Higher anxiety
What’s normal, what’s not, when to intervene

+ Diagnosing depression in preschoolers

Pediatric Pharmacology
Anesthetic neurotoxicity

Dermatology
Erythematous plaque on an infant’s cheek

Infectious Disease
Pneumococcal vaccine

Respiratory Disorders
RSV linked to asthma

Metabolic Disorders
Type 1 diabetes

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Postpartum depression screening in primary care
How to make it a success

Pediatricians are the ideal first-line providers to help identify, refer, and support new mothers affected by postpartum depression.

Postpartum depression (PPD) screening is now considered a cornerstone of infant preventive care. Postpartum depression is a prevalent condition with direct impacts on the health and well-being of the infant and the family.1-3 These include behavioral and attachment issues, early cessation of breastfeeding, and overuse of healthcare services. Given that pediatricians see mother-baby dyads an average of 8 times during the first year of life, whereas mothers typically see their own doctor only once in that time frame, assessing for PPD within the pediatric clinic makes intuitive sense and opens a window for intervention.4

The United States Preventive Services Task Force (USPSTF) endorsed routine PPD screening in 2016.5 Prior to that time, new mothers were only screened by their obstetrician at their 6-week postpartum visit, if they attended that visit. Beginning in 2018, the American Academy of Pediatrics (AAP) strengthened its recommendation in this regard. Previously, the AAP stated that pediatricians should be alert to a mother’s mood and coping. Now the AAP endorses routine screening using a validated tool such as the Edinburgh Postnatal Depression Screen (EPDS) at the 1-month, 2-month, 4-month, and 6-month well visits.6 Most state Medicaid plans and private payers cover this screening fee when completed during the infant well visit.7,8

Multiple studies have found maternal depression rates as high as 15%.7 Given the myriad of negative consequences that postpartum depression can have on infant social and mental development, it is vitally important that these mothers are identified, offered support, and referred for appropriate mental health treatment. However, incorporating this additional screening tool into 5 infant well visits can feel daunting to busy clinicians. We will outline how PPD screening can be integrated into infant well care in a busy academic pediatric practice. We will also share the key resources to consider and line up prior to instituting this screening into your practice.

Setting and evolution of the screening process
Briarwood Center for Women, Children, and Young Adults is a Pediatrics and Obstetrics/Gynecology practice within Michigan Medicine in Ann Arbor. In 2014, our clinic launched an integrated perinatal mental health program with embedded social workers and perinatal psychiatrists to provide on-site support for pregnant women and new mothers with mental health issues including depression and anxiety.

Starting in 2016, the pediatricians began routinely screening new mothers for PPD using the EPDS. Any mother who screened positive as
indicated by a score of 10 or higher or any positive response to the self-harm item was referred to our social workers. When possible, medical providers would offer a warm hand-off, having the mother meet with the social worker same-day during the clinic visit. For those with current thoughts of self-harm, the same-day hand-off was a requirement. The social workers would complete additional screening and facilitate new referrals or refer back to the mother’s primary care doctor, obstetrician, or psychiatry at our clinic site or our Depression Center. Our social workers would also offer short-term counseling to serve as a bridge until patients were able to connect with mental health providers who could follow them long term.

Beginning in 2018 with the AAP endorsement of routine EPDS screening, we confirmed with our billing department that the code 96161 (standard caregiver screen) was appropriate for use to bill for the administration of this tool at the AAP-recommended intervals. We added this code to the order sets for all infant well visits in the first 6 months of life, to make it easy for clinicians to remember to pay for this screening. We also added tabs to enter the score in our well-visit templates, and a PPD handout to the order sets.

Initial concerns of the pediatricians included the time needed to complete another screening tool. Staff noted that the early infant visits were logistically challenging for new parents, who struggled to get the baby, stroller, diaper bag, and perhaps another sibling (or 2) from home to clinic, car to check-in, and waiting room to exam room. Our workflow including PPD screening added time at check-in to complete all screening tools. Additionally, we are a teaching clinic with medical students and pediatric residents on-site every weekday. This exacerbated the concern for timely completion of all components of the well visits, including EPDS screening, scoring, and discussion with the mother.

Conversely, the pediatricians and staff agreed that pediatric primary care is an ideal setting to identify risk factors in mothers who were known to the practice and who would be following up there for years. We screen for adverse childhood experiences (ACEs) and are aware of the life circumstances of our patients and families, and are thus able to keep mothers with multiple risk factors for PPD on our radar. Overall, the benefits were felt to outweigh the potential downsides and it was not difficult to get staff and faculty on board to commence this screening.

**Clinic data**

We reviewed our initial 16 months of screening (September 2016 to December 2017). Overall, we screened 1119 mother-baby dyads, including some mothers screened twice. Our overall prevalence rate of mothers screening positive for PPD, cumulative over this period, was 8.2%. Our weekly volume of referrals to social work was not overwhelming and did not detract from the various other referral, psychosocial, and tangible needs.

**TABLE 1**

**TELEHEALTH FOR MATERNAL MENTAL HEALTH**

<table>
<thead>
<tr>
<th>States with a maternal mental health telehealth program:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montana</td>
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<tr>
<td>Vermont</td>
</tr>
<tr>
<td>Oregon</td>
</tr>
<tr>
<td>Massachusetts</td>
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<tr>
<td>Michigan</td>
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<tr>
<td>Wisconsin</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Emerging telehealth programs in:</th>
</tr>
</thead>
<tbody>
<tr>
<td>California, Nevada, Arizona (Dignity Health network)</td>
</tr>
<tr>
<td>Florida (limited area)</td>
</tr>
<tr>
<td>North Carolina (limited area)</td>
</tr>
<tr>
<td>Rhode Island</td>
</tr>
<tr>
<td>Washington</td>
</tr>
</tbody>
</table>

**HME VISIT WORKFLOW**

1. Check-in
2. Complete screening on tablet
3. Vitals/rooming
4. MD visit
5. Checkout

Abbreviations: EMR, electronic medical record; HME, health maintenance exam; MA, medical assistant; MD, medical doctor
services provided by social work.

During this time, 22 mothers screened positive for self-harm (question 10 on the EPDS screener); of those, 18 indicated “hardly ever” and only 4 indicated “sometimes” or “very often” regarding thoughts of self-harm. Within this group of higher-risk mothers, 15 received immediate referral to social work to assess safety; 2 on further discussion needed no intervention; 2 were connected to our state maternal infant health program for home visits; 2 could not be definitively tracked on subsequent chart review; and 1 was suffering a psychiatric emergency and was sent to Psychiatric Emergency via ambulance. We recognize that these rare instances where there is concern for self-harm are more time consuming and anxiety provoking for the pediatricians and staff. However, these are the most important mothers to identify by screening to ensure they receive timely and appropriate interventions.

Chart review revealed an overall screening rate of 75% at well visits in babies’ first 6 months. Those not screened (either patient declined or the provider opted out) fall into 3 distinct groups. First, mothers who are known to be in therapy already are not rescreened at all subsequent well visits. Second, multiparous mothers who at the 2-month and later visits endorse no signs or symptoms of PPD can decline to complete screenings. Third, we recognize the important group of mothers whose first language is not English. We currently have the EPDS in English or Spanish and rely on interpreters by phone or in person to help with translation during clinical encounters.

By phone, it is challenging to complete the EPDS and other tools such as developmental screening. We will, in those cases, endeavor to ask some but not all of the screening questions. These visits tend to take longer at baseline and we recognize this additional barrier to effective and routine screening of all mothers in our practice for whom English is not their first language. When noted ahead of time, we book additional check-in and provider time for these babies’ well exams. We are also considering how best to implement EPDS in other languages.12

Translating our experience into other pediatric settings

Our pediatric clinic enrolls approximately 400 newborns annually. We worked with our staff to create a standard workflow to incorporate EPDS screening at infant well visits in the first 6 months of life (Figures 1 and 2). At check-in, the parent is given a tablet to complete social determinants, developmental screening, and update clinical information. The EPDS is given in paper-pencil format with an attached cover page offering information about PPD and resources that we encourage the mother to take home and read carefully after the visit. It takes mothers less than 2 minutes to complete the EPDS while the medical assistant is entering baby’s vitals into the electronic health record (EHR).

In other settings, EPDS may be available online through CHADIS13 (Child Health and Development Interactive System) and/or could be programmed into your EHR for completion. The physician can quickly score and review the EPDS during the visit, discuss mood swings and PPD, and let mothers know our clinic has many resources to help if the mother is struggling in any way. This takes the pediatrician fewer than 5 minutes. We aim for universal screening, to decrease the odds of missing subtle cases of mood disturbance and to destigmatize the postpartum mood swings that many mothers experience. We highlight the common challenges new parents face, and advocate for the RIMP.12

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**TABLE 2**

**POSTPARTUM DEPRESSION ONLINE RESOURCES FOR MOTHERS/CAREGIVERS**

<table>
<thead>
<tr>
<th>Resource</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum Support International</td>
<td><a href="http://www.postpartum.net">www.postpartum.net</a> 800-944-4773 Text: 503-894-9453  ■ Service in English or Spanish, also support for Arabic speakers  ■ Resources and local referral options, also online support meetings  ■ Wednesday chats for mothers and 1st Monday chats for fathers</td>
</tr>
<tr>
<td>MGH Center for Women’s Mental Health</td>
<td><a href="https://womensmentalhealth.org">https://womensmentalhealth.org</a>  ■ Information about treatment options and medications  ■ State listings of resources located: <a href="https://womensmentalhealth.org/resource/patient-support-services/">https://womensmentalhealth.org/resource/patient-support-services/</a></td>
</tr>
<tr>
<td>MCPAP for Moms (Massachusetts Child Psychiatry Access Program)</td>
<td><a href="http://www.mcpapformoms.org">www.mcpapformoms.org</a>  ■ Resources in English and Spanish</td>
</tr>
<tr>
<td>Postpartum Progress</td>
<td><a href="https://postpartumprogress.com">https://postpartumprogress.com</a></td>
</tr>
<tr>
<td>National Suicide Prevention Hotline</td>
<td>800-273-TALK (8255)  ■ If mother in crisis or call local emergency department</td>
</tr>
</tbody>
</table>

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Postpartum Support International

- [www.postpartum.net](http://www.postpartum.net)
- 800-944-4773 Text: 503-894-9453
  - Service in English or Spanish, also support for Arabic speakers
  - Resources and local referral options, also online support meetings
  - Wednesday chats for mothers and 1st Monday chats for fathers

MGH Center for Women’s Mental Health

- [https://womensmentalhealth.org](https://womensmentalhealth.org)
  - Information about treatment options and medications
  - State listings of resources located: [https://womensmentalhealth.org/resource/patient-support-services/](https://womensmentalhealth.org/resource/patient-support-services/)

MCPAP for Moms (Massachusetts Child Psychiatry Access Program)

- [www.mcpapformoms.org](http://www.mcpapformoms.org)
  - Resources in English and Spanish

Postpartum Progress

- [https://postpartumprogress.com](https://postpartumprogress.com)

National Suicide Prevention Hotline

- 800-273-TALK (8255)
  - If mother in crisis or call local emergency department
face and offer tools and resources to manage the feeding, sleep, and other issues this new family member brings to the home.

If we tally a positive screen— including any score greater than 10 or any positive response on the item about self-harm—we then access additional resources. Our clinic social worker or on-call hospital social worker is available during office hours even on Saturdays. If your clinic does not have this most helpful resource, then it is essential to research local and online partners for care prior to initiating this screening.

Local adult primary care physicians and obstetricians often manage mothers with PPD, especially those who require medication. Licensed clinical social workers and psychologists are essential therapeutic partners as well. Identify your resources during the planning phase and assess how to most effectively partner with, refer, and co-manage mothers needing care. This will ensure that the pediatric office has the appropriate referral resources.

We recommend having a list of local therapists who are skilled at working with this patient population. Additionally, there are now excellent telehealth resources in several states (Table 1), especially for those in a rural or low-resourced setting. Online tools (Tables 2 and 3) offer more excellent resources and therapy options for caregivers in your practice.

Conclusions

Identifying and caring for mother-baby dyads is one of the joys of pediatric primary care. Postpartum depression is one of the most common clinical scenarios faced by new mothers. It can have significant impact on attachment and infant development, so it is critical that it is addressed in a routine way to optimize infant mental and physical health.

Pediatricians are ideally situated to help identify, refer, and support mothers who are affected by PPD because we see babies so often during their first year of life and establish close bonds with the families in our practices. Implementing a standard PPD screening using EPDS is very feasible in a busy pediatric primary care practice if local and online resources are identified and a clinic workflow is established ahead of implementation. This practice can destigmatize PPD and set mothers and babies on a trajectory to strong attachment and good health.

