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You might notice a small logo on the cover of this issue—it represents our Medical World News’ channel. If you are not familiar with this 24-7 platform, I invite you to visit it as soon as you have the chance: www.medicalworldnews.com.

Easy to navigate and now in its fifth season, this website dedicated to medical news offers viewers 6 shows:

- **Inside the Practice** highlights a unique, nonclinical aspect of a specialty—for example, a hospital’s celebration to mark a patient’s discharge.
- **Deep Dive** offers an in-depth exploration of a high-impact topic, such as COVID-19 vaccines and children.
- **Wellbeing Checkup** shares health care providers’ tips for staying mentally and physically healthy, including suggestions regarding regular exercise, proper nutrition, and meditation practice.
- **After Hours** reveals what clinicians do when they’re not working: They’re scuba diving, playing piano, traveling, etc.
- **Second Opinion** gives 2 medical experts a platform to discuss a compelling and timely health topic.
- **Behind the Science** poses the same question to multiple physicians, garnering a variety of perspectives on some of the most important issues in the health care space.

We hope you will take some time out of your hectic schedule to enjoy these programs!
Greetings, everyone.

Food allergies are always a source of concern in children. Because dairy is one of the most common allergies reported in pediatric health, this month our regular contributor, Rachael Zimlich, BSN, RN, covers assessing and mitigating this potential problem in children and adolescents.

On the COVID-19 front, we spoke with William J. Muller, MD, PhD, whose positions include scientific director of clinical and community trials at the Stanley Manne Children’s Research Institute at Ann & Robert H. Lurie Children’s Hospital of Chicago in Illinois. He shared with us news on vaccine research for potential new COVID-19 variants, as well as updates on vaccines being looked at for other infectious diseases—in particular, respiratory syncytial virus (RSV). According to the Centers for Disease Control and Prevention, more than 2 million children contract RSV each year; last year, pediatric health care providers reported off-season surges, so it is welcome news that a preventive measure may be on the horizon.

Continuing the topic of infectious/respiratory disease, Editorial Advisory Board member Rana F. Hamdy, MD, MPH, MSCE, shares what every pediatrician should know about antibiotic stewardship for common respiratory illnesses in the pediatric population.

Other don’t-miss articles in this month’s issue address atopic dermatitis and serious diaper rash in infants; offer a look at cannabinoid hyperemesis syndrome; and describe the intriguing case of an infant girl whose right cheek had a warm, red, painful area that was firm to the touch. To learn the diagnosis, check out our Puzzler section.

As 19th-century Canadian physician William Osler said, “The good physician treats the disease; the great physician treats the patient who has the disease.” I believe that doctors who chose pediatrics do this every day: Treat the patient in totality.

Please stay safe and well. As always, I welcome your suggestions, comments, and questions.

With warm regards,

Tina Q. Tan

REFERENCE


email: titan@luriechildrens.org
As providers, you know that STIs are on the rise and can happen to anyone. Not everyone is as aware of the risks, and up to 84% of chlamydia and gonorrhea infections are asymptomatic. The CDC now recommends considering an opt-out approach for young women under 25. Universal screening is an inclusive solution that is proven to decrease STI prevalence, infertility issues and cost. Let’s help protect her reproductive health today, and tomorrow.
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RSV, respiratory syncytial virus.
*According to a study of pediatric hospitalizations between 1997 and 2000.
¹Surveillance data between October 2014 and April 2015. Among 1,176 RSV-hospitalized infants aged under 12 months, 851 had no reported underlying condition (prematurity was classified as an underlying condition in the study).

References:

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THE EDITORS ARE PLEASED TO ANNOUNCE the availability of our new parent company’s continuing education activities. We’ve picked this one especially for our Contemporary Pediatrics® readers. Go to: bit.ly/3J6I6pN

Abigail Donovan, MD, assistant professor of psychiatry at Massachusetts General Hospital in Boston, discusses what brexpiprazole brings to the table for treating schizophrenia in pediatric patients, its adverse events, and who will most likely be prescribing it.

Go to: bit.ly/3J6I6pN

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Which ELGANs are most at risk of low lung function?

In extremely low gestational age newborns (ELGANs), certain demographic factors and less-than-optimal respiratory support in or beyond the neonatal intensive care unit (NICU) can increase the risk of abnormal lung function at 1 year of age. These are the major findings of a study in 135 ELGANs born at 6 hospitals across the United States.

Following the newborns’ discharge from the NICU, investigators collected quarterly data about the infants’ respiratory symptoms; emergency department (ED) or hospital admissions for respiratory indications; cardiopulmonary medications; and use of supplemental oxygen or ventilatory support. Investigators also collected perinatal demographic data and performed infant pulmonary function tests (iPFTs) when the babies were 1 year of age.

Compared with normative values, infant z scores for all iPFT values were significantly lower except lung function and respiratory system resistance, with the latter significantly higher. Of 6 adverse events, just 1 was deemed serious, and the infant recovered immediately after testing.

With regard to correlations between NICU and post-NICU clinical factors and iPFTs, for each week’s decrease in gestational age, forced expiratory flow (FEF) at 75% of forced vital capacity (FVC) decreased 9.5%. Other neonatal factors associated with significantly lower or abnormal iPFTs included intubation at delivery, need for invasive ventilation at more than 30 weeks’ postmenstrual age (PMA) or noninvasive ventilation at more than 36 weeks’ PMA, treatment with diuretics or systemic steroids, and weight below or equal to the 10th percentile at 36 weeks’ PMA.

Prenatal and family factors generally had no effect on iPFTs, but ED or hospital admissions for respiratory indications, cardiopulmonary medication, and use of supplemental oxygen or ventilatory support were significantly associated with lower iPFTs. Among demographic factors, being male and Black increased the likelihood of a significant decrease in forced expiratory volume 0.5 or FEF at 75% of FVC. Just 7% of the infants had reversible airflow obstruction.

I sometimes squeeze infant’s chests (gently) to elicit a wheeze, but it appears it can now be done in a standardized fashion. Prior to this, iPFTs were a pipe dream, but technology marches on. I also note that bronchodilators usually do not help these children, just as they are not of benefit with viral wheezing.

In a case report, surgeons describe performing a right lobectomy using a novel surgical procedure, the transoral endoscopic thyroidectomy vestibular approach (TOETVA), on a 17-year-old adolescent boy with a suspicious thyroid nodule. The patient had a normal postsurgical recovery. His parents and he were satisfied with the cosmetic results: Because TOETVA is performed through a natural opening in the oral cavity, he did not have the scar associated with conventional thyroid surgery.

The procedure called for extending the patient’s neck by placing a pillow under his shoulder in the supine position, putting the chin and sternal notch at the same level for an ergonomic study, and making it unnecessary to break the table from the waist, which is done for a standard thyroidectomy. During trocar incisions, the surgeons paid particular attention to avoid damage to mental nerves located on both sides, given that incision locations are crucial to preserve these structures.

The authors noted several advantages of TOETVA over conventional endoscopic techniques for thyroid surgery. First, it not only leaves no visible scars but also offers a shorter dissection distance than conventional surgery. Also, because TOETVA is done with endoscopic equipment similar to that used in laparoscopic cholecystectomy, it provides easy access. Finally, TOETVA is safe and reproducible because it offers significant anatomical landmarks, such as the location of trocar incisions, cricoid cartilage, trachea, strap muscles, sternocleidomastoid muscles, and sternal notch.

Parents may ask about this, so be prepared. The authors do cite another large study with different conclusions. For me, the bottom line is that the risk of kernicterus outweighs the risk of neoplasm, provided phototherapy is used judiciously. Most infants seen in the office with elevated bilirubin will not have levels warranting more than serial follow-up.

Fever and facial swelling in a neonate

ELIZABETH IMBODEN, MD; AND KYLE SANTERIAN

An 18-day-old girl whose right cheek had become increasingly red and warm over 24 hours was directly admitted to a pediatric inpatient unit from an outpatient pediatric office. In the office, the infant, born full term via an uncomplicated vaginal delivery, was febrile, with a rectal temperature of 100.6 °F. She had firmness and pain to the affected area, fussiness, increased sleeping, and poor feeding, preferring the bottle to breastfeeding.

The infant did not have cough, changes in bowel movements, abdominal distention, emesis, or decreased urination, and she had no recent sick contacts or history of facial trauma. Her mother did not have mastitis. The family had a dog, but there was no direct contact between the pet and the patient. The patient’s father was a veterinarian and her mother worked at a local hospital.

