AI AND Autism

How technology has changed the way we diagnose

Respiratory Disorders
What you need to know about pneumonia right now

Nutrition
Neonatal feeding habits for infants with injury

Contemporary Pediatrics.com
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

• Suicidal Thoughts and Behaviors: Closely monitor all Qelbree-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes.

REFERENCES:

Abbreviation: NCE, new chemical entity.

Please see the brief summary of full Prescribing Information on adjacent pages, or visit QelbreeHCP.com.
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)

In a clinical study in patients 6 to 11 years of age, 34/154 (22%) of 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 worsening patterns are observed. If a patient appears to be at imminent risk, 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 200 mg daily had a 0.2 bpm 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 64/265 (31%) who received the 200 mg dose, compared to 39/262 (15%) of patients in the placebo group, and in 28/101 (27%) of patients who received the 400 mg dose, compared to 24/103 (23%) of patients who received placebo.

In a clinical study in patients 12 to 17 years of age, 22/99 (22%) of patients treated with Qelbree 200 mg daily had a 0.22 bpm increase in heart rate at any time point in the clinical trial, compared to 15/104 (14%) of patients who received placebo. This finding was observed in 69/205 (34%) who received the 400 mg dose, compared to 35/201 (17%) of patients in the placebo group.

In patients ages 12 to 17 years, 52/205 (25%) of patients treated with Qelbree 400 mg daily had a 15 mmHg increase in diastolic blood pressure at any time in the clinical trial, compared to 26/201 (13%) of patients in the placebo group. Assess heart rate and blood pressure prior to initiating treatment with Qelbree, following increases in dosages, and periodically while on therapy.

Activation of Mania or Hypomania

Noroaromatic drugs, such as Qelbree, may induce a manic or mixed episode in patients with bipolar disorder. Prior to initiating treatment with Qelbree, screen patients to determine if they are at risk for bipolar disorder; such screening should include a detailed psychiatric history, including a personal or family history of suicide, bipolar disorder, and depression.

Somnolence and Fatigue

Qelbree can cause somnolence and fatigue. In the short-term, placebo–controlled clinical trials 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.

ADVERSE REACTIONS

Clinical Trials Experience

The safety of Qelbree has been evaluated in 1118 patients (6 to 17 years of age) with ADHD exposed to one or more doses in short-term (6 to 8 weeks), randomized, double-blind, placebo-controlled trials. A total of 692 pediatric patients were treated for at least 6 months, and 347 pediatric patients for at least 12 months with Qelbree.

The data described below reflect exposure to Qelbree in 826 patients who participated in randomized, double-blind, placebo-controlled trials with doses ranging from 100 mg to 400 mg. The population (N=826) was 65% male, 35% female, 54% White, 41% Black, 4% multicultural, and 1% other races.

Adverse Reactions Leading to Discontinuation of Qelbree Treatment:

Approximately 3% of the 826 patients receiving Qelbree in clinical studies discontinued treatment due to an adverse reaction. The adverse reactions most commonly associated with discontinuation of Qelbree were somnolence, nausea, headache, irritability, tachycardia, fatigue, and decreased appetite.

Most Common Adverse Reactions (occurring at ≥5% and at least twice the placebo rate for any dose): somnolence, decreased appetite, fatigue, nausea, vomiting, insomnia, and irritability.

Listed here are adverse reactions that occurred in at least 2% of patients treated with Qelbree and more frequently in the Qelbree-treated patients than in the placebo-treated patients. Data represents pooled data from pediatric patients ages 6 to 17 years who were enrolled in randomized, placebo-controlled trials of Qelbree.

Adverse Reactions Reported in ≥2% of Pediatric Patients (Ages 6 to 17 Years) Treated with Qelbree and at a Greater Rate than Placebo-Treated Patients in Placebo-Controlled ADHD Studies Placebo (N=463); All Qelbree (N=826).


* The following terms were combined: Somnolence: somnolence, lethargy, sedation; Headache: headache, migraine, migraine with aura, tension headache; Upper respiratory tract infection: nasopharyngitis, pharyngitis, sinusitis, upper respiratory tract infection, viral sinusitis, viral upper respiratory tract infection; Abdominal pain: abdominal discomfort, abdominal pain lower, abdominal pain upper; Insomnia: initial insomnia, insomnia, middle insomnia, poor quality sleep, sleep disorder, terminal insomnia.

Effects on Weight: In short-term, controlled studies (8 to 8 weeks), Qelbree-treated patients 6 to 11 years of age gained an average of 0.2 kg, compared to a gain of 1 kg in same-aged patients who received placebo. Qelbree-treated patients 12 to 17 years of age lost an average of 0.2 kg, compared to a weight gain of 1.5 kg in same-aged patients who received placebo. In a long-term open-label extension safety trial, 1097 patients received at least 1 dose of Qelbree. Among the 339 patients evaluated at 12 months, the mean change from baseline in weight-for-age z-score was -0.2 (standard deviation of 0.5). In the absence of a control group, it is unclear whether the weight change observed in the long-term open-label extension was attributable to the effect of Qelbree.

DRUG INTERACTIONS

Drugs Having Clinically Important Interactions with Qelbree

Monoamine Oxidase Inhibitors (MAOIs)

• Clinical Impact: Concomitant use of Qelbree with an MAOII may lead to a potentially life-threatening hypertensive crisis.

• Intervention: Concomitant use of Qelbree with an MAOII within 2 weeks after discontinuing an MAOII is contraindicated.

• Examples: Selegiline, isocarboxazid, phenelzine, tranylcypromine, sarafotoxin, tranylcypromine.

Sensitive CYP1A2 Substrates or CYP1A2 Substrates with a Narrow Therapeutic Range

Clinical Impact: Viloxazine is a strong CYP1A2 inhibitor. Concomitant use of viloxazine significantly increases the total exposure, but not peak exposure, of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates.

• Intervention: Coadministration with viloxazine is contraindicated.

• Examples: Alosoten, duloxetine, ramelteon, tasimelteon, tizanidine, theophylline.

Moderate Sensitive CYP1A2 Substrate

Clinical Impact: Viloxazine is a strong CYP1A2 inhibitor. Concomitant use of viloxazine significantly increases the total, but not peak, exposure of sensitive CYP1A2 substrates, which may increase the risk of adverse reactions associated with these CYP1A2 substrates.

• Intervention: Not recommended for coadministration with viloxazine. Dose reduction may be warranted if coadministered.
Drugs Having Clinically Important Interactions with Qelbree

Moderate Sensitive CYP1A2 Substrate

- Examples: Clonidine, prazosin

CYP2D6 Substrates

- Clinical Impact: Viloxazine is a weak inhibitor of CYP2D6, and increases the exposure of CYP2D6 substrates when coadministered.
- Examples: Amiodarone, atenolol, bupivacaine, carvedilol, desipramine, efavirenz, eslicarbazepine acetate, fluoxetine, fluvoxamine, ibuprofen, indapamide, irbesartan, itraconazole, ketoconazole, lopinavir, metoclopramide, mirtazapine, olmesartan, omeprazole, pantoprazole, propoxyphene, quetiapine, ranitidine, rosiglitazone, saquinavir, sirolimus, spironolactone, talinolol, tolcapone, tolterodine, verapamil, voriconazole

CYP3A4 Substrates

- Clinical Impact: Viloxazine is a weak inhibitor of CYP3A4 which increases the exposure of CYP3A4 substrates when coadministered.
- Examples: Atorvastatin, bedaquiline, buspirone, carbamazepine, ciprofloxacin, cyclosporine, diltiazem, dronedarone, elinoglutide, erlotinib, fexofenadine, fluconazole, fluoxetine, and other drugs with known CYP3A4 inhibition

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/jong).  

  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 toxicities 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 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 62 mg/kg/day. Viloxazine at 82 mg/kg/day caused early and late resorption, delayed fetal development, and possibly caused low incidences of fetal malformations or anomalies (craniorachischisis, missing cervical vertebrae, 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, or food consumption at doses ≥ 87 mg/kg/day but did not cause fetal toxicity at doses up to 130 mg/kg/day. The NOAEL 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, which is approximately equal to the MRHD, based on mg/m². Viloxazine was administered orally to pregnant mice during gestation and lactation at doses of 13, 33, and 82 mg/kg/day, which are approximately less than or equal to the MRHD of 400 mg, based on mg/m², respectively. Viloxazine treatment at 82 mg/kg/day during the gestation period caused maternal deaths and decreased body weight in the offspring. 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

Dosage 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 overdose 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 supportive and supportive treatment as appropriate. In case of overdose, consult a Certified Poison Control Center (1-800-222-1222 or www.poiscon.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.rasH-2 mice treated for 26 weeks at oral doses of 4.3, 13, and 43 mg/kg/day.

Mutagenesis

Viloxazine was not genotoxic in a battery of genotoxicity tests. It was not mutagenic in the in vitro bacterial reverse mutation (Ames) assay or clastogenic in the in vitro 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 oral doses of ≥ 130, ≥ 173, and ≥ 38 mg/kg/day in the rat, mouse, and dog, respectively, which are approximately equal to or slightly higher than the MRHD of 400 mg, based on mg/m² in children.
Winter is coming

A couple of years back, a huge billboard near Pennsylvania Station in Manhattan featured the ominous (and, for those of you who loved Game of Thrones, familiar) statement, “Winter is coming,” showing a large spoon filled with liquid, promoting a well-known cough medicine.

It was a clever advertising campaign, and, this year in particular, winter will be impossible to ignore. Although the Delta variant of COVID-19 continues to rear its ugly head, the new Mu strain has also emerged, still largely an unknown right now in terms of potency and contagion level. Meanwhile, we are moving toward the height of the flu, pneumonia, strep, and respiratory syncytial virus seasons.

That is one reason why you will see targeted coverage of these infectious diseases in Contemporary Pediatrics® over the next couple of months, (such as in this issue’s article, “How to Correctly Diagnose and Treat Community-Acquired Pneumonia,” by Jane M. Carnazzo, MD, FAAP). Which brings me back to September 2020, when MJH Life Sciences™ created a COVID-19 coalition to keep health care professionals like you up-to-date with the latest science and information on the pandemic. The coalition includes a top epidemiologist, an infectious disease expert, a clinical pharmacy professor, a psychiatrist, a Johns Hopkins Center for Health Security senior scholar, and others. You can watch webinars such as “Building Confidence in COVID-19 Vaccination: A Toolbox of Talks From Leaders in the Field” and “Battling Dual Threats: Flu and COVID-19 Converge.” These panels, and more, can be found at https://www.mjhlifesciences.com/covid-19-coalition/#pastprograms.

