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.¹ The CDC now recommends considering an opt-out approach for young women under 25.² Universal screening is an inclusive solution that is proven to decrease STI prevalence, infertility issues and cost.² Let’s help protect her reproductive health today, and tomorrow.

Learn more at

Contemporary Pediatrics® mourns the passing of Michael J. Hennessy Sr, chairman of MJH Life Sciences®, Mike Hennessy Sr., the founder of MJH Life Sciences®, was committed to improving health care, as is seen throughout his career. Following his graduation from Rider University in 1982, he started in medical publishing as a sales trainee, advancing, in 1986, to the position of chief operating officer of Medical World Business Press. The company prospered and was eventually sold to a Boston-based venture capital firm.

Hennessy launched MultiMedia Healthcare, LLC, in 1993 and built a portfolio of award-winning clinical journals. In 2001, Freedom Communications, Inc, acquired MultiMedia HealthCare, about the time that Hennessy was pioneering a new approach to print and digital publishing with Intellisphere®, LLC (now part of MJH Life Sciences®). Hennessy added other companies and capabilities to the MJH Life Sciences® portfolio, including health care market research leader Healthcare Research & Analytics, respected journals Pharmacy Times® and The American Journal of Managed Care®, and the leading accredited continuing medical education company Physicians’ Education Resource®, LLC (PER®).

In 2019, MJH Life Sciences® made its largest acquisition to date with the Healthcare and Industry Sciences divisions of UBM Medica, nearly doubling the size of the company. This acquisition made the organization the largest independently owned medical communications company in North America. Hennessy also elevated his role to Chairman while naming his son, Mike Hennessy Jr, President and CEO. Under Mike Jr’s leadership, the company enhanced its global potential by entering into a long-term partnership with BDT Capital Partners, LLC, in November 2021.

Hennessy’s true passion was his relationship with his wife, Patrice “Patti” Hennessy. After meeting her in college, Hennessy devoted his life to Patti and his family, raising 4 children. Hennessy was Patti’s rock as she bravely battled cancer for almost 10 years until her death in January 2020. Hennessy recently honored Patti by making a donation to Rider University to expand the Science and Technology Center at their alma mater. The Mike and Patti Hennessy Science and Technology Center is set to be completed this year. Hennessy’s legacy and “family first” mantra will live on through his children, their spouses, and his 10 grandchildren. He will be greatly missed by his family, friends, and his MJH Life Sciences® family.
Happy New Year!

It is hard to believe that 2022 (Chinese zodiac Year of the Tiger) has started. We begin the year, unfortunately, with COVID-19 still front and center of health care news. The Omicron variant has, as of this writing, spread to more than 110 countries, including here in the United States. This variant contains 30 mutations in the spike protein, which makes it highly transmissible and has been noted to be the most rapidly spreading of all the SARS-CoV-2 variants. The current COVID-19 vaccines provide some protection against this variant, although less than against the other variants. The risk for breakthrough infections and hospitalizations among those that are fully vaccinated is increased with the Omicron variant.

On a more promising note, ever since the US Food and Drug Administration granted emergency use authorization for the Pfizer/BioNTech vaccine for children aged 5 to 11 years, an estimated 20% of those in this age group (as of this writing) have received at least 1 dose of the vaccine. Let’s hope this trend continues.

This month’s January/February issue packs a number of must-read articles:

- The Pediatric Pharmacology section features an excellent piece on harmful pharmaceutical excipients (eg, protein stabilizers, solvents, preservatives). We don’t think about this problem very often, but some of these agents can cause adverse reactions in certain patients.

- The Mental Health section offers a sobering look at the gun violence crisis, and particularly the dangers it presents for children in underserved areas. This includes commentary by Steven Selbst, MD, a member of the Contemporary Pediatrics editorial board.

- The Nutrition section’s article explores the reasons behind the poor eating habits of adolescents. It also provides some practical recommendations for ways to improve their food choices.

- The Respiratory and Infections Diseases section discusses the crossover symptoms of COVID-19 and influenza, infections that everyone will be seeing in their practices. This piece was cowritten by Russell Libby, MD, also a member of the Contemporary Pediatrics editorial board.

Thank you for providing outstanding care to your patients during these rapidly changing times. “Wishing you a Happy New Year! May it be filled with new adventures and good fortunes.” (Anonymous.)

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

With warm regards,

Tina Q. Tan

e-mail: titan@luriechildrens.org
nutrition

20 Eating habits of children during COVID-19
For decades, adolescents have been known to veer toward processed food choices. And then, along came COVID. Sarah Lowry, MD, and Darla Shores, MD, PhD

puzzler

10 Severe hemorrhage from infantile hemangioma
A 5-month-old girl presents with a large scalp hemangioma. Caitlin Brumfiel, MS, Chelsey Huffman, MD, and Kaiane Habeshian, MD

infectious disease/respiratory disorders

14 Crossover symptoms of COVID-19 and influenza
Here is how to best detect and differentiate. Russell Libby, MD, FAAP; and Mary E. Schmidt, MD, MPH, FIDSA

mental health

24 Impact of poverty on gun violence
A study looks at the gun violence dangers children in underserved areas face. Miranda Hester

pediatric pharmacology

26 Harmful excipients for pediatric patients
Some medication excipients may have adverse effects on children. Amanda Clouser, PharmD; and Emily Diseraod, PharmD, BCPPS

dermatology

32 Generalized, eruptive lichen planus in a pediatric patient
A 14-year-old presents with acute onset of an intensely itchy rash. Joseph George; Taryn Murray, MD, and Michelle Bain, MD

in addition

3 IN MEMORIAM
4 EDITOR’S VIEW
8 JOURNAL CLUB
31 MEDICAL WORLD NEWS®
35 ADVERTISING INDEX

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Gestational diabetes can have lasting effects on child health

Children born to mothers with gestational diabetes mellitus (GDM) are at increased risk of developing asthma and wheeze, according to a study involving more than 1000 mother-child pairs. The participants, who were in the second trimester when the investigation began, were drawn from an existing, predominantly Black study group in Tennessee. Participants responded to questionnaires and provided biospecimens throughout the remainder of their pregnancies. In addition, birth records provided information about pregnancy complications and labor and delivery. Postnatally, 1100 pairs participated in annual in-person clinic visits through the child’s third year and again at about age 4 years. At the 4-year visit (which also included children up to 6.5 years), investigators administered parental questionnaires to assess each child’s history of wheeze and asthma.

Investigators documented GDM for 62 (5.6%) of pregnant participants. Compared with other women in the study, those with GDM were older and had a higher socioeconomic status and pre-pregnancy body mass index. Women with GDM also gained less weight during pregnancy and were more likely to experience preeclampsia/gestational hypertension. In addition, children born to mothers with GDM were larger at birth. GDM status was not affected by maternal history of asthma.

At follow-up, wheeze and asthma were more common among children born to women with GDM than among those born to women without the condition. Overall, reported prevalence of current wheeze and asthma was 19% vs 15.7%, respectively. Among children of women with GDM, 30.6% had current wheeze compared with 18.3% of children of women without GDM; 27.4% vs 15.9%, respectively, had current asthma; and 25.8% vs 13.4% had diagnosed asthma. The differences held even after adjusting for multiple potential confounding factors. Investigators therefore concluded that GDM may be a risk factor for childhood asthma.

Here is another instance where we need to look to our adult medicine colleagues to help optimize health for babies yet to be born. However, the rate of GDM is rising because of increasing obesity/overweight, so if we can support our current patients in establishing and maintaining their recommended weight, we will help keep the next generation of children healthy.

