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Healing kids one layer at a time

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Cannabidiol use in children

Hospital Zone
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AAP, ACOG guidance for GBS testing

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Although accounts of food allergy date back to at least 400 BCE,1 significant concern in the medical literature can be traced back to the late 1980s. In May 1990, the British Medical Journal (BMJ) published a report of 4 deaths due to peanut allergy, noting, “All 4 were aware of their allergies, but could not avoid the allergen.”2 In 1992, Pediatric Annals stated that the most worrisome food allergy problem for pediatricians was peanut allergy because peanut appeared to be the most dangerous of the allergenic foods.3 Practicing physicians were anxious to offer parents a way to reduce their infants’ risk of developing food allergy and researchers were anxious to provide guidance. With a lack of robust evidence, they would have done well to follow the dictum, “Don’t just do something, stand there,” but that is not what occurred. In August 2000, the American Academy of Pediatrics (AAP) Committee on Nutrition established infant feeding guidelines that it described as reasonable, although it was acknowledged that there were no conclusive studies on which to base definitive recommendations.4 The guidelines stated “Solid foods should not be introduced into the diet of high-risk infants until 6 months of age, with dairy products delayed until 1 year, eggs until 2 years, and peanuts, nuts, and fish until 3 years of age.” Despite the lack of supporting evidence, by the late 1990s this advice had become gospel.

Although it may still feel somewhat surprising that guidelines were promulgated without good evidence, it is worth remembering that the concept of evidence-based medicine was not yet firmly established, the term only having been introduced in the 1990s.5,6 Concurrent with the new feeding guidelines, the prevalence of food allergy increased, and it became clear that the strategy of withholding these foods from infants to reduce the risk of developing food allergy had failed. In January 2008, an AAP Clinical Report acknowledged that there was no support for restricting the diet of infants beyond 4 to 6 months of age as a way to protect against the development of allergic disease such as eczema, asthma, or food allergy.7

New insight into peanut allergy
In November 2008, Gideon Lack, MD, and George Du Toit, MD, published a paper noting that despite guidelines recommending avoidance of peanut during infancy in the United States, United Kingdom, and Australia, peanut allergy had increased in these countries.8 They observed in particular that peanut allergy (PA) prevalence appeared to be much lower in Israel, where infants freely ate a peanut-containing snack during infancy. Their study confirmed not only

Early introduction of the “Big Eight” allergenic foods

There is now compelling evidence that the early introduction of allergenic foods to infants might very well prevent the development of food allergy.

RONALD SUNOG, MD

Although accounts of food allergy date back to at least 400 BCE,1 significant concern in the medical literature can be traced back to the late 1980s. In May 1990, the British Medical Journal (BMJ) published a report of 4 deaths due to peanut allergy, noting, “All 4 were aware of their allergies, but could not avoid the allergen.”2 In 1992, Pediatric Annals stated that the most worrisome food allergy problem for pediatricians was peanut allergy because peanut appeared to be the most dangerous of the allergenic foods.3

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The LEAP study demonstrated unequivocally that infants at high risk of developing peanut allergy who ate peanut early and continuously had an at least 80% lower risk of developing peanut allergy than high-risk infants for whom the introduction of peanut was intentionally delayed.9
their observation, but also that it was difficult to attribute this to something other than the early introduction of peanut to infants. (The study controlled for other factors, such as differences in social class, genetic background, and the particular variety of peanuts consumed.)

Lack and Du Toit concluded: “These findings raise the question of whether early introduction of peanut during infancy, rather than avoidance, will prevent the development of PA.” To answer this question, they conducted the Learning Early About Peanut (LEAP) study, which demonstrated unequivocally that infants at high risk of developing peanut allergy who ate peanut early and continuously had an at least 80% lower risk of developing peanut allergy than high-risk infants for whom the introduction of peanut was intentionally delayed.

Over the years there have been other studies that lacked the definitive evidence of LEAP but provided compelling evidence that the early introduction of allergenic foods to infants might very well prevent the development of food allergy.

As far back as 2006, a study published in Pediatrics concluded that delayed initial exposure to cereal grains until after age 6 months may increase the risk of developing wheat allergy and that delayed introduction as a guideline could not be recommended.