Finally, watch for 2 more exciting programs. November will bring a special issue devoted to vaccines, from the history of immunization to new pediatric vaccines in the pipeline. You won’t want to miss it. Also, over the next several weeks, Contemporary Pediatrics® will be announcing the winners of the inaugural Resident Writers Award program. Some 40 residents from the East Coast to the West Coast, from the South to the Midwest, contributed compelling cases for their chance to be this journal’s cover story. Stay tuned over the next few months for more details on who won and where you can find the winning submissions, as well as video interviews with the jurors, residents, and resident directors.
in this issue

**October 2021**

**Developmental Health**

**16 AI, telehealth, & sensor-based technologies facilitate autism diagnosis**
New technology-based tools can help pediatricians to make an accurate diagnosis of autism spectrum disorder. Andrew J. Schuman, MD

**PLUS 20 Assessing autism prevalence**
Miranda Hester

**Infectious Disease**

**28 New findings reveal how many lives COVID-19 vaccines have saved in the United States**
Keith A. Reynolds

**Pediatic pharmacology**

**29 Vaxneuvance study shows promise for use in children**
A 15-valent pneumococcal conjugate vaccine may soon be available for infants. Miranda Hester, Editor

**Respiratory Disorders**

**30 How to correctly diagnose and treat community-acquired pneumonia**
Putting the clues together to decide when to treat CAP with antibiotics. Jane M. Carnazzo, MD, FAAP

**Dermatology**

**31 Puncture wounds and purpura**
A 6-year-old presents with asymptomatic skin lesions. Charles Hyman, MD, FAAP

**Puzzler**

**10 Persistent foot and leg swelling in a 17-year-old female**
A teenager presents with swelling of the left leg. Justine Englanoff; and Eyal Ben-Isaac, MD

**Nutrition**

**22 Neonatal feeding in practice**
Nutrition for the neonate with intestinal injury. Shelly Joseph, MD; and Darla Shores, MD, PhD

**Classifieds**

**5 CHAIRMAN’S LETTER**
The availability of our parent company’s continuing education activities. We’ve picked this one especially for our Contemporary Pediatrics® readers. Go to: bit.ly/3EzsNfE

**Editor’s View**

The editors are pleased to announce the availability of our parent company’s continuing education activities. We’ve picked this one especially for our Contemporary Pediatrics® readers. Go to: bit.ly/3EzsNfE

**In addition**

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

Contemporary Pediatrics® does not verify any claims or other information appearing in any of the advertisements contained in this publication, and cannot take responsibility for any losses which may result from the use of such content.
Greetings!

The Delta variant of SARS-CoV-2 continues to surge throughout the United States, especially in unvaccinated populations, resulting in critical hospital bed shortages in many areas of the country. This has led to a major increase in COVID-19 infections and hospitalizations among children, coinciding with a surge of respiratory syncytial virus infections that also places a strain on available pediatric hospital beds. The COVID-19 pandemic is not over, and everyone who can get vaccinated should do so.

This month’s journal has a number of must-read articles:

- The cover story provides a review of new artificial intelligence apps that help clinicians with the screening and diagnosis of children with autism spectrum disorder. This was written by Andrew J. Schuman, MD, a Contemporary Pediatrics® editorial advisory board member.
- The Respiratory Disorders report is on community-acquired pneumonia (CAP) and how to determine who should receive antibiotic therapy. The decision to use antibiotics remains challenging in patients that present with symptoms of pneumonia, even though viruses are the most frequent cause of CAP. Jane M. Carnazzo, MD, FAAP, also a Contemporary Pediatrics® editorial advisory board member, wrote this article.
- The Infectious Disease news brief discusses how many lives have been saved by COVID-19 vaccines—a sobering reminder of vaccination’s critical role in reducing the mortality associated with COVID-19 infection.
- The Nutrition section offers a practical guide to meeting the challenge of feeding infants who have a history of intestinal injury or resection.

Thank you for providing outstanding care to your patients during these rapidly changing times. Please make time to take care of yourselves—the importance of which I was recently reminded of when a family medical emergency arose. Consider this anonymous quotation: “When life gives you a hundred reasons to break down and cry, show life that you have a million reasons to smile and laugh. Stay strong.” As always, I welcome your suggestions, comments, and questions.

With warmest regards,
Tina
Tina Q. Tan
email: titan@luriechildrens.org
How well do caregivers understand their child’s CP?

Most primary caregivers of children with cerebral palsy (CP) believe they have a substantial understanding of their child’s condition, a belief that is highly associated with the caregiver’s confidence that the provider spent sufficient time explaining the diagnosis, according to a cross-sectional study from a large tertiary medical center in Boston, Massachusetts.

A 31-question, interviewer-administered telephone survey was completed by 52 caregivers of children who had received a diagnosis of CP or a related term, such as hemiplegia or diplegia. Half the questions were open-ended, and the other half were true/false questions about CP. Although all the interviewed caregivers knew that their child had a medical condition involving motor function or movement, only two-thirds confirmed that they were told their child had or could have CP. In addition, only 38% knew the diagnostic subtype of their child’s CP.

Nearly half of caregivers (49%) recalled having the child’s condition first explained by a child neurologist. More than half (55%) were not surprised by the diagnosis, whereas 18% were somewhat surprised and 27% were completely surprised. Caregivers were aware that their child’s condition could be caused by an insult before birth (40%) or at birth (60%) and that it was a lifelong condition (73%). Almost 80% of caregivers identified that CP was a brain problem, and 52% recognized that CP is nonprogressive. Only 21% of respondents answered all the true/false questions correctly.

Most caregivers rated the health care provider’s diagnosis disclosure as good, very good, or excellent in terms of the setting of the diagnosis, the time spent on explanation, and their understanding of this explanation. Whereas 62% of caregivers also believed they had a good, very good, or excellent understanding of the term cerebral palsy, caregivers were actually even more knowledgeable than they thought, with 69% reaching a good to excellent level of understanding of the disease. However, the caregiver’s education level was significantly associated with how well they understood the health care professional’s explanation.

The importance of doing a thorough initial explanation of a dramatic life-altering diagnosis (CP, autism, cancer, etc) cannot be overestimated. One needs to set aside sufficient time. I do these visits after my regular office hours and provide a detailed letter afterward, along with phone follow-up in a few weeks.


Jan Matthew Farber, MD, section editor for Journal Club, is a pediatrician in Woodbridge, Virginia. Marian Freedman is a freelance medical editor and writer in New Jersey. The editors have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of these articles.
The current practice of administering rapid intravenous fluid (IVF) to children with acute gastroenteritis does not result in either early discharge or reduced likelihood of a revisit to the emergency department (ED). These were the primary findings of a retrospective study conducted with 284 patients ranging from infants to adolescents who had received a diagnosis of acute gastroenteritis and moderate dehydration at an ED in Saudi Arabia. Investigators divided patients into 2 groups: those receiving IVF in 2 boluses of 40 mL/kg and those given less than 40 mL/kg. A comparison of outcomes found that the 2 groups did not differ significantly in discharge rate at 4 hours, admission to the ward, or rate of ED revisits. On the other hand, patients who presented with only vomiting/diarrhea were less likely than other patients to revisit the ED, whereas patients with an increased CO2 level and anion gap were more likely to return within 1 week of being discharged.

Even these children, with moderate dehydration, did not benefit from aggressive IV rehydration. I’m also not sure they needed the IV at all. We should continue to move more and more toward oral rehydration in children if they are willing to drink, using ondansetron if needed for vomiting.


Bell and pad alarm therapy should be used as first-line treatment for children with neurodevelopmental disorders (NDDs) and enuresis, according to study findings. Investigators compared retrospective medical record data for almost 3000 children in Australia who were given an enuresis diagnosis with data for typically developing children. Children with an NDD had a clinical diagnosis of attention-deficit/hyperactivity disorder, autism spectrum disorder, or intellectual disability (ID). Treatment success was defined as remaining dry for at least 14 consecutive days and relapse as 1 symptom recurrence per month after treatment was interrupted. The investigators found that the bell and pad alarm was nearly as effective in children with NDDs as in typically developing children. For children with NDD, the success rate was 62%; for typically developing children the rate was 78%. The latter all were successfully dry after the first treatment. Only 59% of children with ID had success after the first treatment, the lowest percentage of all groups analyzed. The number of treatments received, or relapse rates, did not differ significantly between the 2 groups. The results also indicated that a child with a NDD and enuresis is more likely than their peers to be male, be older, and have current constipation aligned with a secondary enuresis diagnosis.


PUBLISHED IN INTERNATIONAL JOURNAL OF PEDIATRICS AND ADOLESCENT MEDICINE

Rapid IV hydration does not affect clinical gastroenteritis outcomes

PUBLISHED IN JOURNAL OF PEDIATRIC UROLOGY

Standard therapy for enuresis works in children with neurodevelopmental disorders
Persistent foot and leg swelling in a 17-year-old female

JUSTINE ENGLANOFF; AND EYAL BEN-ISAAC, MD

A 17-year-old girl presents with a 2-year history of unilateral swelling of the left lower extremity. The patient reports a poorly healed ankle sprain of the affected extremity 3 years prior that slowly resolved but left persistent swelling. She states that the swelling fluctuates, reaching as high as the midcalf, but has persistent baseline enlargement compared with the opposite foot.

History
Medical history includes hypothyroidism, successfully managed with levothyroxine, which was discontinued 3 years earlier as thyroid function tests normalized. She reached thelarche at age 11 years and menarche at age 13 years. Developmental and family history are unremarkable and noncontributory.

Physical exam
Upon examination, vital signs and growth parameters are normal. The left foot is notable for nonpitting edema to the level of the malleoli (Figure 1); it is nontender and without discoloration. Kaposi-Stemmer sign (inability to pinch the skin at the base of the second toe) is positive (Figure 2). The remainder of her examination is normal with no evidence of thyromegaly, lymphadenopathy, hepatosplenomegaly, or swelling of the other extremities.