The infant’s vital signs on admission included rectal temperature of 101.2°F; heart rate, 152 beats per minute; respiratory rate, 46 breaths per minute; and oxygen saturation, 98% on room air. A physical exam demonstrated a well-developed neonate who was irritable but alert and active. The anterior fontanelle was flat, and her head was normal size, without signs of trauma. The conjunctiva were clear, without injection or tearing, and the tympanic membranes were normal bilaterally. The infant did not have rhinorrhea, and her oropharynx was without erythema or exudates. Her right cheek was swollen, firm, erythematous, and warm to the touch.

There was no fluctuance, crepitus, or drainage. Cardiovascular and respiratory examinations were unremarkable. The infant’s abdomen was soft, with normoactive bowel sounds and no evidence of distention. Complete blood cell count, basic metabolic panel, and C-reactive protein (CRP) levels were obtained along with urine blood and cerebral spinal fluid (CSF) cultures due to concern for a possible disseminated infection in a neonate. CSF Gram stain, cell count, and meningitis/encephalitis panel were normal. White blood cell count was 21,600/µL, and CRP was 92 mg/L.

Differential diagnosis
For this patient’s facial swelling, differential diagnosis included
cellulitis, erysipelas, congenital malformations, and neonatal parotid gland enlargement. Infectious etiologies included mumps; extrapulmonary tuberculosis (TB); or, more commonly, suppurative parotitis. Less common conditions were tumor and autoimmune conditions such as Sjögren syndrome (Table 1).

Due to concern for suppurative parotitis as the etiology in this newborn, empiric intravenous (IV) clindamycin and cefotaxime were started for broad-spectrum coverage.

On hospital day 1, an ultrasound of the right cheek was performed to evaluate for abscess. The right parotid gland was enlarged (2 × 1.2 × 1.5 cm), with inhomogeneous echotexture and preserved flow without evidence of an abscess. Pus was expressed from the parotid duct and sent for culture. These findings combined with the patient’s clinical picture suggested an acute infectious/inflammatory process within the right parotid gland, consistent with parotitis.

**Discussion**

Suppurative parotitis is a rare condition in children and neonates. The pathophysiology is thought to be due to ascending bacterial organisms from the oropharynx colonizing the parotid gland. As seen in this patient, the common clinical presentation includes fever, erythema, and swelling of the preauricular area with or without fluctuance. A variety of risk factors have been identified (Table 2) and include situations that promote stasis in the salivary glands, such as dehydration and nasogastric tube feeding. Interestingly, male sex has been associated with a 3-fold increased risk of parotitis, although the reason remains unclear.

In cases of unilateral facial swelling, clinicians must maintain a broad differential diagnosis including cellulitis, lymphadenitis, and traumatic injury, with special attention to potentially life-threatening conditions, such as retropharyngeal, peritonsillar, or oral abscess.

Importanty, suspected suppurative parotitis in neonates must be interpreted in the context of the increased risk of sepsis in infants. As such, it is important to collect blood, urine, and CSF cultures to evaluate for systemic infection. The vast majority of neonatal parotitis cases are caused by gram-positive cocci, with *Staphylococcus aureus* being the most commonly isolated organism. However, case series have identified anaerobes as well as gram-negative bacilli such as *Escherichia coli* and *Klebsiella pneumoniae*.

Initial treatment involves IV broad-spectrum antibiotics such as a third- or fourth-generation cephalosporin. Classically, the diagnostic criteria for parotitis include facial swelling, purulent exudate expressed from the parotid gland, and positive cultures. However, when the diagnosis is unclear or there is no obvious parotid exudate, ultrasound can help evaluate for the presence of abscess and need for surgical drainage. Some cases may call for other imaging to identify congenital anomalies or laboratory work to assess for other infectious etiologies such as HIV, TB, or mumps.

**Case outcome**

The patient had rapid clinical improvement with significant reduction in erythema and swelling. On hospital day 2, IV antibiotics were discontinued, and she was discharged to complete 7 days of oral cephalexin. At 48 hours, salivary duct and blood

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**TABLE 1. DIFFERENTIAL DIAGNOSIS OF FACIAL SWELLING IN INFANTS**

- Cellulitis
- Erysipelas
- Parotitis
- Lymphadenopathy/lymphadenitis
- Congenital etiology (hemangioma, venolymphatic malformation)
- Autoimmune diseases (Sjögren syndrome)
- Manifestation of systemic illness (extrapulmonary TB, HIV)
- Trauma

**Key:** TB, tuberculosis.

**TABLE 2. RISK FACTORS FOR NEONATAL SUPPURATIVE PAROTITIS**

- Prematurity
- Prolonged nasogastric feeding or mechanical ventilation
- Dehydration
- Maternal mastitis
- Male sex
Sleep, depression, and bipolar disorder in children and adolescents

BY LEAH KUNTZ

Seeking to understand the relationship between sleep and both depression and bipolar disorder, UK investigators recently conducted a narrative literature review of affective disorders and sleep difficulties in children and young people.

Monica Comsa, FRACP, of the Child and Adolescent Mental Health Service at Cumbria, Northumberland, Tyne and Wear NHS Foundation Trust, and colleagues found that parasomnias, narcolepsy, and sleep-related movement disorders are associated with depression in children and adolescents. Additionally, children and adolescents with depression can present with a number of sleep difficulties, which are also linked with several other issues, such as higher depression severity, greater fatigue, suicidal ideation, physical complaints, pain, and decreased concentration.

On the other hand, insomnia, obstructive sleep apnea, and circadian rhythm disorders are associated with both depression and bipolar disorder in this age group. Sleep difficulties can occur before, during, and after an episode of depression or bipolar disorder.

“Sleep disturbances among adolescents with bipolar disorder can affect the severity of depressive and manic symptoms, are a poor prognostic indicator, and have been associated with social and academic impairment,” said Comsa and colleagues.1

These sleep difficulties may be the result of medication. According to the investigators, antidepressants and antipsychotics can directly affect sleep architecture, and clinicians should be cognizant of this problem when prescribing and consider nonpharmacologic interventions, which might minimize the risk of relapse in affective disorders.

Investigators suggested that the ideal treatment plan involves a multimodal approach to target both the affective and specific sleep disorders: “Psychoeducation, consistent sleep-wake schedules, and tailored interventions for addressing sleep problems should play an important role in the prevention and treatment of mental health difficulties, at any age. Concomitantly addressing sleep problems can lead to an increased remission rate of depression.”1

More research is required to understand the impact of combined interventions on clinical outcomes, investigators concluded: “Of most importance is the impact of specific treatment for sleep disorders on the long-term outcome of affective disorders. Clinicians need to know if better nights reliably lead to better days.”1

REFERENCE

PUZZLER

Fever and facial swelling

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cultures grew methicillin-sensitive *S. aureus* that was susceptible to cephalosporins but resistant to clindamycin. Two weeks after discharge, the child’s symptoms had resolved, and she was progressing well. It remained unknown to the pediatrics team how this infant obtained the infection, given her lack of obvious risk factors. ■

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The authors have nothing to disclose.

For references, go to ContemporaryPediatrics.com/puzzler-0422

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Diagnosis and treatment of cannabinoid hyperemesis syndrome

KEVIN KLEMCZYYK, MD; JESSICA CALIHAN, MD; AND RACHEL H. ALINSKY, MD, MPH

Here is what pediatric health care providers need to know about this often debilitating disorder.

Background
Cannabinoid hyperemesis syndrome (CHS) is a disabling illness characterized by episodic acute vomiting and associated with chronic cannabis use. First described in 2004, CHS remains poorly understood and challenging to diagnose and manage. With expanding medicinal and recreational use, decreasing perception of risk, and increasing potency of cannabis, the burden of CHS on pediatric patients and clinicians will likely continue to grow.

Epidemiology
Prevalence of CHS is uncertain but likely increasing. A 2015 study of emergency department (ED) presentations in a US state following legalization of medical cannabis found nearly double the rate of cyclic vomiting presentations and higher rates of cannabis use among these patients. Findings of a 2018 study estimated that 2.8 million people in the United States (approximately 1% of the population) use cannabis chronically and have symptoms consistent with CHS. Across study findings, CHS tends to present in the late teens or the 20s. One research group emphasizes challenges in both diagnosis and epidemiology due to widespread use of cannabis to self-treat nausea and the relatively low rates at which patients follow up and stop using cannabis—which is required to meet current Rome IV diagnostic criteria for adults (Table 1).