In August 2008, just 7 months after the AAP established that delaying the Big Eight (peanut, milk, shellfish, tree nut, egg, fish, wheat, and soy) was of no benefit, a paper in Pediatric Allergy and Immunology explored the relationship between starting solids and food intolerance, noting that concern about the practice of delaying foods until age 6 months was increasing. The authors concluded: “Tolerance to food allergens appears to be driven by regular, early exposure to these proteins during a ‘critical early window’ of development.”

In June 2009, Göran Wennergren, MD, PHD, from the Department of Pediatrics, University of Gothenburg, Queen Silvia Children’s Hospital, Gothenburg, Sweden, wrote a paper with the provocative title “What if it is the other way around? Early introduction of peanut and fish seems to be better than avoidance.” Wennergren proposed that the early introduction of foods during infancy might induce tolerance, thereby preventing the development of allergy.

In January 2013, the inaugural issue of the Journal of Allergy and Clinical Immunology: In Practice did a review of the current literature and expert opinion and published recommendations for the prevention of allergic disease through dietary intervention, stating that new information suggests that delaying the introduction of foods to infants might increase the risk of food allergy, and “the early introduction of allergenic foods may prevent food allergy in infants/children.”

In December 2013, the Canadian Pediatric Society in a joint statement with the Canadian Society of Allergy and Clinical Immunology stated that although research in this area was not complete, parents should not delay the introduction of any specific foods beyond age 6 months because this would not prevent, and might even increase, the risk of developing food allergy. It was noted that the strength of evidence for this was in the middle range.

**LEAP changes everything**

The publication of LEAP in February 2015 was met with great acclaim. Anthony S. Fauci, MD, director of the National Institute of Health and Infectious Diseases, stated, “For a study to show a benefit of this magnitude in the prevention of peanut allergy is without precedent. The results have the potential to transform how we..."
approach food allergy prevention.”

In April 2019, the AAP published “The effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, hydrolyzed formulas, and timing of introduction of allergenic complementary foods,” a review and summary of current feeding guidelines stating that Infants at high risk should be fed peanut food at age 4 to 6 months after considering testing first for peanut allergy. For moderate-risk infants, the introduction of peanut-containing food is recommended at 6 months, and for low-risk infants it is recommended that families follow their own preferences and cultural practices. Regarding the other Big Eight allergenic foods, it is only reiterated that there is no evidence that delayed introduction is of benefit.

The current guidelines are no doubt consistent with the strength of the evidence, and the guidelines established in 2000 are nothing if not a cautionary tale about making recommendations based on insufficient evidence. However, implementing guidelines based solely on the strength of evidence may not lead to best practices. An article in the Journal of Medical Ethics in 2004 described epistemological evidence-based medicine (EBM) as “setting the hierarchy and the gold standard of medical knowledge” and practical

ADVOCATES SPEAK With a vast potential for benefit, studies show this benefit is likely and of no risk at all, and the analysis overwhelmingly favors a universal recommendation for the early introduction of the Big Eight allergenic foods to infants. It should come as no surprise, then, that despite the measured AAP recommendation, numerous experts and institutions advocate this very approach:

“My clinical approach has long favored early peanut introduction. For low-risk infants, I encourage home-based introduction of peanut (not as whole nuts).” —George Du Toit, MD, lead LEAP investigator. NEJM online forum; February 25, 2015.

“Studies have very consistently shown that early introduction is the way to go. [Now we say, ‘Give foods early.’]” —Jonathan Spergel, MD, PHD, chief of the Allergy Section at the Children’s Hospital of Philadelphia. In: “Delay food introduction to prevent food allergy? It doesn’t work.” Medscape editorial; May 2015.

“Early introduction in this group (low-risk), though not emphasized in the guidelines, should contribute to lower overall rate of peanut allergy.” —James R. Baker Jr., MD, FARE CEO. Food Allergy Research and Education (FARE) webinar; January 2017.

“Infants without eczema or any other food allergy aren’t likely to develop an allergy to peanuts. To be on the safe side, it’s still a good idea for them to start eating peanuts from an early age.” —Francis Collins, MD, director, National Institutes of Health. In: “Peanut allergy: early exposure is key to prevention.” NIH Director’s Blog; January 10, 2017.

“Have infants eat allergenic foods early and have them eat these foods often.” —David M. Fleischer, MD, co-author of the Addendum Guidelines. In: “Guidelines for life after LEAP.” Contemporary Pediatrics; April 3, 2017.