Laboratory testing and imaging
Thyroid function tests, complete blood cell count, and chemistry panel

Want to read more of your colleagues’ puzzling cases? Find the whole collection at ContemporaryPediatrics.com/pediatric-puzzler
Eucerin® Baby Eczema Relief Cream Body Wash
- Statistically significant improvement in itching (55%), erythema (46%), and dryness (44%) at Week 1 vs baseline
- 2% colloidal oatmeal*, ceramide NP, gentle cleansing system
- Gentle, non-foaming body wash

Eucerin Baby Eczema Relief Cream
- 44% reduction in risk of flare
- 4 out of 5 children remained flare free for 6 months
- 1% colloidal oatmeal*, ceramide NP, licochalcone A

Steroid-free • Fragrance-free • Dye-free • Paraben-free • Non-comedogenic

*A skin protectant
1. Data on File, Beiersdorf Inc.
el obtained at presentation are normal. Abdominal and pelvic ultrasonography do not reveal any evidence of an obstructing mass or other abnormalities. Magnetic resonance imaging without contrast is negative except for an incidental finding of tarsal coalition, mostly fibrous, between the calcaneus and talus.

**Differential diagnosis**

The differential diagnosis for chronic unilateral lower extremity swelling in an adolescent includes lymphatic and venous etiologies of edema, as well as lipedema (Table). Lymphatic etiologies include primary and hereditary processes (often distinguished based on age of presentation), secondary causes, and associated genetic syndromes. Venous etiologies include congenital venous malformations, venous insufficiency, and external venous compression from tumor, trauma, or other mechanical obstruction. Edema from congenital venous malformation would likely present earlier in life, and venous insufficiency would be uncommon in an otherwise healthy adolescent. Furthermore, venous edema is usually pitting and often accompanied by hyperpigmentation of the extremity because of hemosiderin deposition. Although lipedema is caused by fat maldistribution rather than edema, it can present similarly to venous or lymphatic edema. It is often exquisitely tender and nonpitting and spares the foot. Systemic causes of edema such as congestive heart failure, nephrotic syndrome, protein-losing enteropathies, and cirrhosis are more likely to cause bilateral, pitting edema. Myxedema can also be noted in advanced stages of hypothyroidism but is typically accompanied by other findings (eg, bradycardia, weight gain).

Certain medications—notably, calcium channel blockers, corticosteroids, and chronic use of nonsteroidal anti-inflammatory drugs—can cause lower extremity edema. Edema from congenital venous malformation would likely present earlier in life, and venous insufficiency would be uncommon in an otherwise healthy adolescent. Furthermore, venous edema is usually pitting and often accompanied by hyperpigmentation of the extremity because of hemosiderin deposition. Although lipedema is caused by fat maldistribution rather than edema, it can present similarly to venous or lymphatic edema. It is often exquisitely tender and nonpitting and spares the foot. Systemic causes of edema such as congestive heart failure, nephrotic syndrome, protein-losing enteropathies, and cirrhosis are more likely to cause bilateral, pitting edema. Myxedema can also be noted in advanced stages of hypothyroidism but is typically accompanied by other findings (eg, bradycardia, weight gain).

Certain medications—notably, calcium channel blockers, corticosteroids, and chronic use of nonsteroidal anti-inflammatory drugs—can cause lower extremity edema. Edema from congenital venous malformation would likely present earlier in life, and venous insufficiency would be uncommon in an otherwise healthy adolescent. Furthermore, venous edema is usually pitting and often accompanied by hyperpigmentation of the extremity because of hemosiderin deposition. Although lipedema is caused by fat maldistribution rather than edema, it can present similarly to venous or lymphatic edema. It is often exquisitely tender and nonpitting and spares the foot. Systemic causes of edema such as congestive heart failure, nephrotic syndrome, protein-losing enteropathies, and cirrhosis are more likely to cause bilateral, pitting edema. Myxedema can also be noted in advanced stages of hypothyroidism but is typically accompanied by other findings (eg, bradycardia, weight gain).

**Discussion**

Lymphedema praecox is the most common type of primary lymphedema. It develops before age 35 years and often shortly after puberty. It classically affects the lower extremities and is typically unilateral; however, it can affect the upper extremities as well. Edema is usually pitting on initial examination but often becomes nonpitting over time because of fibrosis causing the skin to turn leathery and indurated, leading to the nonpitting edema that represents chronic, irreversible stages of the disease.

The patient reports a poorly healed ankle sprain of the affected extremity 3 years prior that slowly resolved but left persistent swelling.
This is further supported by evidence of children with Turner syndrome who during infancy had congenital lymphedema that spontaneously subsided and then returned shortly after menarche.\(^5\)

Lymphedema praecox is thought to be associated with a variety of genetic loci, but a causal relationship between the disease and any specific genetic defect has yet to be defined, and most cases are sporadic rather than hereditary.\(^6\) Meige disease refers to a familial subtype of lymphedema praecox and is also known as hereditary lymphedema type 2. The late onset of lymphedema praecox despite its congenital nature is thought to result from a secondary event later in life (eg, injury or infection) that leads to a sudden worsening of a previously subclinical lymphatic defect.\(^6\)

The differential diagnosis for lymphedema praecox includes other forms of both primary and secondary lymphedema. The 3 types of primary lymphedema are distinguished by age of onset and include congenital lymphedema, lymphedema praecox, and lymphedema tarda.\(^3,4\) All 3 conditions are caused by primary lymphatic abnormalities that may not manifest until later in life and mainly involve the lower extremity.

Congenital lymphedema is defined as primary lymphedema that presents within the first year of life. Milroy disease is a specific subtype of congenital lymphedema and is also called hereditary lymphedema type 1A. Up-slanting toenails and enlarged leg veins have also been associated with Milroy disease as has hydroceles in male patients. In most cases, the swelling is bilateral and remains constant in severity throughout the patient’s lifetime.\(^7\) Both Milroy disease and Meige disease are inherited in an autosomal dominant manner.\(^3\) Lymphedema tarda is defined as primary lymphedema presenting after age 35 and is associated with impaired wound healing due to stasis of lymphatic flow and ulcers that fail to heal because of regional oxygen deficiency in the diseased tissue.\(^7\)

Secondary lymphedema is caused by impaired lymphatic flow from an acquired cause. It is far more common than primary lymphedema and usually becomes symptomatic later in life compared with primary lymphedema. Most cases of secondary lymphedema result from surgery or local radiation causing mechanical lymphatic obstruction. The most common cause worldwide is lymphatic filariasis, also known as elephantiasis, a mosquito-borne infection caused by the roundworm \textit{Wuchereria bancrofti}. The infection is endemic to India and sub-Saharan Africa.\(^3\) Other causes include an obstructing mass, trauma, polysplenia syndrome, Hodgkin lymphoma, rosacea, chronic venous hypertension, venous ulcers, fluid overload, Kaposi sarcoma, obesity, rheumatoid or psoriatic arthritis, allergic contact dermatitis, and drug-induced lymphedema.\(^3\)

### Diagnosis and management

Several radiological modalities are used for the evaluation and diagnosis of lymphedema. Direct lymphangiography allows for real-time visualization of lymphatic flow and assesses the patency of lymphatic channels. It was once the method of choice for imaging lymphedema but is rarely used now because of potential adverse ef-

TABLE

<table>
<thead>
<tr>
<th>Differential Diagnosis of Lower Extremity Swelling &amp; Edema</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary lymphatic</strong></td>
</tr>
<tr>
<td>Primary/hereditary:</td>
</tr>
<tr>
<td>▪ Congenital lymphedema</td>
</tr>
<tr>
<td>▪ Lymphedema praecox</td>
</tr>
<tr>
<td>▪ Lymphedema tarda</td>
</tr>
<tr>
<td>Genetic syndromes (eg, Turner, Noonan, Prader-Willi)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Systemic</strong></th>
<th><strong>Venous</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>Congenital venous malformations</td>
</tr>
<tr>
<td>Protein losing enteropathy</td>
<td>Venous insufficiency</td>
</tr>
<tr>
<td>Liver disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>External venous compression (eg, tumor)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Nephrotic syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Lipedema</strong></th>
<th><strong>Miscellaneous</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat maldistribution</td>
<td>Medications</td>
</tr>
<tr>
<td></td>
<td>Nutritional deficiencies</td>
</tr>
</tbody>
</table>

\(^{3,4}\)
fects, including hypersensitivity reactions and patient discomfort. Direct lymphangiography has been replaced by less invasive procedures such as magnetic resonance lymphangiography and fluorescence microlymphography, a technique that allows for lymphatic visualization using an injection of fluorescein isothiocyanate-dextran. Lymphoscintigraphy, a radionuclide imaging study, can be used to evaluate lymphatic anatomy, vessel patency, dynamics of flow, and flow reversal. It is considered the most definitive test for diagnosing lymphedema and has a specificity of 100%.

Although there is no definitive cure for primary or secondary lymphedema, effective treatment and symptom relief can be achieved by either surgical or nonsurgical treatment modalities. Symptomatic management of early-stage lymphedema can be achieved with nonsurgical decongestive therapy, which includes massage, lymph drainage, compression therapy, and advanced pneumatic compression. Compression can be achieved with multilayer bandages, compression stockings, or advanced pneumatic compression pumps. Compression garments should be used continuously throughout the day and may be removed at night when the extremity can be elevated. Pneumatic pump compression should be done prior to fibrosclerotic evolution to prevent its development. Both medical and pneumatic compression therapy may be contraindicated in patients with congestive heart failure, deep vein thrombosis, or active infection. Low-level laser therapy has also been shown to decrease pain and physical parameters of lymphedema. It is thought to increase lymphatic drainage as well as stimulate the formation of new lymph vessels.

Although there is no definitive cure for primary or secondary lymphedema, effective treatment can be achieved by either surgical or nonsurgical treatment modalities.

Surgical intervention has been effective in treating lymphedema not responsive to less invasive modalities. Options include direct excision and liposuction. Physiologic techniques, such as lymphatic venous anastomosis or bypass, have also been shown to be effective.

Prognosis and complications
Prognosis for patients with lymphedema varies based on disease chronicity, etiology, resulting complications, and the patient’s adherence with maintenance modalities. Primary lymphedema usually does not progress and often stabilizes after several years. Primary lymphedema is associated with lower morbidity and better outcomes than secondary lymphedema.

