What every pediatrician should know

Headaches

Infectious Disease
The HPV vaccine and pregnant women

Nutrition
Best practices in determining food allergies

Puzzler
An infant with vesicular eruptions

Your Voice
Understanding and treating antenatal hydrencephrosis

Contemporary Pediatrics.com
INTRODUCING

The first new chemical entity launched in ADHD in over a decade1,2

LESS CHAOS

MORE CONTROL1,3

INDICATION
Qelbree is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in pediatric patients ages 6 to 17.

IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
In clinical studies, higher rates of suicidal thoughts and behaviors were reported in pediatric patients with ADHD treated with Qelbree than in patients treated with placebo. Closely monitor all Qelbree-treated patients for clinical worsening and for emergence of suicidal thoughts and behaviors.

CONTRAINDICATIONS
• Concomitant administration of a monoamine oxidase inhibitor (MAOI), or dosing within 14 days after discontinuing an MAOI, because of an increased risk of hypertensive crisis
• Concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range

WARNING & PRECAUTION
• Heart rate, blood pressure increases: Qelbree can cause an increase in diastolic blood pressure and heart rate. Assess these measures prior to starting therapy, following increases in dosage, and periodically during therapy


Please see the brief summary of full Prescribing Information on adjacent pages, or visit QelbreeHCP.com/rethink.
In clinical studies, higher rates of suicidal thoughts and behavior were reported in pediatric patients with ADHD treated with Qelbree than in patients treated with placebo. Closely monitor all Qelbree-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.

CONTRAINdications

Qelbree is contraindicated in patients receiving concomitant treatment with monoamine oxidase inhibitors (MAOIs), or within 14 days following discontinuing an MAOI, because of an increased risk of hypertensive crisis.

Qelbree should not be taken when receiving concomitant administration of sensitive CYP1A2 substrates or CYP1A2 substrates with a narrow therapeutic range.

WARNings AND PREcautions

Suicidal Thoughts and Behaviors (see Above)

Among 1019 patients exposed to Qelbree 100 mg to 400 mg in short-term trials, a total of nine patients (0.9%) reported suicidal ideation (N=6), behavior (N=1) or both (N=2). Eight patients reported suicidal ideation or behavior on the Columbia Suicide Severity Rating Scale (C-SSRS), a validated scale that assesses suicide risk. An additional patient treated with Qelbree reported suicidal behavior during the clinical trials, but did not report it on the C-SSRS. Among 463 patients treated with placebo in these studies, two patients (0.4%) reported suicidal ideation on the C-SSRS. No patients treated with placebo reported suicidal behavior. No completed suicides occurred in these trials.

Patients treated with Qelbree had higher rates of insomnia and irritability. Although a causal link between the emergence of such symptoms and the emergence of suicidal impulses has not been established, there is a concern that these and other symptoms such as depressed mood, anxiety, agitation, akathisia, mania, hypomania, panic attacks, impulsive behavior, and aggression may represent precursors to emerging suicidal ideation or behavior. Thus, patients being treated with Qelbree should be observed for the emergence of such symptoms.

Consider changing the therapeutic regimen, including possibly discontinuing Qelbree, in patients who are experiencing emergent suicidal thoughts and behaviors or symptoms that might be precursors to emerging suicidal ideation or behavior, especially if these symptoms are severe or abrupt in onset, or worsen not part of the patient’s presenting symptoms. Advise family members or caregivers of patients to monitor for the emergence of suicidal ideation or behavior, and to report such symptoms immediately to the healthcare provider.

Effects on Blood Pressure and Heart Rate

Qelbree can cause an increase in heart rate and diastolic blood pressure. In a clinical study in patients 6 to 11 years of age, 34/154 (22%) of patients treated with Qelbree 100 mg daily had a ≥20 bpn per minute increase in heart rate at any time point in the clinical trial, compared to 15/159 (9%) of patients who received placebo. This finding was observed in 66/268 (25%) who received the ≥20 beat per minute (bpm) increase in heart rate at any time point in the clinical trial, compared to 84/268 (31%) who received the ≥20 bpm increase in heart rate at any time point in the clinical trial, compared to 15/159 (9%) of patients who received placebo. Closely monitor all Qelbree-treated patients for clinical worsening, and for emergence of suicidal thoughts and behaviors.

Infectious and infestations

Qelbree should not be used in patients with diabetic ketoacidosis, severe hypoglycemia, severe liver disease, or severe renal disease. In animal studies, Qelbree treatment caused dose-dependent convulsions and death. The effects observed in animal studies have not been systematically evaluated in clinical trials. Deaths and serious drug-related adverse reactions have been reported in patients treated with Qelbree.

The safety and effectiveness of Qelbree have not been established in patients with renal impairment or those with severe hepatic impairment. The recommended dosage of Qelbree has not been established in these patients. In clinical trials of patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed.

Infectious and infestations

Qelbree should not be used in patients with diabetic ketoacidosis, severe hypoglycemia, severe liver disease, or severe renal disease. In animal studies, Qelbree treatment caused dose-dependent convulsions and death. The effects observed in animal studies have not been systematically evaluated in clinical trials. Deaths and serious drug-related adverse reactions have been reported in patients treated with Qelbree.

The safety and effectiveness of Qelbree have not been established in patients with renal impairment or those with severe hepatic impairment. The recommended dosage of Qelbree has not been established in these patients. In clinical trials of patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed.

Infections and infestations

Qelbree should not be used in patients with diabetic ketoacidosis, severe hypoglycemia, severe liver disease, or severe renal disease. In animal studies, Qelbree treatment caused dose-dependent convulsions and death. The effects observed in animal studies have not been systematically evaluated in clinical trials. Deaths and serious drug-related adverse reactions have been reported in patients treated with Qelbree.

The safety and effectiveness of Qelbree have not been established in patients with renal impairment or those with severe hepatic impairment. The recommended dosage of Qelbree has not been established in these patients. In clinical trials of patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed.

Infections and infestations

Qelbree should not be used in patients with diabetic ketoacidosis, severe hypoglycemia, severe liver disease, or severe renal disease. In animal studies, Qelbree treatment caused dose-dependent convulsions and death. The effects observed in animal studies have not been systematically evaluated in clinical trials. Deaths and serious drug-related adverse reactions have been reported in patients treated with Qelbree.

The safety and effectiveness of Qelbree have not been established in patients with renal impairment or those with severe hepatic impairment. The recommended dosage of Qelbree has not been established in these patients. In clinical trials of patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed. In patients with renal impairment, the effects of Qelbree on renal function were assessed.
Clinical trials in pediatric patients with ADHD, somnolence (including lethargy and drowsiness) showed that Qelbree 200 mg daily had a ≥20 bpm increase in heart rate at any time point during treatment. This finding was observed in 84/268 (31%) who received the drug. Qelbree can cause an increase in heart rate and diastolic blood pressure.

Behaviors or symptoms that might be precursors to emerging suicidal ideation or behavior should be observed in patients being treated with Qelbree. Thus, patients being treated with Qelbree should be monitored for the emergence of such symptoms. An additional patient treated with Qelbree reported suicidal behavior during treatment.

**Contraindications**

Qelbree™ (viloxazine extended-release capsules), for oral use

In clinical studies, higher rates of suicidal thoughts and behavior were reported with Qelbree treatment compared to placebo. Therefore, close monitoring is recommended for patients with a history of suicidal ideation or behavior or those at risk. An additional patient treated with Qelbree reported suicidal behavior during treatment.

**Warnings**

**Suicidal Thoughts and Behaviors**

An increase in suicidal thoughts or behaviors was observed in patients treated with Qelbree compared to placebo. Patients with suicide ideation or behavior, or those at risk, should be observed for the emergence of such symptoms.

**General**

Suicidal thoughts or behaviors were reported in patients treated with Qelbree compared to placebo. Therefore, patients with a history of suicidal ideation or behavior or those at risk should be observed for the emergence of such symptoms.

**Intervention**

Not recommended for coadministration with viloxazine. Dose reduction of viloxazine is recommended in patients taking concomitant CYP1A2 substrates, which may increase the risk of adverse reactions and toxicity. Coadministration with viloxazine is contraindicated.

## Drugs Having Clinically Important Interactions with Qelbree (continued)

### Moderate Sensitive CYP1A2 Substrate

- Examples: Clocapine, pefrinidone

### CYP2D6 Substrates

- Clinical Impact: Viloxazine is a weak inhibitor of CYP2D6, and the exposure of CYP2D6 substrates when coadministered is increased.

### CYP3A4 Substrates

- Clinical Impact: Viloxazine is a weak inhibitor of CYP3A4. These patients should be monitored for adverse reactions and adjust dosages of CYP3A4 substrates when coadministered.

### Examples:

- Alfentanil, avarafatin, buspirone, conivaptan, darifenacin, darunavir, ebastine, everolimus, brutinib, lomipitide, lovastatin, midazolam, nilvadipine, nisoldipine, saquinavir, simvastatin, srolimus, tacrolimus, tipranavir, trazolam, tricyclic antidepressants.

### USE IN SPECIFIC POPULATIONS

#### Pregnancy

**Pregnancy Exposure Registry**

Report pregnancies to the National Pregnancy Registry for Psychiatric Medications at 1-866-961-2388, and at the website (www.womensmentalhealth.org/premrg).

**Risk Summary**

Based on findings from animal reproduction studies, viloxazine may cause maternal harm when used during pregnancy. Discontinue Qelbree when pregnancy is recognized unless the benefits of therapy outweigh the potential risk to the mother. Available data from case series with viloxazine use in pregnant women are insufficient to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal outcomes.

In animal reproduction studies, oral administration of viloxazine to pregnant rats and rabbits during the period of organogenesis did not cause significant maternal toxicity but caused fetal toxicities and delayed fetal development in the rat at doses up to 2 times the maximum recommended human dose (MRHD) of 400 mg, based on mg/m². In the rabbit, viloxazine caused maternal toxicity without significant fetal toxicity at doses > 7 times the MRHD based on mg/m². The no-observed-adverse-effect levels (NOAELs) for fetal toxicity are approximately equal to and 11 and times the MRHD, based on mg/m² in the rat and rabbit, respectively. Oral administration of viloxazine to pregnant rats and mice during pregnancy and lactation caused maternal toxicities and deaths at doses approximately 2 and 1 time the MRHD, based on mg/m², respectively (see Data). At these maternally toxic doses, viloxazine caused offspring toxicities. The NOAEL for maternal and developmental toxicity is approximately equal to or less than the MRHD, based on mg/m², in the rat and mouse, respectively (see Data).

#### Data

**Animal Data**

Viloxazine was administered orally to pregnant rats during the period of organogenesis at doses of 13, 33, and 82 mg/kg/day, which are less than, equal to, and 2 times the MRHD of 400 mg based on mg/m², respectively. Viloxazine did not cause maternal toxicity at doses up to 82 mg/kg/day. Viloxazine at 82 mg/kg/day increased early and late resorption, delayed fetal development, and possibly caused low incidences of fetal malformations or anomalies (craniorachischisis, meningocele, vertebral, and morphological changes associated with hydranencephaly). The NOAEL for fetal toxicity and malformation is 33 mg/kg/day, which is approximately equal to the MRHD, based on mg/m².

Viloxazine was administered orally to pregnant rabbits during the period of organogenesis at doses of 43, 87, and 130 mg/kg/day, which are approximately 4, 7, and 11 times the MRHD of 400 mg, based on mg/m², respectively. Viloxazine decreased maternal body weight, weight gain, and food consumption at doses ≥ 87 mg/kg/day but did not cause fetal toxicity at doses up to 130 mg/kg/day. The NOAELs for maternal and fetal toxicity is 43 and 130 mg/kg/day, respectively, which is approximately 4 and 11 times the MRHD, based on mg/m², respectively. Viloxazine was administered orally to pregnant rats during gestation and lactation at doses of 43, 87, and 217 mg/kg/day, which are approximately 1, 2, and 5 times the MRHD of 400 mg based on mg/m², respectively. Viloxazine caused maternal toxicity of decreased body weight, weight gain, and food consumption at doses ≥ 87 mg/kg/day and maternal deaths near term at 217 mg/kg/day. At these maternally toxic doses, viloxazine caused lower live birth, decreased viability, and delayed growth and sexual maturation without affecting learning and memory in the offspring. The NOAEL for maternal and developmental toxicity is 43 mg/kg/day and is approximately equivalent to the MRHD in the rat. The NOAEL for both maternal and developmental toxicity is 33 mg/kg/day, which is less than the MRHD, based on mg/m².