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**TABLE 3**

POSTPARTUM DEPRESSION ONLINE RESOURCES FOR PHYSICIANS/CLINIC

<table>
<thead>
<tr>
<th>Resource</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postpartum Support International</td>
<td><a href="http://www.postpartum.net">www.postpartum.net</a></td>
</tr>
<tr>
<td></td>
<td>- Handouts and referral options</td>
</tr>
<tr>
<td>MGH Center for Women’s Mental Health</td>
<td><a href="https://womensmentalhealth.org">https://womensmentalhealth.org</a></td>
</tr>
<tr>
<td></td>
<td>- 7-page guide for patients and families to consider giving out when concerned or to all new mothers: <a href="https://womensmentalhealth.org/wp-content/uploads/2018/05/postpartum_guide.pdf">https://womensmentalhealth.org/wp-content/uploads/2018/05/postpartum_guide.pdf</a></td>
</tr>
<tr>
<td></td>
<td>- State listing of resources located at: <a href="https://womensmentalhealth.org/resource/for-providers/">https://womensmentalhealth.org/resource/for-providers/</a></td>
</tr>
<tr>
<td>MCPAP for Moms (Massachusetts Child Psychiatry Access Program)</td>
<td><a href="http://www.mcpapformoms.org/">www.mcpapformoms.org</a></td>
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Primary care clinicians play a key role in identifying and treating anxiety disorders in children and helping them learn effective coping skills. Mary Beth Nierengarten, MA

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Oregon has passed several new laws aimed at suicide prevention. Rachael Zimlich, RN, BSN

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Suicide rates among teenagers increased by 30% since 2000. Rachael Zimlich, RN, BSN

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INFECTION DISEASE

Remember measles’ past when talking to parents

With the possibility of the United States losing its measles-free status, Dr Eden remembers a patient who suffered extreme neurologic complications as a result of the disease.

ALVIN N EDEN, MD, FAAP

Emily was a beautiful 19-year-old honors student attending Barnard College in New York, New York, who contracted measles and developed post-measles encephalitis with resulting severe brain damage. I met Emily when visiting with a group of fellow pediatricians at Letchworth Village in Thiells, New York, a former residential institution for the physically and mentally disabled. We soon realized that, unfortunately, Emily was now barely able to function at the developmental level of a child aged 4 to 5 years.

That encounter made an indelible impression that has stayed with me to this day. The year was 1959, 60 years ago, and shortly before the measles vaccine was available. At that time, measles was one of the most common childhood illnesses.

Vaccine success story
Since the approval and licensing of the vaccine in 1963, we have seen a dramatic decrease in the prevalence of measles. The vaccine has been shown to be safe and effective. My office participated in the field trials in 1961. My son was an uncooperative, unwilling participant in the trial as I drew his blood, as were many of my other patients. In those days every practicing pediatrician was quite familiar with measles that was, along with chicken pox, seen very frequently.

The diagnosis of measles at times could be challenging. We learned about the 4 k’s: koplik spots, kough, koryza, and conjunctivitis. However, there were cases that did not present with all these features. Finding the koplik spots, which appeared before the rash, was not easy. Prying the mouth open of a sick and screaming toddler was hard enough. Locating these 1-mm to 3-mm blue white lesions with an erythematous base on the buccal mucosa opposite the first molar was even harder.

During the 1989-1991 outbreak, the mortality rate was 2.2 deaths per 1000 cases.1 Pneumonia was responsible for 60% of the deaths, mostly in children aged younger than 5 years.2 As illustrated by Emily, measles can also cause severe neurologic complications. Post-measles encephalitis is seen in 1 to 2 cases per 1000, usually developing several days after the rash.

The hope at that time was for the vaccine to not only protect against measles, but more importantly to prevent the serious complications, which is exactly what has happened.

The vaccine had been an incredible success, so much so that in 2000 the Centers for Disease Control and Prevention (CDC) declared that measles was officially eliminated in the United States, as a result of so few reported cases in each of the previous few years.

MMR: Victim of its own success
However, now we are suddenly witnessing a major outbreak of measles, and so I am again reminded of Emily. I watch, with increasing frustration and anger, more and more antivaccine parents refusing to immunize their children with the measles/mumps/rubella (MMR) vaccine. As of September 19 this year, 1241 cases of measles have been reported by the CDC, the highest number since 1992. Why is there no public outcry to mandate universal measles vaccination without exception for all children?

“Why is there no public outcry to mandate universal measles vaccination without exception for all children?” –Alvin N. Eden, MD, FAAP

CONTINUED ON PAGE 26
As medicine and science advances, pediatric clinicians are seeing ever increasing numbers of approved immunomodulatory therapies approved by the US Food and Drug Administration (FDA). A few examples of drugs approved in recent years include emapalumab (Gammagard) for primary hemophagocytic lymphohistiocytosis and the expanded approval for tocilizumab (Actemra) for cytokine release syndrome due to chimeric antigen receptor T-cell therapy.

Additionally, clinicians may see increased use of older agents such as anakinra (Kineret) for off-label indications such as macrophage activating syndrome and, of course, there are numerous agents once reserved for use in adult populations that are making their way into the world of pediatric medicine.1 Given this increased prevalence and current state of vaccine compliance within the United States, general practice physicians may find themselves wondering how to best protect patients who previously received an immunomodulatory agent from vaccine-preventable diseases.

State of current knowledge
Whereas many of these therapies are being used in an acute care setting, it is important to remember that immunomodulatory therapies new and old can have ramifications on the immune system for weeks to months after administration. The problem of how to vaccinate children receiving these immunomodulatory agents is being increasingly recognized as evident by the development of guidelines from bodies such as the Infectious Diseases Society of America and the Canadian Paediatric Society.2,3 Both guidelines stress the importance of obtaining vaccination records and vaccinating if at all possible before start-

Dr. Lee’s Clinical pharmacologist’s notebook

Carleton Lee, PharmD, MPH, FASHP, FPPAG, section editor for The Clinical Pharmacologist’s Notebook, is a clinical pharmacy specialist in Pediatrics, Department of Pharmacy, Johns Hopkins Hospital, and associate professor of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Hailey E Steuber, PharmD, BCPPS

Dr. Steuber is a pediatric clinical pharmacist, University of Iowa Stead Family Children’s Hospital, Iowa City, Iowa. The author and section editor have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

Contemporary Pediatrics is meeting your need to stay current on pharmacologic best practices by bringing you this recurring feature titled The Clinical Pharmacologist’s Notebook. Our goal is to provide pediatricians and pediatric healthcare providers with the most up-to-date information—and thinking—as provided by children’s clinical pharmacology experts.
# GUIDELINES FOR VACCINATING CHILDREN RECEIVING IMMUNOMODULATORY AGENTS

<table>
<thead>
<tr>
<th>INTERMITTENT IMMUNOMODULATOR THERAPY</th>
<th>SPECIFIC PRODUCT/DOSE</th>
<th>IMPACTED VACCINES</th>
<th>TIME TO VACCINATE FOLLOWING THERAPY</th>
<th>REFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Steroids</strong></td>
<td>High-dose therapy as defined by IDSA²</td>
<td>Live</td>
<td>1 mo</td>
<td>AAP Redbook⁴; IDSA Guidelines for Vaccination of the Immunocompromised Host⁵</td>
</tr>
<tr>
<td><strong>IVIG</strong></td>
<td>300 to 400 mg/kg</td>
<td>MMR, varicella</td>
<td>8 mo</td>
<td>AAP Redbook⁴</td>
</tr>
<tr>
<td></td>
<td>800 mg to 1000 mg/kg</td>
<td></td>
<td>10 mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2000 mg/kg</td>
<td></td>
<td>11 mo</td>
<td></td>
</tr>
<tr>
<td><strong>Blood products</strong></td>
<td>RBC (washed)</td>
<td>MMR, varicella</td>
<td>None</td>
<td>AAP Redbook⁴</td>
</tr>
<tr>
<td></td>
<td>RBC (packed)</td>
<td></td>
<td>5 mo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Whole blood</td>
<td></td>
<td>6 mo</td>
<td></td>
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<tr>
<td></td>
<td>Plasma/platelets</td>
<td></td>
<td>7 mo</td>
<td></td>
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<tr>
<td><strong>Common immunomodulators</strong></td>
<td>Adalimumab</td>
<td>Live vaccines</td>
<td>Contraindicated during therapy</td>
<td>Prescribing information⁵</td>
</tr>
<tr>
<td></td>
<td>Anakinra</td>
<td>Tetanus/ diphtheria toxoid vaccine</td>
<td>None—No difference detected in antibody response (n=126)</td>
<td>Prescribing information⁶</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>All other live and inactivated vaccines</td>
<td>No data or informal recommendations available</td>
</tr>
<tr>
<td></td>
<td>Emapalumab</td>
<td>Live vaccines</td>
<td>Contraindicated during therapy and for 4 wk after last dose</td>
<td>Prescribing information⁷</td>
</tr>
<tr>
<td></td>
<td>Infliximab</td>
<td>Live vaccines</td>
<td>Contraindicated during therapy; caution advised in infants whose mothers received infliximab during pregnancy</td>
<td>Prescribing information⁸</td>
</tr>
<tr>
<td></td>
<td>Tocilizumab</td>
<td>Live vaccines</td>
<td>Contraindicated during therapy</td>
<td>Prescribing information⁹</td>
</tr>
<tr>
<td><strong>Anti-B-cell antibody</strong></td>
<td>Rituximab</td>
<td>Live vaccines</td>
<td>Contraindicated during therapy</td>
<td>Prescribing information¹⁰</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inactivated vaccines</td>
<td>Prospective cohort study¹¹ (n=14)</td>
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</tr>
</tbody>
</table>

Abbreviations: IVIG, intravenous immunoglobulin; MMR, measles/mumps/rubella; RBC, red blood cell.

From: Infectious Diseases Society of America (IDSA)²; American Academy of Pediatrics (AAP)⁴; Abbott Laboratories⁵; Swedish Orphan Biovitrum⁶; Novimmune SA⁷; Janssen Biotech⁸; Genentech⁹; Genentech¹⁰; Nazi I, et al.¹¹
ing immunomodulatory therapies.

In the case of patients receiving immunomodulator therapy for a stable, chronic condition, it is likely feasible to postpone therapy while live vaccines are completed. Immunosuppressed patients receiving chemotherapy or after bone marrow transplants will likely be under the care of an oncologist and may need to undergo revaccination according to their practice’s protocol. Unfortunately, not all children will fall neatly into either of these categories.

Currently, published guidelines do not address how to modify or return to a child’s normal immunization schedule after therapy has been completed. In a small but growing population of patients, these therapies are not chronically administered, and patients may have already returned to the routine care of their primary care provider. It is critical that primary care providers are fully informed of when such therapies were administered. This overview aims to highlight established recommendations for selected agents and reveal knowledge gaps where specialty guidance may be warranted.

Gaps in the data

As the Table shows, most recommendations for altering a patient’s immunization schedule will apply to live vaccines only. However, there are a few exceptions. Also evident in the Table is the fact that not all agents have established recommendations and that recommendations stemming from robust scientific studies are extremely limited. For example, although the manufacturers of anakinra recommend not administering live vaccines during therapy, the prescribing information does state this is due to a lack of evidence as it has not been studied. A published case series of patients who received interleukin (IL)-1 or IL-6 blockade (n=17) concluded that live attenuated vaccines should also be aware of existing literature for agents such as infliximab or adalimumab but note the role of certain disease states such as inflammatory bowel diseases or rheumatologic indications. In this literature, it can be assumed that the therapies are chronic, and that alteration of the immune system is ongoing due to both the inflammatory condition and the immunomodulating agent itself, and so it may not apply to patients treated off label.

Summary

As pediatric providers begin utilizing new agents previously reserved to the adult population and explore the off-label use of other immunomodulating agents, it is becoming increasingly likely that general practice providers will encounter patients who may have had exposure to immunomodulation. In the era of an infectious outbreak exceeding levels seen in previous decades, it is more important than ever that clinicians do all they can to advocate for patients to receive timely vaccination.

Reviewing established vaccine recommendations after immunomodulatory therapies can help pediatric patients stay on an appropriate schedule and, given the current gaps in knowledge, may help guide practitioners toward the consultation of a specialist when necessary.

For references, go to ContemporaryPediatrics.com/immunomodulation
A mildly overweight 8-year-old Hispanic female in rural Colorado is brought to her primary care provider’s (PCP) office with right neck pain and right-sided neck swelling of a day’s duration. The patient’s mother also stated that her daughter had a maximum temperature (T-max) of 102°F that started that morning. The patient denied any sore throat, rash, headache, rhinorrhea, cough, nasal congestion, abdominal pain, vomiting, or diarrhea.

The patient also denied any swelling of her tongue, hands, or feet. Her mother was concerned that the neck swelling may be related to a recent cat scratch. The patient and her family do not have any cats in the home, but the patient did play with one at a friend’s house in the past week. The mother denied any history of recent travel. No one else in the home had similar symptoms.

Prior to this patient’s presentation, she was in a normal healthy state. She does have a past medical history that includes Kawasaki disease (KD) diagnosed at 3 months of age. She has had regular follow-up with Pediatric Cardiology and there have been no concerns for residual cardiac complications.