REFERENCE
Depressive symptoms in youngsters with celiac disease (CD) account for low quality of life (QOL) at adolescence, but disease-related lifestyle adjustments, such as following a limited diet, are not related to reduced QOL. That surprising finding arose from a prospective survey of 12- to 18-year-old patients with CD and their caregivers, who completed standard measures of adjustment to CD, depression, and QOL. Depression was the only statistically significant correlate of QOL in the study’s 105 patients.

Although both patients and parents reported high levels of depression symptoms in the patients, no associations were found between QOL and age, duration of CD, duration of time on a gluten-free diet, or current symptoms. Investigators also found that depression scores in teens with CD are high and comparable with those reported by psychiatric clinics of adolescents who received diagnoses of mental health disorders. Identifying and addressing these symptoms may improve adherence to dietary guidelines for CD, the investigators noted. In addition, because high rates of depression may affect CD prognosis, screening for depression in these adolescent patients appears critical, according to the authors.

Depression is common in chronic disease, and we should always be on the lookout for it. The results of this study showed that, unlike with other diseases, “worse” CD was not a significant factor, suggesting that depression was more likely to be primary rather than caused by having a chronic illness. As such, “improving” the disease would not be expected to improve depression.

**REFERENCE**


Are you screening for autism when—and as often as—you should?

Primary care providers (PCPs) do not consistently provide developmental and autism spectrum disorder (ASD)-specific screenings recommended by the American Academy of Pediatrics (AAP), according to recent findings. The AAP calls for systematic developmental screening at all 9-, 18-, and 24- or 30-month well-child visits (WCVs) and additional ASD-specific screening at all 18- and 24-month WCVs.

Using self-reported and chart-reviewed data, investigators examined the practices of 94 PCPs from 13 states; 79% of participants were pediatricians, and the remainder included family practice physicians, nurse practitioners, and physician assistants. Just 64% of PCPs administered screening tools at all 9-month WCVs; the rate dropped to 62% for all 18-month WCVs and to 41% for all 24-month WCVs. Over half (51%) of PCPs did ASD-specific screening at all 18-month WCVs, and 41% did so at all 24-month WCVs.

General pediatricians were significantly more likely to follow the AAP guidelines, as were practitioners who were more confident in their ability to screen and identify. PCPs with previous training also demonstrated a significantly higher rate of screening. The years of practitioner experience did not influence screening practices.

**THOUGHTS FROM DR FARBER**

We clearly need to do a better job here. I know there is a shortage of specialists for specifically diagnosing autism, with long waiting lists, but early intervention if delays are confirmed is the key to treatment. The referral process can be started without a formal diagnosis, but only if we screen for the disorder.

**REFERENCE**

Severe hemorrhage from infantile hemangioma

CAITLIN BRUMFIEL, MS; CHELSEY HUFFMAN, MD; AND KAIANE HABESHIAN, MD

A 5-month-old girl with a large scalp infantile hemangioma (IH), present since 6 weeks of age, was evaluated in the emergency department for lethargy and pallor. Two days prior, the patient’s mother witnessed significant bleeding from the tumor that resolved spontaneously.

History and examination
The patient had been on propranolol 2 mg/kg/day for 2 months, managed by an outside provider. On exam, a segmental, mixed-type IH measuring 112.5 cm² was evident on the right temporoparietal and occipital scalp, with foci of ulceration and hemorrhagic crust.

Laboratory and imaging studies
Laboratory results showed that the patient’s hemoglobin was 5.7 g/dL. Her platelet count and coagulation studies were normal. Magnetic resonance imaging (MRI) of the brain and magnetic resonance angiography (MRA) of the head and neck revealed an intensely enhancing mass fed by numerous branches of the internal and external carotid and vertebral arteries. The tumor completely encased the right internal carotid artery and internal jugular vein without significant narrowing and infiltrated the right paraspinal muscles and parapharyngeal, carotid, retropharyngeal, and masti-
cator spaces. No additional vascular anomalies were identified other than an aberrant right subclavian artery arising distal to the left subclavian, possibly a normal variant. Cardiology did not recommend routine monitoring based on this finding. There were no additional findings concerning for PHACE syndrome (posterior fossa anomalies, hemangioma, arterial lesions, cardiac abnormalities/coarctation of the aorta, eye anomalies).

Treatment and patient outcome
The patient was transfused with 15 cc/kg of packed red blood cells. Propranolol was increased to 3 mg/kg/day and prednisolone 1 mg/kg/day was initiated. The lesion responded well to treatment and, after 1 month, had decreased in size without recurrent hemorrhage (Figure 1). Figure 2 depicts the lesion 6 months following hemorrhage and demonstrates further reduction in size.

Differential diagnosis
Given the history and morphology of the patient’s tumor, IH was the most likely diagnosis. However, certain differential diagnoses may be considered in an infant with a similar lesion. Onset and natural history are the most important factors distinguishing IHs from other vascular anomalies of infancy (Table 1). Congenital hemangiomas are present at birth and appear as violaceous or pink vascular plaques or exophytic masses with peripheral pallor, typically on the head, neck, or limbs. They can be divided into rapidly involuting congenital hemangiomas (RICH), noninvoluting congenital hemangiomas (NICH), and partially involuting congenital hemangiomas (PICH) based on their clinical course. Because proliferation of these tumors occurs in utero, congenital hemangiomas are fully formed at birth and do not typically grow postnatally, unlike IHs, which characteristically undergo self-limited proliferation followed by spontaneous involution. Tufted angiomas (TAs) and kaposiform hemangioendothelioma (KHE) are rare vascular tumors that fall under the same neoplastic spectrum and may clinically resemble IHs. TAs appear as indurated, dusky to red plaques or nodules with ill-defined borders, and KHEs present as purpuric subcutaneous masses. TAs and KHEs typically manifest in the first few years of life on the trunk or extremities and, in contrast to IHs, they rarely involve craniofacial areas and do not regress over time. Of note, KHE, and less commonly TA, can be complicated by Kasabach-Merritt phenomenon, which is a life-threatening condition characterized by consumption coagulopathy and thrombocytopenia. Vascular malformations are structural anomalies comprised of capillaries, arteries, veins, and/or lymphatic vessels. They may appear morphologically similar to deep IHs, but are commonly present at birth, grow proportionally with or more rapidly than the child, do not spontaneously regress and can progress in adulthood. We diagnosed this as a case of exceedingly rare, life-threatening hemorrhage from a large IH on the scalp.

Discussion
IHs are the most common vascular tumors in infants and become clinically apparent within the first days to months of life. Approximately half appear on the head and neck. They are classified by pattern: localized (focal), segmental (large lesions spanning a linear/geographic territory), or multifocal, as well as by type: superficial (bright red papule/plaque), deep (skin-colored to blue nodule), or mixed (both

<table>
<thead>
<tr>
<th>DIFFERENTIAL DIAGNOSIS</th>
<th>ONSET</th>
<th>NATURAL HISTORY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital hemangioma</td>
<td>Fully present at birth</td>
<td>Do not proliferate after birth. May rapidly involute in the first days-weeks of life (RICH) or not undergo involution and instead enlarge proportionally with the patient over time (NICH). Some may not fully regress but instead partially decrease in size (PICH).</td>
</tr>
<tr>
<td>Tufted angioma and kaposiform hemangioendothelioma</td>
<td>Infancy or early childhood</td>
<td>Lesions become indurated and firm over time, then typically stabilize and remain unchanged.</td>
</tr>
<tr>
<td>Vascular malformation</td>
<td>Fully present at birth</td>
<td>Grows in proportion to or more rapidly than the child. Often becomes more apparent over time, and can progress in adulthood.</td>
</tr>
</tbody>
</table>