Potential complications of long-standing or untreated lymphedema include recurrent cellulitis and other recurrent bacterial and fungal infections. Patients with a history of chronic lymphedema lasting longer than 10 years have a 10% risk of developing angiosarcoma. Other malignancies associated with long-standing lymphedema include basal and squamous cell carcinoma, Kaposi sarcoma, melanoma, and cutaneous lymphomas. Additional complications can include recurrent skin ulcers and elephantiasis nostra verrucosa, as well as functional impairment, activity restrictions, and cosmetic deformity, which can have significant psychosocial repercussions.

Patient course
Diagnostic imaging was recommended, but the patient’s parents declined because of concern of invasive techniques and if any such procedure would provide additional diagnostic information, given the diagnosis of lymphedema praecox. The patient was instructed to apply Jobst compression garments to the affected extremity to help eliminate the remaining swelling. Physical therapy and lymphatic massage were also recommended. The leg swelling decreased dramatically with therapy but intermittently recurs when therapy is discontinued.

COMMENTS? Email them to levine@mjhlifesciences.com

Eyal Ben-Isaac is an attending physician in the Division of General Pediatrics at Children’s Hospital Los Angeles in California and an associate professor of pediatrics at Keck School of Medicine of USC in Los Angeles.

Justine Englanoff is a medical school graduate from the SUNY Downstate College of Medicine, in Brooklyn, New York.

The authors have nothing to disclose.
Allergies and Infant Formula

Is it cow’s milk allergy or is it intolerance? How do you diagnose in newborns and infants? What are the four specialty formula types, and which factors should most influence your selection for a patient?

Answer these questions and more with an expert-curated resource center from Contemporary Pediatrics®.

Explore it now:
contemporarypediatrics.com/clinical/allergies-and-infant-formula
AI, telehealth & sensor-based technologies facilitate autism diagnosis

ANDREW J. SCHUMAN, MD

Although pediatricians screen for autism spectrum disorder (ASD) in children aged 18 to 24 months during routine health maintenance exams, this neurodevelopmental condition often eludes formal diagnosis until a child is 4 years or older.1,2 One telehealth application is currently expediting the diagnosis of ASD by specialists. Another artificial intelligence (AI)–based diagnostic system, which recently received marketing approval by the US Food and Drug Administration (FDA), may facilitate the diagnosis by pediatricians. This article examines these technology-based tools and explores how they can aid pediatricians.
Diagnostic barriers

Children with ASD have communication and social impairments, frequently demonstrate repetitive or restrictive behaviors, and often have a wide range of comorbidities. The condition is common, affecting 1 in 59 children in the United States. As most pediatricians are not able to diagnose children with developmental and speech delays as having ASD, they refer children to specialists, who include developmental pediatricians, child psychologists, pediatric neurologists, and pediatric psychiatrists. In many circumstances a child suspected of having ASD is referred to a multidisciplinary diagnostic team composed of one of the above specialists as well as educators, speech pathologists, occupational therapists, and physical therapists. There are often wait times of many months until an ASD evaluation is performed. Even after a child is evaluated, they may not meet threshold criteria for an ASD diagnosis, and the assessment is considered inconclusive. In such situations, parents and pediatricians must wait until the child is older and upon repeat assessment receive a diagnosis of ASD or have the diagnosis excluded. The diagnosis of ASD is very important for families (vs “developmental delay”) as it assures that insurance companies and school systems will provide much-needed behavioral interventions and services, which are mandated by most states.

Many factors may delay the diagnosis of ASD. For instance, individuals in low-income communities and minorities have limited access to services necessary to diagnose ASD. Only 60% of pediatricians screen children for developmental delays despite the recommendation from the American Academy of Pediatrics (AAP) to perform screenings at 18- and 24-month well visits. In one study, only two-thirds of those who failed screening were referred for a diagnostic ASD evaluation. In addition, it was recently shown that the Modified Checklist for Autism in Toddlers Revised With Follow-Up (M-CHAT-R/F), used by most pediatricians to screen for ASD, has sensitivities as low as 39% in detecting children with ASD. Lastly, the COVID-19 pandemic has resulted in significant delays in evaluating children with suspected ASD.

Screening for ASD

Pediatricians have a plethora of ASD screening tools available, such as the Ages and Stages Questionnaires, the Communication and Symbolic Behavior Scales, the Parents Evaluation of Developmental Status, the Screening Tool for Autism in Toddlers and Young Children, and M-CHAT-R/F. Most pediatricians use M-CHAT-R/F to screen children for autism at 18 months and 24 months of age. The M-CHAT-R/F queries parents regarding their child’s perception of others, use of gestures, interactive eye contact, vocal communication, and ability to interact with parents and children. When children refer following the ASD screen, or if a parent or pediatrician is suspicious of the diagnosis, the AAP recommends that the child be referred for a diagnostic evaluation.

In 2013, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) consolidated several previous categories of ASD into just 1 category. To meet diagnostic crite-
ria for ASD, a child must have 3 symptoms relating to social communication and interaction, as well as 2 out of 4 symptoms relating to repetitive or restricted behaviors (Box).8

This recharacterization and simplification of the criteria needed for the diagnosis of ASD has facilitated the diagnosis of ASD by specialists. Many use a chart similar to the Box as an intake screening form before proceeding with a diagnostic evaluation.

Developmental pediatricians or child psychologists use the Autism Diagnostic Observation Schedule (ADOS) test and/or the Autism Diagnostic Interview-Revised (ADI-R) for evaluation. The ADOS is an observational play and activity assessment of the child that takes up to an hour to complete, whereas the ADI-R is a 93-point questionnaire that may take several hours.9 Many developmental pediatricians and child psychologists use their own screening methods rather than performing a full ADOS or ADI-R, sometimes using other screening tools such as the Social Responsive Scale and the Childhood Autism Rating Scale. Most importantly, although these aids help with diagnosis, ASD is a clinical diagnosis best rendered by clinicians with the training and expertise to do so.

Sensor-based technologies
Children affected with ASD are a heterogeneous group, with varying degrees of functional limitations. Many have comorbidities that include seizures, attention-deficit/hyperactivity disorder, oppositional defiant disorders, sleep disorders, and speech delay. Researchers have long looked to sensor-based technologies, many employing artificial intelligence algorithms to screen for children with ASD. AI is particularly useful for identifying patterns within data and therefore can be advantageous for investigators to try to identify markers associated with an ASD diagnosis. However, AI algorithms are only as good as the training data sets inputted into a diagnostic system. Over the past few years, several AI-related technologies have been developed to improve medical care.10 Additionally, investigators have had some promising results using sensors to analyze facial expressions, vocalizations, touch sensitivity, eye tracking, movements, and interactions with robots to try to identify children with ASD. Unfortunately, to date, none of these technologies have proved sensitive enough to be used diagnostically.11

Telehealth-based tool facilitates diagnosis
In 2005, Behavior Imaging Solutions (BIS) was founded by Ronald and Sharon Oberleitner after their 3-year-old son received an ASD diagnosis. Developed over the course of several years and first made available nationwide in 2018, the system, called the Naturalistic Observation Diagnostic Assessment (NODA), consists of 2 components. Parents use smartCapture, a smartphone-based application, to fill out a developmental questionnaire and record and upload four 10-minute videos of their child (Figure 1). Various scenarios include the child playing alone, the child playing with others, a family mealtime, and a behavior of parent’s concern.

NODA Connect, a web-based portal, allows an autism specialist to analyze submitted videos for features of ASD (Figure 2). They then complete a DSM-5 checklist for ASD and determine whether the child has ASD. The clinician, not the parent, pays a small fee to BIS for use of the system. Several studies have shown that the BIS system is easy to use and renders diagnoses comparable to those produced by a traditional

![FIGURE 1 With the Naturalistic Observation Diagnostic Assessment, parents upload information and record videos on their smartphone.](https://example.com/figure1.jpg)
ADOS evaluation. In 2017, investigators compared the diagnostic accuracy of the NODA system to in-person evaluations by experienced ASD diagnosticians for 40 families seeking an evaluation for ASD and 11 families with normally developing children. The diagnostic clinicians were blinded as to which group they were evaluating and used ADOS, ADI-R, or other diagnostic tools to render a determination of whether the child being evaluated had ASD. Sensitivity between NODA and the in-person exam was 85%, and the specificity was 94%.

BIS is in the process of integrating AI into NODA, using “vision” algorithms to tag video frames containing suspect diagnostic features. This AI is expected to be incorporated into the NODA Connect portal over the next 2 years and will speed the diagnostic process.

The advantage is that pediatricians can refer to specialists who use the NODA system rather than a formal ADOS, which can considerably shorten the wait time to diagnosis. Best of all, the evaluation can be done remotely, even in a pandemic, and expedite appropriate interventions for the child with ASD.

An AI-based ASD diagnostic looks promising

Cognoa, a digital health care company, has been working on developing a multimodal AI-based system that will enable pediatricians to diagnose ASD. In June, the FDA granted the company approval to market the first FDA-authorized diagnosis aid designed to help physicians diagnose autism in a primary care setting. The prescription only system is called Canvas Dx and is expected to be available before the end of this year.

Cognoa AI software was trained on data sets compiled from ADOS and ADI-R score sheets of children aged 18 months to 7 years supplied by numerous ASD evaluation and treatment centers. Cognoa’s system includes a parental questionnaire, a pediatrician questionnaire, and an analysis of 2 or 3 uploaded videos that are each 1 to 2 minutes long of the child at home during mealtime or playtime (Figure 3). The videos scored by trained analysts for features of ASD who respond to a behavior questionnaire. AI algorithms analyze the questionnaires and video report, then decide on whether the child has ASD or if the evaluation is inconclusive.

A study published in March 2020 validated Cognoa’s system on 375 patients over the course of 2 years, indicating that the system could identify children with ASD with sensitivity and specificity as high as 90% and 83%, respectively.

More recently, the company completed a double-blind clinical trial at 14 sites around the United States, using an improved algorithm to gather data for submission to the FDA. The trial involved 425 participants, aged 18 months to 6 years, whose parents or doctors expressed concern about their development but who had not previously been evaluated for ASD. Each child was assessed twice: using Cognoa’s diagnostic and by a specialist clinician based on DSM-5 criteria. The study ran from July 2019 through May 2020, so some of the children

FIGURE 2 NODA Connect, a web-based portal, allows an autism specialist, in conjunction with an ASD checklist, to analyze videos.
were evaluated remotely during the pandemic. The tool performed equally well when administered remotely, according to the company. The trial also showed that Cognoa’s diagnostic is highly accurate across male and female patients, as well as different ethnic and racial backgrounds.