Cannabis use in the United States has long been associated with racist and classist laws and law enforcement (despite liberalization), whereas access to health care, including mental health- and substance-related care, remains disparate and unjust. Clinicians can help mitigate further harm and disparities through careful and thorough treatment of all patients with possible CHS.

Morbidity
CHS can lead to repeated presentations and admissions, with sequelae including hypovolemia, electrolyte derangements, acute kidney injury, esophageal injury, weight loss, and prolonged debility. There are multiple reports of fatalities believed to be related to CHS, including 1 from torsade de pointes due to electrolyte derangement and antiemetic-driven QT prolongation.
Clinical presentation
CHS has 3 clinical phases: prodromal, hyperemetic, and recovery. The prodrome comprises months of morning nausea while chronically using cannabis and is often accompanied by weight loss. The hyperemetic phase includes acute-onset nonbilious vomiting up to several times per hour, plus diffuse abdominal pain. In both phases, compulsory hot bathing for relief of symptoms is common; for example, in one systematic review, this was reported in 10 of 14 pediatric cases. Rome IV criteria include this feature as a “supportive remark” (Table 1). In true CHS, the recovery phase follows cessation of cannabis use, though symptoms can persist for weeks prior to full remission.

Diagnostic evaluation
The hyperemetic phase often prompts ED presentation, in which vomiting and abdominal pain present a diagnostic challenge. Following basic clinical and lab evaluation (including lipase), patients without diagnoses often undergo abdominopelvic CT and then, if admitted, endoscopic gastroduodenoscopy (EGD). Any testing for substances should be interpreted carefully, as false positives and negatives occur, and quantitative tests may be difficult to interpret. Although CHS may be considered early on, it is vital to avoid anchoring and neglect of other dangerous etiologies while also implementing supportive care. “Mimickers” of CHS that can elude CT and EGD include elevated intracranial pressure, acute intoxication, ovarian or testicular torsion, gastroesophageal dysmotility, mitochondrial disorders, and acute intermittent porphyria (see Table 1).

Pathophysiology
CHS is still considered a “functional disorder” because of the incomplete elucidation of its pathophysiology. However, clinicians should understand probable mechanisms to guide treatment and educate patients. These include (1) known proemetic effects of high-dose tetrahydrocannabinol, likely via dopamine signaling at the chemoreceptor trigger zone; (2) progressive cannabinoid receptor downregulation; (3) abnormal stress response due to dysregulation of the hypothalamic-pituitary axis and sympathetic nervous system; (4) upregulation of the transient receptor potential vanilloid 1 (TRPV1) receptors involved in pain, nausea, and thermoregulation; (5) delayed gastric emptying; and (6) predisposing factors, including genetic polymorphisms and untreated mood disorders.

During the hyperemetic phase, persistent vomiting drives lipolysis, releasing lipophilic THC stores and fueling a proemetic feedback loop exacerbated by starvation ketosis.

Approach to management
We lack high-grade evidence treatments specific to CHS, but essential management includes acute stabilization, longitudinal primary and mental health care to reduce harm of cannabis use, and serial reconsideration of diagnosis.

Acute pharmacotherapy
Treatment during the hyperemetic phase includes rehydration with bolus intravenous (IV) crystalloid fluids, IV dextrose-containing fluids (to arrest ketosis), correction of electrolyte abnormalities, and treatment of nausea (Table 2). Gastric acid suppression, nasogastric tube placement, and gastroenterology consultation should be consid-
pharmacology

The use of medications to mitigate sequelae, including catastrophic esophageal rupture.

In the pediatrics literature, haloperidol and topical capsaicin cream have been reported as effective. Among pediatric patients in 2 systematic reviews published in 2021, benzodiazepines were reportedly effective in certain patients; one review noted that ondansetron was reportedly effective in only 2 of 5 pediatric patients who received it. Medications reported as frequently ineffective in these reviews include metoclopramide, promethazine, and opioids.

Adult research reflects similar patterns. In a recent randomized controlled trial (RCT) of 33 adults, haloperidol (0.05 mg/kg or 0.1 mg/kg IV), which blocks proemetic dopaminergic stimulation at the chemoreceptor trigger zone, was found superior at both doses to ondansetron (8 mg IV) in the primary outcome: the average of changes in abdominal pain and nausea scores at 2 hours. Three of the patients who received the higher dose of haloperidol had specific adverse effects (AEs): 2 dystonic reactions and 1 akathisia.

Topical capsaicin cream (0.025%–0.1%) applied to the abdomen has been reported to be effective for treating CHS in adults, via activation of TRPV1 receptors (downregulated in CHS), leading to decreased substance P signaling in the brain stem. TRPV1 receptors are also activated by temperatures over 43°C, explaining relief from hot-water bathing and abdominal hot packs. Oral aprepitant, often used for chemotherapy-induced nausea, was reportedly effective in 1 adult case report of CHS, via inhibition of neumedin K tachykinin receptor-binding by substance P.

Haloperidol and topical capsaicin have pathophysiologic bases and evidence for use in CHS. They are likely more effective than 5-HT3 antagonists (eg, ondansetron), though evidence amounts to systematic reviews of cases and 1 small RCT. Benzodiazepines have been reported effective in some cases but can pose a risk of dependence.

**First described in 2004, CHS remains poorly understood and challenging to diagnose and manage.**

**Nonpharmacologic management**

Adolescents with CHS and cannabis use disorder (CUD) benefit from a combination of pharmacologic treatment, behavioral interventions, and family support.

By Rome IV criteria, the diagnosis of CHS is confirmed only when symptoms resolve upon ceasing use. Clinicians should help patients toward this goal following physiologic stabilization. To approach substance use disorders, the American Academy of Pediatrics recommends the Screening, Brief Intervention, and Referral to Therapy tool. Evidence-based, validated screening tools for adolescents include Screening to Brief Intervention; the Brief Screener for Tobacco, Alcohol, and Other Drugs; and the Alcohol, Smoking, and Substance Involvement Screening Test. These help quantify the degree of substance use to build insight and direct referrals.

Brief intervention can include motivational interviewing toward reducing harm and/or use. This may include providing information about potential cognitive, psychiatric, and physical harms of cannabis use, plus clear patient-centric recommendations. Many adolescents use cannabis to manage anxiety, depression, and/or prior trauma, in which case it is crucial to offer safer options, including psychotherapy and pharmacotherapy with well-studied efficacy and AEs.

All patients should be referred to practical primary care, with an appointment scheduled and provider handoff given, if feasible. Adolescents with multiple ED presentations for CHS, high-risk substance use (eg, injection use, combination of sedatives), and/or cooccurring mental health disorders may benefit from referral to specialty care. The American Society of Addiction Medicine criteria can guide appropriate level of care, whereas the Substance Abuse and Mental Health Services Administration provider locator can identify local resources. This area requires prompt policy attention, because just 26% of US addiction treatment facilities offer services for adolescents.

Psychosocial treatment modalities, including cognitive-behavioral therapy, motivational enhancement therapy, contingency management, and family-based interventions, have been associated with reduced frequency of cannabis use and dependence severity. The Community Reinforcement and Family Training method aims to improve family members’ understanding of addiction and, by creating a supportive environment, can help motivate adolescents to seek care.
There are limited data for long-term pharmacotherapy for CUD. In 1 RCT of 116 patients (including 20 under age 18), N-acetylcysteine 1200 mg twice daily was associated with an odds ratio of 2.4 for abstinence over 8 weeks, whereas a subsequent RCT of 302 patients over 12 weeks showed no difference between groups, though subgroup analysis suggested benefit among younger patients. Although patients receive treatment for CUD, they should continue receiving any medication that is safely and effectively treating CHS-related nausea, with the mutual expectation that nausea should decrease over days to weeks. Any patient stopping or reducing use should be monitored and treated for cannabis withdrawal symptoms, including insomnia, anxiety, irritability, and depression (Table 2).35

**Takeaways**

Cannabis is the third most commonly used substance among adolescents in the United States. Potency and societal acceptance are rising, with use increasing further during the COVID-19 pandemic. CHS is one serious consequence. Presentation to care during the prodromal or hyperemetic phases of CHS can prompt a variety of short- and long-term outcomes, from repeated ED visits with catastrophic sequelae to successful symptom control and patient-centric connection with long-term care. When pediatricians are aware, CHS symptoms can be the canary in the coal mine, leading patients to multidisciplinary support, insight, motivation, and long-term recovery.
When it comes to infant feeding, national and global health experts acknowledge that breast milk is the ideal source of nutrition for at least the first few months of life. Yet, according to the World Health Organization (WHO), just 2 out of 3 babies are breastfed for the recommended 6 months.¹

“If there are no contraindications to breastfeeding or breast milk, then there is no reason to use infant formula, as long as the mother is able to breastfeed and/or provide breast milk,” said Lori Feldman-Winter, MD, MPH, chair of the American Academy of Pediatrics (AAP) Section on Breastfeeding and a professor of pediatrics at Cooper Medical School of Rowan University in Camden, New Jersey. “If for some reason the mother cannot breastfeed or provide her baby breast milk, then infant formula is the recommended feeding source until 1 year of age.”²

“Whenever there are no contraindications to breastfeeding or breast milk, there is no reason to use infant formula, as long as the mother is able to breastfeed and/or provide breast milk,” said Feldman-Winter. “If for some reason the mother cannot breastfeed or provide her baby breast milk, then infant formula is recommended as the primary feeding option until 1 year of age.”