On initial exam, the patient was well appearing and was noted to have posterior pharyngeal erythema with asymmetrical tonsils (R 2+, L 1+), and right-sided nonfluctuant anterior cervical/submandibular lymphadenopathy with a supple neck (Figure 1). As the patient was in school at the time with possible exposure, a rapid group A Streptococcus test was obtained (negative), and culture was sent. The mother was also mildly concerned about the possibility of recurrent KD. She (a medical assistant at the PCP’s clinic) was informed that KD could not be diagnosed in the absence of 5 days of fever. Also, the patient had no other symptoms of KD such as cracked lips, desquamation of hands/feet, or conjunctivitis. The patient was sent home with instructions for supportive care for a presumed vi...
Recommend Aquaphor® Baby as the complete solution for babies’ diaper area needs

**Prevent** Aquaphor Baby Healing Ointment
- Provides immediate protection by creating a barrier from wetness, acidity, and chafing
- Uniquely formulated with 41% Petrolatum and 4 key ingredients that protect and soothe to help heal skin

**Treat** Aquaphor Baby Diaper Rash Cream
- 83% of patients had improvement from baseline in diaper rash and irritation by Week 1*
- Formulated with 15% Zinc Oxide, odor-free, preservative-free, and talc-free

*Data on File.
©2019 Beiersdorf Inc.
The patient returned to her PCP’s office 3 days later as she had developed worsening right-sided lymphadenitis and continued to have fevers (her last fever was the previous night). Her mother noted that the patient had complained of fatigue the previous night, but otherwise had no new symptoms. Her fevers occurred nightly. The patient’s exam was consistent with the mother’s history of increasing neck swelling, and “2-cm x 3-cm nonfluctuant, mildly tender to palpation, right submandibular prominence” with full range of motion was documented. She remained well appearing.

It was time to supplement the differential diagnosis (Table 1) with further laboratory evaluation (Table 2).

Testing was notable for an elevated C-reactive protein (CRP) count (21.1) and erythrocyte sedimentation rate (ESR, 61), with mild leukocytosis (11.9) and elevated liver enzymes (alkaline phosphatase [ALP], 299; aspartate transaminase [AST], 86; alanine transaminase [ALT], 104). *Bartonella henselae* polymerase chain reaction (PCR) analysis was sent and later came back negative. A thyroid-stimulating hormone (TSH) test was within normal limits, and blood cultures did not grow any bacteria at 48 hours. The patient’s monospot test was positive, and Epstein-Barr virus (EBV) PCR serology was sent. See Table 2 for additional laboratory information.

At this time, the patient was given the diagnosis of mononucleosis, although some doubt lingered as to whether all the patient’s symptoms could be attributed to mononucleosis-associated EBV or cytomegalovirus (CMV). Abscess/cellulitis was also considered. She had no obvious

### Table 1. Differential Diagnosis Includes Supportive and Nonsupportive Factors

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mononucleosis infection (EBV or CMV)</td>
<td>Positive monospot, reports of fatigue, cervical LAD</td>
<td>Negative EBV serology, no prodrome, no HSM, no BL LAD</td>
</tr>
<tr>
<td>Bartonella henselae infection</td>
<td>Unilateral LAD with cat exposure</td>
<td>Negative Bartonella serologies</td>
</tr>
<tr>
<td>Tuberculosis infection</td>
<td>Unilateral LAD</td>
<td>No risk factors including travel to endemic area, negative CXR at tertiary care center, negative PPD</td>
</tr>
<tr>
<td>Neck abscess</td>
<td>Unilateral neck swelling</td>
<td>Negative neck ultrasound at tertiary care center</td>
</tr>
<tr>
<td>Recurrent Kawasaki disease (KD)</td>
<td>CRP 21.1, albumin 2.7, history of KD, elevated liver enzymes, presence of cracked lips and conjunctivitis, persistent fever</td>
<td>Rare late in life, so many years after initial occurrence, more common in males</td>
</tr>
<tr>
<td>Oncologic process—lymphoma</td>
<td>Mildly elevated WBC, fevers</td>
<td>No other symptoms of malignancy, mildly elevated WBC, no HSM</td>
</tr>
<tr>
<td>Adenovirus infection</td>
<td>Conjunctivitis</td>
<td>10.4 (low) % lymphocytes negative viral panel, minimal viral symptoms</td>
</tr>
<tr>
<td>Enterovirus infection</td>
<td>Conjunctivitis, acral lesions</td>
<td></td>
</tr>
<tr>
<td>Bacterial LAD (Staphylococcus aureus, GAS, anaerobes)</td>
<td>Unilateral LAD, Initial labs with L shift, + WBC, elevated CRP</td>
<td>CRP elevation seems out of proportion</td>
</tr>
<tr>
<td>Ectopic thyroid tissue</td>
<td>Enlargement of neck tissue</td>
<td>Normal TSH, no other symptoms of hyperthyroidism</td>
</tr>
<tr>
<td>Systemic juvenile idiopathic arthritis (JIA)</td>
<td>Elevated CRP and ESR, recurrent episodes</td>
<td>No evidence of joint swelling or rashes, only 2 episodes, no daily fever</td>
</tr>
<tr>
<td>Acute hepatitis</td>
<td>Elevated liver enzymes</td>
<td>No liver enlargement or jaundice on exam</td>
</tr>
<tr>
<td>Polyarteritis nodosa (recurrent autoimmune vasculitis)</td>
<td>Coronary vessel abnormality, recurrent inflammatory episodes</td>
<td>Resolution of symptoms with IVIG/infliximab, no arthritis, resolution of inflammation, 7 y between episodes</td>
</tr>
</tbody>
</table>

Abbreviations: BL LAD, bilateral lymphadenopathy; CMV, cytomegalovirus; CRP, C-reactive protein; CXR, chest x-ray; EBV, Epstein-Barr virus; ESR, erythrocyte sedimentation rate; GAS, group A Streptococcus; HSM, hepatosplenomegaly; IVIG, intravenous immunoglobulin; LAD, lymphadenopathy; PPD, purified protein derivative; TSH, thyroid-stimulating hormone; WBC, white blood cell.
trauma or puncture wound to the outside of the neck. She also had no dental abnormalities or signs of dental abscess on initial or repeat exam. Given the leukocytosis and elevated inflammatory markers, infection seemed likely. Antibiotics were considered including sulfa-trimethoprim and clindamycin as coverage for *Staphylococcus aureus* or oral flora lymphadenitis.

The patient was also considered to have ectopic thyroid tissue as in an ectopic thyroiditis. This was less likely as the condition is rare and the patient had a normal TSH. Tuberculosis was also considered as a potential infectious cause of the patient’s symptoms but also seemed less likely as she had no risk factors including travel to an endemic area. A chest x-ray done later was negative, as was a tuberculin skin test. Malignancy was considered a potential cause of the swelling as the patient had a mildly elevated white blood cell (WBC) count and low-grade fevers, but again this was moved to the bottom of the list as she had no other symptoms concerning for malignancy and the duration of symptoms was short. The patient’s elevated liver enzymes were mildly concerning for acute hepatitis but she had no liver enlargement or jaundice on exam. See Table 1 for an expanded differential diagnosis.

With laboratory testing pending, the patient’s condition progressed over the weekend. Her fevers continued nightly, and she developed red eyes (no discharge, no pruritus) and mild cough (for 2 days only) on day 5 of illness. She was seen again in the clinic on day 7 of illness for these new symptoms and persistent fevers. At this time, she had not developed swelling/changes of extremities, joint pains, or any rash that would be consistent with juvenile arthritis.

Adenovirus was also considered to be a potential cause of the new onset conjunctivitis. A viral panel (and continued lack of viral symptoms) performed this same day later ruled out viral etiology. Recurrent KD seemed more likely at this time as the patient had fevers for more than 5 days and had developed conjunctivitis. Labs were repeated and notable for decreased leukocytosis and mildly decreased CRP (18). See Table 2.

On day 7 of illness, the patient’s PCP spoke with 2 pediatric Infectious Disease (ID) specialists specifically regarding likelihood of recurrent KD versus other causes of fever, fatigue, and swelling. The PCP was concerned that mononucleosis was not the correct diagnosis. The first pediatric ID specialist did not suspect KD at this point and suggested adding an antibiotic for the lymphadenopathy. The second ID specialist was a fellow, and after discussion with her attending it was decided to have the patient admitted the following morning for imaging of her neck, including an ultrasound to rule out abscess and Kawasaki protocol echocardiogram to rule out KD. Both ID specialists expressed extreme doubt regarding a diagnosis of recur-

### Table 2: Laboratory testing results

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Values</th>
<th>Day of Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid group A <em>Streptococcus</em>: Analysis/group A <em>Streptococcus</em> culture</td>
<td>Negative</td>
<td>Negative</td>
<td>1</td>
</tr>
<tr>
<td>Respiratory viral panel PCR</td>
<td>Negative</td>
<td>Negative</td>
<td>7</td>
</tr>
<tr>
<td>Liver function panel</td>
<td>ALP: 299, 251, AST: 86, 12, ALT: 104, 50, Albumin: 3.3, 2.7</td>
<td>ALP (46-116 U/L), AST (1-37 U/L), ALT (12-78 U/L), Albumin: (2.9-2 g/dL)</td>
<td>4, 7</td>
</tr>
<tr>
<td>Complete blood count</td>
<td>WBC 11.9, 11.7, Segmented neutrophils: 78, 55.5, Eosinophils: 4, 5.1, Hg: 12.3, 11</td>
<td>(5-10), (45-65%), (0-5%), (11.3-16 g/dL)</td>
<td>4, 7</td>
</tr>
<tr>
<td>CRP</td>
<td>21.1, 18.6</td>
<td>(0-0.9 mg/dL)</td>
<td>4, 7</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>61, 85</td>
<td>(0-20 mm/h)</td>
<td>4</td>
</tr>
<tr>
<td>Monospot</td>
<td>Positive</td>
<td>Negative</td>
<td>4</td>
</tr>
<tr>
<td>Epstein-Barr virus PCR</td>
<td>Negative</td>
<td>Negative</td>
<td>4</td>
</tr>
<tr>
<td><em>Bartonella henselae</em> PCR</td>
<td>Negative</td>
<td>Negative</td>
<td>4</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>1.0001</td>
<td>(0.704-4.01 mLU/mL)</td>
<td>4</td>
</tr>
<tr>
<td>Blood cultures x 2</td>
<td>No growth at 48 h</td>
<td></td>
<td>4</td>
</tr>
</tbody>
</table>

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; CRP, C-reactive protein; HG, hemoglobin; PCR, polymerase chain reaction; WBC, white blood cell.
rent KD due to statistical unlikelihood (one quoted a <1% chance).

The patient was seen the next morning in the emergency department (ED) of the tertiary care center where she could be evaluated by the pediatric ID team. She was then admitted with a final diagnosis of recurrent KD after echocardiogram revealed dilated coronary arteries.

**Management**

The patient’s admission exam at the tertiary care center was notable for prominent tongue papillae, dried/cracked lips, and limbic sparing conjunctival injections without discharge. An echocardiogram during admission demonstrated mild dilation of the right main coronary artery (z score, 2.73, 3.67 mm), preserved ejection fraction (EF) of 60.7%, and no other cardiac abnormalities.

Rheumatology consult ruled out other causes of recurrent vasculitis such as polyarteritis nodosa and autoinflammatory disorders such as systemic juvenile idiopathic arthritis (Table 1). Previous echo per Kawasaki follow-up had been obtained 9 months prior and showed no vessel dilation. The patient was treated with infliximab followed by intravenous immunoglobulin (IVIG; both KD treatment protocol at this facility), and high-dose aspirin at the tertiary care center.

**Discussion**

Kawasaki disease is an acute febrile illness with an unknown cause that was first described in Japan by Tomisaku Kawasaki in 1967. Patients typically present with fever, rash, swelling of the hands and feet, conjunctival erythema, swollen lymph nodes in the neck, and inflammation of the mouth, lips, and throat. Kawasaki disease is the leading cause of acquired heart disease among children in developed countries, causing coronary artery dilations and aneurysms. Treatment of KD includes IVIG and aspirin. Kawasaki disease mostly affects young males. The disease is very rare, affecting 9 to 19 per 100,000 in children aged younger than 5 years.

Kawasaki disease recurrence occurs only in a small percentage of patients with a history of the disease. Most sources agree that the recurrence rate of KD is well under 2%. Kawasaki disease recurrence is most common in the first 2 years following diagnosis and significantly decreases each year after 2 years from initial diagnosis, with recurrent episodes occurring 83% of the time in the first 3 years after the initial episode.

Other risk factors associated with recurrence are being male and aged younger than 3 years at the initial episode. The patient in this case, an 8-year-old female, was nearly statistically safe from the diagnosis, although her mother and her PCP were cautiously suspicious from the onset.

Surprisingly consistent with the data, this patient had mild dilation of the right coronary artery (RCA) and left anterior descending (LAD) coronary artery at age 3 months, which resolved with initial treatment and recurred with her second episode. Yang and colleagues found that “coronary artery complications are more likely to occur in children with recurrent KD if they were present during the first episode.” Also, children with longer durations of fever, lower hemoglobin levels, and higher AST levels may be at increased risk for KD. See Table 2 regarding elevated AST and decreased hemoglobin.

**Patient outcome**

The patient responded well to treatment and was discharged home on low-dose aspirin within 48 hours of admission. She had follow-up appointments with ID, Rheumatology, and the PCP clinics. One week after discharge, the patient’s mother noted desquamation of the skin on her daughter’s hands and around her mouth (Figure 2). Repeat echocardiograms were consistent with resolution of dilated coronary arteries within 2 weeks of treatment.