TABLE 1. DIFFERENTIAL DIAGNOSIS
superficial and deep components). IHs classically undergo a proliferative phase, which is most rapid in the first several months and can last up to 1 year. This is followed by a gradual involution phase, with most involution occurring by 3 to 4 years of age. Thicker hemangiomas leave behind fibrofatty residue that may be amenable to excision, but scarring can be significant. American Academy of Pediatrics (AAP) guidelines exist to help pediatricians identify high-risk IH that require early treatment with propranolol.1

Ulceration occurs in 10% to 25% of IH,2,3 usually during the proliferative phase when demand surpasses blood supply to proliferating capillaries. Mild bleeding is common in ulcerated IH but is rarely clinically significant.4 Life-threatening hemorrhage is exceedingly rare, with only 5 other reported cases in the literature, 4 of which required transfusion (Table 2).2,3,5,6 Most occurred in large, bulky mixed-type IHs, known to have increased risk of ulceration, severe bleeding, and a prolonged proliferative phase.5 These IHs likely had numerous large or anomalous feeder vessels more readily damaged by minor trauma or ulceration. Imaging with arteriography may be helpful in further characterizing the extent of feeder vessels that supply these lesions and may aid in risk stratification for potential hemorrhage. In 1 case of a neck IH, arteriography demonstrated feeders from an aberrant collection of vessels from the thyrocervical trunk, subclavian, external carotid, and vertebral arteries.6 MRA of our patient’s IH demonstrated numerous feeders from the internal carotid, external carotid, and vertebral arteries. The lesion also extended into internal spaces and encased critical vessels. Theoretical complications include internal hemorrhage, serious infection, and massive stroke. The extent of the other reported IHs on imaging was not described, possibly due to inconsistent imaging prior to 2016 PHACE syndrome screening guidelines.7

A subset of bulky mixed-type IHs are at a small but serious risk of hemorrhage and should counsel families accordingly. Imaging with MRI and MRA should be performed of large (> 5 cm), bulky, segmental, mixed-type IHs of the head and neck as soon as possible to characterize blood supply, anatomic boundaries, and complication risk.3 AAP guidelines help identify high-risk hemangiomas that require early treatment with propranolol.1 Life-threatening hemorrhage from IHs warrants further study to optimize risk stratification.

Kaiane Habeshian is an assistant professor of dermatology and pediatrics at George Washington University School of Medicine and Health Sciences and Children’s National Hospital in Washington, DC. Chelsey Huffman is a dermatologist at MedStar Washington Hospital Center in Washington, DC. Caitlin Brumfiel is a medical student at Georgetown University School of Medicine in Washington, DC. The authors have nothing to disclose.

### TABLE 2. CHARACTERISTICS OF ULCERATED CUTANEOUS INFANTILE HEMANGIOMAS CAUSING SEVERE HEMORRHAGE

<table>
<thead>
<tr>
<th>AGE</th>
<th>SEX</th>
<th>LOCATION</th>
<th>SIZE (CM²)</th>
<th>MORPHOLOGY</th>
<th>IMAGING</th>
<th>PUBLISHED</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 months¹</td>
<td>F</td>
<td>Temporoparietal and occipital scalp</td>
<td>112.5</td>
<td>S</td>
<td>Yes</td>
<td>2022</td>
</tr>
<tr>
<td>1 month³</td>
<td>F</td>
<td>Cheek</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>2020</td>
</tr>
<tr>
<td>8 months²</td>
<td>F</td>
<td>Occipital scalp</td>
<td>24</td>
<td>N</td>
<td>No</td>
<td>2017</td>
</tr>
<tr>
<td>NA³</td>
<td>NA</td>
<td>Extremity or face</td>
<td>144</td>
<td>S</td>
<td>NA</td>
<td>2007</td>
</tr>
<tr>
<td>NA³</td>
<td>NA</td>
<td>Extremity or face</td>
<td>59</td>
<td>S</td>
<td>NA</td>
<td>2007</td>
</tr>
<tr>
<td>2 months⁶</td>
<td>F</td>
<td>Neck</td>
<td>55.5</td>
<td>S</td>
<td>Yes</td>
<td>2009</td>
</tr>
</tbody>
</table>

**KEY**

*This case | NA, not available; N, nonsegmental; segmental
With easing restrictions expect increasing respiratory infections.

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It is hard to believe that in the fall of 2019, the No. 1 winter viral threat to the health of our communities was influenza. Based on its quasi-predictable genetic markers, we urgently promoted vaccination, stocked up on Clinical Laboratory Improvement Amendments–waived test kits, and prescribed antiviral medications for patients and their families to protect our communities and reduce the potential for spread. Most of us were not prepared for what was coming and how it would dwarf the severity and impact of a viral pandemic that had been the historic standard by which we measured suffering.

COVID-19’s global impact has touched every aspect of our lives and precipitated a redesign of health care as we knew it. The morbidity and mortality seen in the senior and chronically ill populations have not been seen in children, although, as of this writing, hospitalizations for children have been spiking across the United States. It is hard to estimate the incidence and severity from reported data, and the variants and availability of vaccines make it even more so. Before Omicron, 0.1% to 1.8% of children with COVID-19 needed hospitalization, whereas 0.5% to more than 10% of adults (increasing with age) were hospitalized. Less than 0.03% of infected children died; for adults, that rate was about 1% and significantly higher in those over age 65. The fatality rate for children is dwarfed by that caused by unintentional accidents.1

Hospitalization for influenza and COVID-19 in children has been most notable with specific underlying conditions. A retrospective analysis of 315 laboratory tests confirmed SARS-CoV-2, and 1402 laboratory tests confirmed cases of influenza A and B showed a significant increase in hospitalization for COVID-19 in children who had a neurologic diagnosis with global development delay or seizures (20% vs 8%). COVID-19 and seasonal influenza had similar rates of hospitalization, intensive care unit admission, mechanical ventilation, and duration of ventilator support.2

As we became obsessively careful with sanitizers, masks, social distancing, and quarantines, we came to recognize that COVID-19 is very different from influenza. COVID-19 is more contagious and more significant in short- and long-term morbidity yet more variable in its manifestation from asymptomatic to rapidly fatal. Symptoms can be nearly identical and only testing can differentiate, but the overlap seems to stop there, with COVID-19 adding a more diverse menu of symptoms and complications. The Table lists some similarities and differences in symptoms, complications, and the diagnosis and treatment of influenza and COVID-19.

Most pediatricians used a fever and fatigue threshold for testing for influenza, but COVID-19 testing is done for anyone, even those with no symptoms. Incidence and outcomes are all local, and following local epidemiological reports is essential for helping to differentiate what is affecting communities, but with COVID-19, vaccination rates, infection precautions such as masks, and social determinants of health can have a disproportionate impact.

We often overlook some of the complicating features that are so infrequent with influenza in kids but can be devastating. A major difference between influenza and COVID-19 is the expectation that, with influenza, once the illness has
subsidied, the impact of that infectious agent is over, with the secondary infection or organ damage as separate residua. COVID-19, on the other hand, has the potential to directly incite the immune system and can have lingering effects that are disabling and potentially fatal.