#### Lactation

**Risk Summary**

There are no data on the presence of viloxazine in human milk, the effects on the breastfed infant, or the effects on milk production. Viloxazine is likely present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for Qelbree and any potential adverse effects on the breastfed child from Qelbree or from the underlying maternal condition.

**Pediatric Use**

The safety and effectiveness of Qelbree in pediatric patients ages 6 to 17 years of age with ADHD have been established based on randomized, placebo-controlled studies in pediatric patients. The safety and effectiveness of Qelbree have not been established in pediatric patients younger than 6 years old.

Patients treated with Qelbree should be monitored for suicidal thoughts and behavior, and for changes in weight.

**Juvenile Animal Toxicity Data**

Viloxazine was administered orally to juvenile rats from postnatal day (PND) 23 through PND 79 at doses of 43, 130, and 217 mg/kg/day, which are approximately 1, 2, and 3 times the MRHD of 400 mg, based on mg/m² in children, respectively. Viloxazine decreased body weight, weight gain, and food consumption in both sexes at 217 mg/kg/day. Sexual maturation, reproductive capacity, and learning and memory were not affected. The NOAEL for juvenile toxicity is 130 mg/kg/day, which is approximately 2 times the MRHD, based on mg/m² in children.

**Geriatric Use**

Clinical trials of Qelbree in the treatment of ADHD did not include sufficient numbers of patients aged 65 and older to determine whether or not they respond differently from younger patients.

**Renal Impairment**

Dose reduction is recommended in patients with severe (eGFR of < 30 mL/min/1.73m² [MDRD]) renal impairment. No dosage adjustment of Qelbree is recommended in patients with mild to moderate (eGFR of 30 to 89 mL/min/1.73m² [MDRD]) renal impairment. The exposure of viloxazine increases in patients with renal impairment.

**Hepatic Impairment**

The effect of hepatic impairment on the pharmacokinetics of viloxazine is unknown. Qelbree is not recommended in patients with hepatic impairment.

**OVERDOSAGE**

**Human Experience**

The pre-market clinical trials with Qelbree do not provide information regarding symptoms of overdose.

Literature reports from post marketing experience with immediate-release viloxazine include cases of overdosage from 1000 mg to 6500 mg (2.5 to 16.25 times the maximum recommended daily dose). The most reported symptom was drowsiness. Impaired consciousness, diminished reflexes, and increased heart rate have also been reported.

**Treatment and Management**

There is no specific antidote for Qelbree overdose. Administer symptomatic and supportive treatment as appropriate. In case of overdose, consult a Certified Poison Control Center (1-800-222-1222 or www.poisnon.org).

**NON-CLINICAL TOXICOLOGY**

**Carcinogenesis, Mutagenesis, and Impairment of Fertility**

**Carcinogenesis**

Viloxazine did not increase the incidence of tumors in rats treated for 2 years at oral doses of 22, 43, and 87 mg/kg/day. The high dose of 87 mg/kg/day is approximately equal to the MRHD of 400 mg, based on mg/m² in children.

Viloxazine did not increase the incidence of tumors in Tg.rasH2 mice treated for 26 weeks at oral doses of 4.3, 13, and 43 mg/kg/day. No evidence of carcinogenicity was observed in male and female rats treated up to 104 weeks at doses up to approximately equal to the maximum recommended human dose (MRHD) in dogs.

**Mutagenesis**

Viloxazine was not genotoxic in a battery of genotoxicity tests. It was not mutagenic in the in vitro bacterial reverse mutation (Arnes) assay or clastogenic in the in vivo mammalian chromosomal aberration assay or in the in vivo rat bone marrow micronucleus assay.

**Impairment of Fertility**

Viloxazine was orally administered to male and female rats prior to and throughout mating and continued until completion of the second littering at doses of 13, 33, and 82 mg/kg/day, which are less than, equal to, and 2 times the MRHD of 400 mg, based on mg/m², respectively. Viloxazine did not affect male or female fertility parameters in the rat. The NOAEL for male and female fertility is 82 mg/kg/day, which is approximately 2 times the MRHD, based on mg/m².

**Animal Toxicology and/or Pharmacology**

In animal studies, viloxazine treatment caused dose-dependent convulsions at doses ranging from 130 mg/kg in rats, 43 mg/kg in mice, and 360 mg/kg in rabbits, respectively, which are approximately equal to or slightly higher than the MRHD of 400 mg, based on mg/m² in children.

**RA-912-BS-HCP-V1**

Revised: 04/2021
Based on: PI 04/2021
Office- and hospital-based pediatricians and nurse practitioners use Contemporary Pediatrics® for timely, trusted, and practical information to enhance their day-to-day care of children. We advance pediatric providers’ professional development through in-depth, peer-reviewed clinical and practice management articles, case studies, and news and trends coverage.
Contemporary Pediatrics®

in this issue

MAY 2021

developmental health
14 Children and headaches
A guide to treating children aged 1 month or older for headaches, which presents in more than half the pediatric population. Plus, the red flags and triggers for this condition.

Susy Jeng, MD

puzzler
10 A 3-week-old girl with vesicular rash
An infant with vesicular eruptions receives a diagnosis of varicella.
Christine Chang, MD; and Aslam Khan, DO

respiratory disorders
18 Asthma: Everything you need to know
New recommendations and treatment options. Rachael Zimlich, BSN, RN

infectious disease
19 HPV vaccine in pregnancy not linked to adverse birth outcome
A new study examines the effects of the 9-valent HPV vaccine on pregnant women.
Miranda Hester

practice improvement
20 2021 Evaluation and management coding update
This year, the Centers for Medicare & Medicaid Services implemented a new coding system for outpatient visits. Here’s the nuts and bolts of the plan.
Andrew J. Schuman, MD

nutrition
26 The Dx and Rx of food allergies
Tips on assessing children’s food sensitivities, the difference between lactose intolerance and milk allergies, and much more. Elizabeth LeFave, DNP, APRN, PNP-BC, AE-C; and Jennifer Thompson, MD

pediatric pharmacology
32 FDA approves device for nonsurgical treatment of congenital heart defects
The Harmony Transcatheter Pulmonary Valve System eliminates the need for open-heart surgery.

Miranda Hester

dermatology
33 A 6-month-old male with solitary mastocytoma
An otherwise healthy baby boy has a 1-cm area of recurrent blistering on his right cheek. Maria Fazel, MS3, MA; and Bernard Cohen, MD

in addition
5 CHAIRMAN’S LETTER
7 EDITOR’S VIEW
8 JOURNAL CLUB
34 MEDICAL ECONOMICS®
35 ADVERTISING INDEX

THE EDITORS ARE PLEASED TO ANNOUNCE the availability of our new parent company’s continuing education activities. We’ve picked this one especially for our Contemporary Pediatrics’ readers. Go to: bit.ly/3apPvkB
Almost there

Tina Q. Tan, MD, FAAP, FIDSA, FPIDS
Professor of Pediatrics, Feinberg School of Medicine, Northwestern University; Pediatric Infectious Diseases attending; Medical Director, International Patient Services Program; Co-Director, Pediatric Travel Medicine Clinic; Director, International Adoption Clinic, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, Illinois

editor’s view

It is astonishing how fast 2021 is flying by—it is hard to believe that summer is almost here! On the COVID-19 vaccine front, clinical trials are being conducted in the pediatric population down to 6 months of age. With the encouraging preliminary results from the Pfizer/BioNTech COVID-19 vaccine clinical trials in children aged 12 to 15 years showing 100% efficacy, a vaccine may be available for those aged 12 years and older just in time for school. This month’s issue has several “must-read” articles covering topics that all of us in pediatric medicine encounter:

- The cover story on headaches is an excellent review for the practitioner. It sums up the different headache types, signs, and symptoms. Most importantly, it gives you guidance on when a patient needs to be referred to a specialist for further evaluation.
- The respiratory section provides an update on current guidelines and treatment regimens for asthma. With spring a peak time for asthma and other variants of reactive airway disease, the report is especially timely.
- The practice improvement article provides details of the nuances of the new 2021 evaluation and management coding system for outpatient visits, which became effective on January 1. You’ll learn the best way to write patient notes that are compliant with the new guidelines and how to optimally bill for the services that you provide.
- The nutrition section report updates parents on what they need to know about food allergies, including the latest information on Palforzia. Palforzia is the first FDA-approved oral immunotherapy indicated for the mitigation of severe peanut allergic reactions in patients aged 4 to 17 years. This is very exciting news for the 1.2 million children and adolescents in the United States with peanut allergy.

Thank you for providing outstanding care to your patients during these challenging times, and stay safe and well. How this anonymous quote rings true! “Always find time for things that make you feel happy to be alive.” And, as always, I welcome your suggestions, comments, and questions.

With warmest regards,

Tina Q. Tan

email: titan@luriechildrens.org

editorial advisory board

Nina L. Alfiere, MD, MS
Instructor of Pediatrics, Feinberg School of Medicine, Northwestern University. Attending Physician, Academic General Pediatrics, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, Illinois

Amin J. Barakat, MD, FAAP
Professor of Clinical Pediatrics at Georgetown University Medical Center, Washington, DC

Jane M. Carnazzo MD, FAAP
Pediatrician for Children’s Physicians, Omaha, Nebraska, assistant clinical professor, Creighton University Medical School, Omaha, co-editor for SOID (Section of Infectious Diseases) newsletter, CODe (Committee on Development) member for AAP

Harlan R. Gephart, MD
Clinical Professor of Pediatrics Emeritus, University of Washington School of Medicine, Seattle, Washington

W. Christopher Golden, MD
Associate Professor of Pediatrics Neonatologist, Division of Neonatology Medical Director, Newborn Nursery Director, Pediatrics Core Clerkship, Johns Hopkins University School of Medicine, Baltimore, Maryland

Donna Hallas, PhD, CPNP, PPCNP-BC, PMHS, FAANP, FAAN
Clinical Professor, New York University Meyers College of Nursing, and Director, Pediatric Nurse Practitioner Program, New York, New York

Rana F. Hamdy, MD, MPH, MSCE
Assistant Professor of Pediatrics, George Washington University School of Medicine and Health Sciences; Pediatric Infectious Diseases Attending, Director, Antimicrobial Stewardship Program, Associate Fellowship Program Director, Children’s National Hospital, Washington, DC.

Michael S. Jellinek, MD
Professor of Psychiatry and of Pediatrics, Harvard Medical School, Boston, Massachusetts

Candice Jones, MD
Board-certified general pediatrician in group practice in Orlando, Florida, former National Health Service Corps Scholar, AAP member, spokesperson and author

Russell Libby, MD
Founder and president of the Virginia Pediatric Group, Fairfax, Virginia. He is also an Assistant Clinical Professor of Pediatrics, University of Virginia and George Washington University Schools of Medicine, and a board member of the Partners Foundation

Andrew J. Schuman, MD
Clinical Assistant Professor of Pediatrics, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire

Steven M. Selbst, MD
Professor of Pediatrics, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, Pennsylvania, Attending Physician, Pediatric Emergency Medicine, Nemours/ Alfred I duPont Hospital for Children, Wilmington, Delaware

MAY 2021 | CONTEMPORARYPEDIATRICS.COM 7
A quality improvement initiative of 2 interventions showed that documenting the use of sleep hygiene for sleep disturbances in children with neurodevelopmental disorders (NDD) improves adherence to evidence-based sleep hygiene strategies. Parents were given a screening questionnaire related to the child’s sleep and embedding prompts in the electronic medical record (EMR) to guide assessment.

In the first intervention, 144 parents completed the BEARS sleep screening tool (bedtime issues, excessive daytime sleepiness, night awakenings, regularity and durations of sleep, and snoring), which was adapted for this population to help identify patients with sleep disturbance. Sleep hygiene was considered documented if the provider used the term or documented behaviors or environmental conditions pertaining to sleep. In the second intervention, 2 evidence-based SmartPhrases were embedded within the EMR system. The first SmartPhrase was used during history collection in response to positive answers on the BEARS screening tool and contained evidence-based prompts to guide the assessment. The second intervention inserted individualized, evidence-based strategies for sleep hygiene into the patient instruction section of the discharge summary.

Investigators compared EMR data after implementation of the practice change with the same data obtained before implementation 13 weeks earlier. In the 6 months before implementation, 44 patients had received diagnoses of sleep disturbance, insomnia, or behavioral insomnia in the EMR. Sleep hygiene was documented in 27% of the identified charts. After the interventions, the number increased, with 53 patients’ having received 1 of the 3 diagnoses. Sleep hygiene documentation in the EMR of identified patients nearly doubled. The postimplementation query also found a 55% increase in documentation of sleep hygiene when melatonin was initiated. Of those patients prescribed melatonin for the first time, 100% had documentation for sleep hygiene.