**For references, go to ContemporaryPediatrics.com/puzzler-1019**
Anxiety disorders in primary care

Primary care clinicians play a key role in identifying and treating anxiety disorders in children and helping them learn effective coping skills. This article summarizes some of the current guidance.

MARY BETH NIERENGARTEN, MA

Anxiety disorders are the most prevalent psychiatric condition in children and adolescents, affecting between 15% to 20% of youth.¹ Some data estimate an even higher prevalence, up to 31% in young persons aged 13 to 18 years.²

Recently reported data also highlight the steady rise in anxiety disorders in adolescents, showing an increased prevalence of 20% between 2007 and 2012.³ A further recent report highlighted that up to 30% will develop an anxiety disorder in their lifetime.⁴

The impact of these types of disorders in the young cannot be understated. Children and adolescents who struggle with an anxiety disorder face difficulties with academic, social, and family functioning, and are at increased risk for other mental health issues such as depression, substance abuse, and suicide.¹,²

Despite the high prevalence and associated negative impacts, pediatric anxiety disorders can go unrecognized as it can be difficult for parents and clinicians to differentiate an anxiety disorder from anxiety a child experiences as part of growing, developing, and adapting to new situations and experiences. Whereas this latter type of anxiety is characterized by transient fears as part of normal development, anxiety disorders are characterized by their persistence and the extensive distress and functional impairment they cause. In addition, a child with an anxiety disorder will typically respond with a disproportionate amount of fear to a threat that reason cannot allay.²

Early diagnosis and treatment of pediatric anxiety disorders are critical to both minimize the negative impacts on the child’s life as well as to lessen the negative impacts that can impair a child long into adulthood if left untreated. Data suggest that although the onset of anxiety disorders usually begins in childhood, these disorders typically are chronic and persistent and can evolve into a pattern of multiple anxiety disorders (ie, depressive or substance use disorders) into early adulthood.¹ Primary care clinicians play a key role in identifying and treating anxiety disorders in children and helping them to learn effective coping skills. This article summarizes...
some of the current data on screening, diagnosis, and treatment of pediatric anxiety disorders.

**Clinical presentation and diagnosis**

Differentiating an anxiety disorder from developmentally appropriate anxiety or other conditions that may mimic an anxiety disorder is challenging. To help make the differential diagnosis, recognizing the risk factors is important as well as knowing a number of hallmark features that present in adolescents with anxiety disorders (Tables 1 and 2). In addition, clinicians should be aware that children and parents/caregivers may describe anxiety-related symptoms in terms that misinterpret anxiety for something else (eg, parents may describe their child as sensitive, picky, or shy, or attribute symptoms of irritability, crying, or tantrums as signs of disobedience or oppositional behavior, while children may use words such as angry, upset, tense, or uncomfortable to describe their anxiety).2

A particular challenge is differentiating an anxiety-related disorder from other childhood problems, such as major depressive disorder, bipolar disorder, oppositional mood dysregulation disorder, and attention-deficit hyperactivity disorder (ADHD)—all of which can share similar symptoms of inattention, difficulty sleeping and eating, behavioral outbursts, social difficulties, and restlessness.2 Unlike these other childhood problems that are more pervasive across situations, one key distinguishing feature of an anxiety disorder is that it involves avoidance and distress that is more situational and triggered by a perceived threat. Identifying the source of the threat and the feared stimuli can help clinicians determine the type of anxiety disorder.2 (See Table 3 for types of anxiety disorders).

Once the clinical presentation suggests a child may have anxiety, other steps can be taken to confirm the diagnosis. A parent or caregiver interview is key. It is important to include the child in the interview process as much as possible, taking into account the child’s developmental level. Clinicians should ask the child about their anxiety and how it relates to their symptoms. They should also ask about the frequency, duration, and severity of the symptoms. The interview should also include questions about the child’s thoughts, feelings, and behaviors related to their anxiety.

**Resources for Primary Care Clinicians**

- **American Academy of Pediatrics**
  **Pediatric Anxiety: Tools and Resources for Primary Care**
  Provides tools, apps, and activities to help teach children how to manage anxiety, as well as books for parents and for children and adolescents on anxiety.
  www.aappublications.org/news/2018/12/14/anxietyresources121418

- **American Academy of Child and Adolescent Psychiatry**
  **Anxiety Disorders Resource Center**
  Provides a range of clinical resources including practice parameters for the assessment and treatment of anxiety disorders in children and adolescents, workbooks on treatment approaches, and apps for helping children to manage their anxiety.
  www.aacap.org/AACAP/Families_and_Youth/Resource_Centers/Anxiety_Disorder_Resource_Center/Home.aspx
a number of standardized tests are available to assess the type and severity. Table 4 lists screening tools for both parents and children that are easy and quick to complete.

In 2015, the American Academy of Pediatrics (AAP) published guidance for pediatricians on how to implement behavioral and emotional screening in clinical practice. Among the key points highlighted is the need to establish office routines for screening in which children are screened for behavioral and emotional problems at regular intervals, similar to developmental screening. Such screening should be done with standardized measures beginning in infancy through adolescence.

**Treatment**

Appropriate early treatment of anxiety disorders is crucial to prevent or reduce the negative impacts on children’s lives, as well as to reduce the long-term potential adverse effects into adulthood. Both nonpharmaceutical and pharmaceutical approaches are indicated.

The goal of all treatment approaches is to reduce symptoms of anxiety and increase a child’s ability to cope with his/her anxiety without avoiding the feared object or situation. For children with milder forms of anxiety disorder, this goal may be accomplished by using nonpharmaceutical approaches such as cognitive behavioral therapy (CBT) and mindfulness-based therapies. Cognitive behavioral therapy is one of the most commonly used approaches and has shown efficacy for patients with several types of anxiety disorders. Key components of CBT include education of both the child and parents about the nature of anxiety; techniques for managing physical symptoms such as relaxation training and diaphragmatic breathing; reframing anxiety-provoking thoughts; as

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**TABLE 3**

<table>
<thead>
<tr>
<th>TYPES OF ANXIETY DISORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANXIETY DISORDER</strong></td>
</tr>
<tr>
<td>Separation anxiety disorder: Excessive fear/anxiety about being separated from a major person of attachment.</td>
</tr>
<tr>
<td>Generalized anxiety disorder: General feeling of dread linked to the perception of the unpredictability or uncontrollability of events or situations.</td>
</tr>
<tr>
<td>Social anxiety disorder: Fear of embarrassment or humiliation by others.</td>
</tr>
<tr>
<td>Panic disorder: Fear of panic attacks or consequences.</td>
</tr>
<tr>
<td>Agoraphobia: Fear of being in places where escape may be difficult or help not available.</td>
</tr>
<tr>
<td>Specific phobia: Fear of specific object or situation.</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder (OCD) Fear of unwanted thoughts, images, or urges.</td>
</tr>
</tbody>
</table>

*Types of anxiety disorders listed in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), except for OCD that is now listed in “Obsessive-Compulsive and Related Disorders” category. From Chiu A, et al.2

---

**TABLE 4**

<table>
<thead>
<tr>
<th>SCREENING TOOLS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>For children aged 8-18 y</strong></td>
</tr>
<tr>
<td>Screen for Child Anxiety Related Emotional Disorders (SCARED)</td>
</tr>
<tr>
<td>Child version</td>
</tr>
<tr>
<td>Parent version</td>
</tr>
</tbody>
</table>

| **For children aged 6-18 y** |
| Spence Children’s Anxiety Scale | [www.scaswebsite.com](http://www.scaswebsite.com) |

| **For preschool children aged 3-6 y** |
| Spence Children’s Anxiety Scale | [www.scaswebsite.com](http://www.scaswebsite.com) |
| Preschool Anxiety Scale | [www.scaswebsite.com/docs/scas-preschool-scale.pdf](http://www.scaswebsite.com/docs/scas-preschool-scale.pdf) |

From Weitzman CC, et al.4
ADDITIONAL NONPHARMACEUTICAL INTERVENTIONS FOR ANXIETY

- Establish regular routines for the child.
- Make sure the child gets sufficient sleep.
- Prepare child for changes in routines.
- Don’t allow parental anxiety to overwhelm the child.
- Educate parents that childhood should not be "stress-free."

From Neal P.8

well as systematic exposure to feared stimuli or situations.1 (See “Additional nonpharmaceutical interventions for anxiety,” *above.*)

For a child with significant anxiety, the addition of a pharmacologic agent to CBT has been shown to be effective. Selective serotonin reuptake inhibitors (SSRIs) are considered the first-line treatment for pediatric anxiety.1,2,6,7 Other agents used include serotonin-norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants, but these are usually reserved as second- or third-line therapies because of more adverse effects.7 The use and efficacy of these agents to treat anxiety in children is based on a better understanding of the neurobiology of pediatric anxiety gained through imaging studies of children with anxiety disorders that show dysfunction in areas of the brain involved in the regulation of fear and emotion.1

As with any medication, using an SSRI to treat anxiety in a child needs to be balanced against the risks. Adverse effects can include headache, gastrointestinal symptoms, and sleep disturbance.6,7 Children on SSRIs need to be closely monitored to assess improvements in anxiety as well as adverse effects. It is also suggested that children be assessed for suicidal ideation at each follow-up given the black box warning on many antidepressants of an increased risk of suicide.7 (See “Resources for primary care clinicians,” page 24, for more on treating pediatric anxiety disorders.)

For references, go to ContemporaryPediatrics.com/pediatric-anxiety-disorders

Measles CONTINUED FROM PAGE 14

there no public outcry to mandate universal measles vaccination without exception for all children?

I am certain that every parent wants only the best for his/her child, and this includes the antivaccine group. When I am faced with a parent who is hesitant or refuses to immunize his or her child, I explain to them how safe and effective the vaccine has been for over 50 years, but I also tell them about Emily and who she was before and after she caught measles.

Many practicing pediatricians have little or no experience with measles and its complications, unless, like me, they started practicing pediatrics before the routine use of the measles vaccine in 1963 or before the last major outbreak of measles that occurred 25 years ago. (The MMR vaccine was licensed in 1971 and recommended to be administered in 2 doses in 1989.)

What we can do

For those community pediatricians who have little or no experience in diagnosing or treating measles, I implore you to emphasize to all your patients the absolute necessity to fully immunize every child on time and without delay, and explain to any reluctant parents that the group that questions the safety or effectiveness of the measles vaccine is not only wrong but is jeopardizing the health and well-being of their children. Tell them that the British physician who first reported that the MMR vaccine could cause autism was found to be a dangerous fraud and so lost his license to practice.

The antivaccine group must be made more aware of the terrible complications of measles. In my opinion, not vaccinating a child against measles is not only idiotic, it is immoral and dangerous.

Please remember Emily.

Dr Eden is clinical professor of Pediatrics, Weill-Cornell Medical Center, New York, New York. He has nothing to disclose.

For references, go to ContemporaryPediatrics.com/your-voice-measles
FLARES AREN’T GOING TO PREVENT THEMSELVES

DAILY USE OF ECZEMA RELIEF BODY CREAM REDUCES THE INCIDENCE OF FLARE AND INCREASES THE TIME-TO-FLARE RECURRENCE¹

44% reduction in risk of flare in pediatric subjects

4 out of 5 children remained flare-free for six months¹

Steroid-free | Fragrance-free

Diagnosing depression in preschoolers

Clinically significant depression can occur in children aged as young as 3 years. Here’s how to recognize the symptoms and identify risk factors in your young patients.

MICHAEL A SHAPIRO, MD

Depression in childhood is rare (Figure 1). It is not too early to look for it in preschool-aged children, however, and pediatricians are likely to be the first to suspect the condition. Detection requires understanding of the presenting features of depression in preschool-aged children combined with an age-adjusted approach to evaluation. Knowledge of associated risk factors also can enable recognition of depression in a preschool-aged child and will direct appropriate intervention that is important for optimizing the child’s well-being and his or her developmental and mental health trajectory.

The idea that depression occurs in preschool-aged children may be difficult to fathom considering that childhood is often regarded as a happy and carefree period. The idea also may be discarded based on the idea that such young children lack the developmental maturity to experience the core cognitions associated with depression. In fact, however, several studies document that clinically significant depression can occur in children aged as young as 3 years.2

There is limited information about the prevalence of depression in preschool-aged children. Available research indicates that boys and girls are equally affected and report that the rate ranges between 0.08% and 2%.3,4 It has been suggested, however, that because of underrecognition, the prevalence of preschool-aged depression may be underestimated.2

Because of underrecognition, the prevalence of preschool-aged depression may be underestimated.2

Although genetics may increase a child’s vulnerability to depression, depression in preschool-aged children most often develops because of an environmental issue that causes psychosocial stress. These problems can include a negative home environment, a caregiver with depression or other serious illness, problematic peer relations, and stressful life events, such as loss of a parent or a separation involving a person of significance to the child.3

Recognizing depression
Identifying preschool-aged children affected by depression can be challenging. Very young children are less able to articulate
their internal emotional state and therefore are unlikely to verbalize feelings of sadness that raise suspicion of the diagnosis. Age-adjusted questioning may identify sadness and other diagnostic findings including excessive guilt, lack of pleasure in activities and play, and decreased energy.