“We should uniformly recommend that allergenic solids not be delayed and should be introduced in the first year of life.” —Katie Allen, MD. In: “Results from the LEAP study should be applied to food other than [just] peanut.” Presented at: American College of Allergy, Asthma, and Immunology meeting; San Francisco, California; November 2016.


“All infants should be given allergenic solid foods including peanut butter, cooked egg, dairy, and wheat products in the first year of life. This includes infants at high risk of allergy.” —Australasian Society of Clinical Immunology and Allergy. “ASCIA guidelines: Infant feeding and allergy prevention,” based on current published evidence and the consensus of participants. Presented at: Infant Feeding Summit, hosted by the Centre for Food and Allergy Research; May 2016.
Adding the Big Eight to an infant’s diet makes it more varied and nutritious, and studies show this increases the chance that the child will remain a healthy eater.25 EBM as “a term describing the optimal way to practice medicine.”17 Analyzing the costs and benefits of early introduction results in a powerful argument that the guidelines ought to strongly recommend the early introduction of the Big Eight to all infants as a best practice.

The full benefits of a broad recommendation to eat the Big Eight cannot be fully quantified, but the potential is vast:
- A universal recommendation of early introduction of peanut would benefit high-risk infants who are not recognized as such.
- Many new cases of peanut allergy annually are in the low-risk group, and although LEAP categorized infants as high-, medium-, and low-risk, risk falls on a continuum. It seems quite likely, then, that some number of these low-risk infants would benefit from early introduction.
- Based on current prevalence, 320,000 of the children born this year can be expected to develop food allergy and, as already noted, there is significant, if not conclusive, evidence of benefit in a number of studies. My own review of common illnesses and their treatments shines a light on the (perhaps obvious) reality that medical interventions are often broadly accepted in the absence of definitive evidence, if for no other reason than the simple fact that definitive evidence can be so difficult to obtain.24

The diet of many children is suboptimal. Adding the Big Eight to an infant’s diet makes it more varied and nutritious, and studies show this increases the chance that the child will remain a healthy eater.25 In other words, Eat the Eight—early and often.

Dr Sunog is a pediatrician in private practice in Massachusetts for more than 30 years and the author of Eat the Eight, Preventing Food Allergy with Food and the Imperfect Art of Medicine, published by The Nasiona. He discloses that he is medical advisor to and investor in Puffworks, makers of organic, non-GMO peanut butter puffs, including Puffworks Baby, designed for the early introduction of peanut to infants.

For references, go to ContemporaryPediatrics.com/big-8-allergenic-foods

MENTAL/BEHAVIORAL/DEVELOPMENTAL HEALTH
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For Contemporary Pediatrics, Dr. Bobby Lazzara examines a new report from the US Department of Health and Human Services Office of Inspector General (OIG) that found children enrolled in Medicaid who were diagnosed and treated for attention-deficit hyperactivity disorder (ADHD) are not receiving appropriate follow-up care and behavioral therapy within guidelines from the American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry, and describes strategies the OIG recommends to improve outcomes for these children.

ContemporaryPediatrics.com/ADHD-care-video
Supplemental oxygen can be delivered safely to patients in their home. Here experts discuss the indications for oxygen therapy, the amount needed, and the interface for delivery.

**Oxygen delivery in the home setting**

**Parisa Kaviani, MD; Joseph M. Collaco, MD, PhD**

There are a number of respiratory conditions in infants and children that can lead to hypoxemia, requiring supplemental oxygen (with or without ventilation) in the home setting. Some of the more common diagnoses that may require home supplemental oxygen include bronchopulmonary dysplasia (BPD) and chronic lung disease (CLD). It is important to identify the indication for oxygen therapy, the amount needed, and the interface for delivery (Table).

For treatment of hypoxemia, in a patient without cardiac disease, typically a goal saturation of ≥92% is often used as a threshold at sea level. Patients with congenital heart disease with mixing lesions or shunts may have different goal saturations depending on their physiology. Oxygen is a pulmonary vasodilator, thus patients with pulmonary hypertension may have higher recommended goal saturations (≥95%).