If mothers choose not to breastfeed even though they are able, infant formula is a viable option, though Feldman-Winter called it “a recognized and significantly substandard method of feeding.”²

Both AAP and the WHO recommend exclusive breastfeeding for at least the first 6 months of life. Beyond that, continued breastfeeding is recommended until at least age 1 but in conjunction with the introduction of complementary nutritious solid foods.¹²

Because there is no defined reason to transition from breastfeeding or use of breast milk to formula, Feldman-Winter said, there really is no official recommendation on the best time to make that move. “The only thing that may impact timing is if a mother becomes unable to continue breastfeeding or breast milk feeding for some reason, and at that time, infant formula is recommended,” she said. “The longer the mother breastfeeds or provides her milk for the baby, the better the health outcomes.”

Pediatricians should base guidance on the infant’s health and nutrition and counsel parents on the options and best practices for feeding.

There is no clinical evidence that 1 type of infant formula is better than another, according to Feldman-Winter. “If and when infant formula is introduced, it really does not matter which formula is selected, as long as it is commercially available and meets US Department of Agriculture (USDA) standards and is reconstituted according to guidelines developed by the USDA, the Centers for Disease Control and Prevention (CDC), and AAP,” she said.

Giving a bottle should be done with responsive feeding practices, following the baby’s cues to avoid overfeeding, Feldman-Winter said. “Bottle-feeding should follow the AAP guidance on responsive feeding, using bottles until about 6 months, and the infants may transition to staged cup feeding depending on development,” she said. “If feeding formula, the formula should be mixed according to guidelines provided by the manufacturer and not altered. Some babies...
prefer warm breast milk or formula to mimic the temperature of direct breastfeeding.”

The CDC echoes AAP’s position that breast milk is the healthiest option for both infants and mothers in the first few years of life, but the agency also acknowledges that both mothers and babies may decide to stop breastfeeding at any point.3

According to the CDC, common reasons parents stop breastfeeding early include:
- difficulty with lactation,
- latching problems,
- insufficient infant nutrition or weight gain,
- concerns about medications the mother is taking,
- challenges related to work or parental leave policies,
- lack of family or cultural support, and
- lack of support from health care providers and/or hospitals.

The timing of weaning, from breast milk to both formula and solid foods, is a personal decision, the CDC states.3 The agency suggests that parents interested in weaning an infant from breast milk to formula substitute 1 formula feeding for a breast milk feeding per day to start, gradually increasing the frequency of substitutions.4

Breastfeeding rates have not risen much in the past few decades, but the push to increase the practice really took hold in the mid-2010s. That is when the Breast Is Best initiative launched a campaign to encourage hospitals to achieve a Baby-Friendly designation and support breastfeeding mothers. By the end of the campaign, overall breastfeeding rates grew by about 4%, and exclusive breastfeeding increased from 39% to 61%.”

However, in the years since the campaign’s launch, some researchers and advocacy groups have questioned the “breast is best” narrative, suggesting that proper nutrition, not how it is provided, is key.6 The Fed Is Best Foundation, a national nonprofit group staffed by volunteer health care professional and parents, suggests that research findings point to a rise in hospitalizations of exclusively breastfed infants due to feeding complications from poor milk production or constitution. In 2018, a paper in the Journal of Human Lactation called the Breast Is Best campaign into question, arguing that anxiety, depression, and mental health complications mothers face in the breastfeeding process should be considered when weighing the risks vs benefits of breastfeeding.7

La Leche League International suggests that parents who plan to switch from breastfeeding to bottle-feeding breast milk wait until about the fourth week of breastfeeding.8 If supplementation is needed, several types of manufactured formulas, including cow’s milk, soy based, and hypoallergenic, are available to meet infants’ needs.9

Pediatricians should be sure that formulas offered to infants are USDA approved and warn parents never to use homemade formulas or stray from the manufacturer’s mixing guidelines.9

Increase in food allergies signals similar rise in cow’s milk allergy

Experts note that, with cow’s milk allergies seemingly on the rise, pediatric health care providers can help parents be vigilant.

BY RACHAEL ZIMLICH, BSN, RN

On the surface, it seems the prevalence of food allergies—or at least parents’ awareness of them—is on the rise. The Centers for Disease Control and Prevention reports that from 1997 to 2011, food allergies in children increased by about 50% overall and now affect roughly 2 children in every classroom.1,2

Cow’s milk allergy (CMA) is one of the most common food allergies reported in infants and young children, but estimating its true prevalence has proved difficult. Not all suspected cases are tested and diagnosed, but CMA prevalence is estimated at 2% for children under 4 years of age, with roughly 1.6 million children affected as of 2018.2

Despite difficulties in establishing prevalence in children, experts warn that, based on facility-based observations, CMA cases are presumably rising. This makes it all the more important for pediatricians to know how to recognize and treat these allergies.

Obstacles to pinpointing prevalence

There are several accepted methods for assessing and diagnosing CMA but no clear standard, and related data are not collected frequently on a national basis. The National Health and
nutrition

Nutrition Examination Survey didn’t uncover significant increases in dairy allergies between the 1990s and mid-2000s, but these figures are estimated only once per decade, and many health facilities continue to report higher numbers of food allergies, including dairy.

Together, these issues present a challenge to establishing overall prevalence and a benchmark for surveillance. Testing methods have improved over the years, too, raising the question of whether more accurate results and a better understanding of gut health may be skewing the perception of a rise in allergy prevalence.

“The American diet has been changing [with more processed foods and less fruits and vegetables], which is affecting the microbiome of the gut,” said Sarah Lowry, MD, a pediatric gastroenterology fellow at Johns Hopkins Medicine in Baltimore, Maryland. “This may be contributing to immunogenicity and allergies, but more studies are needed for this to be identified as a true cause. I think there is a higher prevalence overall—again, based on changes in the gut microbiome, diet, and exposure—but there are also better testing methods.”

Diagnosis begins with a parental history report and recognition, which Lowry said have improved as a process overall. Parent groups on social media have also raised awareness and opened the door to more questions about these allergies, Lowry said.

CMA is the second most common food allergy in children, behind peanut, Lowry said. It presents earlier—around age 2—than other food allergies but usually produces a less severe reaction. Considering the limitations of reporting, overall prevalence of dairy allergies in children is estimated at 5%, representing about 20% of all food allergies in children, Lowry said.

Varying symptoms in reactions to CMA
Different symptoms and prevalence rates characterize the various types of CMA, said Vivian Hernandez-Trujillo, MD, FAAP, FAAAAI, FACAAI, a pediatric allergist and division director of the allergy and immunology program at Nicklaus Children’s Hospital in Miami, Florida. She offered the following summary:

**IgE mediated:** This type can affect the skin as urticaria, angioedema, or eczema, as well as cause respiratory symptoms (eg, cough, nasal congestion, rhinorrhea) and gastrointestinal symptoms (nausea, vomiting, diarrhea). A combination of several symptoms can lead to anaphylaxis in patients with severe CMA.

**Non-IgE mediated:** Infants and children with this type of allergy may develop vomiting and blood or mucus in the stool, similar to the symptoms seen with food protein–induced enterocolitis.

**Lactose intolerance:** This is an enzyme deficiency of lactase as opposed to a true allergy to cow’s milk.

Hernandez-Trujillo noted that CMAs can resolve by adulthood, which also presents a challenge in estimating their true burden. Lowry noted that study results suggest that up to 80% of teenagers develop tolerance and essentially outgrow their CMA allergy.

“While rates of food allergy are increasing, it is not clear whether rates of cow’s milk allergy are increasing,” Hernandez-Trujillo explained. “Because the natural history of cow’s milk allergy leads to resolution in many patients, it is difficult to say whether increases are occurring over time.”