Most commonly, however, young children with depression exhibit somatic symptoms, such as frequent headaches or stomachaches, and they may develop changes in sleep, appetite, and social interactions. Changes in sleep can include both difficulties going to sleep, staying asleep, and sleeping too much, whereas appetite issues in preschool-aged children usually involve not eating enough rather than overeating. Their mood may appear more irritable than outright sad.

General questions asked during a routine wellness visit or when a child is brought in for unexplained somatic complaints can explore concerns about possible depression and the need for further evaluation. The child’s parent/caregiver should be asked about changes in behavior or mood, but not specifically if the child is depressed because most adults would not consider that depression can occur in a preschool-aged child.

Screening instruments for use in this age group are limited. The Preschool Feelings Checklist that includes 16 “yes” or “no” questions is a quick and simple screening tool that might be used to identify young children who might warrant referral for further assessment by a mental health specialist. The Pediatric Symptom Checklist is another rating scale that assesses for difficulties in psychosocial functioning and has been validated for children aged as young as 4 years.

**Other risk factors**

If there is concern that a child is depressed, pediatricians should look for an associated risk factor. Problems to explore include whether the child’s parent is depressed or if the child is living in a situation where there is conflict, neglect, or abuse. Maternal depression or illness resulting in inability to tend to the child’s emotional needs can be a common finding in the history of a young child who is depressed. A child or parent with a chronic medical illness has a modestly increased risk for depression, but how the family is adjusting to the illness may be the biggest determinant of the child’s mental well-being.

Bullying is another common issue, and in particular, it can lead to comorbid anxiety. Anxiety is more common than depression in early childhood, and the manifestations of anxiety can be similar to those of depression. Children with anxiety may complain of headaches or stomachaches, balk at going to school, exhibit separation issues, or express worry about bad things happening. Anxiety in young children often develops because the child is worried that something will happen to the parent/caregiver, and so practitioners should consider if the parent or caregiver was involved in a traumatic event.
matic incident, suffered an illness, or was separated from the child. Because anxiety and depression can be comorbid and have overlapping symptoms, the goal should be to try to identify the underlying cause for the child’s distress rather than to identify the specific diagnosis.

A risk of suicide in children who are depressed usually does not emerge as a concern until adolescence. Among younger children, risk for suicide most often occurs in the context of attention-deficit/hyperactivity disorder (ADHD), which suggests that these children are more likely acting impulsively on a feeling of distress rather than on a cognitive appraisal of the sadness of their life situation. With that information in mind, screening and treating for ADHD is important in a child who may appear depressed.

It has been reported that preschoolers diagnosed with major depressive disorder were more likely than healthy preschoolers to cause self-injury during a tantrum episode.9 Young children may be asked questions to screen for suicidal ideation or self-harm, but the questions should be phrased using age-appropriate terms. Because young children may not know what suicide or dead means, it may be more appropriate to ask if they ever wish they could disappear or go away. To investigate self-harm, children may be asked if they ever want to hurt themselves rather than if they ever hurt themselves, which may be misinterpreted as ‘accidental injury.

**FIGURE 2** FDA-approved pediatric age ranges and indications for antidepressant medications

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<th>Age Range in Years</th>
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*Flouxetine is FDA approved for the treatments of MDD in pediatric patients aged to 18 years. Abbreviation: FDA, Food and Drug Administration; GAD, generalized anxiety disorder; MDD, major depressive disorder; OCD, obsessive-compulsive disorder.

From Centers for Medicare and Medicaid Services.12

Pharmacologic intervention

There is very limited evidence to support the use of antidepressant medications to treat depression in preschool-aged children. No medication is approved by the US Food and Drug Administration (FDA) for treatment of depression in preschool-aged children (Figure 2).12 The agent with the lowest age of approval to treat major depressive disorder is fluoxetine, and it is indicated only for use in children aged 8 years and older. Other antidepressants have been studied in children but failed to show benefit and were associated with high rates of adverse events.5,12 Of particular concern is evidence that young children may be more susceptible to the activating adverse effects of selective...
serotonin reuptake inhibitors (SSRIs) antidepressant medications.13,14

Antidepressant treatment is only considered if a child has very severe depression or has failed to respond to appropriate psychotherapies. Florida Medicaid guidelines recommend that in children aged younger than 6 years, behavioral therapy, psychotherapy, or social intervention be given a trial of 6 to 9 months before considering a medication.15 If antidepressant treatment is used, it should be combined with psychotherapy. It should never be prescribed as standalone treatment because of poor access to appropriate psychotherapeutic intervention.

Antidepressant treatment may be best prescribed by a psychiatrist who is familiar with its dosing, safety, and monitoring needs in the pediatric population.

Due to concerns about possible adverse effects, antidepressant treatment may be best prescribed by a psychiatrist who is familiar with its dosing, safety, and monitoring needs in the pediatric population. Furthermore, antidepressants should only be prescribed to a child whose family or caregiver can be relied on to watch for possible adverse effects. In addition, parents need to be informed that psychotherapy and behavioral interventions are considered first-line treatments, and that treatment with medication is off-label and that there is little evidence regarding its efficacy and safety, including long-term effects on growth and development.

Referral and collaboration
It may initially be important to obtain information from the child’s school or daycare to determine whether the child is exhibiting any symptoms outside the home. Being able to refer children and families properly is important to accessing timely care. Therefore, pediatricians should familiarize themselves with local resources, such as community mental health centers, child advocacy centers, and social services.

Before considering an antidepressant medication for a preschool-aged child, it is important to evaluate for neglect or abuse; consider whether the parent/caregiver is suffering from a mental or physical illness and refer properly; and, if necessary, refer the child for behavior therapy or psychosocial intervention. Pediatricians should familiarize themselves with community providers and understand who provides behavioral interventions, for which age ranges of children, and who provides medication management. Forming collaborative relationships with other healthcare providers is important.

Conclusion
It is very rare that a preschool-aged child will be affected by depression, but pediatricians should be aware that it can occur so that they will explore the diagnosis in a child who presents with unexplained somatic symptoms or other age-related signs. Children at risk for depression can also be identified through screening for the presence of adverse experiences and distressing environmental factors. As young children’s brains are still developing, early identification and treatment of such issues could have everlasting implications on the child’s physical, emotional, social, and cognitive development.

For references, go to ContemporaryPediatrics.com/depression-in-preschoolers

Depression and Suicide Social Media Resources

What if someone is posting suicidal messages or something disturbing on social media?
If you see messages or live streaming suicidal behavior on social media, call 911 immediately; contact the toll-free National Suicide Prevention Lifeline at 1-800-273-TALK (8255); or text the Crisis Text Line (text HOME to 741741).

Some social media sites also have a process to report suicidal content and get help for the person posting the message. Each offers different options on how to respond. For example:
- Facebook’s Suicide Prevention web page can be found at www.facebook.com/help/5949377257121/ (use the search term “suicide” or “suicide prevention”).
- Instagram uses automated tools in the app to provide resources, which can also be found online at https://help.instagram.com (use the search term “suicide,” “self-injury,” or “suicide prevention”).
- Snapchat’s Support provides guidance at https://support.snapchat.com (use the search term “suicide” or “suicide prevention”).
- Tumblr Counseling and Prevention Resources web page can be found at https://tumblr.zendesk.com (use the search term “counseling” or “prevention,” then click on “Counseling and prevention resources”).
- Twitter’s Best Practices in Dealing With Self-Harm and Suicide at https://support.twitter.com (use the search term “suicide,” “self-harm,” or “suicide prevention”).
- YouTube’s Safety Center webpage can be found at https://support.google.com/youtube (use the search term “suicide and self-injury”).

Turn to page 32 to read more about suicide prevention.
New Oregon laws address mental health and suicide prevention

Oregon has passed several new laws aimed at suicide prevention, including one offering students excused mental health days.

Sometimes, it’s not just the body that needs a break. Recognizing that students often face mental health challenges that can make learning difficult and can take time to address, Oregon leaders enacted a new law that allows students to take up to 5 excused absences in a 3-month period for mental health reasons.

“It is important for adolescents to have a voice for their mental health needs and to make sure that they get the help they need before it is a crisis,” says Cora Breuner, MD, MPH, FAAP, professor of Pediatrics in the Division of Adolescent Medicine and adjunct professor of Pediatrics in the Department of Orthopedics and Sports Medicine at the University of Washington School of Medicine, Seattle. Breuner also serves as a member of the Forum Management Committee at the American Academy of Pediatrics (AAP).

Breuner says this new law is extremely important. “It prioritizes the mental health needs of a community that desperately needs them now,” she says.

The new law took effect July 1, 2019, alongside Adi’s Act, which Oregon Governor Kate Brown signed into law in June. Adi’s Act requires all Oregon school districts to develop comprehensive suicide prevention policies. These new efforts are aimed at stifling the increasing number of suicides, which reached a record high of 825 in Oregon in 2017. Suicide was the second-leading cause of death for Oregon residents aged 15 to 24 years, and the third-leading cause of death for children aged 5 to 14 years, according to the Oregon Health Authority.

Suicide rates for children have been rising nationwide, with the Centers for Disease Control and Prevention (CDC) ranking suicide as the second-leading cause of death for 10- to 34-year-olds. From 1999 to 2016, suicide rates increased in all 50 states, according to the CDC, with some regions facing bigger problems than others. In North Dakota, suicide rates increased the most—by 57.6%, the CDC reveals—with several other states following close behind. Suicide rates increased in Utah by 46.5% and in Oregon by 28.2%, the CDC notes.

“Boys are 4 times more likely than girls to die by suicide, although girls are more likely to attempt suicide.”
—Cora Breuner, MD, MPH, FAAP

Whereas these 2 new laws may be seen as trendsetting, Minnesota also passed a bill in 2009 that excused students for absences related to ongoing treatment for a mental health diagnosis when accompanied by a note from a healthcare professional.

How such laws will help
The important statistics to remember in practice are that boys are 4 times more likely than girls to die by suicide, although girls are more likely to attempt suicide, Breuner says. Guns are used in more than half of suicides, she adds. The question that remains, she says, is what causes teens to commit suicide?

“The teenaged years are a stressful time. They are filled with major
Suicide rates among teenagers increased by 30% since 2000, with the majority of the increase occurring over the last decade.

RACHAEL ZIMLICH, RN, BSN

Suicide rates among teenagers are spiking, but experts aren’t quite certain why.

“Suicide rates are rapidly rising in adolescence, especially in boys,” says Oren Miron, MS, a research associate in biomedical informatics at Harvard Medical School, Boston, Massachusetts, and co-author of a report published as a research letter in *JAMA*. “Pediatricians should account for this rise when deciding if a child shows enough suicidal signs to warrant further steps,” he says.

Miron and his colleagues note that there was a 30% increase in teen-aged suicides over the last 2 decades. Although the exact cause of this increase isn’t known, the investigators have correlated increases in social media use, anxiety, depression, and self-inflicted injuries with the rise in suicide. More detailed research is needed to analyze specific trends in these age groups, their report points out.

“Further studies are required, and they should focus on factors from recent years since those the years when we start to see a faster rise in suicide,” Miron says. “For example, we are examining the connection of this suicide epidemic to the opioid epidemic, since opioid abuse is known to be a risk factor for suicide.”

Miron’s suggestion is mirrored in a recent study published in *JAMA Psychiatry*, which tied parental opioid use to increased rates of teenaged suicide. According to the study, parental opioid use was associated with doubling the risk of suicide attempts by their children.

Miron’s letter references data from the Centers for Disease Control and Prevention’s (CDC) Underlying Cause of Death database and reveals that there were 6421 suicides in young adults aged 15 to 24 years in 2017 alone. The majority—5016—of those were males, and 1225 were females. Suicide rates stayed steady from 2000 to 2007 at a rate of about 8 per 100,000, according to the report, but increased by 3.1% from 2007 to 2014, and even more—by 10%—from 2014 to 2017. Suicide rates among boys spiked dramatically.
“I hope the report would help pediatricians in assessing suicide risk, and that it will help policymakers bring more resources to this tragic suicide trend.”

—Oran Miron, MS

males actually decreased from 2000 to 2007, only to increase by 2.6% from 2007 to 2015 and by 14.2% from 2015 to 2017. Suicide rates among females increased by 1.8% from 2000 to 2010, then by 8.2% from 2010 to 2017, according to the data.

“I was surprised by the surge of suicide among boys, since previous studies reported more of a rise among girls,” says Miron.

Although there were little data about the causality of these increases in the letter, another recent study published in JAMA Psychiatry notes that suicide rates increased by 12.7% in 10- to 19-year-old males and 21.7% among females during the height of social media popularity surrounding the series “13 Reasons Why.” The popular show about teenage suicide is based on a 2007 novel and was released on Netflix in 2017 with 2 additional seasons airing in 2018 and 2019. In August 2019, a fourth and final season of the show was ordered by Netflix.