When discussing COVID-19 infection with families, pediatricians will often include a caution for the infrequent possibility for multisystem inflammatory syndrome in children (MIS-C), but probably the most common and actionable concern is cardiac, especially for adolescent athletes. (Of note: Since June 2020, there have also been several reported cases of MIS in adults3). We have come to recognize that myocarditis, pericarditis, and rhythm abnormalities are common to both influenza and COVID-19 yet more common, lingering, and possibly more subtle with COVID-19. The immediate focus on COVID-19 has made it more of a concern and promulgated a set of recommendations for screening patients with specific symptoms and a severity-related algorithm and staged return to sports for adolescent athletes. Although the cardiac problems can be associated with influenza or COVID-19 infection, COVID-19 has the added etiologies of MIS-C and an adverse effect of the vaccine, especially in adolescent male patients.

Both the influenza and the COVID-19 messenger RNA vaccines have been associated with Guillain-Barré syndrome, but not at the frequency seen with actual infection. The incidence after vaccination is rare enough and the public and individual health benefit large enough to recommend vaccination against both.4

Certainly, there are so many other areas of overlap, especially as we see new formulations of vaccines that can adapt and generalize antigens that may provide better specificity and immunocompetence. However, for now we continue to deal with a hit-or-miss influenza vaccine and viral mutations that can reduce vaccine effectiveness and, unfortunately, feed the reluctant and refusers with self-justification. The elevation of COVID-19 and its identity as a pandemic magnifies the reality of both our vulnerability and our potential to effectively respond with the development of vaccines and treatments. ■

COMMENTS? Email them to llevine@mjhlifesciences.com

For references and additional resources, go to ContemporaryPediatrics.com/crossover-symptoms-COVID-19-influenza

Russell Libby is founder and president of the Virginia Pediatric Group in Fairfax, Virginia; assistant clinical professor of pediatrics at the University of Virginia and George Washington University schools of medicine; a board member of the Physicians Foundation; and a member of the Contemporary Pediatrics® Editorial Advisory Board.

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The authors have nothing to disclose.
Eating habits of children during COVID-19

Disruptions to routines and economic troubles have affected the diets of families. Here’s how to foster better nutrition.

SARAH LOWRY, MD; AND DARLA SHORES, PHD, MD

Obesity has increased in many segments of the population over recent decades, including children and adolescents. The COVID-19 pandemic has accelerated that trend, bringing to light changing patterns in eating habits, disparities in access to healthy food, decreased activity, and increased risk of poor health outcomes.

Historically, food was transformed for improved palatability, as well as preservation and storage. Foods have been processed to make them more appealing for both convenience and taste. Since the 1970s, ultraprocessed foods have been available in most of the world and over the past 20 years have become a major source of calories, comprising an average of 3 out of 5 calories consumed daily (Table 1).

Ultraprocessed foods are easy to manufacture, which reduces industrial costs for companies. Food corporations have focused on advertising and marketing of these products to improve sales, but eating more ultraprocessed foods leads to a decline in dietary content of important vitamins, minerals, protein, and fiber.

The National Health and Nutrition Examination Survey reviewed 10 cycles of 24-hour recall to understand what children were eating daily. They found that consumption of ultraprocessed foods increased as children got older, with the highest percentages of daily intake occurring in adolescents.

Increased consumption of ultraprocessed foods has paralleled an increase in obesity, now involving low- and middle-income countries as well, contributing to a global health crisis. Children are an especially vulnerable population because they have higher nutritional needs for healthy growth, and critical nutrients are often absent from a diet of mostly ultraprocessed
Adequate nutrition is necessary to support the immune system and prevent infection. Eating a diet low in nutritional value increases risk of malnutrition and rates of chronic diseases. The NOVA classification system, developed by investigators at the University of São Paulo in Brazil, separates food into 4 categories based on their constitution and alteration. Foods with significant processing classically have been viewed as detrimental to overall health with promotion of weight gain and risk of chronic disease; however, there has been some discussion of the pitfalls that come with the classification system. Some foods are processed to add nutrients, such as iron-fortified cereal. Processing also may be important to ensure the safety of foods consumed. Nevertheless, ultraprocessed foods are generally of low nutritional quality with high-energy density and are associated with the development of chronic noncommunicable diseases with long-term effects on health. Consumption of ultraprocessed foods is associated with a high glycemic response and reduced satiety, which may contribute to overeating. Noncommunicable chronic diseases, including cardiovascular disease and metabolic syndrome, account for 70% of deaths worldwide.

### Table 1.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultraprocessed foods</td>
<td>61.4%</td>
<td>66.4%</td>
<td>67%</td>
</tr>
<tr>
<td>Unprocessed foods</td>
<td>28.8%</td>
<td>25.2%</td>
<td>23.5%</td>
</tr>
<tr>
<td>Ready-to-eat meals</td>
<td>2.2%</td>
<td>11.1%</td>
<td></td>
</tr>
</tbody>
</table>

The NOVA classifications are:

- **UNPROCESSED FOODS**: foods consumed whole without major alterations or changes. These include fresh or frozen fruits, vegetables, meats, or legumes with minimal processing. The food itself is not changed and is considered a whole food.

- **PROCESSED CULINARY INGREDIENTS**: food items used in cooking to add flavor and taste or that are part of unprocessed foods. These include table salt, sugar, oil, and other substances extracted from unprocessed foods.

- **PROCESSED FOODS**: foods taken from nature and altered with added substances, often sugar or salt, to create more stable and appealing foods. This includes canned fruits and vegetables, simple breads, and cheeses.

- **ULTRAPROCESSED FOODS**: foods with a combination of several ingredients creating a packaged food or meal that is sustainable, convenient, and appetizing. In addition to added culinary ingredients (sugar, salt, and oils), ultraprocessed foods also include nonculinary products such as high fructose corn syrup and artificial sweeteners. Added sugars, saturated fats, emulsifiers, and preservatives can extend the shelf life for months to years.

Added sugars include brown sugar, cane sugar,
Adolescent eating habits

Recent research into the dietary habits of adolescents around the world has focused on exposure to ultraprocessed foods. The National Health and Nutrition Examination Survey reviewed 10 cycles of 24-hour dietary recall to understand what children and adolescents were eating daily. They reviewed 2 different time periods, 1999-2000 and 2017-2018 to look at dietary eating habits. They found that consumption of ultraprocessed foods increased as children got older, with the highest percentages of daily intake occurring in adolescents.

Adolescence is a crucial time for emotional, mental, and physical development as individuals gain autonomy and independence. Several factors influence eating habits of adolescents, including their physical surroundings and social environment, self-awareness of food preferences and nutritional needs, and their exposure to the digital world of social media and advertisements. Adolescents believe the definition of healthy includes a balanced diet, consistent physical activity, and maintenance of a healthy body weight, but they sometimes struggle with how to characterize energy-dense and processed food. Food marketing targeted at children and adolescents through television and social media has been linked with a preference for those ultraprocessed foods that tend to be unhealthy. In 2009, $1.8 billion was spent on marketing to adolescents of ultraprocessed foods such as sugary carbonated beverages, snack foods, cookies, potato chips, and cakes. The World Health Organization has recommended reducing advertisements targeted toward children and developing a nutritional criterion for advertising. Governing bodies have encouraged a reduction of targeted marking of ultraprocessed foods to children and adolescents. The Better Business Bureau’s voluntary Child Food and Beverage Initiative in 2006 promoted reduced marketing. Seventeen large corporations agreed to advertise only healthy foods to children but in the end only a few companies actually reduced their marketing.

Other governing policy changes have led to a slight decrease in ultraprocessed foods available at schools, however there is still a lot left to do to improve the health of children and adolescents.