**Low-flow nasal cannula**

Low-flow nasal cannulas are used for treatment of hypoxemia without ventilation needs. There are 2 settings that can be controlled: the flow rate and the fraction of inspired oxygen (FiO₂). Optional humidification can be achieved through cold bubble or heated humidification devices. The flow rate can range from 1/32 L/min to 10 L/min based on the concentrator and flow meter, but typically the maximum flow rate is 4 L/min as higher flows may generate turbulence and not successfully deliver a higher oxygen concentration.

Whereas inpatient devices can deliver oxygen concentrations between 21% (room air) to 100% FiO₂, outpatient devices can only deliver 100% FiO₂. It should be noted that as the nasal cannula is an open oxygen delivery system, 100% FiO₂ is diluted with room air in the nasal passages, so the effective FiO₂ delivery to the lungs generally does not exceed 40%.

**High-flow nasal cannula**

High-flow nasal cannula is a newer means of home oxygen delivery and use in the home setting is still evolving. It has been used for obstructive sleep apnea (OSA) and laryngotracheomalacia. Both the interface (cannula) and humidification system differ from low-flow nasal cannula. The settings are similar in that both the flow and the FiO₂ can be titrated to deliver heated and humidified air. However, it allows delivery of effectively higher inspiratory flows and oxygen concentrations to the lungs.

Although this is also an open system, the flow provided is presumably higher than...
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the intrinsic inspiratory flow, which will decrease trapping of room air and mixing in the upper airway.\(^3\) The use of high-flow can eliminate dead space, overcome airway resistance in the nasopharynx, improve compliance, and deliver some level of positive pressure.\(^6,7\) Devices can deliver as much as 70 L/min of flow. In the acute setting, flows of 2 L/min per kilogram have been used.\(^8\)

**Noninvasive positive pressure ventilation**

Oxygen can also be delivered as part of noninvasive positive pressure ventilation (NIPPV) through a nasal mask or pillows. The 2 most common modalities prescribed for home use are continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP).

The CPAP modality is used for treatment of sleep apnea with gas exchange abnormalities. The settings include an inspiratory positive airway pressure (IPAP), expiratory positive airway pressure (EPAP), optional backup rate, and supplemental oxygen. Similar to CPAP, the oxygen is typically prescribed in L/min, but some machines can calibrate and display the FiO\(_2\).\(^9\)

**Mechanical ventilation**

Oxygen can also be delivered via mechanical ventilation, which is implemented for chronic respiratory failure. A tracheostomy is required for mechanical ventilation at home. Ventilator settings typically include FiO\(_2\) (21%-100%) and most ventilators can calibrate and display the FiO\(_2\). The amount of oxygen in L/min of flow necessary to achieve a specific FiO\(_2\) depends on the air flows through the ventilator and can vary by machine and patient. Typically, an FiO\(_2\) of 40% is the upper limit of support that can be provided in the home setting. This implies a high level of support, and also beyond this maintaining oxygen supply would be difficult.

**Face masks**

Face masks are typically not used for delivery of oxygen at home in pediatric patients. It is difficult to estimate reliably how much oxygen the patient is receiving, so use is reserved for hospitals where monitoring is closer. One exception to this is comfort care, when the patient does not tolerate a nasal cannula. It is important to note that high flows of oxygen (10-15 L/min) may be required in order to prevent rebreathing of CO\(_2\).

**Equipment**

Oxygen delivery at home typically requires an oxygen concentrator or pressurized oxygen tanks. Concentrators are powered by electricity, utilize room air to generate flows up to

---

**TABLE**

**SUMMARY OF DIFFERENT HOME OXYGEN DELIVERY DEVICES**

<table>
<thead>
<tr>
<th>OXYGEN DELIVERY DEVICE</th>
<th>COMMON INDICATIONS</th>
<th>INTERFACE</th>
<th>RANGE OF OXYGEN FLOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-flow nasal cannula</td>
<td>Hypoxemia</td>
<td>Cannula</td>
<td>0-4 L/min</td>
</tr>
<tr>
<td>High-flow nasal cannula</td>
<td>Obstructive sleep apnea Laryngomalacia</td>
<td>Cannula (different than low-flow)</td>
<td>0-70 L/min</td>
</tr>
<tr>
<td>CPAP</td>
<td>Sleep apnea with gas exchange problems</td>
<td>Nasal mask • Nasal pillows Full-face mask (not recommended)</td>
<td>0-10 L/min bled in CPAP pressure (cm H(_2)O)</td>
</tr>
<tr>
<td>BiPAP</td>
<td>Sleep apnea with gas exchange problems, chronic respiratory insufficiency</td>
<td>Nasal mask • Nasal pillows Full-face mask (not recommended)</td>
<td>0-10 L/min bled in IPAP/EPA</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Chronic respiratory failure</td>
<td>Tracheostomy</td>
<td>21%-40% FiO(_2)</td>
</tr>
</tbody>
</table>

Abbreviations: BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure; EPAP, expiratory positive airway pressure; IPAP, inspiratory positive airway pressure.