Miron says he hopes the results of his team’s research will lead to more research on teenage suicide rates and highlight awareness among pediatricians. “I hope the report would help pediatricians in assessing suicide risk, and that it will help policymakers bring more resources to this tragic suicide trend,” he says. ■

REFERENCES

Ms Zimlich is a freelance writer in Cleveland, Ohio. She writes regularly for Contemporary Pediatrics and sister publications Managed Healthcare Executive and Medical Economics. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.
Pediatricians need to have informed discussions with parents and caregivers about procedures for their children requiring sedation or general anesthesia. This evidence can help with those decisions.

In 2016 and 2017, the US Food and Drug Administration (FDA) issued a warning and subsequent labeling change for anesthetic drugs with concerns that repeated or lengthy use of sedation and general anesthesia in children aged younger than 3 years may impact brain development. Although not calling for delay of medically necessary procedures, the FDA did state that healthcare providers should consider delaying elective procedures when medically appropriate.

Prior to the late 1980s, the concept of neonatal pain during procedures was not acknowledged and thought to be a behavioral reflex rather than a conscious experience of pain. However, multiple studies subsequently demonstrated neonates did respond to painful stimuli and that these stimuli could be managed. Further failure to manage pain can lead to both short- and long-term complications. These warnings need to be considered within that context.

This article will review both animal and human studies so that pediatricians can have informed discussion with parents and caregivers whose children may be faced with procedures requiring sedation or general anesthesia.

What’s the concern?
Multiple animal studies have demonstrated significant long-term and possible permanent damage to the developing brain in the areas of behavior, learning, and memory following administration of anesthetic agents. Pathophysiologic mechanisms for the neurodevelopmental effects include increased apoptosis of neurons, glia, and oligodendrocytes; impaired neurogenesis; synaptic and axonal dysgenesis; perturbed neurotrophic signaling; mitochondrial dysfunction; and neuroinflammation.
Specific agents in rodent models

TRIPLE COCKTAIL OF ANESTHESIA
A 2003 study administering midazolam, isoflurane, and nitrous oxide (a triple cocktail commonly used in pediatric anesthesia) to 7-day old rat pups demonstrated apoptotic neurodegeneration and deficits in hippocampal synaptic function following 6 hours of anesthesia. The baby rats demonstrated immediate, persistent, and ongoing deficits in learning, working memory, and reference memory as evidenced by performance in several different maze activities. In animal studies, there appears to be a direct correlation with time under anesthesia and abnormalities seen in the brain.

LAUGHING GAS/NITROUS OXIDE/XENON
Several studies have demonstrated that xenon, nitrous oxide, or midazolam administered alone were not associated with neurodegeneration. Administered with other agents, xenon or nitrous oxide may also attenuate the impact of other anesthetics. A 2007 study showed nitrous oxide or xenon alone did not cause cell death and that xenon reduced isoflurane-induced cell death. Other rodent studies have demonstrated similar results with xenon and nitrous oxide attenuating neurodegeneration and hypoxia making it worse.

Jevtovic-Todorovic’s 2003 study examined both single exposures as well as continuous infusion of anesthetic agents and found that rat pups suffered no immediate or long-term neurodegeneration with administration of nitrous oxide or midazolam alone, but combination with isoflurane was associated with increased cell death and neurodegeneration. Other studies have found conflicting results with only administration of midazolam but that the administration of melatonin prior to anesthesia has an attenuating effect on neurodegeneration.

Specific agents in nonhuman primates

KETAMINE
Given that outcomes in rats may not truly represent outcomes in humans, studies have also been performed in primates. A 2012 study administered intravenous ketamine for 5 hours to rhesus neonates (day 6 of life) or to pregnant rhesus females at 120 days’ gestation (full-term is 165 days). Pregnant rhesus females were delivered via cesarean delivery 3 hours following infusion. Both fetal and neonatal brains exposed to ketamine experienced significantly more brain apoptosis compared with controls. Fetal exposure led to 2.2 times more neurodegeneration compared with neonatal exposure. Other rhesus monkey studies with ketamine also have demonstrated neurodegeneration and poor long-term outcomes.

PROPOFOL
Because common anesthetics such as ketamine and isoflurane demonstrated neurodegeneration, other investigators examined other anesthetic agents in nonhuman primates. Propofol anesthesia was delivered to fetal rhesus macaques at gestational age 120 days, or rhesus neonates using the same protocol as described above. Compared with isoflurane, propofol infusion for 5 hours led to less neurodegeneration in both fetal rhesus macaques and rhesus neonates. Unlike ketamine exposure, neurodegeneration was similar in both fetal and neonatal rhesus monkeys.

Takeaways for pediatrics
Although it’s clear that administration of anesthetics leads to neurodegeneration in rats and primates, children receive lower doses (in terms of mg/kg) and are generally exposed for much shorter durations of time, and the animals were not undergoing a painful surgical procedure. Similarly, these experimental studies did not monitor the animals as closely as a child undergoing surgery would be monitored.

There is also the question of whether adverse developmental outcomes in rats are similar, meaningful, and equivalent to poor developmental outcomes in children. However, better-controlled studies in progressively larger animals (sheep, pigs, monkeys) did not account for all the developmental issues seen post-anesthesia. As a result, the pediatrician needs to acknowledge preclinical data indicating the possibility that anesthesia may be neurotoxic and potentially damaging to pediatric development.

Human data
A variety of studies have attempted to examine neurotoxicity in children following anesthesia.
[D]ata from the MASK, PANDA, and GAS studies provide strong evidence that a one-hour or less single exposure to general anesthesia is not associated with an increased risk of neurodevelopmental deficit in later childhood.14

RAINE STUDY
The Western Australian Pregnancy Cohort (Raine) study was originally designed to examine the effects of prenatal ultrasound on 2608 infants born between 1989 and 1992.15 Detailed demographics and medical history were collected prenatally and included assessments at ages 1, 2, 3, 5, 8, 10, 13, and 16 years. In this group, 321 children were exposed to anesthesia before age 3 years and 2287 children were unexposed.

NEUROPSYCHOLOGIC AND FUNCTIONAL TESTING at the 10-year follow-up visit was the primary outcome for this study and utilized validated and reliable tests:15

- **Cognition:** Symbol Digit Modality Test (SDMT); Raven’s Colored Progressive Matrices (CPM)
- **Language:** Clinical Evaluation of Language Fundamentals (CELF); Peabody Picture Vocabulary Test (PPVT)
- **Gross/Fine Motor Function:** McCarron Assessment of Neuromuscular Development (MAND)
- **Behavioral problems:** Child Behavior Checklist (CBCL)

Anesthesia was associated with significantly worse scores in tests of receptive, expressive, total language, cognition, and abstract reasoning measured by CPM. Differences were not seen between exposed and unexposed children in behavior and motor function domains. After adjusting for confounders, anesthesia before age 3 years was associated with increased risk of disability in receptive language (CELF), expressive language (CELF), total language (CELF) and abstract reasoning (CPM).

MASK STUDY
The Mayo Anesthesia Safety in Kids (MASK) study16 examined whether (unexposed, singly exposed, and multiply exposed children born in Olmsted County, Minnesota, from 1994 to 2007) children requiring general anesthesia before age 3 years suffered adverse neurodevelopment outcomes. In the cohort, 997 children underwent neuropsychologic testing (full-scale intelligence quotient [IQ] standard score of the Wechsler Abbreviated Scale of Intelligence) at ages 8 to 12 years or 15 to 20 years. Results demonstrated the IQ did not vary significantly across groups. However, processing speed and fine motor abilities did vary significantly in the multiply exposed compared with singly exposed children. Parents of multiply exposed children also reported more problems with behavior and reading. It is important to note that all the differences seen were secondary outcomes and should be interpreted with caution.

Interestingly, one of the tests administered to rhesus monkeys, the Operant Test Battery (OTB), can be and was also administered to children in the MASK study. The OTB examines aspects of learning, motivation, impulse control, and short-term memory. Children exposed to general anesthesia did not experience similar deficits on OTB tasks that were previously observed in nonhuman primates.17

PANDA STUDY
The Pediatric Anesthesia Neurodevelopment Assessment (PANDA) study16 looked at 105 sibling pairs born within 3 years of each other with one of the children undergoing inguinal hernia repair under general anesthesia before age 3 years and the other not having any anesthesia exposure before age 3 years. The goal was to determine if a single anesthesia exposure before age 3 years in otherwise healthy children was associated with impaired neurocognitive development and abnormal behavior between ages 8 to 15 years. Children prospectively underwent a neurocognitive and behavior battery that included measures of IQ; expressive and receptive language; verbal reasoning; memory; attention; executive function; motor skills; academic skills; adaptive skills; and parental rating.

Clinical data from the surgical procedure and anesthesia were retrospectively abstracted from hospital records. Mean duration of anesthesia was 84 minutes with a range of 20 to 240 minutes. Mean age of IQ testing was 10.6 for children receiving anesthesia and 10.9 for those not. The IQ scores were not statistically or clinically different between the 2 groups (difference, 0.2 IQ points).18 Similarly, there were no significant differences in the secondary outcomes of mean scores of memory, attention, visuospatial function, executive function, language, motor and processing speed, or behavior.

It is important to note that this study utilized similar comprehensive neuropsychologic assessments and did not find similar secondary outcomes as the MASK study did.16 Thus, among healthy children undergoing a single anesthesia expo-
Is it better to have all planned procedures for an individual patient coordinated under one anesthetic procedure, or should the procedures be separated as several short anesthetic exposures? There is no good answer to this question.

General Anesthesia Study (GAS) trial\textsuperscript{19} is the only completed randomized controlled trial (RCT) of anesthesia-induced neurotoxicity.\textsuperscript{14} This international open-label trial randomized 772 children aged younger than 5 years undergoing inguinal herniorrhaphy to either an awake-regional anesthesia group or to a sevoflurane-based general anesthesia group in a 1:1 fashion. The primary outcome measure was full-scale IQ (FSIQ) on the Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III), and assessors were blinded to treatment arm. Secondary outcomes at age 2 years included cognitive scores on the Bayley Scales of Infant and Toddler Development and various measures of language, memory, attention, executive function, motor skills, academic skills, adaptive skills, and parental ratings at age 5 years.\textsuperscript{14} Median duration of anesthesia was 54 minutes with an average of less than 34 minutes. Mean FSIQ were equivalent for the awake-regional anesthesia group and the sevoflurane-based general anesthesia group. Likewise, differences in secondary outcomes were not clinically significant.

General Anesthesia Study (GAS) trial\textsuperscript{19} is the only completed randomized controlled trial (RCT) of anesthesia-induced neurotoxicity.\textsuperscript{14} This international open-label trial randomized 772 children aged younger than 5 years undergoing inguinal herniorrhaphy to either an awake-regional anesthesia group or to a sevoflurane-based general anesthesia group in a 1:1 fashion. The primary outcome measure was full-scale IQ (FSIQ) on the Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III), and assessors were blinded to treatment arm. Secondary outcomes at age 2 years included cognitive scores on the Bayley Scales of Infant and Toddler Development and various measures of language, memory, attention, executive function, motor skills, academic skills, adaptive skills, and parental ratings at age 5 years.\textsuperscript{14} Median duration of anesthesia was 54 minutes with an average of less than 34 minutes. Mean FSIQ were equivalent for the awake-regional anesthesia group and the sevoflurane-based general anesthesia group. Likewise, differences in secondary outcomes were not clinically significant.

Certain medical, socioeconomic, or psychosocial comorbidities may confer higher risk and may not be easily studied. Children with congenital heart disease will often experience significantly more exposure to anesthesia than described in the MASK, PANDA, and GAS studies. It is not feasible to perform a GAS-like RCT in these groups. As a result, less rigorous observational and nonrandomized designs will be implemented and the results are subject to bias and residual confounding. However, several such studies of cardiac patients have shown inverse associations in children’s IQ scores at age 4 to 5 years.\textsuperscript{20} Importantly some of the studies in congenital heart patients have not shown adverse outcomes for several years identifying the importance of long-term follow-up.\textsuperscript{21}

Conclusions
Whereas animal and retrospective studies demonstrating possible neurotoxic and developmental impacts following anesthesia should concern the pediatrician, data from the MASK, PANDA, and GAS studies provide strong evidence that a one-hour or less single exposure to general anesthesia is not associated with an increased risk of neurodevelopmental deficit in later childhood.\textsuperscript{14} Given that more than half of all pediatric procedures in children aged younger than 3 years last less than one hour should also be reassuring.\textsuperscript{13}

However, there are many practical questions that remain unanswered: Is it better to have all planned procedures for an individual patient coordinated under one anesthetic procedure/exposure or should the procedures for a given individual be separated as several short anesthetic exposures? There is no good answer to this question as it has not been addressed in animal or human studies. Similarly, recommendations for particular mixtures of anesthetic agents are not possible based on the current state of knowledge.

The pediatrician needs to be aware of ongoing research and development so that he or she can be aware and recommend adjuvants in development that might prevent anesthesia-associated neurotoxicity; report findings to the FDA that may be related to anesthetic exposure; and have appropriate discussions with patients’ parents and caregivers regarding anesthesia.