**COVID-19 pandemic**

The COVID-19 pandemic disrupted dietary habits with the transition from work and school to home for many families. The pandemic heightened the consumption of ultraprocessed foods as schools closed and access to food changed. In the early months of the pandemic, more meals were cooked and prepared at home to allow for social distancing and infrequent trips to restaurants and stores. However, this also meant that foods with longer shelf lives and sustainability, such as high-calorie snacks and nonperishable goods, were purchased more often. With the economic burden of the pandemic, families attempted to cope with food insecurity by purchasing foods with long shelf lives and low cost to ensure there would be food in the house.

The environment in which food was consumed in the home also has been altered during the pandemic. Adolescents reported eating more snacks rather than daily structured meals, and a study of 24-hour diet recall in several countries found increased intake of ultraprocessed foods during the COVID-19 pandemic’s first year. Additionally, sleeping patterns were disrupted, and there was an increase in screen time for both school and leisure, especially in low-income families. Given these extra stressors and isolation, adolescents reported an increase in “comfort food” consumption, which also contributed to excess weight gain.

Increased weight gain associ-
Households with less financial stability and fewer resources often are those with higher rates of obesity.13 Children living in poverty also are experiencing higher rates of infection and severe disease during the COVID-19 pandemic.17

During the COVID-19 pandemic, food insecurity increased and families purchased ultraprocessed foods more often due to lower cost and the foods’ longer shelf life.14 Decisions about the most cost-effective methods to provide food were influenced by lower costs for higher-calorie foods.13 During lockdown with social distancing, acquiring foods became even more difficult for families with food insecurity, and most families experienced a further reduction in income, only exacerbating the problem.14 Food insecurity rates in families tripled 6 weeks after the lockdown and overall food insecurity rates increased by approximately 20% in the United States and contributed to poor quality of diet.13,14 Children are often aware of their family’s food insecurity despite parental attempts to shelter them of that fact.15

**Long-term solutions**

For clinicians, engaging with both parents and adolescents during visits creates an environment of shared decision-making, and motivational interviewing can lead to the most success for implementing dietary changes. Potential engaging questions that lead to action are included in Table 2. Utilizing a multidisciplinary approach, including access to behavioral psychologists and dietitians to help with decision-making and meal planning, also can be helpful.

Screening for social determinants of health with a focus on food security is becoming a common practice in pediatrician offices due to the frequency of visits, even if they are virtual. Whereas education is important, it alone does not have the desired impact on food insecurity. Recognition of social stressors associated with poverty is important due to its disruption of development and contribution to chronic disease. Addressing the “hunger vital sign” to screen for food insecurity can be done at all visits, both in person and virtual.13 Normalization and recognition of the struggle that families face, especially during the COVID-19 pandemic, can help families be more willing to discuss options for assistance.13 Primary care providers should be prepared to discuss social determinants of health in addition to having knowledge about weight concerns and obesity. Providing resources to families and ensuring adequate follow-up are crucial to promote long-term health.14 Active and passive referrals for food resources can be done by providing information for food shelters or giving foods directly to families at the visit.15

**Since the 1970s, ultraprocessed foods have become a major source of calories, comprising an average of 3 out of 5 calories consumed daily.**

Food deserts and food insecurity

Food deserts are areas in low-income neighborhoods with limited food resources, particularly for healthy and fresh foods such as fruits, vegetables, and whole grains. There is a larger presence of fast-food restaurants and convenience stores offering predominantly ultraprocessed foods.13 Food insecurity is defined as limited or uncertain access to food that is nutritionally adequate due to lack of money or ways to acquire food.14

The COVID-19 pandemic not only exacerbated racial and ethnic disparities present in the US with higher rates of COVID-19 infection and severe outcomes in Hispanic and non-Hispanic Black children, but it also disproportionately affected food access in these communities.15

Previously, the National School Health Program benefited children of low-income households, allowing access to predictable meals throughout the week. There were attempts to expand the summer lunch program during the COVID-19 pandemic to provide food to families, however, due to a lack of resources, the efforts proved difficult to implement.13

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

For references, go to ContemporaryPediatrics.com/eating-habits-during-COVID-19
Impact of poverty on gun violence

BY MIRANDA HESTER

Firearm-related injuries are the second leading cause of death among children and young adults, accounting for nearly a quarter of all deaths among people aged 15 to 24 years.\(^1\) Ninety-one percent of firearm deaths worldwide in children aged 0 to 14 years occur in the United States.\(^2\) In a recent study, investigators examined whether living in a county with a large poverty concentration was linked to a child or teenager’s risk of death related to a firearm.\(^3\)

The investigators ran a cross-sectional study that analyzed US firearm fatalities among children and young adults aged 5 to 24 years from January 2007 to December 2016. They used data from the Centers for Disease Control and Prevention’s Compressed Mortality File (CMF) and the US Census Bureau’s annual intercensal population data. Poverty concentration was defined as a population living below the poverty level ($21,027 in 2007 and $24,339 in 2016 for a family of 4) and divided into 5 groups: 0% to 4.9%, 5% to 9.9%, 10% to 14.9%, 15% to 19.9%, and 20% or higher.

The cohort included 67,905 firearm-related deaths and mainly comprised males (60,164). Among total deaths, 42,512 were homicides, 23,034 were suicides, and 1627 were considered unintentional. The investigators found a stepwise increase in firearm-related mortality risk tied to increasing county poverty concentration. Compared with counties with the lowest poverty concentration, those with the highest concentration saw increased rate of total deaths related to firearms (adjusted incidence rate ratio [IRR], 2.29; 95% CI, 1.96-2.67), homicides (adjusted IRR, 3.55; 95% CI, 2.80-4.51), suicides (adjusted IRR, 1.45; 95% CI, 1.20-1.75), and unintentional deaths (adjusted IRR, 9.32; 95% CI, 2.32-37.4). Overall, 3,833,105 years of potential life were lost.

Investigators noted they could report only association and not causation. Also, because neighborhoods may have varying levels of poverty, and there is an inability to determine income data for the teenagers and young adults, researchers could not determine the implications of individual-level vs county-level poverty.

Counties with a higher level of poverty concentration were linked to increased rates of total firearm deaths, homicides, suicides, and unintentional deaths, the investigators concluded. More than 50% of the firearm-related deaths and more than two-thirds of all homicides tied to firearms in the age group could be linked to living in a county with a higher poverty concentration.

For references and additional content, go to ContemporaryPediatrics.com/gun-violence

Commentary from Steven Selbst, MD:

This important article shows the dramatic impact of poverty on firearm-related deaths in the United States. It is no surprise that deaths from gun violence are related to poverty, but the numbers reported here and the strong association with higher county poverty concentration are staggering. It is well known that school shootings have increased in the United States in recent years, and these tragic events understandably capture national attention. This article makes us look closely at the more subtle epidemic of gun-related deaths that occur daily on the streets of our country. The authors briefly describe the impact of children living in neighborhoods with a high poverty concentration. Children in these communities often have inadequate housing, limited access to high-quality schools, and increased toxic stress. It is no surprise that they also have a disproportionate number of firearm-related deaths. The New York Times reported that Chicago, Illinois, had 101 gun-related homicides in residents under age 20 in 2021, up from 76 in 2019. In my own city of Philadelphia, Pennsylvania, 2021 brought a new record for homicides (562), and the large majority of these deaths was by firearms. More than 200 teens were caught in the cross fire with the rising gun violence in Philadelphia, and at least 36 were killed in 2021. The large majority of these shootings also occurred in sections of the city with an increased concentration of poverty.\(^4\)

In 2016, the American Academy of Pediatrics noted that almost half of children in the United States live in or near poverty. The association issued a policy statement indicating its commitment to “reducing and ultimately eliminating poverty in the United States.” This is a daunting task, as is ending the crisis of gun violence in our country. The authors of this study mention some helpful interventions such as the Child Tax Credit; Head Start; and the Special Supplemental Nutrition Program for Women, Infants, and Children. They also note the importance of firearm regulation legislation.\(^5\) Our country seems to be a long way off from this.