Cognoa plans to promote their diagnostic to pediatricians to be used (1) when a child does not pass a routine ASD screening tool, or (2) the diagnosis is suspected by parent or provider by history or observed behavior. Using the diagnostic in this fashion will help identify children who should be referred to ASD specialists to corroborate the diagnosis and help educate families and recommend services. Undoubtedly, Canvas Dx will be scrutinized via independent studies. Pediatricians will look to the AAP’s Council on Children With Disabilities for recommendations regarding its use. Additionally, it may take considerable time until insurance companies pay for the test. Therefore, Cognoa has hired former AAP president Colleen A. Kraft, MD, MBA, FAAP as its senior medical director for clinical adoption to promote the system.

Conclusion
Diagnosing ASD remains a challenge, and recent advances in technologies may expedite the identification of affected children. A child identified with ASD at a younger age can receive behavioral therapy and other interventions at a time when they can be most beneficial. Looking ahead, various smart device-based applications are either in development or will soon be available that may assist parents in socializing children with ASD. Progress is being made, and soon parents and providers will leverage technologic advances to better care for patients with ASD.

COMMENTS? Email them to llevine@mjlifesciences.com

Assessing autism prevalence
Results of a large study in England showed marked differences across races, ethnic groups, and geographic areas.

Autism spectrum disorder has a prevalence of 1% to 2% of the global population. Very little research has been done in the non-White population, which could have an impact in planning a variety of services. An investigation in JAMA Pediatrics looked at the prevalence of autism spectrum disorder in the state school population in England to measure differences among race, as well as sex and socioeconomic levels.

The investigators performed a case-control prevalence cohort study, which used the Spring School Census 2017 from the Pupil Level Annual Schools Census of the National Pupil Database. These data encompassed all children, teenagers, and young adults aged 2 to 21 years who were in state-funded education. There are 2 levels of support that a child may receive: SEND support, which includes school-specific learning programs for pupils, and Education, Health and Care Plans, which were introduced as part of the Children and Families Act 2014.

The population included a total of 7,047,238 pupils. In this cohort were 119,821 pupils with autism spectrum disorder, 21,660 of whom had learning difficulties. The investigators found that the standardized prevalence of autism spectrum disorder was 1.76% (95% CI, 1.75%-1.77%), with female pupils having a prevalence of 0.65% (95% CI, 0.64%-0.66%) and male pupils having a prevalence of 2.81% (95% CI, 2.79%-2.83%), creating a male-to-female ratio (MFR) of 4.32:1. Black pupils had the highest standard prevalence (2.11% [95% CI, 2.06%-2.16%]; MFR, 4.68:1). Pupils with autism spectrum disorder were more likely to speak English as an additional language (adjusted prevalence ratio, 0.64; 95% CI, 0.63-0.65) as well as face social disadvantages (adjusted prevalence ratio, 1.61; 95% CI, 1.59-1.63).

The investigators concluded that there were significant differences in autism spectrum disorder prevalence across not only racial/ethnic groups, but geographic areas and local districts. These findings are in line with research that found higher rates of autism spectrum disorder in immigrants with foreign-born mothers in the United States, but contrast with other studies that indicate lower rates in the Black community and individuals with a lower socioeconomic status. The investigators believe their results highlight the need to have a better understanding of who receives a diagnosis, when they get it, what support is offered, and how much social determinants of health affect autism spectrum disorder status.

REFERENCE
Stelatopia®
A complete range of natural, fragrance-free products specifically designed for eczema-prone skin and newborns and up

Formulated with Avocado Perseose® and Sunflower Oil Distillate®
2 patented natural active ingredients that target the deficiencies caused by AD

Avocado Perseose®
- Reinforces the skin barrier
  +32% Ceramides*
  +49% Involucrine*
- Maintains the hydration level of the epidermis
  +47% Hyaluronic acid*
  +175% Transglutaminase*
- Protects the skin’s stem cell supply
  +80% Integrim® preserved**

Sunflower Oil Distillate®
- Stimulates filaggrin expression
  +57%*
- Stimulates involucrine expression
  +99%*
- Actives PPARα
  Ceramides × 3*

To learn more about Mustela® and to receive samples, visit www.MustelaMD.com
Infants who have a history of intestinal injury as neonates can pose challenges for the pediatricians who care for these babies after they are discharged from the hospital. Here are some of the causes, feeding guidelines, and approaches to feeding difficulties that you can use in your practice.

Common causes of neonatal intestinal injury include necrotizing enterocolitis (NEC), spontaneous intestinal perforation, gastroschisis, intestinal atresia, and volvulus (Table 1). Intestinal injury in the neonate typically presents acutely with vomiting, inability to tolerate enteral feeds, abdominal distention, and bloody stools. Treatment typically requires at least the temporary adoption of bowel rest and parenteral nutrition.\(^1\)

Intestinal failure is generally defined by the loss of normal function of the intestine, regardless of length of residual small bowel, resulting in reliance on parenteral nutrition for calories and fluid to sustain life.\(^2\) NEC and gastroschisis are the most common causes of long-term intestinal failure in infants, which results in significant morbidity, mortality, and cost to families and medical systems.\(^3\) Those infants who undergo significant intestinal resection and intestinal failure, and thus need long-term parenteral nutrition, require specialized care in multidisciplinary intestinal rehabilitation centers. However, the majority of infants with intestinal injury will tolerate enteral nutrition by hospital discharge.\(^3\) Therefore, the majority of these infants will be cared for by their primary pediatri-

**TABLE 1. CAUSES OF NEONATAL INTESTINAL INJURY\(^2\)**

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrotizing enterocolitis(^*)</td>
</tr>
<tr>
<td>Gastroschisis(^*)</td>
</tr>
<tr>
<td>Intestinal atresia (eg, duodenal atresia, jejunal atresia)</td>
</tr>
<tr>
<td>Volvulus</td>
</tr>
<tr>
<td>Intestinal aganglionosis</td>
</tr>
<tr>
<td>Spontaneous intestinal perforation</td>
</tr>
<tr>
<td>Long-segment Hirschsprung disease</td>
</tr>
<tr>
<td>More than 1 of the above(^*)</td>
</tr>
</tbody>
</table>

\(^*\)Indicates the most common causes.
cians, who should be aware that these infants are prone to a variety of ongoing nutritional challenges.

Feeding difficulties include poor oral intake, failure to thrive, nutrient deficiencies, gastroesophageal reflux disease (GERD), and intestinal dysmotility. Intestinal dysmotility secondary to resection or injury can cause chronic vomiting, diarrhea, abdominal distention, and small intestinal bacterial overgrowth (SIBO). More than 50% of infants with intestinal injury are prescribed medications to address 1 or more of these issues. Overall positive prognostic indicators for successful tolerance of enteral feeds in these infants include the residual length of the small bowel following resection (the longer the residual bowel, the better), the presence of an intact ileocecal valve, and an intact colon; therefore, it is important to understand the infant's surgical course, residual anatomy, and any neurodevelopmental sequelae.

**General feeding guidelines and principles**

The importance of feeding guidelines and algorithms for preterm and other critically ill infants who are at increased risk of NEC are well established. However, guidelines for feeding following intestinal injury are not standardized; they can be highly variable across institutions and even among providers at the same institutions.

Enteral feeding stimulates the intestine to heal and grow. Data have shown that early implementation of enteral feeds following intestinal injury (<5-7 days) promotes intestinal adaptation and is not associated with worse outcomes or recurrence of NEC. In fact, early feeding with the use of consistent, standardized feeding advancement has been associated with shorter length of stay, quicker achievement of enteral feeding goals, fewer infectious complications, and reduced overall cost to the patient and health system. For those patients who require surgery for intestinal injury, guidelines support early postoperative enteral feeding with breast milk if available.

Once infants are advanced to full enteral feeds, close monitoring of weight is needed to ensure age-appropriate weight gain. A follow-up study of infants with intestinal injury demonstrated that a majority of these infants will be discharged and even among providers at the same institutions.

---

**TABLE 2. SUMMARY OF COMMON INFANT FORMULAS AND PROPERTIES**

<table>
<thead>
<tr>
<th>FORMULA</th>
<th>PROPERTIES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Standard</strong></td>
<td>- Intact proteins from cow’s milk</td>
</tr>
<tr>
<td></td>
<td>- Protein size ~14-65 kD</td>
</tr>
<tr>
<td><strong>Preterm</strong></td>
<td>- Intact proteins from cow’s milk and whey proteins</td>
</tr>
<tr>
<td></td>
<td>- Protein size ~14-65 kD</td>
</tr>
<tr>
<td></td>
<td>- Increased kcals 20-30</td>
</tr>
<tr>
<td><strong>Partially hydrolyzed</strong></td>
<td>- Proteins partially broken down; not considered hypoallergenic</td>
</tr>
<tr>
<td></td>
<td>- Protein size ~3-10 kD</td>
</tr>
<tr>
<td><strong>Extensively hydrolyzed</strong></td>
<td>- Proteins extensively broken down</td>
</tr>
<tr>
<td></td>
<td>- Hypoallergenic</td>
</tr>
<tr>
<td></td>
<td>- Protein size &lt;3 kD</td>
</tr>
<tr>
<td><strong>Elemental/amino-acid</strong></td>
<td>- Proteins completely broken down to amino acids</td>
</tr>
<tr>
<td></td>
<td>- Hypoallergenic</td>
</tr>
</tbody>
</table>

*Table includes commonly used formulas but is not a complete list.
with some proportion of supplemental tube feeding via nasogastric or gastrostomy tube, but most will be weaned to primarily oral feeds by the time they are aged 1 year. Those with a history of NEC and spontaneous intestinal perforation were found to have poor weight gain 3 months after discharge. In some studies, poor weight gain in children with surgical NEC persisted through the first 2 years of life. Infants with intestinal injury therefore require frequent feeding adjustment and weight checks in those early months to account for higher caloric requirements for optimal growth. Foods that are complementary to formula and breast milk should be added to the diet as developmentally appropriate, with the provision that fruit juices and sugary foods can produce a high solute load in the small bowel. Children with intestinal dysfunction or resection may be more prone to the osmotic diarrhea caused by these foods.