As much as I appreciate melatonin, which has been a boon for many parents of children with NDD, we should not necessarily jump to it as the first approach. This study is a reminder to look at traditional sleep hygiene techniques (eg, bedtime routine with a wind-down, turning off electronic devices) before advising medication.
Predictive testing for ASD: Should it be done and for whom?

The ethics of the clinical application of predictive testing for infants at high risk for autism spectrum disorder (ASD) are still unclear, according to a recent report. Given that a predictive test for ASD does not allow for immediate treatment, the benefits of testing are questionable.

However, an immediate benefit may be relief from parental anxiety caused by uncertainty or, when results are positive, targeted access to intervention, such as frequent monitoring for emerging ASD symptoms and enrollment in individualized behavioral intervention as soon as development begins to diverge from the norm. On the negative side, behavioral intervention could pose logistical or financial burdens on families. In addition, societal harm could result from introducing children who had received a predictive ASD diagnosis into an already highly stressed service system. The authors also noted that the relative weight of the benefits and harms of ASD prediction vary with the different perspectives and priorities of parents, clinicians, investigators, and neurodiversity advocates. What is clear, however, is that efforts to develop and evaluate predictive testing for infants at high risk for ASD are ethically warranted.

For those who believe that ethical early diagnosis issues apply only to conditions such as Huntington disease, or that early intervention is a no-brainer, this article is food for thought. Because in most instances a prediagnosis of autism will be far from certain, I will still stick with careful monitoring and referral once delays are noted.

For reference, go to ContemporaryPediatrics.com/JournalClub-predictive-testing-ASD

Approaches to skin conditions vary with skin color

A recently-published report shares dermatologic clinical pearls for examining and treating pediatric and adolescent patients with skin of color in light of the empathy, effective communication, and shared decision-making that are key to patient satisfaction and good outcomes.

- **Acne**: The increased potential for postinflammatory hyperpigmentation (PIH) with acne in skin of color calls for aggressive treatment. Use of topical retinoids is particularly important because it can start the treatment process for the PIH. Daily sunscreen use and patience also are essential.

- **Atopic dermatitis**: Follicular prominence may be the only sign of atopic dermatitis in this population. Using the tips of your fingers to examine the skin may help determine whether a flare is present.

- **Seborrheic dermatitis**: Encourage patients to wash their hair at least once every 1 to 2 weeks with antidandruff shampoos that contain tar, selenium sulfide, pyrithione zinc, or ketoconazole. To avoid excess dryness, counsel patients to apply the shampoo to the scalp only, rinse, then follow with a moisturizing shampoo and conditioner. For patients who use heavy pomades and oils, provide a topical steroid in ointment form.

- **Traction alopecia**: Advise against hairstyles that place chronic tension on the hair. If you see signs of traction alopecia, educate the patient and family early on the risk factors and sequelae of traction alopecia.

This article has useful advice. One size does not fit all in dermatology. This applies not only to skin color, but, for example, to relative oiliness of the skin in deciding what products or formulations (eg, cream vs ointment) to use.

For reference, go to ContemporaryPediatrics.com/JournalClub-skin-conditions-color
A 3-week-old girl with vesicular rash

CHRISTINE CHANG, MD; AND ASLAM KHAN, DO

History
A 3-week-old previously healthy full term girl presented to the pediatric emergency department with 2 lesions on the body that had developed 3 days earlier—1 lesion on the forehead and 1 perianal lesion. Her parents said that she had recently developed mild nasal congestion and fussiness but denied fever, purulent drainage, bleeding from the lesions, or rashes elsewhere. The infant had been feeding well with appropriate urine output for age. Her mother had a history of genital warts, but neither parent had a history of oral or genital herpes simplex virus (HSV) infection. The patient presented to her pediatrician earlier that day and after evaluation, given her young age, she was referred to the emergency department for work-up of a possible HSV infection.

Physical examination
In the pediatric emergency department, the infant appeared well. Her temperature was 37.3°C, heart rate was 156 beats per minute, respiratory rate was 33 breaths per minute, and her oxygen saturation level was 100% on room air. She weighed 3.3 kilograms. Physical examination was significant for a ruptured 3-mm vesicle with a central crust on the medial aspect of the right eyebrow (Figure 1) with some tiny pustules and scattered erythema and scale on the forehead, nasal bridge, and eyelids with the right side lesions more prominent than the left. She also had a 3-mm crust with a narrow scaly border and surrounding erythema on the right buttock (Figure 2). Her parents brought a photo of the right eyebrow lesion from 2 days before it ruptured that showed a 4-mm intact vesicle with a narrow rim of erythema (Figure 3). The patient had normal tone, normal strength, and open, flat anterior and posterior fontanelles. There was no appreciable hepatosplenomegaly, lymphadenopathy, or rash noted elsewhere.
Differential diagnosis
Given her age and presentation, HSV infection was the leading and most concerning diagnosis in the differential diagnosis, but varicella and staphylococcal infections were also considered. A differential diagnosis for vesicular lesions in infants is shown in Table 1 and includes infectious etiologies and well as congenital and neonatal bullous disorders.

Laboratory studies
A complete neonatal sepsis rule-out was performed given the infant’s age. Laboratory studies revealed an unremarkable complete blood cell count in addition to differential, comprehensive metabolic panel, C-reactive protein, procalcitonin, and urinalysis. A lumbar puncture produced blood-tinged fluid on the second attempt, and initial cerebrospinal fluid (CSF) studies showed 416 white blood cells per microliter and 605,000 red blood cells per microliter, with 4% neutrophils, 83% lymphocytes, 1% reactive lymphocytes, and 12% monocytoïd cells. The laboratory was unable to run protein and glucose studies on the CSF. No organisms were seen on CSF Gram stain. Cultures from blood, urine, and CSF were sent in addition to multiplex polymerase chain reaction (PCR) testing with a respiratory pathogen PCR panel from the nasopharynx and a CSF meningitis/encephalitis panel. The patient was started on empiric intravenous ampicillin, gentamicin, and acyclovir and admitted to the neonatal intensive care unit (NICU) for further treatment.

Diagnosis
Shortly after admission, the infant’s CSF meningitis/encephalitis panel resulted positive for varicella-zoster virus (VZV) and her respiratory pathogen PCR panel resulted positive for coronavirus (not SARS-CoV-2). Pediatric infectious diseases (ID) was consulted, given the presence of varicella infection in a newborn with no clear history of exposure. The ID consult recommended HSV and VZV PCR tests from the patient’s blood, CSF, and a skin lesion, as well as HSV PCR tests from her conjunctiva, nares, oropharynx, and rectum. All HSV PCR tests resulted negative. Notably, the patient’s PCR test results were positive for VZV in the skin lesion and blood but not in the CSF. As the CSF VZV PCR test was negative, the VZV result from the CSF meningitis/encephalitis panel was thought to be representative of sampling from the blood introduced from the traumatic lumbar puncture. Nevertheless, the infant was found to have positive VZV PCR testing from multiple sources (ie, skin lesion, blood).

Discussion
Varicella, commonly known as chickenpox, is caused by a primary VZV infection. It most often affects children unimmunized against the disease, with the highest incidence in children aged between 1 and 9 years.\(^1\) VZV is usually results in mild to moderate illness in otherwise healthy individuals, but trends to be more severe in infants, teenagers, and adults compared with school-aged children.\(^4\) Asymptomatic cases are rare.\(^5\) Some presentations of varicella can be severe and life-threatening, especially in cases of vertical transmission (ie, either fetal infection after the development of maternal varicella or neonatal infection around the time of delivery).
and in immunocompromised individuals. Possible complications include bacterial superinfection of skin lesions, pneumonia, and central nervous system involvement. The risk of hospital admission or dying from varicella in infants is higher than that in children.

Varicella presents with a pruritic rash with vesicles in different stages of development, often accompanied by fever, malaise, and decreased appetite. The rash tends to be more prominent on the face and trunk than on the extremities. VZV is transmitted via airborne droplets or vesicular fluid. It is thought to multiply in regional lymph nodes, then to spread to the viscera. The incubation period for varicella varies between 10 to 21 days. Individuals with varicella are contagious from 1 to 2 days before the onset of rash until all of the lesions have crusted over, which is typically at least 5 days after the onset of rash.

Varicella can be diagnosed clinically by the presentation of a characteristic rash. In cases that require laboratory confirmation, the diagnostic method of choice for varicella is a VZV DNA PCR test from vesicular fluid or a scab—vesicles contain large amounts of virus and PCR is more sensitive than a viral culture or a direct fluorescent antibody assay.

In otherwise healthy children, treatment for varicella is supportive care to address fever and pruritus and to maintain adequate hydration. Varicella in a newborn does not universally require antiviral treatment, and there is no consensus by experts in the literature about management.

The antiviral treatment of choice is acyclovir, which prevents viral DNA synthesis by inhibiting the viral DNA polymerase and is most effective if administered intravenously within 72 hours of disease.

Blumental et al recently recommended acyclovir treatment for all patients less than 1 month of age with clinical signs of varicella.

Varicella, commonly known as chickenpox, is caused by a primary VZV infection.

Both of the infant’s parents reported having a childhood illness consistent with varicella and tested positive for VZV immunoglobulin G. As the patient’s mother tested positive, it is likely that maternal transfer of antibody contributed to a less severe course of varicella (though this is confounded by the fact that the infant was started empirically on intravenous acyclovir upon admission).

Given varicella’s incubation period, we presume the patient was exposed to VZV during the first week of life. Though no clear source of infection was ultimately identified, it is most likely that the infant was exposed in her pediatric clinic, as she was seen in clinic on days of life 3, 5, 6, and 14 for weight and jaundice checks and a routine 2-week well care visit.

**Treatment and patient outcome**

The day after admission, the infant developed additional vesicular lesions on her trunk and extremities. Given the patient’s positive CSF meningitis/encephalitis panel—despite the history of a traumatic lumbar puncture and the negative dedicated VZV PCR from the CSF—ID recommended a plan to treat for at least 7 days while continuing to monitor the infant. Intravenous acyclovir was continued, but antibiotics were discontinued by 48 hours as there was less concern for bacterial infection and negative cultures. Amplitude-integrated electroencephalography was unremarkable. The patient had 1 isolated temperature to 38.0 °C that resolved without medication. She was continued on intravenous acyclovir for 1 week until hospital discharge. At that time, all cultures were negative for bacterial infection and the infant’s vesicular lesions had scabbed over.

This case highlights the importance of providers including varicella in the differential diagnosis of vesicular lesions in infants, as often its consideration is overshadowed by the concern for possible HSV. Continuing to administer routine varicella vaccinations is also important from a public health perspective, in order to maintain herd immunity in populations.

**COMMENTS?** E-mail them to llevine@mjhlifesciences.com

**Christine Chang** is a general pediatrician at Palo Alto Medical Foundation in Sunnyvale, California.

**Aslam Khan** is a fellow, pediatric infectious diseases at Stanford University School of Medicine in Stanford, California.

The authors have nothing to disclose.

For references, go to ContemporaryPediatrics.com/pediatric-puzzler
When it comes to meningitis, time to diagnosis is critical.

Get patients on the right therapy sooner with rapid results from BioFire.

Diagnosing deadly pediatric meningitis without the right tools can feel like a race against time—especially with ambiguous overlapping symptoms. Fast, comprehensive laboratory results from the BioFire® FilmArray® Meningitis/Encephalitis (ME) Panel can fast track answers, shortening time to diagnosis by four days.¹ Identifying the probable cause sooner means you can prescribe targeted treatment and impact antimicrobial therapy—reducing both acyclovir and antibiotic duration by two days.² Every minute counts when it comes to meningitis. The BioFire ME Panel can help.

1 Test. 14 Targets. ~1 Hour.

“*It has impacted my practice here and I don’t think I’d want to practice without it because I do feel the patients receive better care because we do have this available.*”

Estela O’Daniell, MD, FAAP
Medical Director Emergency Department
Driscoll Children’s Hospital

biofiredx.com

FEATURE

Children and headaches
Red flags, triggers, and rescue treatments

Headaches are 1 of the top 5 health problems of childhood. Because 58.4% of children and adolescents aged 1 month or older will develop headaches at some point,\(^1\) general pediatric practitioners may have many opportunities to evaluate and treat patients with headaches.