To make any progress in reducing gun-related violence, we need data. This study provides very valuable data that will at least help us target our efforts.
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Harmful excipients for pediatric patients

AMANDA CLOUSER, PHARMD; AND EMILY DISEROAD, PHARMD, BCPPS

Evidence suggests some pharmaceutical excipients in medications may have adverse effects on pediatric patients. Here’s what you should know.

The United States Pharmacopeia (USP) defines pharmaceutical excipients as substances other than the active pharmaceutical ingredient that is intentionally included in an approved drug delivery system or finished drug product.¹ There is a growing body of literature to suggest pharmaceutical excipients contained in commercially available and extemporaneously compounded medications may have adverse clinical effects on pediatric and adult patients. The US Food and Drug Administration (FDA) requires over-the-counter (OTC) products marketed under their respective drug monographs to contain only suitable inactive ingredients which are administered in safe amounts; however, it is entirely under the responsibility of the manufacturer to comply with these standards.² Due to the vast differences in metabolism and clearance of medications in various stages of development, it is difficult to assess precise harmful levels of pharmaceutical excipients and the extent to which they will impact patients. Pediatric pharmacokinetic and pharmacodynamic profiles can vary drastically, and with this variability ultimately comes variance in safety profiles. Many of these discoveries have been attributed to therapeutic misadventures, such as the discovery of the neonatal gasping syndrome when physicians started to use bacterial static saline flushes containing benzyl alcohol.³ In a 2019 study surveying 42,052 oral solid dosage forms from the Pillbox database, an American database regulated by the National Institutes of Health, medications were found on average to contain 8.8 inactive ingredients.⁴ Given the overall prevalence of potentially harmful pharmaceutical excipients in various medications, the potential risks posed to children remains a pertinent topic for discussion.

Ethanol
Ethanol is the second most commonly used solvent in oral liquid medications, preceded by water. Ethanol additionally has antimicrobial properties. Patients with impaired alcohol dehydrogenase enzyme systems, including children aged less than 6 years, patients with hepatic disease, and patients treated with disulfiram or metronidazole are at greatest risk of toxicity, as alcohol dehydrogenase activity is less than 20% of adult enzymatic activity in children under the age of 6 years. Prenatal exposure to ethanol may result in fetal alcohol syndrome. The FDA, American Academy of Pediatrics (AAP), and European Medicines Agency (EMA) have all published dose limits related to ethanol-containing medications; however, these standards are based on acute central nervous system (CNS) toxicity after single-dose administration.⁵ While most are familiar with the signs and symptoms of ethanol intoxication and acute poisonings in adults, children may present with hypoglycemia, hypothermia, acidosis, tachycardia, seizures, and disorders of consciousness. These effects should be treated promptly with supportive care measures and the drug should be discontinued if possible. Very
### Table. Continued on page 30
#### OTHER MISCELLANEOUS HARMFUL EXCIPIENTS

<table>
<thead>
<tr>
<th>EXCIPIENT</th>
<th>PURPOSE</th>
<th>WHERE EXCIPIENT IS FOUND</th>
<th>DAILY ADMISSIBLE INTAKE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arginine</td>
<td>Protein stabilizer</td>
<td>cefepime and ceftazidime</td>
<td>Not established</td>
</tr>
</tbody>
</table>

**ADVERSE REACTION**
- In the setting of arginase deficiency, a rare metabolic disease characterized by the inability to process arginine, arginine administration can lead to a buildup of ammonia.\(^{14}\)
- Hyperammonemia can present as feeding problems, vomiting, poor growth, seizures, and increased reflexes and progress to developmental delays, microcephaly, lethargy, and coma.\(^{14}\)
- Treatment includes restriction of protein in the patient’s diet and avoidance of arginine-containing medications. Glycerol phenylbutyrate is FDA approved for the treatment of arginase deficiency in those at least 2 months of age.\(^{14}\)

| Aspartame | Sweetener | azithromycin suspension powder, sugar-free chewing gum, montelukast sodium chewable tablet | < 40 mg/kg |

**ADVERSE REACTION**
- Aspartame is a disaccharide made from aspartic acid and phenylalanine as the methyl ester. It should be avoided in those with phenylketonuria who lack the gene required to breakdown phenylalanine.
- May cause neurological reactions (neurotoxicity, epilepsy, headache, panic attack, and hallucinations), hypersensitivity reactions (vascular and granulomatous panniculitis) and cross-reaction with sulfonamides.

| Cyclodextrins | Disintegrant | IV itraconazole and Johnson & Johnson/Janssen COVID-19 vaccine | Not established |

**ADVERSE REACTION**
- Cyclodextrins are used to improve the aqueous solubility of hydrophobic compounds through encapsulation.
- In vitro studies reported hemolytic effects after high amounts of cyclodextrin administration, but these effects have not been demonstrated in vivo. Although generally considered safe, patients with severe renal impairment should be monitored closely as cyclodextrin is renally eliminated.
- Potential exists for the hydrophobic interior of cyclodextrin to form a complex with compounds other than the intended; however, this has only been studied in vitro and further pharmacokinetic studies in patients are needed to address clinical relevance of this interaction.\(^{15}\)

| Parabens (propyl-, methyl-, ethyl-, butyl-) | Preservative | aripiprazole (Abilify) oral solution, amphetamine (Adzenys ER and Dyanavel XR) oral suspension, amlodipine besylate oral solution, clonidine oral solution, furosemide oral solution (extemporaneously compounded) | < 10 mg/kg |

**ADVERSE REACTION**
- The main metabolite is hydroxyparabenzoic acid, which is structurally similar to aspirin and may result in cross hypersensitivity.\(^{16}\)
- Parabens may also displace bilirubin in neonates and cause hyperbilirubinemia.\(^{17}\)

| Polyethylene glycol (PEG) | Surfactant | Inactive ingredient: acetaminophen tablets, famotidine tablets, cyclobenzaprine tablets, PEG-asparaginase, Pfizer-BioNTech COVID-19 vaccine, Moderna COVID-19 vaccine Active ingredient: polyethylene glycol 3350 (Miralax) | Not established |

**ADVERSE REACTION**
- PEG has been linked to IgE-dependent hypersensitivity reactions.\(^{18}\) Type 1 hypersensitivity reactions secondary to PEG of various molecular weights are exceedingly rare but may be life-threatening.
- There have been a small number of case reports of mRNA-based COVID-19 vaccines eliciting anaphylaxis directly attributable to PEG.\(^{19,20}\)
- Patients with confirmed or suspected PEG allergy should consider vaccination with Johnson & Johnson’s/ Janssen COVID-19 vaccine.
CONTINUED FROM PAGE 26
little is understood about the long-term effects of ethanol exposure in children; however, the clinical benefits of administering ethanol-containing medications may outweigh the potential risks. For this reason, administration of extemporaneously compounded buprenorphine sublingual drops (30% ethanol), phenobarbital elixir and oral solution (15% ethanol), and methadone oral solution (9.8% ethanol) in neonatal abstinence syndrome has remained controversial. Additional examples of medications containing ethanol include dexamethasone oral solution (30% ethanol), furosemide oral solution (11.5% ethanol), digoxin oral solution (10% ethanol), and many others. Alternative formulations or medications should be considered if possible, especially when the product contains more than 5% ethanol by volume.