For references, go to ContemporaryPediatrics.com/anesthetic-neurotoxicity

Segmental hemangioma on a newborn’s face
ContemporaryPediatrics.com/dermcase-0919

Emergent itchy rash in a 5-year-old boy
ContemporaryPediatrics.com/dermcase-0819

Rapidly growing nodule on an infant’s finger
ContemporaryPediatrics.com/dermcase-0719
PCV13 serotypes still contribute to pneumococcal disease

The 13-valent pneumococcal vaccine (PCV13) is performing well since its 2010 introduction but still has some flaws, according to a new report.

RACHAEL ZIMLICH, RN, BSN

The 13-valent pneumococcal conjugate vaccine (PCV13), approved for use in the United States in 2010, has substantially decreased the burden of disease from some forms of pneumococcal bacteria, but nearly a quarter of US pediatric cases are still caused by the strains covered by the vaccine.

The PCV vaccine protects against just 13 of the more than 90 serotypes of pneumococcal bacteria that can cause disease, according to the new report.

The new study published in Pediatrics points out that invasive pneumococcal disease (IPD) in children has dropped since routine administration of the pneumococcal conjugate vaccine (PCV7) began in 2000, followed by the administration of a 13-valent pneumococcal conjugate vaccine—covering serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F—in 2010. A 23-valent vaccine is also available for children aged 24 months to 18 years with specific underlying conditions, but most of predominant serotypes found in IPD cases in children are covered by the PCV-13 vaccine.

Despite the success of the vaccine, however, researchers have noted that there have been some cases described around the world in which children have developed IPD due to PCV13 serotype isolates despite having received at least 2 doses of the vaccine. Serotypes 3 and 19A were the most common in these cases and did not occur in children in the United States, according to the report. The children who did develop IPD from these serotype isolates often did not have immune evaluations completed or had normal immune workups, the report notes.

What researchers found

The study evaluated children with IPD at 8 US hospitals between 2014 and 2017 and found that PCV13 serotypes accounted for 23.9% of the IPD isolates during that period. Serotypes 3, 19A, and 19F made up 91% of these cases, with the most common non-PCV13 serotypes being 35B, 23B, 33F, and 22F. The study notes that 40% of the children with IPD from serotype isolates found in the PCV13 vaccine received only 1 or no doses of the vaccine. The research team concluded that PCV13 serotypes continue to account for nearly a quarter of IPD cases in children aged 4 to 7 years, even years after the introduction of the PCV13 vaccine.

Sheldon Kaplan, MD, professor and executive vice chair, and head of the Section of Infectious Diseases in the Department of Pediatrics at Baylor College of Medicine, Houston, Texas, and chief of the Infectious Disease Service and head of Pediatric Medicine at Texas Children’s Hospital, Houston, led the study and says although the vaccine is clearly effective in preventing IPD due to most serotypes in the PCV13 vaccine, there is still more work to be done.

“Pediatricians need to continue to educate the parents of their patients about the importance of having their children immunized against vaccine-preventable infections and following the recommended vaccine schedule.”

—SHELDON KAPLAN, MD

“Since the introduction of PCV13, about 75% of pneumococcal isolates causing IPD were non-PCV13 serotypes. Of those children with non-PCV13 serotype IPD, more than half have some underlying condition compared with about 25% of children with IPD due to a PCV13 serotype isolate having an underlying condition,” Kaplan says. “IPD due to serotype 3 remains a challenge for prevention.”

Key takeaways

Kaplan says the report emphasizes how well PCV13 prevents IPD for most of the serotypes—with the exception of serotype 3—in the vaccine. He says that he hopes his research will help inform selection of
pneumococcal serotypes for the next generation of PCVs, and that it also provides data regarding the utility of routine immune evaluations for children who have received 2 or more doses and still have an IPD episode due to 1 or more of the isolates found in the vaccine.

Kaplan says he had expected immune evaluations for children with IPD from the PCV13 serotypes, despite having received 3 or 4 doses of the vaccine, would have uncovered more potential immune abnormalities. According to the report, of the 28 children with IPD who had received 3 or more doses of the vaccine, just 1 was found to have an immunodeficiency.

Kaplan says the study, despite finding weaknesses in the vaccine pertaining to serotype 3, should highlight the importance of all routine vaccination—especially with PCV13.

“As they have been doing, pediatricians need to follow the recommended CDC-AAP-AAFP vaccine schedule for infants and children,” Kaplan says. “Pediatricians need to continue to educate the parents of their patients about the importance of having their children immunized against vaccine-preventable infections and following the recommended vaccine schedule. Parents need to know that Streptococcus pneumoniae can cause infections that are potentially fatal or lead to terrible brain injuries and/or deafness.”

REFERENCE


RESPIRATORY DISORDERS

RSV in infancy linked to asthma later in childhood

Severe respiratory syncytial virus (RSV) infection in a child’s first year may increase risk for acute asthma and recurrent wheezing.

RACHAEL ZIMLICH, RN, BSN

Respiratory syncytial virus (RSV) is a frequently battled illness in the youngest patients, but a study shows that while infection frequency might slow as infants age, the lasting effects of the virus may be more significant.

A study published in the Journal of Infectious Diseases reveals that whereas younger infants become infected most often with RSV to the point of requiring hospitalization, older infants who are hospitalized for RSV may face increased risk of developing asthma and/or chronic wheezing later in childhood.

“Children who develop severe RSV infection—RSV bronchiolitis in the first 12 months of life—are at increased risk of developing subsequent asthma and/or recurrent wheeze, and this risk is higher in children who develop RSV bronchiolitis after 6 months of age,” says Nusrat Homaira, MBBS, MPH, PhD, senior lecturer and National Health and Research Council early career fellow in Pediatrics at the University of New South Wales, Kensington, Australia, respiratory researcher at Sydney Children’s Hospital, and co-author of the report.

Respiratory syncytial virus was responsible for an estimated 3 million hospitalizations in children aged younger than 5 years in 2015 alone, according to the study, with the highest incidence found in children aged between 6 weeks and 6 months. Whereas this illness alone is a burden at this age, there is growing evidence suggesting that severe RSV in a child’s first year of life can increase incidence of asthma or recurrent wheezing developing later in life.

Previous studies have shown that children who fall ill with RSV in their first year have a 2- to 4-fold higher risk of developing acute asthma later.

The current study sought to determine if there was an association between the age at which a child experiences his/her first RSV illness and an asthma diagnosis later in childhood. Researchers found that the incidence of asthma-associated
hospitalization per 1000 child-years among children who were hospitalized for RSV when aged younger than 3 months was 0.5; 0.9 when the child was hospitalized for RSV between ages 3 and 6 months; 2 when they were hospitalized for RSV between ages 6 months and 1 year; and 1.7 when hospitalization occurred between ages 1 and 2 years. The study authors determined the ratio for hospitalization for asthma was 2- to 7-fold higher in children who were hospitalized for RSV when they were aged 6 months and older, compared with children who were hospitalized for RSV between birth and age 6 months. So, although more children younger than 6 months fall sick with RSV, the chances of developing asthma subsequently is higher in those who develop RSV infections at age 6 months and older.

The study assessed records from children born in New South Wales, Australia, between 2001 and 2010 who had RSV before age 2 years. Out of 888,154 births during that period, 18,402—2%—were hospitalized for RSV in the first 2 years of life. Fifty-seven percent of them were hospitalized for RSV by age 6 months and older, compared with children who were hospitalized for RSV between birth and age 6 months. So, although more children younger than 6 months fall sick with RSV, the chances of developing asthma subsequently is higher in those who develop RSV infections at age 6 months and older.

What the study found
Researchers suggest that the development of asthma after early RSV infection is likely due to both short- and long-term alterations and airway immune response from the airway caused by RSV infection. Younger infection beyond 6 months of life," Homaira says. “Though this was a first-of-its-kind research and needs to be substantiated with further work, we hypothesize that maternally derived anti-RSV antibody may provide some protection against the extent of airway damage in the first 6 months of life. Also, there is rapid lung alveolar multiplication in the first 6 months of life and it is possible that any lower airway damage due to RSV infection is transient.”

Alveolar multiplication and airway remodeling that naturally occurs in the first 6 months of life may also help to stave off permanent airway damage, the report notes. By age 2 to 3 years, lung alveolarization is complete and the RSV disease process is more likely to cause permanent disruption on alveolarization and adverse lung function.

Unfortunately, there is little pediatricians can do to prevent RSV infection, other than to provide basic infection control education to parents and families.

There are currently no preventive treatment—or screening test—for RSV infection apart from palivizumab, which is only recommended for high-risk children,” Homaira says. “However, healthcare providers can promote hand and respiratory hygiene, especially during the winter season, to limit transmission. Additionally, it’s important for pediatricians to bear in mind that children who are admitted to the hospital in infancy with bronchiolitis can present to them beyond 2 years of age with recurrent wheeze, which may then be diagnosed as asthma.”

There is little pediatricians can do to prevent RSV infection, other than to provide basic infection control education to parents and families. infants who become sick with RSV may be able to stave off later airway damage and disease development due at least in part to the presence of maternal antibodies, which can last through nearly the first 3 months of life and help protect immature lungs and immune systems. To confirm this theory, the research team notes an observed dose-response relationship between increased risk of hospitalizations for asthma and increasing age at first severe RSV disease, which could be due to waning maternal antibody levels.

“What the study found
Researchers suggest that the development of asthma after early RSV infection is likely due to both short- and long-term alterations and airway immune response from the airway caused by RSV infection. Younger
er that children who have yet to be diagnosed as asthmatic are simply more susceptible to RSV, Homaira says it’s a question that can’t really be answered just yet.

“This is almost like the ‘egg first or the chicken’ type question, which is not very easy to prove,” Homaira says. “However, there is now a body of work that suggests that early severe RSV infection has a causal association with asthma and that children who develop severe RSV infection can then go on to develop asthma even in absence of atopy or family history of asthma.”

Developing an RSV vaccine has been a global health priority, and the report notes that there are currently at least 20 different RSV vaccines in various phases of clinical trials. These vaccines may not only help prevent these dangerous early RSV infections but also chronic airway diseases that may develop later.

“Currently there is no effective treatment or vaccine against RSV infection in children. However, several vaccines and antibodies are being tested in different phases of clinical trials, and the most advanced is a maternal vaccine that will protect infants in the first 6 months of life through placental transfer of enhanced levels of maternal anti-RSV antibody,” Homaira says, “although children aged older than 6 months will have a beneficial impact on the long-term consequences of RSV disease as well. We will need several effective RSV vaccines and complementary measures such as monoclonal antibodies to prevent severe RSV disease and chronic respiratory morbidity associated with early severe RSV disease in children.”

When effective RSV vaccines become available, passive immunization through maternal vaccination, followed by active immunization in the first 2 years of life, may help in lowering the burden of acute and chronic childhood respiratory diseases associated with RSV.

REFERENCE


Mental/Behavioral/Developmental Health

How legalization impacts teenagers’ marijuana use

RACHAEL ZIMLICH, RN, BSN

Whereas opponents of marijuana legalization for medicinal or recreational purposes may worry about increased access for youths, a new study suggests that the legalization of marijuana may actually help to curb use among teenagers.

The study, discussed in a research letter published in JAMA Pediatrics, was conducted using a national sampling of more than 1.4 million high school students. Data from the biennial Youth Risk Behavior Survey between 1993 and 2017 was used to compare marijuana usage rates among high school students as an average across all states compared with usage by teenagers in states that had legalized marijuana for either medical or recreational purposes.

“The general takeaway from our research is that there is no evidence that legalization of marijuana for medical or recreational purposes had led to increased teen use,” says D. Mark Anderson, PhD, associate professor in the Department of Agricultural Economics and Economics at Montana State University, Bozeman, Montana, and lead author of the research letter. “This is now one of a handful of studies that all reach the conclusion of no effect on teen marijuana consumption.”

Previous research using the Washington Healthy Youth Survey pointed to decreases in marijuana use among teenagers in Washington State after marijuana was legalized for recreation purposes. The authors aimed to take the research a step further in this national study. Results of their research showed that recreational marijuana laws were associated with an 8% decrease in marijuana use overall among high school students when compared with before legalization, and a 9% drop in frequent marijuana use that was self-reported by teenagers. There was no significant association with marijuana use before
or after legalization for medical purposes, according to the report.

Anderson says the research team wasn’t able to pin down the precise mechanism for the decline in marijuana use, but the researchers gave credence to the suggestion in previous studies that it is more difficult for teenagers to obtain marijuana from licensed dispensaries after legalization than it is from drug dealers before legalization.

No real surprises
Anderson says there wasn’t really much about the study that surprised him. “The null findings for medical marijuana laws were consistent with results from a previous study on the same topic in 2014,” Anderson says. "As for the negative association between recreational marijuana laws and teen use, we weren’t surprised by this either. This finding is consistent with a story where the relative cost of selling to underage individuals goes up when these laws are passed."

Anderson couldn’t comment on the importance of his research to clinical practice, but says the data is highly relevant as policymakers weigh the costs and benefits of marijuana legalization.

The American Academy of Pediatrics (AAP) has been clear on its stance against the legalization of marijuana for either medical or recreational purposes, most recently reaffirming its policy statement about marijuana legalization in 2015. The organization discusses concerns that increased availability to adults—even with restrictions—will increase access for young persons. The AAP does, however, advocate for decriminalization of marijuana, according to the policy statement.