SUSY JENG, MD

Urgent versus nonurgent headaches

Many conditions can present initially with headache, so it is important to have a list of “red flag” risk factors, symptoms, and exam findings to keep in mind during the initial assessment. Red flag risk factors would include a patient aged younger than 6 years, history of neurocutaneous syndrome, systemic illness, immunodeficiency, known malignancy, or hypercoagulability.\(^2\)

Red flag symptoms include new (<1 month) or quickly worsening headache type, focal and sidelocked headache, headache maximal at onset (thunderclap headache), infectious symptoms (eg, fever, meningismus, sinus or ear pain), or pressure-dependent features (eg, positional headache), headache worse in the middle of the night or first thing in the morning, headaches triggered by cough or Valsalva maneuvers, vomiting that is persistent and increasing in frequency. Focal neurologic symptoms or exam findings (eg, seizures, vision changes, papilledema, ataxia) also require urgent evaluation. Etiologies that cannot be missed include mass lesions, infections (eg, meningitis/encephalitis, brain abscess), and vascular etiologies (eg, stroke, hemorrhage, aneurysm, arteriovenous malformation, cerebral venous sinus thrombosis). Any of these symptoms or exam findings should prompt urgent consideration of brain imaging and/or lumbar puncture. Less than 1% of brain abnormalities in patients present with chronic headache as the only symptom.\(^3\)

Primary versus secondary headaches

Once urgent headache etiologies are no longer of concern, the next objective is to distinguish between primary and secondary headaches. Unlike secondary headaches, primary headaches, such as migraine and tension-type headaches, are not a symptom of an underlying issue. Whereas a child may develop migraine-type headaches due to obstructive sleep apnea, the diagnosis of primary headache is only made after excluding the possibility of a secondary headache disorder. Depending on the history and physical exam, as well as diagnostic testing when needed (eg, screening blood tests or sleep study), the differentiation between primary and secondary headache can be made.

Primary headaches

The diagnosis of primary headache is made primarily through identifying classic characteristics of the headache, as there are no con-
firmatory diagnostic tests. The International Headache Society has created an International Classification of Headache Disorders to aid clinicians and investigators.4,5

The diagnosis of episodic childhood migraine is adapted from adult migraine. It is defined as an episodic headache with 5 or more attacks that last 2 to 72 hours. It must have 2 or more of the following: unilateral or bilateral location, pulsating quality, moderate to severe pain, or aggravation by routine physical activity. It must also have 1 or more of the following: nausea or vomiting, and photophobia and phonophobia. For childhood migraine, experts argue that headaches are often shorter, lasting 30 minutes or more, and often fitting 1 or more of each category.6 Premonitory signs also are different in childhood migraine than in adult migraine. They are most commonly fatigue, mood changes, neck stiffness, cranial autonomic symptoms, and cutaneous allodynia, rather than visual disturbance or dizziness.7

Diagnosing episodic childhood tension-type headache requires 10 or more episodes lasting from 30 minutes to 7 days. It must have 2 or more of the following: bilateral location, pressing or tightening quality (nonpulsating), mild or moderate intensity, and it cannot be aggravated by routine physical activity. There cannot be nausea or vomiting, and no more than 1 of photophobia or phonophobia.

Children and adolescents may present with both migraine and tension-type headaches, making it difficult to have separate treatment trials. In fact, it is unclear whether they are actual separate biological entities.8 Most treatments are geared toward migraine management, but the overall approach for both should be 3-pronged, addressing lifestyle modifications, a rescue plan, and a preventative plan.

**Headache treatment: lifestyle modification**
The most common triggers for childhood headache include stress/anxiety, lack of sleep, warm climate, and video games.9 Other triggers include glare, eye strain, high altitude, menstruation, medications, fasting, dehydration, certain foods (eg, simple sugars, smoked meats, chocolate), caffeine use, and lack of exercise.

The first step in headache treatment is to better characterize the headaches and triggers by keeping a headache diary documenting possible triggers, time of day, days per month, headache intensity, and response to treatment. The number and/or intensity of headaches over time influences what types of treatment are needed. For example, episodic headaches (less than 2 times a week) can be treated with rescue medications alone, whereas headaches more frequent than that will require preventative treatment as well as rescue medications.

The general categories for lifestyle modifications are water and food intake, sleep regulation, daily exercise, and stress reduction.

**Headache treatment rescue plan**
Tip: Tell patients and their caregivers that the rescue plan should be implemented right at the beginning of the headache.

Because of the nature of the headache/pain cycle with amplification over time, the longer it takes to treat, the harder it is to break the cycle. Taking rescue measures early and taking the full dose of the abortive medication are more effective than waiting and then giving a half dose followed by another half dose.

Caregivers should be cautioned that these medications are only meant for rescue. Taking them more than 2 or 3 times a week over a month-long period can lead to medication overuse headache syndrome.

Nausea and vomiting are most common in younger children as part of the headache syndrome,10 and antiemetics can be used in conjunction with headache medications. As patients who are nauseated may not tolerate swallowing pills, many headache medications come in oral-dissolving or intranasal formulations.

The first line for abortive headache treatments includes acetaminophen, ibuprofen, and other nonsteroidal anti-inflammatory drugs. Randomized trials for pharmacologic rescue treatments efficacy show acetaminophen at 54% and ibuprofen at 68.76%.11

Triptan medications, the second line for rescue headache treatments, were designed specifically to abort migraine headaches. Because they have selective activity on atypical 5HT1B and 5HT1D receptors, their mechanisms of action include cranial vasoconstriction, peripheral trigeminal inhibition, and inhibition of the trigeminovascular system.
developmental health

of transmission via the trigeminal cervical complex. They are typically well tolerated. Common adverse effects include paresthesia, sleepiness, dizziness, and tightness in chest or throat. They should not be used more than 2 times a week and should be avoided in patients with cardiovascular disease, who are pregnant, or who have complicated migraines. Rizatriptan (efficacy 73-74%) is the only treatment approved for patients aged 6 to 12 years. Sumatriptan nasal spray (64-86%), combination sumatriptan/naproxen, almotriptan (72-73%), and zolmitriptan nasal spray (62%) are approved in patients aged 12 to 17 years.11

Further pharmacologic rescue treatments typically have to be administered intravenously in the emergency department setting. Of the dopamine antagonists, prochlorperazine (Compazine) IV is the most effective abortive in randomized trials at 84.8% pain relief, followed by metoclopramide (Reglan) and pro-methazine (Phenergan).12,13

**Headache treatment-preventive plan**

Whereas patients with episodic headache can often be treated with lifestyle changes and rescue medications alone, others with chronic headaches (>15 days a month) and severe headaches will benefit from a preventive plan that aims to decrease both headache severity and frequency.

Tip: it is important to distinguish rescue from preventive treatment, so patients do not stop taking preventive treatments within few days when it “doesn’t work.”

Patients should understand that preventive treatment has to start at a low dose to minimize adverse effects and build up slowly. Within 6 to 8 weeks of taking it constantly, the goal would be a decrease in headache frequency and intensity by at least 50%.

For many years, the use of pharmacologic preventive medications in childhood headache was based on adult studies. A seminal paper published in The New England Journal of Medicine in 2018 based on the CHAMP trial (NCT01581281) compared children with episodic migraine in 3 prospective randomized groups taking placebo, topiramate 2 mg/kg, or amitriptyline 1 mg/kg.15 The trial was stopped early because the placebo group did as well as the other 2 groups with fewer adverse effects. It was noted that patients had an average of 11 days per month of headache (suggesting more of an episodic than chronic headache picture) and that the placebo group received appropriate lifestyle management and rescue plan counseling. This underscores the efficacy of lifestyle and rescue management independent of pharmacologic preventive therapy.

Following this study, many practitioners chose to offer nutraceuticals for headache prevention before going straight to pharmacologic treatments. Nutraceuticals include vitamins, minerals, herbal supplements, and dietary supplements. Magnesium, riboflavin (vitamin B2), coenzyme Q10, and vitamin D, all have demonstrated efficacy in some pediatric trials for headache prevention,15-18 although there are limited studies with a placebo group. Importantly, the adverse effect profile for nutraceuticals is better than for pharmacologic agents.

If headaches continue to be troublesome despite lifestyle management, good rescue therapy, and a sustained trial of nutraceuticals, it is reasonable to consider pharmacologic preventatives. Cyproheptadine (Periactin), an antihistamine, has no clinical trial data but has probably been used the longest for pediatric headache prevention. Although it is well-tolerated in younger children, patients 8 years of age and older typically experience too much sedation for it to be acceptable. Topiramate, an epileptic medication, received FDA approval in 2014 for the prevention of headaches in adolescents aged 12 to 17 years. Potential common adverse effects include cognitive slowing, paresthesias, appetite suppression, and renal stones. Amitriptyline, an antidepressant, can be helpful for patients with migraines who also have insomnia and/or depression. Besides somnolence, it can cause appetite increase, tachycardia, and dry mouth. Propranolol, a β-blocker, has 1 randomized control

### COMMON TRIGGERS

- Stress/anxiety (75.5%)*
- Lack of sleep (69.6%)*
- Warm climate (68.6%)*
- Video games (64.7%)*
- Glare/refractive error
- High altitude
- Menstruation
- Medications
- Fasting/dehydration
- Foods/caffeine

*Most common triggers

A trial from 1974 showing efficacy, but subsequent studies have been negative. Possible adverse effects include exercise intolerance, depression, and light-headedness.

Finally, there are many other nonpharmacologic interventions that have been shown to be helpful in mitigating childhood headache and may have a synergistic effect with preventive medications. Cognitive behavioral therapy (CBT) in combination with amitriptyline was more beneficial than CBT alone for a group of adolescents. There is some convincing evidence for biofeedback (teaching patients to regulate physical responses to stress) in the prevention of pediatric migraine, sometimes in combination with relaxation therapy. At Stanford Children’s Health, occupational therapists and pediatric pain psychologists are trained in multiple modalities such as CBT, biofeedback, and relaxation therapy. If there is a history of neck/shoulder pain or tenderness to palpation of the scalp, neck, or shoulders, a physical therapist can help strengthen and realign a patient’s posture to prevent cervicogenic headache. There is 1 positive study on acupuncture for pediatric headache, and many adult studies demonstrate efficacy in chronic pain and headache. It is important to explain to the patient that acupuncture needles are much thinner and less painful than typical needles; children who have had acupuncture before seem to prefer this method.

When to refer to a neurologist

Instances in which consultation with a neurologist could be helpful would include headaches that are severe, prolonged, or intractable. Neurology consultation would be indicated for patients with a complicated aura (e.g., hemiplegic migraine or migraine with brainstem symptoms such as dysarthria, vertigo, tinnitus, or diplopia). Referral is advised when a pediatric practitioner is reconsidering the diagnosis of primary headaches and would like guidance on workup for secondary headaches. Finally, a practitioner may feel comfortable implementing first- or second-line therapies but will seek help with less conventional treatments, such as the new class of anti-cGRP monoclonal antibodies. These have not yet been approved in children but are increasingly being prescribed off label for adolescents with intractable migraines. The American Headache Society Section on Pediatric-Adolescent Headache offers guidelines for administering these new treatments. Several neuromodulatory devices have been developed for the headache population, with 2 approved by the FDA for adolescents, but the studies have very small sizes (9–45 patients) and the cost for renting these devices is often prohibitive.

Childhood headache can be dangerous, debilitating, or both. After excluding dangerous causes, it is important to provide the patient and caregiver with a plan for headache management that includes education on lifestyle management, rescue plan, and preventive measures. During the current pandemic, screen time and eye strain have become more significant triggers, whereas, conversely, being able to sleep in later on school days appears to be beneficial for teenagers. The more that children and their caregivers are empowered to understand and manage childhood headaches, the better for all involved.

COMMENTS? Email the m to llevine@mjhiflsciences.com

For references, go to ContemporaryPediatrics.com/children-and-headaches

Register for our eNewsletter to receive similar content
Scan this QR code
Asthma

Everything you need to know

New recommendations and treatment options for this common condition

RACHAEL ZIMLICH, BSN, RN

The last update to national asthma guidelines was in 2007, but a number of recommendations are coming forward that could go into the next set of updates when they are published.

Asthma is the most common chronic childhood disease, affecting approximately 5.5 million children in the United States. Good control of asthma is necessary to preserve lung function and prevent exacerbations, but approximately 40% of all pediatric asthma patients don’t have their condition under control. There are a number of reasons for this, including nonadherence and inadequate treatment regimens.

The National Asthma Education and Prevention Program published updates to its asthma management recommendations in December 2020. The update included focus on:

- use of exhaled nitric oxide,
- control of indoor allergies,
- medications for intermittent wheezing,
- use of long-acting muscarinic antagonists,
- immunotherapy, and
- bronchial thermoplasty.