Propylene glycol
Propylene glycol is a solvent used in many oral, topical, and intravenous medications and as a humectant in some topical medications. It is metabolized to lactaldehyde by alcohol dehydrogenase. Lactaldehyde is converted by aldehyde dehydrogenase to lactate, and accumulation may lead to an anion gap metabolic acidosis. Propylene glycol may additionally result in direct organ toxicity through an unknown mechanism, manifesting as CNS depression and seizures, cardiac arrhythmias, hypotension, respiratory depression, hemolysis, and acute kidney injury. Patients with impaired alcohol dehydrogenase systems, as discussed in the ethanol section above, and renal impairment are at greatest risk. This becomes most clinically relevant in patients receiving continuous infusions of medications containing propylene glycol as an excipient. Examples include esmolol (25% propylene glycol), lorazepam (80% propylene glycol), and phenobarbital (40% to 70% propylene glycol). Manifestations of toxicity should be treated promptly and the drug should be discontinued if possible. Propylene glycol is considered safe. Clinicians should use caution and monitor lactate, comprehensive or basic metabolic panels, anion gap, serum osmolarity, pH, and neurologic, cardiovascular, and respiratory status in patients at risk for accumulation and systemic toxicity, particularly those on continuous infusions.

Benzalkonium chloride
Benzalkonium chlorides (BAC) are cationic surfactants commonly used for their broad-spectrum antimicrobial properties in topical sanitizers, nasal sprays, ophthalmic solutions, and nebulized solutions. The mechanism of toxicity is not abundantly clear, but may be related to oxidative stress. BAC is generally considered safe and can be found in OTC nasal decongestant sprays, including sodium chloride and oxymetazoline. Nasal sprays containing less than 0.1% BAC have been found to be safe. Some data suggest it may damage the human nasal epithelia and/or cause exacerbation of rhinitis medicamentosa at higher concentrations. When used in ophthalmic preparations such as prednisolone acetate ophthalmic suspension (0.01% BAC), various OTC eye lubricants, and others, BAC may cause dry eye, trabecular meshwork degeneration, ocular inflammation, and mitochondrial effects. Adverse effects have been demonstrated in concentrations as low as 0.0001%. Recommending short courses of BAC-containing nasal sprays or ophthalmic products is the ideal way to avoid these adverse effects. Examples of inhaled medications containing BAC include nonsterile, multidose 0.5% albuterol solutions; nonsterile, screw-cap, unit-dose 0.083% albuterol nebulizer solutions; and nonsterile, multidose metaproterenol solutions. Use of BAC-containing products has resulted in poor pulmonary outcomes including decline in forced expiratory volume 1 by 20% or more, increased risk of requiring additional respiratory support, and lower likelihood of stopping continuous albuterol in patients with asthma when compared to preparations without BAC. Albuterol preparations without BAC should be used preferentially as they are now available as 5-mg/mL mul-

Evidence suggests that some pharmaceutical excipients in medications may have adverse effects on pediatric patients.

CONTINUED ON PAGE 30
Opt-Out Chlamydia Screening

Our Partner Perspective highlights that Opt-Out Chlamydia Screening should be part of routine adolescent health care services. This testing can significantly increase screening rates and lead to a decrease in overall chlamydia prevalence, helping women’s health providers identify more STIs and prevent more life-altering adverse health outcomes such as infertility.
**TABLE. continued from page 27**

## OTHER MISCELLANEOUS HARMFUL EXCIPIENTS PART 2

<table>
<thead>
<tr>
<th>EXCIPIENT</th>
<th>PURPOSE</th>
<th>WHERE EXCIPIENT IS FOUND</th>
<th>DAILY ADMISSIBLE INTAKE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polysorbate 80</strong></td>
<td>Surfactant</td>
<td>Vaccines (DTaP-IPV-Hib vaccine, HBV vaccine, Johnson &amp; Johnson/Janssen COVID-19 vaccine and MMR vaccine at extremely low amounts), amphetamine (Dyanavel XR), doxetaxel, epoetin/darbepoetin, and fosaprepitant vitamin E (intravenous)</td>
<td>Not established</td>
</tr>
<tr>
<td><strong>Sodium benzoate</strong></td>
<td>Preservative</td>
<td>Ammonul, caffeine (benzoate salt), oral alprazolam, Children’s Tylenol Cold and Cough and Sore Throat solution (acetaminophen/dextromethorphan hydrogen bromide), and trimethoprim-sulfamethoxazole</td>
<td>Not established</td>
</tr>
<tr>
<td><strong>Sorbitol</strong></td>
<td>Sweetener and plasticizer22</td>
<td>Children’s Tylenol Cold and Cough and Sore Throat solution (acetaminophen/dextromethorphan hydrogen bromide), sodium polystyrene sulfonate, aminocaproic acid syrup, calcium carbonate suspension, carbamazepine suspension, amantadine hydrochloride solution, furosemide solution, isoniazid solution, and pseudoephedrine syrup</td>
<td>European excipient review is limited to 5 mg/kg in children 0-2 years of age, and 140 mg/kg in those older than 2 years16</td>
</tr>
</tbody>
</table>

**ADVERSE REACTION ♦**
- Polysorbate 80 may potentially lead to hypersensitivity reactions in neonates due to immature detoxification systems if large quantities are administered.21
- Similar to benzyl alcohol, metabolism is dependent on benzoic acid conjugation with glycine.
- Due to incomplete liver maturation, neonates are at highest risk for metabolic acidosis and neurotoxicity.
- Other adverse effects include hives and allergic reactions proposed to be due potentially to either an IgE and histamine mediated reaction and/or structural similarities of sodium benzoate with acetyl salicylic acid that may act on eicosanoid production.
- Treatment of benzyl alcohol and sodium benzoate induced metabolic acidosis and respiratory distress is predominately managed with respiratory support and administration of alkaline fluids.
- At higher doses, it can act as a laxative and cause abdominal pain, swelling, and osmotic diarrhea.
- Nosocomial diarrhea typically begins within 72 hours of administration.23
- Patients experiencing sorbitol-induced osmotic diarrhea are advised to discontinue sorbitol-containing agents, and manage symptoms of dehydration with oral electrolyte and fluid repletion.

CONTINUED FROM PAGE 28

Tidose concentrate for continuous nebulization and 2.5 mg/3 mL-unit dose bullets.

**Benzyl alcohol**

Benzyl alcohol is a preservative used in medications for its antibacterial properties. Due to incomplete liver maturation, benzoic acid may not be converted to the renally excreted metabolite hippuric acid in infants and children. Large administrations in neonates may lead to elevated benzoic acid concentrations, metabolic acidosis, respiratory depression, and gasping syndrome. Gasping syndrome occurs when metabolic acidosis and respiratory depression progress to gasping respirations, renal failure, CNS depression, seizures, and hypotension. Due to these concerns and documented evidence of increased mortality in infants weighing less than 1250 g receiving intravascular catheter washes containing benzyl alcohol, benzyl alcohol is contraindicated in patients less than 3 years of age.22 The EMA has suggested dos-
es greater than 100 to 200 mg/kg/24h are linked to neonatal gasping syndrome. A report published by the Centers for Disease Control and Prevention suggested a similar range of 99 to 405 mg/kg/24h may be linked to accumulation of benzyl alcohol in neonates. The FDA recommends the exclusion of benzyl alcohol from medications, intravenous fluids, and heparin washing solutions for newborns. Although benzyl alcohol is commonly found in oral formulations of cetirizine chewable tablets, diphenhydramine tablets, hydroxyurea tablets, montelukast chewable tablets, and olanzapine oral disintegrating tablets, these medications are typically used in older children with the developed metabolic capacity to process benzyl alcohol exposure and are therefore at less risk for toxicity. Benzyl alcohol has been found in some parenteral formulations of aminophylline, amiodarone, bumetanide, diazepam, furosemide, heparin, metoclopramide, midazolam, lorazepam, parenteral vitamin E, multidose vial pediatric trace elements (neonatal single-dose vials should be reserved for neonates), parenteral vitamin K, multivitamin infusion, and trimethoprim-sulfamethoxazole. Treatment of complications due to benzyl alcohol are predominately symptom focused (ie, reversal of metabolic acidosis with sodium bicarbonate, management of respiratory depression with increased respiratory support).