For references, go to ContemporaryPediatrics.com/marijuana-legalization

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

METABOLIC DISORDERS
Type 1 diabetes disrupts educational outcomes

MIRANDA HESTER, EDITOR

Poorer educational outcomes may need to be added to the list of the potential outcomes for children who have type 1 diabetes. A new study published in Diabetes Care examines the connection.

Researchers used 9 databases from across Scotland that included hospital admissions, maternity records, dispensed prescriptions, diabetes registered, death certificates, school absences/exclusions, school examination, annual pupil census, and unemployment, which resulted in a cohort of 766,047 single-birth children who were born and attended school in Scotland between 2009 and 2013. Within that cohort, 3330 children were treated for type 1 diabetes.

The children who were treated for type 1 diabetes were more likely than their peers who did not have the condition to be absent from school, have some form of learning difficulty, be admitted to a hospital, and die. In the cohort of children with type 1 diabetes, the children with a higher HbA1c measurement, particularly those with a measurement in the highest quintile, were more likely to have an increased risk of exclusion, a greater rate of absenteeism, poorer attainment of education, and a higher risk of being unemployed.

The researchers highlighted the need to develop interventions to reduce school absenteeism and to ensure that children with type 1 diabetes are able to attain needed education.
polymorphic ventricular tachycardia (CPVT). We also think of patients with Wolff-Parkinson-White (WPW) syndrome. Patients with ventricular tachycardia fall into this category. Second, there’s a structural category for patients who have a structural abnormality in their heart—things like aortic stenosis, an abnormal coronary artery, or hypertrophic cardiomyopathy. And third are patients who have a low cardiac output state, and these tend to be patients whose heart muscles aren’t functioning well due to things like cardiomyopathy from other causes such as a dilated cardiomyopathy or myocarditis. So, in thinking about these cardiac causes that are relatively rare but that we always have to have in the back of our minds, it’s important to ask a thorough detailed history about this event.

I think that there are 6 really important questions to ask related to any of these events.

FIRST is the circumstances of the event. Was there anything different about that day? Where was the patient when this happened? What was the patient doing when this happened?

SECOND, were there any triggers leading up to the event? Was it particularly hot that day? Had the patient been standing for a prolonged period of time? We have all heard of the syncope that occurs during blood draws or during videos in school that make somebody feel queasy, but it’s important to think of triggers like exercise or even emotional exertion.

THIRD is to ask about the presence of a prodrome. This is a very important question. My favorite question to ask these patients is, did you know you were going to pass out when this happened? People describe a prodrome as vision changes. It can be vision turning black, tunnel vision, seeing spots. They can also describe lightheadedness or nausea as part of this prodromal feeling.

FOURTH, what other associated symptoms did you have? Did you have chest pain before this happened? Did you have palpitations? Did you have any trouble breathing?

FIFTH is the duration of the event.

SIXTH is asking about the post-event period. What did you feel like when you came to? Were you confused? And ask the person who was there, of course. Did the patient look confused? Ask about other kinds of symptoms when waking up. Were there palpitations when the patient woke up? And how did the patient then feel for the rest of the day or the following few days around that event?

So, again, the questions around the event are: What were the circumstances of the event? What were the triggers leading up to the event? Was there a prodrome? What were other associated symptoms? How long did the event last? What was the post-event period like?

After asking these questions about the event itself, it’s important to think about other factors that could have played a role—things like, has this ever happened before, or what medications is the patient taking? Specifically, is this patient taking any QT-prolonging medications? Is there family history of sudden death or accidents? Is there a history of any cardiac problems? Does anyone in the family have a pacemaker or a defibrillator? And finally, is there a history of syncope seizures or hearing loss in the family as well? These are all important questions for us to ask surrounding these events.

Q. What are the best treatment options for syncope in children?

A. This is very important to think about, of course, and it’s all based on what the level of suspicion is whether this is a cardiac versus a noncardiac event. If a provider thinks that an event could be cardiac—and I’ll emphasize the red flags that can point us toward the cardiac cause here—the red flags are, did this episode of syncope occur during exercise or emotional exertion? I say emotional exertion on purpose because when somebody’s really worked up, emotional exertion can have the same effect or even more of an effect on a patient than physical exertion can have.

A second red flag is, was there an absence of a prodrome? Third, is there a family history of sudden death, malignant syncope, or other concerning findings? Next is, was the patient taking QT-prolonging meds? Was there an abnormal physical exam finding? For example, if the
patient has a murmur that seems to be an outflow murmur, that could be a red flag. Also, if the patient injured himself or herself during the event, that’s a red flag. And then preceding symptoms are palpitations, chest pain, difficulty breathing. Those things could all point us in the direction of a cardiac cause of syncope.

What’s really important is to have these patients evaluated by a cardiologist if this is a concern. It can be helpful to get an electrocardiogram, an EKG, as this can be really helpful to then further delineate a cardiac cause. These visits for potential cardiac causes of syncope are often expedited because we also find them to be very important to figure out. As cardiologists, we are always happy to have conversations with providers to help determine the best plan of action to help make decisions around what to do. Also, these patients with suspicion for a cardiac cause of syncope should be exercise restricted, and I’ve even recently expanded that to be restricted from highly emotional activities such as these video games that seem to be very emotion provoking.

So, it’s these 3 things, really: to get an EKG, if possible; to expedite care to a pediatric cardiologist (and we’re all happy to help make that happen); and third, exercise restriction in that setting. There are some really helpful management strategies and treatments for vasovagal or benign syncope, but that would probably take another session for us to cover completely.

Q. Dr. Beach, is there anything else you’d like to add as a final thought for our community pediatricians?

A. I really would stress that we as pediatric cardiologists, no matter where you are, are always happy to help you figure this out. We recognize that these decisions are not black and white. It’s not always easy, even when you take a thorough history and you do a thorough physical exam, to make the decision about what this is. So, I am happy to take phone calls, happy to see patients, and happy to help with anything else you need.

Dr Johanek is a staff pharmacist at Southwest General Health Center, Middleburg Heights, Ohio. She has nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article.

**CONTEMPORARY PEDIATRICS CLINICAL VIDEO EXCLUSIVE**
Dr. Bobby Lazzara discusses findings published in *Pediatrics* about the potential effect of acid suppression therapy on bone fracture risk in a 12-year retrospective cohort of children given proton pump inhibitors alone or together with H2 receptor antagonists.

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sibility of such complications necessitates clinical monitoring of patients with SCFN.

Poststeroid panniculitis characteristically presents in children who are on high doses of systemic corticosteroids followed by rapid withdrawal. Erythematous subcutaneous nodules develop within several days of steroid cessation, most commonly on the cheeks, again attributed to the high concentration of fat in this area as occurs with steroid therapy. The lesions are typically asymptomatic, but they can ulcerate and scar.

In the absence of a characteristic history for cold panniculitis, punch biopsy can be performed to support the diagnosis and rule out other conditions. Subcutaneous fat necrosis of the newborn is characterized by a radial pattern of needle-shaped crystals on histology. Unlike cold panniculitis wherein infiltrates are limited to the upper subcutis, inflammation in SCFN involves the entire subcutaneous fat layer. Poststeroid panniculitis can appear identical to SCFN on biopsy but is easily distinguished with clinical correlation of high dose steroid use.

Sclerema neonatorum is a panniculitis most commonly seen in premature infants with infection or heart disease. Diffuse woody induration starts on the buttocks and thighs, with rapid extension to include other areas of the body. Feeding and respiration can be impaired if involvement is extensive enough to limit movement. Despite the ill appearance of the infant, histology may reveal only mild changes with little to no inflammation. Infectious cellulitis may also be considered in the differential diagnosis in the setting of a febrile and ill-appearing infant.

Management
No treatment is required for cold panniculitis. In the setting of an appropriate history and characteristic morphology, the patient can be monitored for improvement. The lesions typically progress from red to purple in color, with gradual improvement of induration. Complete resolution is expected in a period of weeks to months.

Patient outcome
On examination, the child was playful and afebrile. Upon further questioning, mother reported that the child lived in Alaska and spent time outside when at daycare.

At the time of this patient’s evaluation, 3 weeks after onset of the rash, the mother reported that the child’s lesion was spontaneously improving. Examination revealed a well-demarcated purple to red plaque, with greatly reduced erythema compared with the initial lesion (Figure 2). The mother was reassured of the benign nature of cold panniculitis and the expectation for full resolution. Ongoing protection from extreme cold exposure was recommended.

Ms Osborn is a medical student at the Medical College of Georgia, Augusta University, Augusta, Georgia.

Dr Brown is a clinical assistant professor of Medicine (Dermatology), University of Louisville, Louisville, Kentucky.

Dr Davis is professor and chair, Department of Dermatology, and director, Residency Program, Medical College of Georgia, Augusta University, Augusta, Georgia.

Dr Cohen, section editor for Dermcase, is professor of Pediatrics and of Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland. The authors and section editor have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of this article. Vignettes are based on real cases that have been modified to allow the authors and editor to focus on key teaching points. Images also may be edited or substituted for teaching purposes.

For references, go to ContemporaryPediatrics.com/dermcase-1019
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Erythematous plaque on an infant’s cheek

LINDSAY P OSBORN, BS; ASHLEY D BROWN, MD; LORETTA S DAVIS, MD

A healthy, afebrile, 12-month-old girl presents for evaluation with an asymptomatic nodule on her left cheek that has been present for 3 weeks (Figure 1). She was initially seen by her pediatrician, diagnosed with cellulitis, and prescribed an oral antibiotic, which was not administered by her parents.

COLD PANNICULITIS

Etiology/Epidemiology

Cold panniculitis is a phenomenon that occurs primarily in infants and young children due to a higher proportion of saturated fats in subcutaneous fat compared with older children and adults. Saturated fats become solid with cold exposure at a relatively higher temperature than unsaturated fats, leading to the potential for fat crystallization and adipocyte damage with short exposures to cold.

Development of cold panniculitis after exposure to popsicles and cold environments has been reported particularly in young children. Red, indurated plaques typically develop 24 to 72 hours after exposure, frequently occurring on the cheeks or chin due to a higher amount of subcutaneous fat in these areas.

Whereas a clinical diagnosis can be made by physical examination in the setting of an appropriate history, histopathology is confirmatory but usually not necessary. A lobular panniculitis with a lymphocytic and histiocytic inflammatory infiltrate is present at the junction of the dermis and subcutaneous fat.

Differential diagnosis

Included in the differential diagnosis of cold panniculitis are the other panniculitides seen in the pediatric population. These include subcutaneous fat necrosis of the newborn (SCFN), poststeroid panniculitis, and sclerema neonatorum. Subcutaneous fat necrosis of the newborn appears in full-term infants and may be associated with perinatal complications. Erythematous to violaceous indurated plaques or subcutaneous nodules appear within days to weeks of birth. Much of the body can be involved, but the anterior trunk is classically spared. Although benign, SCFN should be differentiated from cold panniculitis due to the potential for metabolic derangements, specifically hypercalcemia. The pos-
Focus on syncope

This month’s spotlight is Pediatric Cardiology as Contemporary Pediatrics sits down exclusively with pediatric cardiologist Cheyenne Beach, MD, assistant professor of Pediatrics, Pediatric and Adult Congenital Electrophysiology, Section of Pediatric Cardiology, Yale New Haven Children’s Hospital, New Haven, Connecticut, to discuss the one key condition for which she believes community pediatricians should be especially aware—syncope.

ERIN JOHANEK, PHARMD

Q. Dr. Beach, can you tell us what syncope is and why you think it is something of particular concern for pediatricians?

A. Syncope is essentially passing out. Technically, the definition of syncope is an abrupt, transient, complete loss of consciousness with loss of postural tone. And this is something that is important for us as pediatricians to think about and talk about, first because it’s really common—about 15% of pediatric patients have at least 1 episode of syncope during their pediatric lifetime—and also because syncope can be really anxiety provoking, both for family members and friends who witness events and also for providers who know that syncope can be a symptom of a life-threatening condition.

Q. What do you think are the underlying reasons for the increase in the frequency and severity of syncope specifically in children?

A. I don’t think that there’s necessarily been an increase in episodes of syncope in children, but more and more we’re hearing publicized cases of malignant or dangerous types of syncope, so I think it’s something that has been more anxiety provoking, both for people throughout the community and again also for providers taking care of these patients.

Q. What advice could you offer as far as diagnostic clues that pediatricians should be on the lookout for to properly diagnose syncope in their patients?

A. This is a topic we can cover in a few minutes here but I feel like I could talk about this for a long time. It’s something I see pretty often in our arrhythmia clinic and I’ve become pretty accustomed to trying to use these diagnostic tools. So first, when we see patients with syncope we have to determine if this is an episode of benign or usually vasovagal syncope or if it’s syncope from another more concerning cause. I’ll note that syncope can have a neurologic cause, something like a seizure, but I won’t focus on that today, instead really differentiating benign or vasovagal syncope versus a cardiac cause of syncope.

Cardiac causes of syncope can fall into 3 large categories and there’s a fair amount of overlap among these categories. The first is a primary arrhythmogenic cause of syncope—things like an inherited channelopathy, long QT syndrome, or something called catecholaminergic...
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