CMA prevalence also appears to depend on the test used for diagnosis, she adds. Current data show prevalence rates based on the following methods:

- 1.2% to 1.7%, self-reporting
- 0.2% to 2.5%, skin prick testing (SPT) alone
- 2% to 9%, serum IgE testing (sIgE)
- 0% to 2%, symptoms and sensitization (SPT ≥ 3 mm or sIgE ≥ 0.35 kU/L)
- 0% to 3%, food challenges

Although data suggest that food allergies overall are rising, Hernandez-Trujillo said, it is not really clear if that includes CMAs, specifically. Geographic locations can alter prevalence too, she added.

Assessing CMA at the patient level
Because dairy allergy is a common allergy that is usually first noticed by the parent, Lowry emphasized the importance of a detailed history as part of the assessment. Additional testing and referral to a pediatric allergist are common after dairy allergies are suspected, but even then, avoidance remains the primary treatment strategy, she added.

When a true CMA is confirmed, Hernandez-Trujillo said, it is crucial that the child avoid not only milk but also other dairy products, including butter, yogurt, cheese, and ice cream. “Any product with cow’s milk should be avoided, especially in patients with severe cow’s milk allergy or anaphylaxis,” Hernandez-Trujillo said. “Food-label reading is essential.”

Avoidance isn’t always enough,
though. Hernandez-Trujillo emphasized that pediatricians must teach parents how to handle severe reactions when accidental exposure occurs.

**Moving forward and mitigation**

It’s important to monitor children with dairy allergies closely, because they have a higher risk of other food allergies too, Lowry said. Dairy allergies also appear to come with a higher tolerance, so monitoring patients as they age and offering food challenges later may help reduce allergy prevalence in later childhood or adulthood, she said.

Managing CMAs in the long run requires vigilance, with individual surveillance and education, Hernandez-Trujillo notes. Many nutritional alternatives to cow’s milk are available, and parents can benefit from having both a pediatrician and an allergist involved in their child’s care. Nuances of CMA can vary among patients, and coordinated care efforts can help identify where exceptions to avoidance might be made. Although some patients must avoid all dairy, others may need to steer clear of only uncooked forms, she said. Baking alters some of the milk proteins and reduces allergenicity.

“Depending on the patient’s clinical presentation and severity, pediatric allergists can work with pediatricians to identify patients who may be able to tolerate some form of cow’s milk,” Hernandez-Trujillo said. “The majority of pediatric patients will outgrow the cow’s milk allergy over time, and follow-up to determine when they outgrow the CMA is essential. For patients who do not outgrow the CMA, continued strict avoidance and immediate access to epinephrine are needed.”

Lakiea Wright, MD, MPH, a board-certified allergist and immunologist at Brigham and Women’s Hospital in Boston, Massachusetts, said that although the main treatment strategy for CMA is avoidance, an epinephrine autoinjector should be prescribed for individuals who have a physician-diagnosed IgE-mediated allergy. She adds that one large study of parent-reported food allergy found that just 26% of children with CMA had a current epinephrine autoinjector prescription. “Being prepared to treat a severe allergic reaction is also imperative,” Lowry added. “For patients with severe reactions or anaphylaxis, strict avoidance of cow’s milk products and carrying injectable epinephrine at all times is essential.”

Caregivers also need to be educated on milk allergen avoidance, as well as how and when to use an epinephrine autoinjector. Investigators are testing different protocols for CMA immunotherapy to help achieve a maintenance dose and develop a tolerance for milk proteins, according to Wright. Until those tools are available, she said, it’s key to educate parents about CMA, including true allergy vs intolerance, and the importance of learning how to introduce common foods early to early to prevent common food allergies.

Rachael Zimlich is a freelance medical writer in Cleveland, Ohio. She has nothing to disclose.
Vaccines for COVID-19 and RSV: An update

William J. Muller, MD, PhD, discusses COVID-19 vaccinations for children and what is on the horizon for a potential RSV vaccine.

Contemporary Pediatrics®: Could you explain in some detail what caused the delay in allowing children 4 years and younger to be eligible for the COVID-19 vaccine?

William J. Muller, MD, PhD: The Pfizer/BioNTech delay has been related to the second of the 2-dose series not inducing the same level of antibody response in younger children, those between the ages of 2 and 5 years. A lot of the pediatric studies have not been designed to show efficacy against preventing either symptomatic disease or hospitalization in this age group. Everybody is aware by now that children are not as severely affected as adults are by COVID-19. So...
it was reasonable for all the vaccine studies that I’m aware of in children to be designed to use surrogate end points—basically, how good are the immune responses produced?—and antibody levels are a reasonable surrogate for that. That’s the way that the companies have gone into studying these vaccines in children.

I think Pfizer/BioNTech was not expecting as low of an antibody response in that age group as they measured in later stages of the study. That’s what they’re studying now, and it takes time to do that. They needed to bring all the participants back in for an additional dose, and they needed to get additional consent from the parents because that was not part of the initial study design. There are also concerns in adolescent and young adult males, in particular about possible cardiac effects of the mRNA vaccines, so that will be on their radar throughout the study. That added to the complexity and the amount of time it will take to get through all the data.

That’s for the Pfizer/BioNTech vaccine. We may not need 3 doses of the Moderna vaccine, which is studying 2 doses for children aged 6 months to 12 years. The expectation is that 2 doses will be sufficient to induce an immune response.

**CP:** As far as COVID-19 variants, going forward, where are we at in trying to be proactive?

**WJM:** The mRNA vaccine platforms are easily adapted to generating new variant vaccines. The technology that goes into putting a piece of mRNA into the lipid nanoparticle that is delivered as part of the vaccine doesn’t change when there’s a new variant; only the material that’s put into the vaccine would change. So from that standpoint, it’s not that difficult for a company to make a new vaccine for a variant.

Do the vaccines need to show the same level of efficacy? Probably not; I think they really need to show safety and some level of an immune response. All that said, it seems the existing vaccines now have a 3-dose series in adults; we don’t know necessarily yet for children if 2 or 3 doses will be necessary for all the mRNA vaccines, but there are reasonably good data that the immune responses induced may still provide a level of protection that is reasonable. Whenever there is a new variant, there are basic science laboratories in various parts of the world that are poised to immediately do studies with model systems in which they can put the variants into a virus that is not pathogenic and ask the question “Do the antibodies from some of the recipients of the vaccine provide some level of protection in a laboratory study?”

With the Omicron surge being so big, we were able to get a pretty good idea of whether people who had received the vaccine were significantly less likely to have significant consequences from infection. And the answer is that they seem to be much more protected from infection. Children aged 5 years and older who have been eligible for vaccination were really protected from hospitalization during the Omicron surge, and even at our hospital [Ann...
& Robert H. Lurie Children’s Hospital of Chicago in Illinois, we have good evidence that the increased number of hospitalizations in children was largely among either the unvaccinated or those who were not eligible for the vaccine.

**CP:** Do you foresee a time in the near future when the COVID-19 vaccine for adults and eligible children will be just part of the annual vaccination schedule, like with influenza?

**WJM:** I think there will be an expectation of a recommended vaccine for children and adults on some scheduled basis. And I think that the unanswered question right now is “Will we need it every year, like we recommend the influenza vaccine every year, or can it be spaced out over a longer time period?” It’s certainly too soon to tell if the current vaccines will offer lifelong protection. I don’t think I would expect that to be true. But, I don’t want to get too far off from what we know now.

**CP:** What about other COVID-19 vaccines?

**WJM:** More vaccines will become available. Recently, Sanofi and GSK [GlaxoSmithKline] asked for authorization for a protein-based vaccine for adults. As far as I know, the data are not yet sufficient in children to ask for authorization. But that will give families a potential alternative, which may be beneficial in situations where, for example, somebody has an allergic reaction to mRNA vaccines. Another company, Novavax, is also making a protein-based vaccine, so there will be 2 additional protein-based options.

Currently, there is 1 other protein-based option under study, which is a vaccine being made from plants, Covifenz, from Medicago and GSK. [Editor’s note: As of this writing, Covifenz is approved for use in Canada for adults aged 18 to 64 years.]. So, if somebody has objections to the manufacturing process associated with some vaccines, this could alleviate those concerns. I expect there to be more options within the COVID-19 vaccine area.

The other questions will involve alternative dosing schedules. There’s been some discussion recently about extending dosing between the first and second dose in adolescents and young adults. Early on in the pandemic, there were reasons to get the 2 doses close together. First, it made the studies go faster, and we needed something authorized quickly. That was a reasonable thing to do. Second, we wanted to get people protected sooner. That’s becoming less true as there is more population immunity. Maybe spacing out the doses [further] would be a practical approach.