**TYPE OF FEEDING**

Breast milk has long been favored as the initial choice for feeding infants both with and without intestinal injury or resection. Breast milk reduces the risk of NEC. Breast milk attenuates the proinflammatory pathway that is mediated by a molecular signaling protein, Toll-like receptor-4, which plays a prominent role in the pathogenesis of NEC. The exclusive use of preterm formula instead of breast milk might contribute to maturation of less-favorable intestinal flora, and it lacks the protective effects against NEC that are seen in preterm infants who are fed breast milk. If maternal breast milk is not available to infants with intestinal injury, donor breast milk should be used, if available. Donor milk has also been shown to be protective against further intestinal injury, despite the need for pasteurization.

Breast milk also has a multitude of beneficial bioactive and immunomodulating components that not only provide nutrition but also provide anti-inflammatory and antioxidant compounds. Examples include epidermal growth factors, which promote mucosal healing; secretory immunoglobulin A for immune function; lactoferrin to promote enterocyte growth; and prebiotic substrates, such as human milk oligosaccharides (HMOs), which promote a diverse gut flora. HMOs are carbohydrates found in human milk; they have antimicrobial properties that prevent the adhesion of some pathogenic intestinal bacteria. HMOs diminish intestinal leukocyte adhesion and migration, thereby dampening some of the proinflammatory processes in the gut. Synthetically produced HMOs are now available, but not all are functionally equivalent to endogenously produced HMOs.

Despite breast milk’s many benefits, not all infants with intestinal injury will have access to it or will tolerate it. Formula selection should take into consideration the degree of intestinal injury and other comorbidities. A list of infant formulas and their properties is shown in Table 2.

Among infants who had significant bowel injury requiring parenteral nutrition, those who were fed amino acid–based formula, also known as elemental formula, or breast milk required parenteral nutrition for a shorter duration, indicating that amino acid–based formula was also well tolerated by such infants. Extensively hydrolyzed formulas should be considered in patients who have suspected milk protein intolerance. Infants who are born extremely prematurely and/or who are critically ill have been found to have worse outcomes with the use of intact-protein, cow’s milk–based formulas. These formulas are associated with developing NEC, which can be recurrent; therefore, they should be used cautiously in infants with a NEC history. The elemental formulas (amino-acid based) may be better tolerated; however, more complex intact proteins and other macronutrients promote a greater

| TABLE 3 |
| SIBO TREATMENT REGIMENS |

<table>
<thead>
<tr>
<th>ANTIBIOTIC</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metronidazole</td>
<td>10 mg/kg twice daily (BID) x 7-10 days</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>15 mg/kg BID x 7-10 days</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>5-10 mg/kg BID x 7-10 days</td>
</tr>
<tr>
<td>Rifaximin</td>
<td>10-15 mg/kg BID x 7-10 days</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>5 mg/kg BID x 7-10 days</td>
</tr>
</tbody>
</table>

SIBO: small bacterial intestinal overgrowth
degree of intestinal growth and adaptation after intestinal resection. Intact cow’s-milk proteins may be tolerated later in those infants with more significant bowel injury or resection as the infant’s immune system matures. Term infants with minimal resection may tolerate an intact cow’s milk-based formula initially following intestinal injury.

**APPROACH TO FEEDING DIFFICULTIES**

Even if they are successfully weaned from parenteral nutrition, infants with bowel injury may still be prone to feeding difficulty due to anatomic changes, dysmotility, and developmental delay. Nearly 60% of infants who experience NEC will have neurodevelopmental delay, which can have a negative impact on their ability to feed orally. Common symptoms of feeding intolerance include oral aversion, vomiting, fussiness with feeding, abdominal distention, and change in stool frequency and consistency. Treatment and evaluation should be tailored to the infant’s symptoms and medical history.

Certain infants—those with a history of neurodevelopmental delay or who required prolonged periods of bowel rest and parenteral nutrition early in life—may experience poor development of oral-motor coordination or oral aversion. Clinical signs of this include dysphagia, gagging with feeds, or oral feed refusal. Such children might require swallow evaluation with a speech-language pathologist and referral for feeding therapies with a multidisciplinary feeding rehabilitation program. Clinical reflux is also a common cause of vomiting and fussiness with feeds. However, the possibilities of delayed gastric emptying or partial obstruction also need consideration, particularly in infants with a history of NEC, gastrochisis, or intestinal reanastomosis; all are prone to dysmotility and strictures.

Radiographic studies can aid in the diagnostic evaluation of anatomic etiologies. They can include (1) abdominal x-ray, to assess for evidence of bowel obstruction or ileus; (2) contrast upper gastrointestinal series or contrast enema to evaluate for stricture, dilatation, or malrotation; and (3) abdominal ultrasound to evaluate both the intestines (intussusception, stricture, or gastric outlet obstruction) and surrounding organs (hydronephrosis). If no structural cause for vomiting is identified, medications and feeding changes may be indicated. Empiric treatment with 4 to 8 weeks of histamine-2 blockers, proton pump inhibitors (PPIs), or pro-motility agents such as erythromycin can be trialed for suspected reflux. Potential feeding interventions include providing a smaller volume of food with each feeding, more frequent feedings, transitioning to an extensively hydrolyzed or amino acid-based formula, or, ultimately, continuous feeding via nasogastric or gastrostomy tube if other measures fail. Some infants may also require enteral tube feeding due to dysphagia or severe oral aversion. Management of ongoing enteral tube feeding or poor response to formula or medication changes warrants referral to a pediatric dietician and gastroenterologist.

Infants with a history of intestinal injury or bowel resection who experience abdominal distention or bloating without obstruction, feeding intolerance, and changes in stool patterns may have SIBO. Factors that predispose an infant to SIBO include anatomic intestinal abnormalities, dysmotility, bowel resection, ileocecal valve resection, and prolonged use of PPIs that alter the gut flora. In severe cases, SIBO can cause malabsorption, severe diarrhea, acidosis, and altered mental status. The diagnosis of SIBO can be challenging, as the gold-standard diagnosis technique requires bacterial quantification of jejunal secretions.

---

**TABLE 4. NUTRIENT DEFICIENCIES**

<table>
<thead>
<tr>
<th>DEFICIENCY</th>
<th>CLINICAL FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>Xerophthalmia</td>
</tr>
<tr>
<td></td>
<td>Bitot spots on conjunctiva</td>
</tr>
<tr>
<td></td>
<td>Impaired immunity</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>Rickets</td>
</tr>
<tr>
<td></td>
<td>Poor growth</td>
</tr>
<tr>
<td></td>
<td>Hyperparathyroidism</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>Neuropathy</td>
</tr>
<tr>
<td></td>
<td>Ataxia</td>
</tr>
<tr>
<td></td>
<td>Muscle weakness</td>
</tr>
<tr>
<td>Iron</td>
<td>Microcytic anemia</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Pallor</td>
</tr>
<tr>
<td>Copper</td>
<td>Anemia</td>
</tr>
<tr>
<td></td>
<td>Poor wound healing</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
</tr>
<tr>
<td></td>
<td>Pallor</td>
</tr>
<tr>
<td></td>
<td>Myalgias</td>
</tr>
<tr>
<td>Zinc</td>
<td>Poor wound healing</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
</tr>
<tr>
<td></td>
<td>Hair loss</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td></td>
<td>Gait abnormalities</td>
</tr>
<tr>
<td></td>
<td>Loss of deep tendon reflexes</td>
</tr>
<tr>
<td></td>
<td>Hypotonia</td>
</tr>
<tr>
<td></td>
<td>Poor feeding</td>
</tr>
</tbody>
</table>

---

For stricture, dilatation, or malrotation; and (3) abdominal ultrasound to evaluate both the intestines (intussusception, stricture, or gastric outlet obstruction) and surrounding organs (hydronephrosis).
Nutrition

via endoscopy or hydrogen breath testing, neither of which is easily obtained in infants or young children. Therefore, empiric treatment with antibiotics is often trialed if there is a strong clinical suspicion of SIBO. A variety of SIBO treatment regimens in children have been proposed (Table 3); however, there is no consensus guideline for pediatric regimens. Empiric treatment is typically prescribed for a 7- to 10-day course, with some infants requiring long-term cycled antibiotics: alternating 1 or 2 antibiotics every 2 to 4 weeks in an effort to prevent development of bacterial resistance. The antibiotic doses for SIBO are typically lower than those in traditional regimens for treating infection, as the goal is to overall reduce the gut bacterial flora.

PROBIOTICS AND PREBIOTICS

There has been great interest in the use of probiotics and prebiotics in infants in recent years. Probiotics are live microorganisms that are administered as an oral supplement to help maintain the balance of beneficial gut bacteria and gut health. Prebiotics are nondigestible oral supplements, usually made up of oligosaccharides, that serve as substrates for nonpathogenic gut bacteria. The positive balance of pathogenic and nonpathogenic intestinal microorganisms has an effect on underlying gut inflammation and health.

Preterm infants have later acquisition of and fewer beneficial gut bacteria, including Bifidobacterium and Lactobacillus, when compared with term infants. This lack of diversity is multifactorial and related to mode of delivery, exposure to antibiotics, the hospital environment, and feeding methods. The use of probiotics and prebiotics has served to promote and maintain the balance of nonpathogenic gut bacteria, with some data indicating benefits of certain probiotic strains including Lactobacillus rhamnosus, Bacillus infantis, Bacillus lactis, Streptococcus thermophilus, and Bifidobacterium.

Recent American Gastroenterological Association guidelines recommend the use of probiotics in preterm and low-birth-weight infants that contain a combination of Lactobacillus and Bifidobacterium species to prevent mortality and NEC. However, the benefit of probiotics in infants following intestinal injury is unclear and, currently, insufficient evidence recommends the routine use of probiotics following intestinal injury. There is no consensus regarding the optimal dose or frequency of probiotics or prebiotics in children, and it is important to note that there have been case reports of bacterial translocation and bacteremia associated with probiotic use in infants. Although probiotics and prebiotics have shown promising beneficial effects in some pediatric patients, their use should be determined on a case-by-case basis in lower-risk infants.

NUTRITIONAL DEFICIENCIES AND PITFALLS

Even those infants with relatively short segments of bowel resection should be monitored for nutrient deficiencies. Risk is related to the particular location of resected bowel and the degree of dysmotility causing diarrhea with malabsorption. For example, copper is absorbed primarily in the proximal small intestine, so resections or dysfunction of the duodenum and proximal jejunum can lead to copper deficiency. Vitamin B12 is absorbed only in the terminal ileum, and B12 deficiency may not become apparent for several months after resection of the terminal ileum. Additional common nutrient deficiencies to be aware of include iron-deficiency anemia, copper-deficiency anemia, and deficiencies of fat-soluble vitamins (A, D, E, K) and of trace minerals such as selenium and zinc (Table 4). Depending on clinical signs and symptoms, and on the infant’s pattern of bowel injury, these levels should be monitored 1 to 2 times per year for the first 2 to 3 years, or more frequently if repletion is needed.