Angela Duff Hogan, MD, FAAAAI, FACAAC, FAAP, a member of the American Academy of Pediatrics’ Section on Allergy and Immunology and a practitioner at Children’s Hospital of The King’s Daughters in Norfolk, Virginia, says that updates also need to be made on availability and use of medications.

“Since 2007 there has been numerous medication changes,” Hogan says. “There was a time when we felt all asthmatics should have an inhaled steroid year-round with albuterol to use as needed. But based on research, we know that most patients do not adhere to this regimen.”

Although some medications have been changed or removed like short-acting β-agonists, new ones have been introduced, and the way others are used have changed. One specific change is the use of controller medications. Previously, it was recommended to keep children on inhaled albuterol treatments all year, Hogan said. Now, new guidelines suggest children aged 4 years and younger with recurrent wheezing due to upper respiratory infections stop treatments once the infection or symptoms resolve. The guideline also addresses single-inhaler maintenance and reliever therapy (SMART), which uses inhaled corticosteroids and formoterol for both maintenance therapy and rapid symptom relief.

“The new guidelines recommend in children between the ages of 0 and 4 with recurrent wheezing episodes due to viral infections, that inhaled corticosteroids be used with the onset of the upper respiratory infection along with short acting beta agonist (SABAs) and stopped when the symptoms resolve. The new guidelines also talk about SMART therapy. Smart therapy is single maintenance and reliever therapy. It recommends using ICS/formoterol for both reliever therapy and daily therapy,” Hogan explains. “If these guidelines are adopted, it means patients could have 1 inhaler that they use at the beginning of their symptoms if they have milder forms of asthma or daily for rapid relief of symptoms.”

An official update to the guidelines likely will include more recommendations, but here are a number of medication changes that may be included.

**Bronchodilators**

Bronchodilators, or short-acting β-agonists, aren’t used to manage asthma, per se, but can be used for as-needed relief of asthma symptoms. Children with asthma should be treated with a controller medication regimen, according to the Global Initiative for Asthma (GINA). Albuterol and levalbuterol are the 2 bronchodilators approved for use in the US. A new generic version of albuterol called ProAir HFA was released in 2020.

**Corticosteroids**

Low-dose inhaled corticosteroids often are used for maintenance therapy. Some changes to options of this medication class are as follows:

- Pulmicort Flexhaler (budesonide) was approved for children 6 years and older.
**Respiratory**

- QVAR RediHaler (beclomethasone) was approved for children 4 years and older. It replaces the former metered dose inhaler.
- Fluticasone propionate HFA and the dry powder inhaler (DPI) can be used in children 4 years and older.
- Twisthaler (mometasone) was approved for children 4 years and older.
- Fluticasone furoate DPI and mometasone HFA are now available to younger children 5 years and older.

**Combination therapies**

Inhaled corticosteroids and long-acting β-agonists (LABAs) can be used to control chronic inflammation as well as asthma, symptoms. In 2017, the United States Food and Drug Administration (FDA) removed safety warnings for LABAs.

**Leukotriene receptor antagonists**

For mild asthma or allergy-related or exercise-induced asthma, antileukotriene medications such as montelukast can be helpful. However, the FDA has added a warning to montelukast after behavior and mood changes were noted in some individuals taking this medication. Patients who take montelukast should be monitored for neuropsychiatric changes.

Hogan says the updates will reflect some of the recommendations released in 2019 by GINA, as well as other international organizations that update asthma guidelines each year. One of these recommendations was to stop treating adolescents and adults who have asthma with short-acting β-agonists alone. Instead, patients with mild asthma should receive inhaled corticosteroids for chronic management or symptomatic relief.

In addition, “The recommendations were that sublingual immunotherapy is not recommended in the treatment of asthma, and that subcutaneous immunotherapy should not be used in patients with severe or unstable asthma,” Hogan says.

“In terms of environmental control measures...allergen reduction should only be used in those individuals who have allergen-induced symptoms and sensitization to specific indoor allergens,” Hogan continued. “There is little evidence to support [the idea that] isolated single interventions really make much impact on asthma control, exacerbations, and other relevant outcomes.”

COMMENTS? Email them to llevine@mjlifesciences.com

For references/complete article, [ContemporaryPediatrics.com/asthma-2021](http://ContemporaryPediatrics.com/asthma-2021)

Rachael Zimlich is a freelance writer in Cleveland, Ohio. She has nothing to disclose.

---

**INFECTIOUS DISEASE**

**HPV vaccine in pregnancy is not linked to adverse birth outcome**

A study examines the effect of such exposure on birth outcomes.

**MIRANDA HESTER**

The 9-valent human papillomavirus (9vHPV) vaccine is recommended for individuals aged 11 to 26 years, and recently expanded to women up to 45 years old. A study in *JAMA Network Open* offers data on whether exposure is linked to adverse birth outcomes.

The investigators used data from 7 health systems in the Vaccine Safety Datalink, which included pregnancies among females aged 12 to 28 years that ended between October 2015 and November 2018. Vaccine exposures were distal (9vHPV or 4-valent HPV [4vHPV] vaccine administered from 22 to 16 weeks before last menstrual period [LMP]), peripregnancy (9vHPV vaccine administered from 42 days before LMP until LMP), and during pregnancy (9vHPV vaccine administered from LMP to 19 completed weeks’ gestation).

The study included 1493 pregnant participants. The investigators found that administering the 9vHPV vaccine during pregnancy was not linked to an increased risk of spontaneous abortion (HR, 1.12; 95% CI, 0.66-1.93) when compared with a distal vaccine exposure. Similar findings were found with peripregnancy 9vHPV vaccine exposures. When looking at the live births, exposure to 9vHPV vaccine during pregnancy was not linked to preterm birth or small-for-gestational-age birth. Across all exposure groups, birth defects occurred in approximately 1% of live births.

The investigators concluded that exposure to the 9vHPV vaccine either during or around pregnancy is not a common occurrence and that, when exposure does happen, it is not linked to either spontaneous abortions or select adverse birth outcomes.

For references and full article, go to [bit.ly/3uZMi30](http://bit.ly/3uZMi30)
2021 Evaluation and management coding update

Effective January 1 this year, the Centers for Medicare & Medicaid Services (CMS), with guidance from the American Medical Association (AMA), implemented a new evaluation and management (E/M) coding system for outpatient visits. The first change in 25 years, it was developed to ease the documentation burden on medical providers. This article details the nuances of the 2021 E/M coding system, to help keep office notes in compliance with the new guidelines.

Implications for medical practice

In order to comply with the pre-2021 coding guidelines, physicians were spending too much time writing bloated notes to justify the level of service billed; many were frequently completing their notes at home. This was just one of many factors contributing to physician burnout. Recognizing the burden that documentation was placing on medical providers, CMS launched their “Patients Over Paperwork” initiative in 2017, and finalized guidelines based on the 2020 AMA relative value scale (RVS) Update Committee (RUC) suggestions. A benefit of the updated guidelines is that pediatrician work relative value unit (wRVU) productivity will increase for well visit codes and acute visit codes. As a consequence, compensation will likely increase by as much as 9% for pediatricians whose pay is based predominantly on wRVU output.1

On December 22, 2020, congress adjusted the Medicare Physician Fee Schedule (MPFS) conversion factor, a change that will likely improve 2021 pediatrician compensation further.2

Prior to 2021, billing for an outpatient visit required a very complicated mixture of documenting appropriate elements of the patient’s history and physical along with the medical decision-making (MDM) associated with the visit or time spent counseling patient or coordinating care. The updated CMS guidelines are based only on 1) a clearer method of assigning MDM or 2) a new methodology for assigning a time component to the visit on the date of service.

Medical decision-making: 2021 guidelines

As they did previously, CMS recognizes 4 levels of MDM (straightforward, low complexity, moderate complexity, and high complexity). MDM quantifies the complexity of establishing a diagnosis and/or selecting management options by measuring:

• The number and complexity of problems addressed at the encounter
• The amount and/or complexity of data to be reviewed and analyzed
• The risk of complications and/or morbidity with patient treatment

This year, to guide MDM decisions, providers must become familiar with the coding table on page 21. As in the past, the table columns list the number and complexity of problems addressed at the encounter. The amount and/or complexity of data to be reviewed and analyzed, and the risk of complications and/or morbidity with patient treatment.

CONTINUED ON PAGE 22

The AMA, who developed the Current Procedural Terminology (CPT) coding system, commissioned a study that indicated that the new guidelines would produce a conservative reduction of 2.11 minutes per visit. Thus, a physician that sees 20 patients per day could realize over 180 hours of freed time over 1 year to focus on care.

ANDREW J. SCHUMAN, MD

The AMA, who developed the Current Procedural Terminology (CPT) coding system, commissioned a study that indicated that the new guidelines would produce a conservative reduction of 2.11 minutes per visit. Thus, a physician that sees 20 patients per day could realize over 180 hours of freed time over 1 year to focus on care.
### TABLE 1: MDM CODING TABLE

<table>
<thead>
<tr>
<th>MDM LEVEL</th>
<th>PROBLEMS ADDRESSED</th>
<th>DATA REVIEWED AND ANALYZED</th>
<th>RISK OF ADDITIONAL TESTING/TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Check boxes</td>
<td>Each unique test, order, or document contributes to the combination of 2 or 3 items in Category 1.</td>
<td>Circle 1</td>
</tr>
<tr>
<td>Low (99203/99213)</td>
<td>2 or more self-limited or minor problems OR 1 stable chronic illness OR 1 acute, uncomplicated illness or injury</td>
<td>Need 1 of 2 categories Category 1: Tests and documents</td>
<td>Low risk of morbidity from further testing or treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Record number or check boxes</td>
<td>Recomend OTC medications, physical, occupational, or speech therapy</td>
</tr>
<tr>
<td>Moderate (99204/99214)</td>
<td>1 or more chronic illnesses with exacerbation, progression, or adverse effects of treatment, stable OR 1 undiagnosed new problem, uncertain prognosis OR 2 or more stable chronic illnesses OR 1 acute illness with systemic symptoms OR 1 acute complicated injury</td>
<td>Need 1 of 3 categories Category 1: Tests and documents</td>
<td>Moderate risk of morbidity from further testing or treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Record number or check boxes</td>
<td>Examples: Prescription drug management Minor surgery with patient risk factors Elective major surgery without risk factors Diagnosis/treatment affected by social determinants of health</td>
</tr>
<tr>
<td>High (99205/99215)</td>
<td>1 or more chronic illnesses with severe exacerbation, progression, or adverse effects of treatment OR 1 acute or chronic illness or injury that poses a threat to life or bodily function</td>
<td>Need 2 of 3 categories Category 1: Tests and documents</td>
<td>High risk of morbidity from additional diagnostic testing or treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Record number or check boxes</td>
<td>Examples: Drug therapy requiring intensive monitoring for toxicity Major surgery with risk factors Emergency major surgery Hospitalization Decision not to resuscitate or de-escalate care due to poor prognosis</td>
</tr>
</tbody>
</table>

**KEY:** MDM, medical decision-making
dressed, the data reviewed for the visit, and the risk associated with treating the patient. The performance and interpretation of in-office tests (rapid strep, rapid flu tests, etc.) as well as external tests, such as complete blood count (CBC) or an x-ray done at a hospital are appropriate to consider as data elements. Each test counts as 1, if it is performed or evaluated on the day of service (see Figure 1 below).

Looking at the coding table, determining the level of MDM associated with a visit depends on 2 of 3 scores associated with elements of care columns. To qualify for an MDM level, 2 of the 3 elements for that level of decision-making must be met or exceeded. Keep in mind that, for pediatricians, the majority of outpatient visits are low complexity (level 3 – 99203 new patient, 99213 established patient) and moderate complexity (level 4 – 99204 new patient, 99214 established patient).

**Level 3 visits**

Level 3 low-level visits are associated with the evaluation of 2 self-limiting or minor problems, 1 stable chronic illness, or a new uncomplicated illness or injury. Data to meet threshold criteria for a low-complexity visit include reviewing documents from an external source or ordering or reviewing tests (that are not in-office tests). Each document and unique test or order is counted and must add up to 2 or higher to meet the threshold for data analysis for a level 3 visit.

Alternatively, obtaining a history from an independent historian (ie, a parent or guardian in the case of a pediatric visit) alone satisfies the data element for a level 3 visit. The risk associated with level 3 visits is associated with a low risk of morbidity from additional tests or treatment, such that there would be a minimal amount of discussion involved in completing the visit.