**CP:** What about vaccines for other infectious diseases in pediatrics—is there anything of particular interest?

**WJM:** There certainly has been a lot of discussion recently about another illnesses of significant importance in pediatrics, notably RSV [respiratory syncytial virus]. Different strategies have been looked at to try to protect babies against severe disease from RSV infection. The first would be maternal vaccination—if the mom was able to get sufficient levels of antibodies, passive immunity could be passed from her to the baby. So far, those study findings have not necessarily shown protection. But as we learn more from the research, other vaccines might be developed to increase the mother’s ability to generate a protective response that doesn’t necessarily require the baby to get a separate immunization. I know that there are some studies as well that involve immunization of the baby, which could be active immunization for RSV—similar to the COVID-19 vaccine, in which the immune response that’s generated against the vaccine is what’s providing protection. And then there is passive immunity: That would provide protection against RSV by getting an antibody into the baby as opposed to inducing the production of antibodies. So, we will have to wait and see.

**REFERENCE**


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Diaper dermatitis is a common presentation seen in dermatology. The differential diagnosis is broad and varies based on numerous risk factors, including patient age, gastrointestinal disorders, diaper hygiene practices, diaper breathability, and genetics. It is essential that pediatricians and dermatologists recognize the various forms of diaper dermatitis to effectively diagnose and treat it. The following 5 instructive cases of diaper dermatitis include the differential diagnosis (Table) and treatment options.

Match the photos to the answer choices below.
A. Seborrheic dermatitis
B. Candidiasis
C. Jacquet dermatitis
D. Psoriasis
E. Staphylococcal pustulosis

Turn the page for answers.
This 18-month old boy with a family history of psoriasis presented for evaluation of an erythematous rash on the scrotum, suprapubic skin, and perineum, consistent with infantile psoriasis. Similar to adult psoriasis, infantile psoriasis presents as well-defined, often symmetrically distributed erythematous papules and plaques. In contrast to psoriasis in adults, psoriatic plaques in childhood tend to be thinner, smaller, and less scaly and are more likely to develop on the face, trunk, and flexural areas, although they can develop on any skin area. In young children, infantile psoriasis is often diagnosed with a diaper rash that is unresponsive to irritant diaper dermatitis treatment.

**PREVALENCE.** Psoriasis affects approximately 2% to 3% of the population worldwide, and it is estimated that up to half of cases begin before age 20 years. The incidence increases with age. Results of one study showed that the total rate of psoriasis in children under 18 years old was 0.71%, with rates increasing linearly from 0.12% at 1 year of age to 1.2% by 18 years. Findings of another study were similar, showing a prevalence of 0.55% in children aged 0 to 9 years compared with 1.37% in patients aged 10 to 19 years.

**DIFFERENTIAL DIAGNOSIS.** Making a diagnosis of psoriasis is often more difficult in children because of atypical characteristics. Lesions in children may be thinner, softer, less scaly, and less well-defined than in adults. The differential diagnosis should include tinea corporis/cruris, atopic or nummular dermatitis, irritant contact dermatitis, seborrheic dermatitis, *Candida* dermatitis, and inverse pityriasis rosea.

**WORK-UP.** Diagnosis of infantile psoriasis is often clinical and, in unclear cases, can be aided by biopsy; however, biopsy is often not necessary and should be avoided in uncomplicated cases. Histology is similar to that of adult psoriasis and would reveal neutrophils overlying parakeratosis, loss of the granular cell layer, variable spongiosis, and elongated rete ridges.

**TREATMENT.** First-line therapy for infantile psoriasis is topical corticosteroids. Medium- to high-potency topical steroids can be used up to 4 weeks during the initial flare and then up to 2 weeks for subsequent flares. Using topical corticosteroids in combination and rotation with nonsteroidal topicals such as topical calcineurin inhibitors, vitamin D analogues, tar, and keratolytics can optimize efficacy while reducing the risk of adverse effects. It is important to know the ages of approval for steroid-sparing agents. Calcipotriene is approved for children 4 years or older, and topical calcineurin inhibitors are approved for patients 2 years or older. Crisaborole (Eucrisa) can be considered in patients 3 months or older. Phototherapy can also be considered for extensive or refractory disease. For moderate to severe plaque psoriasis in children, systemic therapy should be considered. Etanercept (Enbrel) is approved for children 4 years or older; ustekinumab (Stelara), ixekizumab (Taltz), and secukinumab (Cosentyx) are all approved for children 6 years or older. Studies have shown significant improvements in quality of life and psoriasis area and severity index scores for children with moderate to severe plaque psoriasis on systemic immunomodulators. Pediatricians should monitor patients for comorbidities associated with psoriasis, including obesity, hypertension, hyperlipidemia, rheumatoid arthritis, and diabetes. The patient in the vignette responded well to topical steroids.

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**Figure 2. Answer: C—Jacquet dermatitis**

This 6-month-old girl presented with an erosive diaper rash following diarrhea with viral gastroenteritis. These findings were consistent with Jacquet erosive diaper dermatitis. Jacquet dermatitis is a rare, severe form of irritant diaper dermatitis characterized by ulcerated or eroded papules and nodules in the genital and perianal areas. It is typically associated with frequent loose stools, infrequent diaper changes, and poor hygiene. It is also more common in patients with chronic diarrhea or incontinence.

**DIFFERENTIAL DIAGNOSIS.** Milder forms of irritant diaper dermatitis often occur in infants with short episodes of loose stools associated with viral gastroenteritis and administration of oral antibiotics for otitis media and other infections. The differential diagnosis for severe erosive diaper dermatitis includes perianal pseudoverrucous papules and nodules, granuloma gluteale infantum, **CONTINUED ON PAGE 30**
# Differential Diagnosis Summary

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Clinical Presentation</th>
<th>History</th>
<th>Work-Up</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psoriasis</strong></td>
<td>Well-defined, symmetrically distributed erythematous papules and plaques</td>
<td>Family history of psoriasis; can occur at any age; affects 2%-3% worldwide, with prevalence increasing with age</td>
<td>Diagnosis is typically made by clinical examination but can be aided by biopsy neutrophils overlying parakeratosis, loss of the granular cell layer, variable spongiosis, and elongated rete ridges.</td>
<td>A. Topical corticosteroids are the treatment of choice. B. Calcipotriene, topical calcineurin inhibitors (for patients &gt; 2 years), and phototherapy can be used in conjunction. C. Systemic therapy is reserved for moderate to severe plaque psoriasis, consisting of etanercept for children ≥ 4 years or older and ustekinumab, ixekizumab, and secukinumab for children ≥ 6 years or older.</td>
</tr>
<tr>
<td><strong>Jacquet dermatitis</strong></td>
<td>Ulcerated or eroded papules and nodules in the genital and perianal areas</td>
<td>Associated with a history of frequent loose stools, infrequent diaper changes, and poor hygiene, chronic diarrhea, or incontinence</td>
<td>Clinical; can consider KOH and bacterial culture</td>
<td>A. Frequent diaper changes and use of diapers with absorbent gel material B. Barrier ointments C. Low-potency topical steroids D. Topical antifungals or antibacterial if secondary infection present E. Oral antibiotics or corticosteroids for severe cases</td>
</tr>
<tr>
<td><strong>Staphylococcal pustulosis</strong></td>
<td>Pustules in the diaper area</td>
<td>Previous or current <em>Staphylococcus aureus</em> infection</td>
<td>Bacterial culture for confirmation. Biopsy is typically not performed, but histology would show subcorneal pustules with neutrophils and acantholysis.</td>
<td>A. Limited skin disease is treated with topical mupirocin ointment. B. Systemic symptoms require oral antibiotics, such as amoxicillin for <em>S aureus</em> and TMP/SMX for MRSA coverage.</td>
</tr>
<tr>
<td><strong>Seborrheic dermatitis</strong></td>
<td>Erythematous rash with salmon-colored plaques and greasy scales</td>
<td>NA</td>
<td>Diagnosis is typically made by history and clinical examination. In unique cases, a biopsy may be required, which would show neutrophilic follicular scale/crust and/or shoulder parakeratosis.</td>
<td>A. Emollients B. Short courses of low-potency topical steroids</td>
</tr>
<tr>
<td><strong>Candidiasis with irritant dermatitis and candidiasis pustules</strong></td>
<td>Erythematous papules coalescing into plaques, peripheral satellite lesions, a few scattered pustules, skinfolds, vesicles, and erosions</td>
<td>NA</td>
<td>KOH preparation will confirm the presence of yeast and pseudohyphae. A biopsy is typically not required but, if performed, will show neutrophils, vertically oriented pseudohyphae in the stratum corneum, crusting, and hyperkeratosis.</td>
<td>A. Antifungals effective against <em>Candida</em>, such as nystatin and clotrimazole, are required. B. Education on breathable diapers can prevent recurrence.</td>
</tr>
</tbody>
</table>

KOH, potassium hydroxide; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not available; TMP/SMX, trimethoprim/sulfamethoxazole.
dermatology

CONTINUED FROM PAGE 28
diaper dermatitis with superimposed bacterial and fungal infections, cutaneous Crohn disease, Langerhans cell histiocytosis, and acrodermatitis enteropathica.