Conclusion

Infants with a history of intestinal injury from neonatal conditions such as NEC, gastrochisis, and other etiologies of intestinal resection are predisposed to feeding difficulties and nutritional deficiencies. The infant’s surgical history and remaining bowel anatomy need to be considered when monitoring feeding tolerance, growth, and nutritional status. These infants often require the use of hydrolysate or elemental formula if breast milk is not tolerated; however, the use of breast milk should be prioritized given its unique immunologic and probiotic benefits. Feeding intolerance, poor growth, GERD, and dysmotility can also be managed with feeding volume and rate adjustments, and with the assistance of various medications if anatomic etiologies, such as stricture, have been excluded.

COMMENTS? Email them to llevine@mh lifesciences.com

For references, go to ContemporaryPediatrics.com/neonatal-feeding-practices
Never miss a thing.


Sign up for our eNewsletter and take us anywhere.

contemporarypediatrics.com/enews
New findings reveal how many lives COVID-19 vaccines have saved

KEITH A. REYNOLDS

The NIH reports that the COVID-19 vaccines have saved more than 139,000 lives.

According to a news release from the National Institutes of Health, a study was performed to assess the impact of state-level vaccination campaigns. Investigators analyzed the period from December 21, 2020 to May 9, 2021 and compared the amount of time each state took to reach a series of milestones, beginning with 5 doses per 100 adults to 120 doses per 100 adults. They also calculated the number of vaccine doses per 100 adults at the end of each week.

During the first 5 months they were available, COVID-19 vaccines prevented more than 139,000 deaths, according to the results. By May 9, there were 570,000 US deaths related to COVID-19. The model used for the study projected this number would have been 709,000 deaths without the vaccine, the release says.

The investigators estimated that the economic value of saving these lives was between $625 billion and $1.4 trillion.

The reduction in deaths varied in different states, with vaccinations in New York leading to an estimated 11.7 fewer COVID-19 deaths per 10,000, whereas Hawaii saw the smallest reduction, at just 1.1 fewer deaths per 10,000, the release says.

“This study brings into focus the dramatic success of the early months of the nation’s coronavirus vaccine rollout,” said Christopher Whaley, policy researcher at the RAND Corporation, who helped lead the research team.

The investigators note that the study has limitations, such as an inability to distinguish between the role of vaccination from increases in natural immunity or social distancing policies on the number of COVID-19 deaths, according to the release.

COMMENTS? Email them to llevine@mjhlfsciences.com

REFERENCE


Want to learn more? Check out additional resources at https://www.medicalworldnews.com
Merck recently reported the topline results of the PNEU-PED (V114-029) study, which evaluated the safety, tolerability, and immunogenicity of the 15-valent pneumococcal conjugate vaccine Vaxneuvance.\(^1\)

The trial included 1720 healthy infants aged between 42 and 90 days. The participants were given a 4-dose regimen of either the licensed 13-valent pneumococcal conjugate vaccine or Vaxneuvance. Doses were received at 2, 4, 6, and 12 to 15 months of age. The study’s primary end points showed that the safety profile of Vaxneuvance was comparable to the 13-valent vaccine at any vaccine dose. Thirty days after the third dose, Vaxneuvance was found to be noninferior to the 13-valent pneumococcal conjugate vaccine for all 13 of the shared serotypes. The same was true 30 days after the final dose. A secondary end point illustrated a statistically superior immune response from Vaxneuvance compared with the vaccine for shared serotype 3 and unique serotypes 22F and 33F.

In July, the Food and Drug Administration approved Vaxneuvance for use in patients aged 18 years and older for active immunization. Merck indicated that the vaccine is on track for the submission of a supplemental regulatory licensure application to allow use in children by the end of 2021.

COMMENTS? Email them to mhester@mjhlifesciences.com

REFERENCE
How to correctly diagnose and treat community-acquired pneumonia

JANE M. CARNAZZO, MD, FAAP

While health care professionals remain on high alert for COVID-19 and all its variants, many pediatricians also witnessed a respiratory syncytial virus (RSV) surge this past summer, typically a winter illness.¹ Now that winter is almost here, this is what you should know about pneumonia.

Community-acquired pneumonia (CAP) can appear year-round but late fall and winter tend to be prominent months as viral respiratory illnesses are more common during this time. A majority of CAP is viral, including influenza, RSV, enterovirus, and others, but we have to remember the bacterial causes that include Streptococcus pneumonia, Haemophilus influenzae and Streptococcus group A. CAP is one of the most common serious infections in children and is responsible for a significant number of outpatient visits and hospitalizations.²

Many patients present with fever and cough, so how do you decide who has pneumonia and who should be treated with antibiotics? This is where the art of medicine plays a role. There are subtle findings that can help identify the child with pneumonia, such as grunting or an increased work of breathing; fever persisting beyond a few days; and sometimes it is just that the child looks sicker. You may hear decreased breath sounds or some crackles on the affected side. I have seen some patients come in with only a persistent fever and minimal other signs or symptoms. This is where the chest x-ray (CXR) could be helpful. However, even the CXR may not give us the answer, showing up as normal early in a pneumonia, and sometimes positive when it isn’t pneumonia at all. Unilateral findings are typically more suggestive of a bacterial cause, with bilateral infiltrates being more commonly viral—but again, not always. It is not an easy task to differentiate bacterial from viral pneumonia and determine who needs antibiotics.

So what do we do? As pediatricians and diagnosticians, we have to put it all together: Is there a history of prior upper respiratory symptoms? Has fever been higher than expected and persistent? How does the child look? What are the vitals including oxygen saturations; and what are other findings on exam? Many times you can make the decision on a clinical basis, but a CXR can assist in the diagnosis. It is important to correctly diagnose CAP, yet there are no validated prognostic tools to help in the diagnosis. In the office setting, I do not find obtaining lab findings particularly helpful because the results are very nonspecific to viral vs bacterial pneumonia. If the white cell blood count (WBC) and/or CRP are elevated, what does

CONTINUED ON PAGE 33
The lesions were apparently fresh and probably occurred that morning because the child’s mother first became aware of them when the nurse inquired about the wounds. The mother reported that the family had a rambunctious 8-month-old kitten in the home that loved to play and sleep with all the family members, particularly the patient. The mother had similar lesions from a week ago, but the puncture wounds had healed, leaving flat pinpoint and surrounding ring purpura (Figure 2). The mother reported that except for the time of the bite, the lesions were not painful and healed quickly.

One week prior to discovery of the child’s new lesions, the mother observed the kitten “attacking” the child’s leg and causing scratches in addition to claw and bite punctures. This behavior had not previously occurred. The child was not in distress, and the lesions required no additional care. The mother obtained and placed claw caps on the kitten.

Unfortunately, at initial evaluation in the pediatric emergency department (ED), the history of the kitten as the cause of the injury was rejected, and there was concern for the injury occurring in the setting
of child abuse because of the wound pattern. Specifics about what made the wound pattern concerning for abuse were not given.

The child was transferred to a children’s hospital. The diagnosis of cat bite was not considered by the general pediatric staff. Two child abuse pediatrics (CAPs) rejected the mother’s history of the kitten being in close contact with the child and concluded that because the wounds could not have been self-inflicted, there was no plausible history and, therefore, the child’s injuries were consistent with child abuse.

Apparently, none of the physicians or nurses were familiar with wounds from cat and dog bites.

Discussion
The literature suggests that approximately half of all people in the United States will be bitten by either an animal or another human being at some point.1–3 Most of the estimated 2 million annual mammalian bite wounds1 are minor, and the victims never seek medical attention. The lack of medical consultations in these cases could perhaps explain why many primary care physicians and some urgent care and ED physicians are not knowledgeable of the many presentations of animal bites.

Cat bites are the second most common form of mammalian bite. Ginsburg et al note that approximately 450,000 cat bites occur annually in the United States, nearly all of which are inflicted by household cats.3 Many of these bites are not reported.

The general literature on feline behavior notes that even domesticated cats can exhibit their instinctual predatory nature, which includes pursuing and possessing moving objects. This behavior is more unrestrained in kittens; they can be more boisterous and exhibit such predatory behaviors as part of playing.4

Animal bites can present with different lesions, such as punctures, avulsions, tears or lacerations, crush injuries, and/or abrasions.5 Also, puncture wounds can appear with irregular spacing like those seen on the patient’s mother (Figure 2). The literature regarding dog bites shows that similar irregular spacing can occur from their bites as well.6

Unfortunately, at initial evaluation, the kitten as the cause of injury was rejected, and there was concern for the injury occurring in the setting of child abuse.

A potential cause of confusion between animal bites and other causes of bruising is the peripuncture blue discoloration visible in the patient’s and mother’s wounds. The literature does not address the causes of these discolorations. Bilo et al attribute this to trauma from jaw pressure.5 Another consideration may be an inflammatory process from an animal salivary protein or its microbiota that can cause small-vessel inflammation and diapedesis of red blood cells.

Following this injury, the mother removed the kitten from their home. The child was asymptomatic, and no treatment was needed. The lesions cleared within a week.

It is important to analyze the cause of this misdiagnosis.

The CAPs who evaluated the skin findings rejected the mother’s history based on their erroneous conclusion that the pattern of skin lesions was not compatible with kitten bites. They did this without producing any objective supporting facts and without the support of medical literature. Consultants were not used. These physicians did not describe any abusive mechanisms that could have caused the child’s skin lesions. A differential diagnosis was not offered. The lack of putting forth a diagnosis based upon the medical facts of the case makes the diagnosis of abuse in this case a default diagnosis that lacked objective evidence and proper scientific reasoning.7–9

In a formal inquiry regarding unsubstantiated diagnoses of abuse, Justice Stephen T. Goudge, who served on the Court of Appeal for Ontario, Canada, for many years, stated that the use of a default diagnosis is unscientific and does not represent the evidence-based scientific approach. Default diagnoses infer rather than prove causality. They lack transparency, which prevents independent reviewability. Furthermore, a default diagnosis can be produced from confirmation bias.10

A similar term for a default diagnosis is diagnosis of exclusion (DOE). Without objective support for a given diagnosis, a DOE is an educated guess that could be unreliable and unsafe.11

Because no objective evidence of inflicted trauma was appreciable in this case and the specific abusive mechanisms that could have caused the child’s lesions were not given, “undetermined”—rather than abuse—would have been a proper default diagnosis by the CAPs.