**Conclusion**

Ultimately, there is a paucity of safety data for several of the pharmaceutical excipients discussed. There is a great need for further investigation to evaluate the safety of pharmaceutical excipients. There is also a need for more transparency and improved labeling regarding excipient content of various medications. Clinicians should be mindful of pharmaceutical excipients in medications and monitor for signs and symptoms of toxicity.

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

Amanda Clouser is a pediatric pharmacy resident at The Johns Hopkins Hospital in Baltimore, Maryland. She has nothing to disclose.

Emily Diseroad is an intensive care unit float clinical pharmacy specialist at Cincinnati Children’s Hospital Medical Center in Cincinnati, Ohio. She has nothing to disclose.

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Flurona: the facts doctors need to know

**BY TODD SHRYOCK; AND LOGAN LUTTON**

Flurona is a term being used for patients who are infected with both influenza and COVID-19. Unfortunately, there is also a lot of misinformation and misconceptions about this double infection.

1. **Flurona is not a combination super virus.** Flurona is when a patient is infected with both COVID-19 and influenza at the same time.

2. **Numbers are small.** To date, cases of flurona double-infections are not rising in any significant numbers.

3. **Vaccinations are still key.** There is little data on how flurona affects patients, but experts stress that vaccines for both are the most effective way to prevent severe infections.

4. **Both viruses are transmitted through droplets and aerosols that can be passed on by coughing, sneezing, speaking, singing or breathing.** The spread of both can be stopped by masking.

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For references and commentary, go to ContemporaryPediatrics.com/harmful-excipients-patients
A healthy 14-year-old boy presented at our dermatology practice with acute onset of an intensely itchy rash that first appeared 2 months prior (Figures 1 and 2). The patient had no family history of skin disease, was on no medications, and denied a history of preceding viral symptoms.

Clinical findings
The rash consisted of symmetrical and diffusely scattered violaceous to hyperpigmented papules with overlying silver scale coalescing into plaques. Affected areas included the entire trunk, extremities, and genitals. A punch biopsy demonstrated a lichenoid dermatitis consistent with lichen planus. In light of the presentation, the findings were consistent with pediatric eruptive generalized lichen planus (LP).

Etiology/epidemiology
LP is a pruritic, inflammatory dermatitis first described in 1869. The clinical appearance is classically described by the 6 P’s: purple, polygonal, planar, pruritic papules, and plaques. Additionally, a network of fine, reticular white lines called Wickham striae may be seen within the skin and mucosal lesions. Similar to psoriasis, The Koebner phenomenon (skin lesions appearing in areas of skin trauma, especially scratching and picking), which is also seen in psoriasis, is classically seen with LP. Several clinical subtypes, based on morphological pattern, have been described. Classic LP (also known as papular) is the most common subtype. \(^1\) LP variants include actinic, annular, atrophic, hypertrophic, inverse, bullous, and ulcerative.

LP is rarely seen in children, with just 1% to 4% of total cases diagnosed in the pediatric population. \(^2\) Children are more likely to present with
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HIGHLIGHTS
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HIGHLIGHTS
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CONTINUED FROM PAGE 32

atypical manifestations. Although oral mucosal involvement occurs more than over half of adult patients and may be the only site of disease, it is rare in children. Pruritus, a hallmark symptom of LP in adults, is frequently absent in children. Nail involvement, which can include nail thinning, pterygium (overgrowth of nail fold onto nail bed of the skin surrounding the nail and the skin under the nail plate), and subungual hyperkeratosis (thickened skin underlying the nail plate), is more common in adults compared with children.

The most common pattern in pediatric patients is the classic form. The second most common form in children is eruptive (16%), as seen in this patient. Many children have a polymorphic and heterogeneous disease phenotype; in these cases, LP is classified based on the most dominant pattern. Pediatric patients are more likely than adults to have a more severe disease course.

A variety of drugs and dental materials have been implicated as inciting factors. Several autoimmune diseases have been linked to LP, including vitiligo, Hashimoto thyroiditis, myasthenia gravis, and alopecia areata. Other disease associations include liver disease (particularly hepatitis C and primary biliary cholangitis) and thymoma. The aforementioned associations have been described in adult patients with LP. It is important to note, however, that these risk factors do not appear to apply to pediatric patients.

Several studies show a disproportionate number of cases of pediatric LP in the Indian subcontinent. Here, Black children may be more affected than other races.

There is evidence that CD8+ T cells are strongly implicated in the pathogenesis of LP because they cause apoptosis (programmed cell death) of keratinocytes, but the true pathogenesis remains unknown. Diagnosis is typically confirmed by punch biopsy.

Differential diagnosis

The differential diagnosis for LP can be extensive, but 2 common considerations are lichenoid drug eruption (LDE) and psoriasis. A history of medications that can trigger an LDE, including antihypertensives, diuretics, and nonsteroidal anti-inflammatory drugs, is critical in differentiating it from LP.

LP and psoriasis are both considered papulosquamous disorders. One key differentiator is the presence of Wickham striae in LP compared with overlying scale in psoriasis. LP can also remit without treatment after about 1 year, whereas psoriasis is generally a lifelong condition.

Treatment and management

There is no cure for LP, and treatment is aimed at managing symptoms. Topical corticosteroids are often used as a first-line option, and most patients show an excellent response. For treatment-resistant disease, systemic steroids and dapsone can be prescribed. Following resolution of the rash, postinflammatory hyperpigmentation (PIH) and cicatricial alopecia can be seen. Management of PIH includes topical hydroquinone and a retinoid.

With treatment, pediatric LP generally carries a good prognosis. However, the eruptive pattern of LP can have severe, acute manifestations. In addition, long-term complications of LP involving the genitals can include scarring, urethral strictures, and urethral stenosis. Although there is no associated risk of skin cancer, LP with oral involvement has been linked to the development of oral squamous cell carcinoma. These potential complications underscore the need for prompt treatment.

Patient outcome

The patient started on triamcinolone 0.1% ointment twice daily for affected areas, hydrocortisone 2.5% ointment twice daily for the genital area, and oral hydroxyzine 25 mg nightly.

At follow-up 2 weeks later, the patient had mild improvement in pruritus and appearance of the rash. Fluocinonide 0.05% ointment twice daily was added for the most pruritic areas. At 8 weeks’ follow-up, pruritus had resolved and the rash had improved, with a few remaining foci of activity and residual PIH (Figure 2). Hydroxyzine and fluocinonide were stopped, and oral metronidazole 500 mg twice daily was added. A prior authorization for narrow band UV-B 3 times per month for 3 months was submitted.

At 12 weeks’ follow-up, metronidazole 500 mg twice weekly was continued for an additional 4 weeks, as was triamcinolone 0.1% ointment twice daily to the worst areas and hydrocortisone 2.5% ointment twice daily to the less involved areas.

For references, go to ContemporaryPediatrics.com/lichen-planus-in-pediatrics

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