For most pediatricians, level 3 or low-complexity visits are straightforward. The American Academy of Pediatrics (AAP) suggests assigning level 3 visits to the following conditions:
### TABLE 2 TIME ASSOCIATED WITH VISITS, 2021

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>2021 TOTAL TIME MINUTES/VISIT</th>
</tr>
</thead>
<tbody>
<tr>
<td>99202 New patient</td>
<td>15-20</td>
</tr>
<tr>
<td>99203 New patient</td>
<td>30-44</td>
</tr>
<tr>
<td>99204 New patient</td>
<td>45-59</td>
</tr>
<tr>
<td>99205 New patient</td>
<td>60-74</td>
</tr>
<tr>
<td>99212 Established patient</td>
<td>10-19</td>
</tr>
<tr>
<td>99213 Established patient</td>
<td>20-29</td>
</tr>
<tr>
<td>99214 Established patient</td>
<td>30-39</td>
</tr>
<tr>
<td>99215 Established patient</td>
<td>40-54</td>
</tr>
<tr>
<td>99417 (see text)</td>
<td>15</td>
</tr>
</tbody>
</table>

For 99205 and 99215 visits requiring more time, you can additionally code for a 99417 visit in 15-minute units.

**KEY:** CPT, current procedural terminology

- Mild upper respiratory infection and mild diaper rash, with home care recommendations
- Pharyngitis with negative streptococcal test, with independent historian
- Acute gastroenteritis, with limited data, drug management
- Follow-up of stable attention-deficit hyperactivity disorder (ADHD), with limited data, prescription drug management
- Follow-up of stable asthma, with limited data, antiemetic drug, oral rehydration plan
- Uncomplicated hand, foot, and mouth disease, with advice for home care and infection control
- Allergic rhinitis due to pollen, with advice for over-the-counter medication
- Minor sprain, with recommendation for use of soft brace
- Wound repaired in emergency department or urgent care requiring evaluation and suture removal
- Overuse injury requiring order for physical therapy
- Fever, cough, and third episode of otitis media within 3 months in infant; antibiotics prescribed
- Acute gastroenteritis with dehydration; administration of antiemetic drug, oral rehydration plan
- Follow-up of stable ADHD; discussion with school nurse, medication management
- Asthma with exacerbation but not respiratory distress, requiring prescription drug management
- Asthma with report of increased symptoms, requiring medication change
- Follow-up for stable asthma and stable anxiety disorder with medication management
- Symptoms and findings supporting strep throat; positive streptococcal test, antibiotic prescribed
- Unexplained bruising; with independent historian and 2 or more laboratory tests ordered and/or results reviewed
- Follow-up of head injury with brief loss of consciousness with intermittent headaches and confusion; order for cognitive testing, review of radiology report from initial treatment at hospital, and independent historian
- Foreign body in ear, with decision regarding removal of foreign body under anesthesia
- Caregiver refusal of testing or consultation for an undiagnosed new problem due to out-of-pocket costs

### Level 4 visits

Level 4 moderate-level visits are associated with the evaluation of 1 or more chronic illnesses with exacerbation, progression, or adverse effects of treatment; 2 or more stable chronic illnesses; 1 undiagnosed new problem with uncertain prognosis; 1 acute illness with systemic symptoms; or 1 acute complicated injury. Data required to meet the threshold criteria for moderate-complexity visits require satisfying 1 out of 3 categories. The first includes the data count described in a level 3 visit, including a data point if the history is obtained in full or in part from an independent historian. Credit for category 1 of level 4 visits requires a data count of 3 or higher. The second data category is the interpretation of a test performed by another physician, and the third is a discussion of treatment with an external physician.

The risk associated with moderate-complexity visits includes prescribing medication, decisions regarding minor surgery with risk factors, decisions regarding elective major surgery without risk factors, or diagnosis or treatment limited by social determinants of health. Social determinants of health refer to a patient’s ability to adhere to recommendations based on their economic situation (eg, insurance status) or social situation (eg, homelessness). However, when a physician is deciding whether a visit merits a level 4 designation, the landscape can be murky. What about an uncomplicated conjunctivitis for which an antibiotic is prescribed? How about when a patient presents with an ear infection with pain or fussiness and no other symptoms? Fortunately, as with level 3 visits, the AAP gives examples of the types of encounters that merit a level 4 evaluation. These include, but are not limited to:

- Fever, cough, and third episode of otitis media within 3 months in infant; antibiotics prescribed
- Acute gastroenteritis with dehydration; administration of antiemetic drug, oral rehydration plan
- Follow-up of stable ADHD; discussion with school nurse, medication management
- Asthma with exacerbation but not respiratory distress, requiring prescription drug management
- Asthma with report of increased symptoms, requiring medication change
- Follow-up for stable asthma and stable anxiety disorder with medication management
- Symptoms and findings supporting strep throat; positive streptococcal test, antibiotic prescribed
- Unexplained bruising; with independent historian and 2 or more laboratory tests ordered and/or results reviewed
- Follow-up of head injury with brief loss of consciousness with intermittent headaches and confusion; order for cognitive testing, review of radiology report from initial treatment at hospital, and independent historian
- Foreign body in ear, with decision regarding removal of foreign body under anesthesia
- Caregiver refusal of testing or consultation for an undiagnosed new problem due to out-of-pocket costs

### Level 5 visits

Level 5 high-level visits are associated with 1 or more chronic illnesses with severe exacerbation or progression. They are also associated with the adverse effects of treatment of an acute or chronic illness or injury that poses a threat to life or bodily function. Data to meet threshold criteria for high-complexity visits must satisfy 2 out of 3 categories (see Level 4 above). The risk associated with high-level visits is a high risk of morbidity from additional diagnostic testing or treatment.
According to the AAP,3 examples of level 5 visits would include:

- Decision for or against hospital admission in a patient with acute respiratory distress (eg, status asthmaticus)
- In-office hydration therapy for dehydration, with plan for hospitalization if patient is unable to tolerate oral rehydration before leaving office
- Infant with fever, tachycardia, lethargy, and dehydration, with decision to admit to hospital
- A patient is seen for recent seizures requiring hospital management. The physician reviews hospital records including recent video electroencephalogram test results read by another physician, obtains history from caregivers who witnessed seizures, and monitors for toxicity due to long-term use of an antiepileptic drug.
- Parents seek hospitalization of their child who planned suicide but was stopped before injury occurred.
- Decision for hospitalization for suspected or confirmed appendicitis

If you use MDM to code, you must accurately determine those elements of MDM that contributed to your determination of the level of service. Usually, your assessment and plan will contain enough details to justify the level of MDM billed for. The prudent pediatrician will conclude a level 4 or 5 note by presenting the MDM elements documented in the note (Figure 1). The note in Figure 1 was presented in table format with invisible borders to conserve space, which enables reading without scrolling. Important components of the note are highlighted to capture the reader’s attention. Documenting MDM at the end of your note reduces the chance of an insurance company audit. It also serves as a reminder to document the elements needed to justify the level of service you submit.

**Coding by time**

Using time to determine a level of service can be less confusing compared to assigning a level of service using MDM. Time now consists of:

- Preparing to see the patient, reviewing tests and external notes
- Obtaining a history from the parent
- Performing an examination
- Ordering medication or tests
- Referring to and possibly communicating with other health care providers on management

Coding by time is dependent on providers being honest in their determination of time elements during a visit. As such, visits coded by time are quite difficult for insurance companies to reject.

**Conclusion**

A brief webinar on the guidelines is available on the medgizmos.com website. You can also visit MDMTool.org (Figure 2) which helps providers code more accurately.

**COMMENTS?** Email them to llevine@mhlfsciences.com

*Developed by Andrew Schuman and Robert Schuman, M.Ed, BS, to facilitate coding according to the 2021 guidelines.
Opportunities for
Point-of-Care Diagnostics
in Outpatient Pediatric Centers
to Influence Antibiotic Prescribing Patterns

Although beneficial, antibiotic use can lead to adverse effects. Unnecessary antibiotic prescribing is a risk factor for antibiotic resistance, which can result in increased healthcare costs, morbidity, and mortality. Judicious prescribing, correct dosage and duration, and minimizing misdiagnoses are fundamental to reducing inappropriate prescribing of antibiotics.*

This supplement to Contemporary Pediatrics examines key findings from a 1-year study of real-world use of a CLIA-waived, point-of-care respiratory PCR panel in a pediatric clinic.

Read this supplement now at:
contemporarypediatrics.com/poc-diagnostics-study

Supported by:

Food allergies can develop in individuals at any age, although many develop during childhood. Milk, eggs, peanut, tree nuts, fish, shellfish, soy, and wheat make up approximately 90% of food allergies in the United States. The National Institute of Allergy and Infectious Diseases (NIAID) defines food allergy “as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.”

When assessing patients for food allergies, the pediatrician should remember that patients reporting a food allergy are far more common than challenge-confirmed food allergy, that food allergies are more common in children and those with atopic diseases, and that a small number of foods account for the great majority of food allergies.

Food allergies can develop in individuals at any age, although many develop during childhood. Milk, eggs, peanut, tree nuts, fish, shellfish, soy, and wheat make up approximately 90% of food allergies in the United States. The National Institute of Allergy and Infectious Diseases (NIAID) defines food allergy “as an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food.”

When assessing patients for food allergies, the pediatrician should remember that patients reporting a food allergy are far more common than challenge-confirmed food allergy, that food allergies are more common in children and those with atopic diseases, and that a small number of foods account for the great majority of food allergies.

Patients are frequently referred to pediatric allergists due to concern that a food might have caused a particular set of symptoms. Common complaints include rash, rhinitis, itchy mouth, loose stools, and/or abdominal pain. It is important to realize that immunoglobulin E (IgE)-mediated food allergy will almost always elicit a response within 2 hours after food ingestion and is reproducible when that type of food is consumed again. For instance, if a rash develops when a patient drinks milk, then a thorough dietary history should include what other types of dairy the patient consumes. If the patient is eating cheese, yogurt, or ice cream without symptoms, then milk allergy can be eliminated from the differential diagnoses.

Another situation is confusion around lactose intolerance and milk allergy. If a patient can tolerate lactose-free cow milk, they are not allergic because the milk protein is still present. A reaction consisting of hives, swelling, vomiting, severe abdominal pain, coughing, wheezing, and other IgE-mediated symptoms is concerning for true food allergy. It is important that patients with a history of a reaction concerning for food allergy see an allergist promptly, especially when milk or egg is presumed to be the culprit. These patients often can tolerate extensively baked products that have milk or egg as ingredients, so a thorough review with an allergist can determine if and when the patients can tolerate these products.

Patients also are commonly referred for consultation following food exposure with complaints of rhinitis. There are no published studies of food allergy presenting with rhinitis symptoms alone. There is no evidence of IgE-mediated food-induced rhinitis symptoms without anaphylaxis with whole-body symptoms (ie, hives, difficulty breathing, or diarrhea); therefore, there is no indication to...
test for food allergens in patients presenting with rhinitis symptoms. Furthermore, there is no reason to eliminate a food a child has been eating and tolerating regardless of specific IgE level or skin prick test results.

Serum IgE levels for an indiscriminate panel of foods should never be drawn when evaluating food allergy. A thorough history that includes foods ingested, timing of symptom onset in relation to the food, symptoms, symptom duration, and subsequent exposure to the food should be obtained. If the patient has been able to tolerate a normal amount of the food following the reaction, food allergy can be eliminated. The misinterpretation of IgE levels often leads to the inappropriate avoidance of a food, which may lead to the development of true IgE-mediated food allergy. Although food-specific IgE levels and skin prick testing can be useful, it is important to recognize that the gold standard for determining if a patient has a true food allergy is ingestion of the food. If it is tolerated without reaction, there is no food allergy and any positive testing results are false positives.

Social media has had positive and negative aspects in the realm of food allergy. Social media allows patients and families to connect with one another to share their experiences, swap recipes geared toward those with food allergies, and find support. However, it also allows for open discussion of food allergy and food sensitivity in which information presented might not be evidenced based or accurate. Advertising for IgG (not IgE) testing has led to inappropriate food allergy testing and unnecessary food avoidance. IgG is a marker of exposure, and one would not be surprised to find that foods that are routinely consumed have detectable IgG values. An elevated IgG value has no role in diagnosing food allergy. IgE or skin prick testing is used to bolster the evidence that there was a particular food responsible for the symptoms that are compatible with allergy; it cannot be used by itself to make the diagnosis of a food allergy. The overuse of serum IgG testing for dietary guidance can lead to unnecessary avoidance of foods, which may lead to nutritional deficient dietary practices, a big concern in a growing child.