WORK-UP. Secondary infection with Candida and bacteria is common in Jacquet dermatitis. Potassium hydroxide (KOH) preparation and bacterial culture can be performed to help guide antimicrobial therapy. If the patient fails to respond to therapy or has systemic findings, biopsy and additional laboratory tests may be indicated.

Figure 3. Answer: E—staphylococcal pustulosis
This 7-month-old boy was brought to the clinic for pustules in the diaper area. These findings were consistent with staphylococcal pustulosis, a relatively uncommon manifestation of infection with Staphylococcus aureus. It can be difficult to diagnose because there is a wide differential for pustular eruption in infants, which includes both infectious and noninfectious etiologies. It is important to be able to distinguish benign causes from more serious causes that require additional management.

DIFFERENTIAL DIAGNOSIS. Noninfectious causes of pustules in an infant include erythema toxicum neonatorum, transient neonatal pustular melanosis, neonatal acne, and neonatal pustular psoriasis. In this case, some of those conditions could be ruled out based on timing. Erythema toxicum neonatorum typically affects full-term infants and presents within 1 to 2 days of birth. It is self-limited and usually resolves by 2 weeks of age. Neonatal pustular melanosis affects 0.2% to 4% of neonates, with a higher prevalence in Black babies. It usually occurs within a few days of birth and resolves spontaneously over a few weeks. Neonatal acne and pustular psoriasis have a wider range of age presentations. Neonatal acne presents as pustules as well as open and closed comedones that are usually limited to the face. It can occur within 3 to 16 months of age, although it usually appears within 3 to 6 months and resolves by 3 to 4 years. Neonatal pustular psoriasis is rare but can occur at any age and has a varied presentation. Pustules typically develop symmetrically and can occur on any area of the body, with a predilection for the diaper area and skinfolds.

Infectious causes include herpes simplex infection and candidiasis. Cutaneous manifestations of vertical herpes simplex virus (HSV) infection have been reported but are relatively rare and occur within a few days of life. Anogenital HSV infection in older babies and toddlers is also rare; it has additional implications and can be a sign of abuse. Candidiasis usually presents on a base of erythema with erythematous macular satellite lesions, neither of which is seen in this case.

To confirm the diagnosis, Gram stain and culture of the pustule fluid can be performed. Gram stain is often negative even in the setting of positive cultures and should not be used alone to rule out staphylococcal pustulosis. HSV polymerase chain reaction can be performed concomitantly if suspected.

WORK-UP. Biopsy typically does not play a role in the diagnosis of staphylococcal pustulosis. Although biopsy is often not performed for these lesions, histology would show subcorneal pustules with neutrophils and acantholysis.

TREATMENT. Jacquet dermatitis treatment is similar to that of uncomplicated irritant diaper dermatitis, with the goal to reduce contact of the skin to urine and feces. This is accomplished through frequent diaper changes, use of diapers lined with absorbent gel materials, and application of barrier ointments. Low-potency topical steroids can also be used to reduce inflammation. Topical antifungal/antibacterial agents may be required in the case of secondary infection. Severe cases may require oral antibiotics and/or oral corticosteroids.

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Figure 4. Answer: A—seborrheic dermatitis
This 3-month-old boy presented for evaluation of an erythematous rash in a diaper distribution; findings were consistent with seborrheic dermatitis. This benign, self-limited condition presents as salmon-colored plaques with greasy scales and typically occurs within the first 3 months of life. Unlike seborrheic dermatitis in adults, which takes on a chronic course, seborrheic dermatitis in children is self-limited and usually resolves without treatment within the first 9 to 12 months of life. Many parents are familiar with the term cradle cap, which is infantile seborrheic dermatitis of the scalp, but the condition can also present on the face, axillae, inguinal folds, and trunk. When it occurs on the face, it tends to involve the eyebrows, nasolabial folds, and hairline. Lesions on the trunk usually involve the lower abdomen and are more sharply demarcated than those seen elsewhere on other body.

DIFFERENTIAL DIAGNOSIS. The differential diagnosis for symmetric, well-demarcated erythematous patches and plaques on a baby’s lower abdomen includes psoriasis, candidiasis, atopic dermatitis, contact dermatitis, and nutritional deficiency. Contact dermatitis is less likely when the skinfolds are affected. It is often difficult to distinguish atopic from seborrheic dermatitis in young children, and there can be overlap of the 2 conditions. However, seborrheic dermatitis is not usually pruritic, and atopic dermatitis typically spares the groin and axillae in young children.

WORK-UP. Diagnosis is usually made by history and physical exam alone. In cases where the diagnosis is not clear or the patient has an unusually prolonged course or lack of response to treatment, biopsy can be performed. Seborrheic dermatitis and psoriasis have similar histopathological findings, with a few key differences. Mounds of parakeratosis with neutrophils and clubbed and evenly elongated rete ridges are seen more often in psoriasis. Neutrophilic follicular scale/crust, shoulder parakeratosis, and lymphocytic exocytosis are seen more often in seborrheic dermatitis.7 A KOH preparation can be performed to rule out candidiasis. Patients with infantile seborrheic dermatitis are otherwise healthy and do not require additional laboratory monitoring.

TREATMENT. The mainstay of treatment for seborrheic dermatitis in infants consists of emollients that help loosen the scale, which can then be gently wiped away with a cloth. Because this is a self-limited disease that resolves without treatment, the risk to benefit ratio of additional therapies needs to be considered. Furthermore, treatments for seborrheic dermatitis in children have not been studied extensively for safety or efficacy, and it is unclear whether these interventions alter the course of the condition.8 Short courses of low-potency topical steroids also can be used. Calcineurin inhibitors and antifungal shampoos are not approved for use in children under the age of 2, so they should be avoided. The patient in the vignette responded well to emollients and topical steroids. He was able to discontinue therapy and did not have recurrence on follow-up a few months later.

Figure 5. Answer: B—candidiasis with irritant dermatitis and candidiasis pustules
This girl between 5 and 6 months of age presented with a red rash in a diaper distribution. Findings showed erythematous papules coalescing into plaques, satellite lesions, and a few scattered pustules consistent with candidiasis, which usually presents as red erythematous papules, plaques, and peripheral satellite lesions in the groin with a predilection for skinfolds. Pustules, vesicles, and erosions can also be seen.

DIFFERENTIAL DIAGNOSIS. The differential diagnosis for an erythematous rash with plaques, papules, and pustules in a diaper distribution includes psoriasis and contact dermatitis.

WORK-UP: For this case, KOH preparation was performed and showed yeast and pseudohyphae. Although biopsy is often not required, histology would show neutrophils and vertically oriented pseudohyphae in the stratum corneum. Crusting and hyperkeratosis are also commonly seen.

TREATMENT. Treatment with antifungal antifungals such as nystatin and clotrimazole is required to achieve clearance. This patient responded well to topical antifungals and barrier cream therapy. Parents also can be educated to use breathable disposable diapers to reduce the rate of recurrence—the survival of Candida is reduced more than 50% in breathable vs nonbreathable diapers.
Less is more: Use the shortest effective duration of antibiotics

Follow best practices when prescribing antibiotics in the pediatric population

Rana F. Hamdy, MD, MPH, MSCE

Pediatricians tend to be more judicious in prescribing antibiotics than our colleagues in adult medicine, but there remains much room for improvement in ambulatory pediatrics. Reducing therapy to the shortest effective duration may be one of the highest-yield practice changes to decrease unnecessary antibiotic exposure in pediatric patients.