The mother was accused of abusing the child. Custody was removed from the mother, and the child was placed in foster care. The following day, the foster parents brought the child back to the ED because of the medical complexities of the child’s care. The child was then released to
the biological mother’s home; the kit-
ten had already been removed from
the home. However, the foster mother
still retained custody, so the mother
had to be supervised by the child’s
step-grandmother.

A second child abuse consultation
with a CAP who presented no object
evidence rejected the mother’s his-
tory and experience with their kitten
and affirmed, by default, the errone-
ous diagnosis of child abuse.

Three months later, the mother’s
attorney presented to the family
court officer and prosecutor a com-
prehensive medical report objec-
tively confirming that the skin le-
sions were due to the kitten bite/paw
punctures. They dismissed the case,
and there was no adjudication of
abuse on the mother’s record.

Björk et al states that a physician’s
private values can modulate reason-
ning and may play a significant role in
the diagnostic process.12 Physicians’
bias is paramount considerations
in evaluating possible cases of child
abuse because those cases can in-
volve significant medical debate and
societal pressures.

We believe that all physicians must
insist upon ethical and medical pre-
cision in diagnoses of child abuse so
that unequivocally abused children
will be removed from abusive envi-
rions and innocent families will
not be subjected to the psychological,
financial, and societal stresses asso-
ciated with being accused of abuse.

We agree with the statement by
Findley et al—regarding a diagnosis
of abuse, we should all strive to “get
it right.”13

COMMENTS? Email them to
llevine@mjh lifesciences.com

Charles Hyman currently has a
forensic pediatric practice in
Redlands, California. He reviews
cases of alleged child abuse and
testifies in court when necessary. He
is usually paid for his work.

RESPIRATORY

How to correctly diagnose and treat
community-acquired pneumonia

that tell you? A recent study of bio-
markers and disease severity in chil-
dren with CAP looked at the useful-
ness of WBC, CRP, and procalcitonin
in predicting severity of CAP. Despite
the usefulness in predicting severity
of disease in adults, CRP and pro-
calcitonin have not proved useful in
children. The investigators did note
that “CRP and procalcitonin may be
useful in predicting the development
of specific severe outcomes, such as
complicated pneumonia and sepsis.”2
Blood cultures are rarely helpful and
should be reserved for the hospital-
ized patient.

Amoxicillin remains the choice
of treatment for suspected bacterial
CAP. Antibiotic stewardship stresses
the importance of the most specific
and least broad spectrum antibiot-
ic for treatment of CAP. The Ameri-
can Academy of Pediatrics Red Book
clearly notes, “Don’t treat uncompli-
cated community-acquired pneumo-
nia in otherwise healthy immunized,
hospitalized patients with antibiotic
therapy broader than ampicillin.”3
In an immunized child or areas
of high penicillin-resistant pneumo-
coccus, then an alternative such as a
cephalosporin should be considered,
especially in the hospitalized child. If
an atypical pathogen is considered,
such as mycoplasma or chlamydia,
then add a macrolide.4

As the temperature drops and the
runny noses increase, we need to be
on alert for the child who has some-
thing more than just an upper respi-

COMMENTS? Email them to
llevine@mjh lifesciences.com

Jane Carnazzo is on the editorial advisory
board of Contemporary Pediatrics®, an assistant
clinical professor at Creighton University
School of Medicine, and a pediatrician with
Children’s Physicians in Omaha, Nebraska. She
has nothing to disclose.

For references, go to
ContemporaryPediatrics.com/
diagnosing-and-treating-CAP
REDUCE YOUR CREDIT CARD PROCESSING FEES

Rates as low as .05%*

- Cash Discount
- Next Day Funding with weekend settlement

OPTIONAL PROGRAMS:
- Curbside Ordering
- Point of Sale Systems
- Recommendations, Solutions & Integrations

GROW YOUR BUSINESS. PARTNER WITH NAB TODAY!

866.481.4604

www.nynab.com

©2023 North American Bancard is a registered DBA of Wells Fargo Bank, N. A., Concord, CA, and The Barclaycard Bank, Philadelphia, PA. American Express may require separate approval. You will receive Chase Card percentages only. A user fee applies to the credit card. **Some restrictions apply. This advertisement is sponsored by an AD of North American Bancard. Apple Pay is a trademark of Apple Inc.
marketplace
PRODUCTS & SERVICES

Pediatric Equipment Bargains
www.medicaldevicedepot.com

**Tools for Increased Reimbursement and Office Efficiency at Discount Prices**

- **MA 1 Handheld Audiometer**
  - List Price: $735.00
  - Our Price: $670.00
  - You save $65.00!

- **MA 25 Audiometer**
  - List Price: $965.00
  - Our Price: $875.00
  - You save $90.00!

- **plusoptik S12R Mobile Vision Screener without Wireless Connection**
  - Our Price: $5,495.00

- **Welch Allyn Spot Vision Screener**
  - List Price: $7,998.00
  - Our Price: $6,880.00
  - You save $1,118.00

- **Hausmann 4906 Pediatric Funtastic Table**
  - List Price: $471.00
  - Our Price: $388.50
  - You save $82.50

- **Clinton Select Series Pediatric Scale/Treatment Exam Table**
  - List Price: $2,751.50
  - Our Price: $1,996.00
  - You save $755.00!

- **Amplivox Otoscope 102-1 Tympanometer (1 Clinical Model)**
  - List Price: $2,595.00
  - Our Price: $2,382.00
  - You save $213.00!

- **Welch Allyn MicroTym 4 Portable Tympanometer**
  - List Price: $4,140.00
  - Our Price: $3,623.00
  - You save $517.00!

- **Mi 24 touchTymp Tympanometer Screener**
  - List Price: $3,580.00
  - Our Price: $3,258.00
  - You save $322.00!

- **Accucold 8 cu ft Upright Refrigerator w/ Solid Door**
  - List Price: $1,730.00
  - Our Price: $1,284.00
  - You save $446.00!

- **LSR 2 cu ft Ultra-Low Temperature Chest Freezer**
  - Our Price: $5,099.00
  - You save $540.00!

- **Amico Pediatric Diagnostic Stations (White, Stool or Bus)**
  - Starting at $1,090.00

- **Astra 300 Spirometer**
  - Our Price: $898.00

- **Welch Allyn 39500 OAE Hearing Screener**
  - List Price: $5,200.00
  - Our Price: $4,550.00
  - You save $650.00!

**CALL to ORDER: 877-646-3300**
www.medicaldevicedepot.com

---

**marketplace
ADVERTISING INDEX**

BEIERSDORF
Aquaphor.................................................................................11
www.aquaphorus.com

Eucerin.................................................................................CV4
www.eucerinus.com

MUSTELA
Mustela..................................................................................21
https://www.mustelausa.com/

SUPERNUS
SUPERNUS........................................................................CV2
www.supernus.com
Provide Relief From Atopic Dermatitis, Contact Dermatitis, and Other Skin Conditions That Cause Itch With Aquaphor Itch Relief Ointment

- 37% reduction in itch severity on Day 1 of use
- up to 12 hours of significant itch relief
- 69.5% reduction in pruritus at Day 7 vs baseline with twice-daily use in children with atopic dermatitis

GENTLE AND SAFE FOR SENSITIVE SKIN, PARABEN-FREE, FRAGRANCE-FREE, HYPOALLERGENIC

RECOMMEND AQUAPHOR ITCH RELIEF OINTMENT FOR PATIENTS WITH ECZEMA FLARES AND SKIN IRRITATIONS

Beiersdorf
Team up with a trusted partner for unique and complex cardiovascular care.

Committed to a Unique Continuum of Care

As 1 of 10 children’s hospitals in the U.S. designated as a Platinum Level Center of Excellence for ECMO, Riley Children’s Health offers your patients leading-edge medicine and superior outcomes that are unmatched. Our integrated continuum of care model focuses on promoting excellent sub-specialty care coordination with a re-imagined approach to cardiac intensive care, including:

- A cardiovascular intensive care unit with a team of intensive care doctors and nurses who monitor patients 24/7, reacting quickly to changes during critical care and healing.
- A specialty-trained team of advanced providers, nursing staff and navigators dedicated to our cardiac patients and families, keeping the care team and patient’s local physicians connected.
- A consulting team of more than 40 pediatric-trained specialties working alongside the Heart Center team.

Delivering Nationally Ranked Pediatric Cardiovascular Care

From fetal diagnoses to complex surgical interventions, Riley Children’s Health is your trusted partner and resource to deliver expert care for the most complex but also the most common cardiovascular conditions patients experience. The care team within the Riley Heart Center includes pediatric cardiologists, cardiac intensivists, cardiac anesthesiologists and neonatologists.

Our pediatric heart program is ranked 5th in the nation by U.S. News & World Report.

To refer a patient to the Riley Heart Center or for more information about the program, visit rileychildrens.org/heart
Care for the Most Complex Conditions

**Cardiac Catheterization** Riley Heart Center specialists use the latest advancements in cardiac catheterization and routinely perform leading edge procedures, including atrial septal defect closure, ventricular septal defect closure, balloon valvuloplasty and transcatheter valve replacement.

**Cardiomyopathy Program** Approved by the Children’s Cardiomyopathy Foundation Centers of Care, our program provides specialized disease management, including genetic evaluation, to children with cardiomyopathy. Since 2016, we’ve assessed more than 500 children for this heart condition.

**Cardiothoracic Surgery** Our cardiac healthcare team has world-class specialists trained in cardiovascular and cardiothoracic surgery, cardiac anesthesiologists, imaging technicians, congenital cardiologists, cardiovascular intensive care specialists and many others who specialize in working with heart defects and thoracic conditions and is one of the many reasons we are among the top 15 high-volume heart programs in the nation for effective outcomes.

**Specialty Programs**
- Pulmonary Hypertension Program
- The Fetal Cardiology Program
- The Home Monitoring Program
- The Cardiovascular Genetics Program
- The Adult Congenital Heart Disease (ACHD) Program

**Highest rating ★★★★★ from the Society of Thoracic Surgeons**