Perhaps the newest breakthrough in the area of food allergy over the past year has been the US Food and Drug Administration approval of Palforzia, an oral immunotherapy product aimed at reducing the severity of reactions to peanut exposure among individuals with a peanut allergy. Although there are allergists across the United States who offer oral immunotherapy for various foods, these are typically not covered by insurance and cost can be a barrier. Whereas Palforzia is not a cure for peanut allergy and does not allow an individual to eat peanut ad lib, it is another option for managing food allergies. With the advancements over the past few years in food allergy, such as recommendations about early peanut introduction in infants at higher risk of developing peanut allergy, patients should be evaluated by an allergist who keeps abreast of the latest developments in the field.

COMMENTS? Email them to llevine@mjhlifesciences.com

For references, go to ContemporaryPediatrics.com/state-of-union-food-allergies-2021

LIKE WHAT YOU’RE READING? Sign up to receive the eNewsletter
Scan this QR code

MILK, EGGS, PEANUT, TREE NUTS, FISH, SHELLFISH, SOY, AND WHEAT MAKE UP APPROXIMATELY 90% OF FOOD ALLERGIES IN THE UNITED STATES.
Antenatal hydronephrosis
A pediatrician’s dilemma: understanding, diagnosing, and treating ANH

Antenatal hydronephrosis (ANH), also referred to as urinary tract dilation (UTD), is one of the most confounding challenges to the practicing pediatrician. When dealing with newborns and children with ANH, pediatricians face understanding the significance of the degree of hydronephrosis, risk assessment, prenatal and postnatal management, and the use of prophylactic antibiotics.

A pragmatic and clinically focused approach to these issues should facilitate the pediatrician in their treatment of infants with prenatally detected hydronephrosis.

The use of routine fetal ultrasound has increased the diagnosis of ANH. ANH, which is dilation of the fetal renal collecting system, is one of the most common fetal anomalies, occurring in 1% to 5% of pregnancies.1,2 However, Hamilton et al reported an incidence of 1% to 2% of pregnancies in the United States, or 40,000 to 80,000 cases annually based on an estimated annual birth rate of 4 million.3 Prenatal ultrasound, which can visualize the kidneys at 12 to 13 weeks’ gestation and identify distinct renal architecture by week 20, has the advantage of allowing follow-up without invasive testing or radiation exposure. Fetal magnetic resonance imaging may be indicated in select cases to further delineate the structural abnormalities of the fetal urinary tract.

ANH may be a sign of underlying severe fetal urinary system anomalies or chromosomal aneuploidies and also may be associated with impaired renal development and fetal renal parenchymal injury.2,4 ANH may be transient in 50% to 70% of cases. It also may be secondary to ureteropelvic junction (UPJ) obstruction in 10% to 30% of cases, vesicoureteral reflux (VUR) in 10% to 40% of cases, ureterovesical junction (UVJ) obstruction in 5% to 15% of cases, multicystic dysplastic kidney in 2% to 5% of cases, posterior urethral valves (PUV) in 1% to 5% of cases, and other anomalies.5

Due to the increase in the detection of ANH, pediatricians had increased responsibility in administering prenatal counseling and pre- and postnatal diagnostic and treatment plans. The rationale for early diagnosis of ANH is to treat urinary tract

---

FIGURE 1  SOCIETY FOR FETAL UROLOGY
CLASSIFICATION OF ANTENATAL HYDRONEPHROSIS10

grade 1  grade 2  grade 3  grade 4

Urine barely splits sinus  Full pelvis, major calyces dilated  Uniformly dilated minor calyces, parenchyma spared  Parenchymal compromise

---

AMIN J. BARAKAT, MD, FAAP; AND H. GIL RUSHTON, MD, FAAP
obstruction and prevent pyelonephritis, renal calculi, loss of renal function, and chronic kidney disease.

**Degree of hydronephrosis**

Three systems are used to classify the degree of ANH: renal pelvic diameter (RPD), Society for Fetal Urology (SFU) criteria, and UTD classification. Although not uniformly accepted, the most common method to determine RPD is measurement of the maximum anteroposterior diameter of the renal pelvis in a transverse plane. An RPD of less than 4 mm at less than 28 weeks’ gestation and less than 7 mm at 28 weeks’ gestation is usually transient and does not usually require postnatal workup or future intervention. These authors found that an anteroposterior diameter (APD) of 4 mm or greater before 33 weeks’ gestation or 7 mm or greater after 33 weeks’ gestation was 100% accurate in identifying patients with abnormal renal function or those who might require intervention postnatally. However, many of these patients will demonstrate spontaneous improvement without surgical intervention. Others have classified RPD as mild, moderate, or severe according to specific measurement criteria (Table 1). An RPD of greater than 10 mm in the second trimester is associated with increased risk for the presence of congenital anomalies of the kidney and urinary tract (CAKUT). However, a clear cutoff value for defining obstruction requiring surgical intervention has not been determined.

In 1993, the SFU proposed a classification based on the appearance of the calyces, renal pelvis, and renal parenchyma to determine the grade of ANH (Table 2) (Figure 1). The SFU grading system is probably the most commonly used system of classification for both pre- and postnatal grading of UTD. In 2014, a multidisciplinary work group proposed a revision to the SFU classification, using “UT dilation” as a common terminology that would lead to a more standardized reporting of abnormal findings. This classification requires more extensive modifiers to determine the level of urinary tract obstruction than the SFU system. In the normal fetus, calyceal dilation is absent, the renal parenchyma has normal thickness and appearance, the ureter is not seen, the bladder is normal, and there is no unexplained oligohydramnios (Table 3). According to the new UTD system, the renal pelvis is considered to be not dilated if the APD measures less than 4 mm at less than 28 weeks’ gestation, less than 7 mm at 28 weeks’ gestation or greater, and less than 10 mm postnatally. A fetus is considered to be at increased risk of postnatal uropathy if the APD of the renal pelvis is 7 mm or greater at less than 28 weeks’ gestation, or 10 mm or greater at 28 weeks’ gestation or greater, or if there is 1 of the following: dilation of peripheral calyces, abnormal parenchymal thickness, appearance of visibly dilated ureter, abnormal bladder, or the presence of oligohydramnios.

Patients with pathological ANH have high SFU and APD grades, and both grading systems may be used as relatively reliable predictors for the outcome of ANH, including ANH regression and postpartum surgery. These authors found that the sensitivity and specificity of the SFU and that of the APD grading system are very similar, indicating that both grading systems have a relatively 

---

**FIGURE 2 POSTNATAL MANAGEMENT OF ANTENATAL HYDRONEPHROSIS**

<table>
<thead>
<tr>
<th>I. Mild unilateral hydronephrosis (SFU grade 1-2; fetal A-P diameter &gt; 7mm)</th>
<th>Initial US ON day of life 1-3:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat US in 3 mos</td>
<td>If worsened (SFU grade 3-4), MAG-3 Lasix renal scan or refer to pediatric urologist/nephrologist</td>
</tr>
<tr>
<td>If improved, no further studies</td>
<td>If stable, repeat US in 6-9 mos</td>
</tr>
<tr>
<td>If stable, repeat US in 6-9 mos</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. Moderate or severe hydronephrosis (SFU grade 3-4; fetal A-P diameter &gt; 15mm)</th>
<th>Initial US AFTER day of life 3:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repeat US in 6-9 mos</td>
<td>If worsened (SFU grade 3-4), MAG-3 Lasix renal scan or refer to pediatric urologist/nephrologist</td>
</tr>
<tr>
<td>If improved, no further studies</td>
<td>If stable, repeat US in 6-9 mos</td>
</tr>
<tr>
<td>If stable, repeat US in 6-9 mos</td>
<td>Antibiotic prophylaxis with amoxicillin 25 mg/kg/day</td>
</tr>
<tr>
<td>Antibiotic prophylaxis with amoxicillin 25 mg/kg/day</td>
<td>MAG-3 Lasix renal scan and/or refer to pediatric urologist/nephrologist</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>III. Bilateral or associated with ureteral dilation, duplicated system, solitary or small dysmorphic kidney</th>
<th>Antibiotic prophylaxis with amoxicillin 25 mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis with amoxicillin 25 mg/kg/day</td>
<td>VCUG and/or refer to pediatric urologist/nephrologist</td>
</tr>
</tbody>
</table>

**KEY:** A-P, anterior-posterior; SFU, Society for Fetal Urology; US, ultrasound; VCUG, voiding cystourethrogram
your voice

high diagnostic accuracy. However, they noted that the combination of both grading systems seems to have a higher diagnostic value compared with that of each system alone regarding the discrimination of pathological ANH from physiological ANH.

Prenatal management
Management of ANH depends on the risk assessment. A fetus categorized as low risk based on ultrasound prior to 32 weeks’ gestation will require only 1 further repeat ultrasound at starting at 32 weeks’ gestation. However, ANH (APD > 4 mm in the second trimester, > 7 mm in the third trimester) requires further follow-up. Findings suspicious of PUV (oligohydramnios, dilated bladder, or bilateral ANH) warrant monitoring every 2 to 4 weeks throughout pregnancy, and any comorbid fetal abnormality also should be investigated. If increasing oligohydramnios is seen after 20 weeks’ and before 32 weeks’ gestation, bladder outlet obstruction is suspected and fetal intervention such as vesicoamniotic (VA) shunting may be considered. This will allow for the return of amniotic fluid in an effort to promote fetal lung development. The middle of the second trimester is the ideal time period to offer prenatal intervention.

Fetal intervention of VA shunting may improve postnatal outcome in fetuses with lower urinary tract obstruction who have favorable fetal renal function parameters. Fetal renal function can be evaluated by combining fetal urinary biochemistry profiles with ultrasound characteristics of fetal kidneys according to gestational age. Increased levels of sodium, calcium, chloride, β₂ microglobulin, and decreased levels of creatinine after 18 weeks’ gestation measured in fetal urine in patients with bilateral obstructive uropathy and oligohydramnios are associated with poor neonatal outcomes and may serve as adjuvants to decide on the need for antenatal intervention. Morris et al reported higher survival in the fetuses receiving VA shunting, whereas Spiro et al reported that prenatal interventions do not improve renal function prognosis of patients with oligohydramnios associated with CAKUT.

Postnatal management
Because there is no consensus on the postnatal approach to ANH, fetuses with persistent antenatal renal pelvis measurements 7 mm or greater in the third trimester should be investigated postnatally. Because physiologic dehydration of the newborn can lead to underestimation of hydronephrosis, an early normal postnatal ultrasound, if done in the first 72 hours of life, does not preclude the presence of urinary tract abnormality.

Lee et al screened 1645 citations, of which 17 studies met inclusion criteria and created a data set of 1308 participants. There was a significant increase in risk of any postnatal pathology per increasing degree of ANH (11.9% for mild, 45.1% for moderate, and 88.3% for severe). The risk of VUR was similar for all degrees of antenatal hydronephrosis. Most cases of ANH are transient and resolve spontaneously with increasing gestational age or soon after birth. Maayan-Metzger et al found that 97.5% of mild prenatal ANH resolved or remained mild on follow-up, although 80% of the moderate and only 20% of the severe cases improved. Barbosa et al showed that 25% of ANH resolved antenatally, including 90%, 75%, and 28% of mild, moderate, and severe ANH cases, respectively.

Because hydronephrosis could be underestimated on an early postnatal ultrasound, newborns with persistent or worsening ANH should be evaluated with a postnatal ultrasound after at least 48 to 72 hours of

<table>
<thead>
<tr>
<th>Degree of HN</th>
<th>Second trimester (mm)</th>
<th>Third trimester (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>4- &lt;7</td>
<td>7- &lt;9</td>
</tr>
<tr>
<td>Moderate</td>
<td>7-10</td>
<td>9-15</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt; 10</td>
<td>&gt;15</td>
</tr>
</tbody>
</table>

HN, hydronephrosis; RPD, renal pelvic diameter; UTD, urinary tract dilation.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal exam</td>
</tr>
<tr>
<td>1</td>
<td>Mild dilation of RP</td>
</tr>
<tr>
<td>2</td>
<td>Moderate dilation of RP and few calyces</td>
</tr>
<tr>
<td>3</td>
<td>Dilation of RP and uniform dilation of all calyces</td>
</tr>
<tr>
<td>4</td>
<td>Grade 3 and thinning of renal parenchyma</td>
</tr>
</tbody>
</table>

RP, renal pelvis.
life. Ultrasound findings (SFU grade 1-2) after 48 to 72 hours of life in patients associated with low risk for postnatal uropathy should be followed up with an ultrasound in 3 to 6 months. If the hydronephrosis improves, longer-term imaging is not necessary, based on the very low risk of progression. Patients with higher-risk (SFU grades 3-4) hydronephrosis should undergo more frequent ultrasounds and, when indicated, a MAG-3 Lasix renal scan to rule out obstruction at the UPJ or UVJ. This allows for the evaluation of both differential renal function and drainage of the dilated collecting system. Consultation with a pediatric urologist or nephrologist should also be considered in these higher-risk patients.