Antibiotic resistance is a growing threat to public health, and antibiotic use (prescribed for a wide variety of pediatric illnesses such as common respiratory disorders) is the primary driving factor that leads to resistance. Many pediatricians may have been taught that not completing a prescribed course could lead to antibiotic resistance. In fact, it is longer exposure to antibiotics that exerts greater selective pressure on bacteria, increasing the risk of resistance.¹

Adverse drug events (ADEs) are another important consideration in the mission to reduce unnecessary antibiotic use. The findings of one study showed that almost half of all emergency department visits for ADEs in children were due to antibiotics.² In one study across a large primary care pediatric network, 29% of all antibiotic courses prescribed for acute respiratory tract infection resulted in an ADE.³ In the inpatient setting, each additional day of antibiotic use has been shown to be associated with a 7% increased risk of developing an antibiotic-related ADE.⁴ Longer duration of therapy is also an important risk factor for Clostridioides difficile infections.⁵

Therapy should be prescribed for the shortest effective duration. For some indications, that means 0 days. This article discusses several childhood illnesses and recommended durations

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<tr>
<th>DIAGNOSIS</th>
<th>DURATION OF THERAPY</th>
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<tbody>
<tr>
<td>Ear, nose, throat infections</td>
<td></td>
</tr>
<tr>
<td>Acute otitis media*</td>
<td></td>
</tr>
<tr>
<td>Nonsevere,* age ≥ 6 years</td>
<td>Watchful waiting recommended; if antibiotics are prescribed: 5 days</td>
</tr>
<tr>
<td>Nonsevere,* age 2-5 years</td>
<td>Watchful waiting recommended; if antibiotics are prescribed: 7 days</td>
</tr>
<tr>
<td>Nonsevere,* age 6-23 months, unilateral</td>
<td>Watchful waiting recommended; if antibiotics are prescribed: 10 days</td>
</tr>
<tr>
<td>Nonsevere,* age 6-23 months, bilateral</td>
<td>10 days</td>
</tr>
<tr>
<td>Severe*</td>
<td>10 days</td>
</tr>
<tr>
<td>Otitis media with effusion</td>
<td>No antibiotics</td>
</tr>
<tr>
<td>Presence of cough, rhinorrhea, hoarseness, or conjunctivitis</td>
<td>Likely viral—do not test for GAS; no antibiotics</td>
</tr>
<tr>
<td>GAS pharyngitis</td>
<td>10 days</td>
</tr>
<tr>
<td>Acute bacterial sinusitis*</td>
<td></td>
</tr>
<tr>
<td>Severe signs (fever &gt; 39 °C, purulent rhinitis &gt; 3 days)</td>
<td>10 days</td>
</tr>
<tr>
<td>Worsening symptoms/new fever after initial improvement</td>
<td>10 days</td>
</tr>
<tr>
<td>Persistent symptoms &gt; 10 days without improvement</td>
<td>Watchful waiting recommended; if symptoms worsen: 10 days</td>
</tr>
<tr>
<td>Viral upper respiratory tract infection</td>
<td>No antibiotics</td>
</tr>
<tr>
<td>Community-acquired pneumonia</td>
<td>5 days</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>No antibiotics</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>No antibiotics</td>
</tr>
<tr>
<td>Skin infections</td>
<td></td>
</tr>
<tr>
<td>Cellulitis*</td>
<td>5 days*</td>
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<tr>
<td>Subcutaneous abscess without surrounding cellulitis</td>
<td>Incision and drainage No antibiotics</td>
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<tr>
<td>Genitourinary infections</td>
<td></td>
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<tr>
<td>Urinary tract infection</td>
<td></td>
</tr>
<tr>
<td>Simple cystitis</td>
<td>3 days</td>
</tr>
<tr>
<td>Pyelonephritis*</td>
<td>7 days</td>
</tr>
<tr>
<td>Asymptomatic bacteriuria*</td>
<td>No antibiotics</td>
</tr>
</tbody>
</table>

GAS, group A streptococcal

*Severe signs of acute otitis media: fever > 39 °C, severe otalgia > 48 hours.

*May be extended if infection has not improved in this time period or shortened for minor infections with rapid improvement.
[Antibiotic] therapy should be prescribed for the shortest effective duration. For some indications, that means 0 days.

Respiratory infections

Acute otitis media
Acute otitis media (AOM) is the most common indication for antibiotics in children, and 95% of children with AOM are prescribed antibiotics. However, most children with AOM will improve without antibiotics. The number of patients needed to treat for symptomatic benefit after 2 to 3 days is 20, whereas the number needed to harm with an antibiotic-related ADE is 4. For this reason, the 2013 American Academy of Pediatrics (AAP) clinical practice guidelines recommend watchful waiting for children older than 6 months with mild to moderate unilateral AOM. Findings have shown that for most children with AOM given antibiotics, there is no difference in treatment failure between those who receive 5 days and those who receive 7 or more days of therapy. When antibiotics are prescribed, high-dose amoxicillin remains the first-line antibiotic treatment for AOM.

Pharyngitis
Group A streptococcal (GAS) pharyngitis is the second most common indication for antibiotics in ambulatory pediatrics. Although the standard recommended antibiotic duration for confirmed GAS pharyngitis remains 10 days, the greatest opportunity for antibiotic stewardship in this setting lies in testing for GAS pharyngitis only when indicated; this reduces the likelihood of identifying and treating false positives that represent chronic pharyngeal GAS colonization in patients with viral pharyngitis. Because 20% of healthy, asymptomatic children can be chronic pharyngeal GAS carriers at any given time, it is important to test only when there is a high pretest probability for GAS vs viral pharyngitis. This means not testing when a patient has viral upper respiratory infection symptoms including cough, rhinorrhea, congestion, conjunctivitis, and hoarseness or in a child younger than 3 years who has a low likelihood of GAS pharyngitis.

Community-acquired pneumonia
In the past year, the results of 2 multi-institutional, randomized controlled trials showed no difference in treatment failure or recurrence of infection in children who received short-course (5 days) vs long-course (10 days) antibiotics. High-dose amoxicillin remains the first-line antibiotic treatment for community-acquired pneumonia believed to be bacterial.

Cellulitis
Skin and soft-tissue infections are unique in that clinical improvement is easily visible, so antibiotic duration can easily be tailored based on clinical improvement. Clinical practice guidelines from the Infectious Diseases Society of America recommend 5 days of antibiotics for cellulitis. For an extensive case, if evidence of active infection remains after 5 days of therapy, then the course should be extended. On the other hand, for a more minor skin infection, if clinical resolution is shown after 3 days of therapy, then antibiotics could be discontinued. For abscesses without surrounding cellulitis, the guidelines recommend incision and drainage alone, without additional need for antibiotics.

Urinary tract infections
For simple cystitis (ie, symptomatic urinary tract infection with pyuria and positive urine culture but without symptoms suggesting pyelonephritis, such as flank pain, costovertebral angle tenderness, or fever), it has long been known that for adult patients, short courses of antibiotics (1-3 days, depending on antibiotic choice) are sufficient. Pediatric guidelines recently adopted these standards to shift recommendations to short courses (3 days). For pyelonephritis, the AAP’s 2011 guidelines recommend a range of 7 to 14 days. More recent data show that a 7-day course for pyelonephritis results in similar outcomes, including infection recurrence or treatment failure, with lower rates of ADEs compared with longer courses.

Conclusion
When prescribing antibiotics, the first consideration is whether antibiotics are indicated: How certain is the diagnosis (eg, otitis media with effusion vs AOM, viral vs bacterial pneumonia)? Is this a condition (eg, AOM, sinusitis) for which watchful waiting is a safe option? When antibiotics are definitely indicated, the shortest effective duration must be prescribed to minimize harm to patients.
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For the first time in nearly 80 years, there is a clinically studied generic hypoallergenic formula that delivers comparable tolerance as a leading brand in patients with confirmed CMA.¹

Parents need and deserve an affordable option that is safe, efficacious and meets the same AAP hypoallergenicity standards² as the expensive name brands. And as their pediatric provider, you can now recommend a lower cost option with confidence.

**Non-reactivity incidence (%)**

<table>
<thead>
<tr>
<th>AAP Criterion</th>
<th>Store Brand Hypoallergenic (G19) &amp; a leading national brand meet AAP hypoallergenic criterion.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>98.3%</strong></td>
<td><strong>98.3%</strong></td>
</tr>
<tr>
<td><strong>One-sided lower 95% bound of mean non-reactivity rate &gt;90%</strong></td>
<td><strong>One-sided lower 95% bound of mean non-reactivity rate is &gt;94.3%</strong></td>
</tr>
</tbody>
</table>

For U.S. Healthcare Professionals