Opinions differ on the indication for VCUG in patients with ANH. Many centers screen all patients with grades 3 to 4 hydronephrosis to look for clinically significant dilating VUR (grade > 3). However, more specific selection criteria for VCUG have been proposed, including ureteral dilation, duplication of the collecting system, and/or renal dysmorphia, which were shown to have the same yield for detection of dilating VUR but with only approximately half as many patients requiring VCUG.21

Patients with risk of more severe postnatal uropathy, such as those with suspected PUV, bilateral severe hydronephrosis, or solitary hydronephrotic kidney, should be routinely evaluated with a VCUG and MAG-3 Lasix renal scan during the first 1 to 2 weeks of life to determine renal function, renal drainage, and the possible need for early neonatal surgical intervention versus close serial monitoring with renal function studies and ultrasounds.3,9,21 Prophylactic antibiotics may be considered at this stage. Unfortunately, there are not enough data to support strong recommendations in many instances, and some decisions are left to the discretion of the specialist. An algorithm of the postnatal management of ANH is shown in Figure 2.

**Urinary tract infection and the use of prophylactic antibiotics**

Female gender, uncircumcised males, high-grade UTD, and VUR were found to be independent high-risk predictors of febrile urinary tract infection (UTI) in patients with ANH.23,24 The benefits of continuous antibiotic prophylaxis in patients with ANH are controversial.21 In a systematic review of the literature, which included 3876 infants, UTI rates in patients with low-grade hydronephrosis were similar regardless of continuous antibiotic prophylaxis status: 2.2% on prophylaxis versus 2.8% not receiving prophylaxis.26,27 However, when looking at high-grade UTD, a significant decrease in the rate of UTI was seen (14.6% treated vs 28.9% untreated; \( P < .01 \)). The estimated number of patients needed to treat to prevent 1 UTI in those with high-grade UTD was 7.

In a meta-analysis of prenatal UTD in 2008, Lee et al reported a 4%, 14%, 33%, and 40% incidence of UTI in SFU grades of 1 to 4, respectively, which indicated the presence of a linear relationship between the degree of UTD and risk of developing UTI.28 Higher rates of UTI in higher-grade UTD as compared with lower-grade UTD also were reported.27 It appears from these studies that the presence of moderate to severe UTD does place the neonate at risk of UTI. Prophylactic antibiotics may have to be considered to prevent UTI and risk for kidney damage.

Ureteral dilation has shown to be an independent risk factor for UTI.23,24 Herz et al in a 10-year retrospective experience in patients with prenatally detected UTD, reported the incidence of febrile UTI on prophylactic antibiotics to be 7.9% versus 18.7% without treatment.29 The authors found that ureteral dilation of more than 11 mm in patients not maintained on prophylactic antibiotics afforded a 5-fold higher risk of developing a febrile UTI.

**TABLE 3 NORMAL VALUES FOR UTD CLASSIFICATION SYSTEM**

<table>
<thead>
<tr>
<th>Ultrasound findings</th>
<th>Time at prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16-27 weeks' gestation</td>
</tr>
<tr>
<td>Anterior-posterior (RPD)</td>
<td>&lt; 4 mm</td>
</tr>
<tr>
<td>Calyceal dilation</td>
<td></td>
</tr>
<tr>
<td>Central</td>
<td>no</td>
</tr>
<tr>
<td>Peripheral</td>
<td>no</td>
</tr>
<tr>
<td>Parenchymal thickness</td>
<td>Normal</td>
</tr>
<tr>
<td>Parenchymal appearance</td>
<td>Normal</td>
</tr>
<tr>
<td>Ureter(s)</td>
<td>Normal</td>
</tr>
<tr>
<td>Bladder</td>
<td>Normal</td>
</tr>
<tr>
<td>Unexplained oligohydramnios</td>
<td>No</td>
</tr>
</tbody>
</table>

N/A, not applicable; RPD, renal pelvic diameter; UTD, urinary tract dilation.
The US Food and Drug Administration has approved the Harmony Transcatheter Pulmonary Valve System, the first nonsurgical heart valve to treat both pediatric and adult patients with certain congenital heart defects (CHDs). The device improves the blood flow to the lungs without open-heart surgery.

The device is used in patients with a native or surgically repaired right ventricular outflow tract. Its safety and efficacy were assessed in a prospective, nonrandomized, multicenter clinical study. In the study, 70 patients had the device implanted. Patients were scheduled for examinations at the start of the study, at implant procedure, at discharge, and post implant at 1 month, 6 months, and annually through 5 years. The primary safety end point for the study was no procedure- or device-related death within 30 days of receiving the implant, which was achieved in 100% of the participants. Primary efficacy end point was the percentage of patients who had no additional surgical or interventional procedures linked to the device and also had acceptable heart blood flow function at 6 months, with 89.2% of participants reaching the efficacy end point.

The device is contraindicated for patients who have an infection in their heart or elsewhere, can’t tolerate blood-thinning drugs, or who have a sensitivity to titanium or nickel.

For references, go to ContemporaryPediatrics.com/antenatal-hydronephrosis

H. Gil Rushton is chief emeritus, Division of Urology at Children’s National Medical Center; and professor of urology and pediatrics at George Washington University School of Medicine, both in Washington, DC.

Amin J. Barakat is a professor of clinical pediatrics at Georgetown University School of Medicine in Washington, DC.

The authors have nothing to disclose.

For reference and full article, go to bit.ly/3oTTkGB

Subscribe to our eNewsletter to get our latest articles
Scan this QR code
Clinical findings
Mastocytosis is a condition that involves an accumulation of mast cells in 1 or more organ systems such as the skin, liver, bone marrow, or small intestine. Cutaneous mastocytosis (CM) is usually found in very young children and predominantly involves dermal infiltrates of mast cells. The condition can be divided into maculopapular CM, diffuse CM, and solitary CM. The prognosis of solitary CM is excellent, with most patients experiencing spontaneous resolution before puberty. However, in patients with disease onset after age 2 years, solitary CM may continue into adulthood. Children with solitary lesions, multiple skin lesions, or diffuse mastocytosis confined to the skin (rare in infants) all have a good prognosis. Diffuse cutaneous disease with systemic involvement is much less common in infants and is often persistent. It is rarely associated with myeloproliferative disease.

Epidemiology/etiology
The incidence of CM is estimated to be around 5 to 10 new cases in 1 million individuals, or 1 in every 1000 to 8000 dermatology outpatients, but it may be as often as 1 in 200 first-time patients at pediatric dermatology clinics. It is estimated that 10% to 15% of all pediatric cases of CM are solitary CM. Although the condition typically affects infants, particularly in the first 3 months of life, there have been reported cases of adult onset.

Most cases of mastocytosis are due to a gain-of-function mutation in the c-KIT gene, which encodes a receptor tyrosine kinase that regulates cell growth and division in addition to regulating the production of mast cells. Most of these somatic mutations occur spontaneously and are therefore not heritable. However, there have been some case reports of familial cases.

Differential diagnosis
When the patient’s skin lesion is stroked or rubbed, mast cell degranulation occurs, leading to an immediate eruption of hives or urticaria. This is known as the “Alder reaction.” The presence of a significant number of mast cells in the dermis and the absence of eosinophils can help distinguish CM from other conditions such as dermatitis herpetiformis or Sweet’s syndrome.

An otherwise healthy 6-month-old boy has a 1-cm area of recurrent blistering with surrounding erythema on his right cheek that developed shortly after birth.
ululation occurs and forms a wheal known as Darier sign. Blisters result from buildup of tryptase between the epidermis and dermis. Although not usually necessary, diagnosis can be confirmed by a skin biopsy, which would show a dense infiltrate of mast cells. Additionally, during an attack, tryptase and histamine levels may be increased. An absence of systemic systems should be noted to rule out systemic mastocytosis, which could show more extensive blistering in a larger surface area, a high serum total tryptase level, gastrointestinal disturbances, osteolysis, organomegaly, ascites, or cytopenias.

Treatment and management
Patients should avoid triggers of mast cell degranulation. Common triggers include heat, friction, alcohol, narcotics, sunlight, nonsteroidal anti-inflammatory drugs, anesthetics, bee stings, and more. When symptoms are triggered, they can be managed with antihistamines, sodium cromoglycate, acetylsalicylic acid, or ketotifen. Topical steroids may be used to manage lesion progression, and topical antibiotics can be used to prevent infection in blisters.

Patient outcome
When the area with recurrent blistering was rubbed, the infant developed a blister with surrounding urticarial erythema, typical of a positive Darier sign. The patient was given an oral antihistamine for symptomatic treatment, and a discussion was had with his parents about ways to avoid rubbing the area. Over the next 3 to 4 months, the blistering stopped and the redness with rubbing improved dramatically. The patient’s parents were counseled that continued regression of the lesion and improvement in symptoms should be expected.

COVID-19 was third-leading cause of death in US in 2020
The viral disease, surpassed only by heart disease and cancer, was a factor in more than 377,000 deaths, study results show
KEITH A. REYNOLDS

COVID-19 was the underlying or contributing cause of 377,883 of the approximately 3.36 million deaths in the United States in 2020; it was the third-leading cause of death after heart disease and cancer, according to study results published in Morbidity and Mortality Weekly Report. The age-adjusted death rate in the US rose for the first time since 2017; it increased 15.9% in 2020 compared with 2019, the results showed. COVID-19 death rates were highest among males and older adults; the highest numbers of overall deaths occurred in April and December. The disease replaced suicide as 1 of the top 10 causes of death, according to the study’s authors.

COVID-19 death rates were lowest among children aged 1 to 4 years and children and adolescents aged 5 to 14 years. Females showed lower age-adjusted death rates from COVID-19 than males by approximately one-third. Age-adjusted death rates were lowest among Asian and Hispanic individuals and highest among Black and Native American individuals, the study results showed.

The study’s authors noted that their findings were limited due to the data being provisional and numbers possibly changing as more information is received, timelines of death certificate submission varying by jurisdiction, certain categories of race reported on death certificates possibly being misclassified, and the limited availability of COVID-19 testing at the beginning of the pandemic possibly leading to an underestimation of deaths associated with the disease.

REFERENCE
**PRACTICE FOR SALE**

**SOLO PEDIATRIC PRACTICE FOR SALE**
Suburban city in Michigan, close to a major university and excellent school district. Surrounded by golf courses, downhill skiing and lakes. Excellent place to raise a family. Busy practice with major hospitals nearby.

**Gross revenue in excess of $800K**
- Terms Negotiable –

Call (810) 355-6134 or email plowe058@gmail.com with any inquiries

**CAREERS | GEORGIA**

One practitioner in thriving Stockbridge, GA peds office seeking full-time partner....

reply to cjpediatrics@cjpeds.com

**Reach your target audience.**

**Our audience.**

Contact me today to place your ad.

Joanna Shippoli
(440) 891-2615
jshippoli@mjhlifesciences.com

**Advertising Index**

**BIOFIRE**
BioFire.................................................................13
www.biofiredx.com

**QUIDEL**
Sofia2/LymeFIA....................................................CV4
www.quidel.com

**SUPERNUS**
SUPERNUS............................................................CV2
www.supernus.com

**CALL to ORDER:** 877-646-3300
www.medicaldevice depot.com
Ticks don’t know the meaning of “Social Distancing.”

Sofia 2 Lyme FIA: CLIA-waived Results in minutes, at your point-of-care

With kids home and parents looking for things to do that include “social distancing,” more families will take to the outdoors. The only thing, ticks don’t play by the same rules, so Lyme disease could end up on the rise. When patients aren’t feeling well, anxiety levels could be especially high – and now more than ever they’ll ask to be tested. Sofia 2 Lyme FIA uses a finger-stick whole blood sample to provide accurate, objective and automated results in as few as 3 minutes, getting practitioner and anxious patient on a path to treatment much sooner.

- IgM and IgG differentiated results
- CLIA waived
- Point-of-care testing
- Less than 1 minute hands-on-time
- Accuracy comparable to laboratory testing methods

For more information contact Quidel Inside Sales at 858.431.5814
Or go to our website at Sofia2Lyme.com