Author created.
10 L/min, and can provide up to 95% FiO₂ when bled into an oxygen delivery device. Small portable oxygen tanks can be provided for transport, and for a patient requiring 3 L/min of flow typically last 100 minutes. Tanks must be placed in holders or secured to the ground. In special circumstances (ie, airplane travel), a battery-powered portable oxygen concentrator can be prescribed. As a general safety rule, the battery time should be double the flight time.

An alternative to concentrators and pressurized oxygen tanks is liquid oxygen, which is prescribed for disease processes that are more sensitive to variation of inspired oxygen. These tanks are heavy and carry a risk of freezing regulators. Ordering a pulse oximeter is critical to allow for accurate monitoring of oxygen saturations on any patient on home oxygen. Ordering the appropriate size and type of pulse oximeter probes is also essential for accurate measurements.

**Risks**

Just as with other therapies, there are risks and safety hazards to consider. Oxygen toxicity can lead to generation of free radicals, pulmonary edema, and absorption atelectasis. Length of oxygen tubing can be hazardous depending on the mobility of the child, and measures should be taken to secure tubing as best as possible. Oxygen itself is not flammable but can contribute to rapid spread of fire.

Aside from the physical risk, oxygen should be titrated with caution, and only with direct instructions from providers. Patients with significant hypercarbia and OSA rely on the hypoxic respiratory drive to breathe, and blunting hypoxemia by increasing the inspired fraction of oxygen in a patient who is hypoventilating can be fatal. Also, oxygen acts as a vasodilator and can lead to pulmonary overcirculation and cardiac failure if dosed incorrectly in a patient with congenital heart disease.

**Takeaway for pediatricians**

Home oxygen therapy has liberalized patients with chronic conditions from the confines of the hospital. Oxygen can be delivered safely, but it is imperative to focus on the indication, and to titrate delivery of the lowest FiO₂ required by the patient.
Port-wine stains (PWSs) are a type of congenital vascular malformation estimated to occur in 0.3% to 0.5% of newborns. These birthmarks, which represent dilated capillaries and postcapillary venules in the dermis, appear as pink or erythematous flat patches that reflect the increased hemoglobin content in the skin.

These patches vary in size and can occur anywhere on the body, but approximately 80% of PWS lesions are present on the face and neck. The vast majority of PWSs are isolated findings. A facial PWS involving the distribution of the V1 (ophthalmic) branch of the trigeminal nerve, however, is a hallmark feature of Sturge-Weber syndrome, and babies with this presentation should be referred to an ophthalmologist and neurologist to screen for glaucoma and brain involvement.

Other than Sturge-Weber syndrome, which is very rare, the most significant concern for children with a PWS is the potential that they will experience stigmatization and psychosocial morbidity because of the disfiguring birthmark. Published studies document the negative emotional and quality-of-life consequences that a PWS has on affected children and how these problems are lessened by treatment that improves the appearance of the lesion.

When a baby is born with a disfiguring port wine stain, parents may be anxious for options to eliminate the lesion. Laser treatment is an effective option, and it is best begun early.

The vascular-selective pulsed dye laser represents the gold standard treatment of PWS.

Dr Geronemus is the director, Laser & Skin Surgery Center of New York, and clinical professor of Dermatology, New York University Medical Center, New York, New York. He discloses that he is an investigator for and is on the medical advisory board for Candela.
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PWS, parents may be anxious for options to eliminate the lesion. Pediatricians can help these families by referring them to a dermatologist who has expertise treating PWSs in infants.

The vascular-selective pulsed dye laser (PDL) represents the gold standard treatment of PWS. Performed with proper parameters and with repeated sessions until a plateau in response is reached, the procedure has excellent safety and the potential to provide complete to near-complete clearance. With early initiation of treatment in infants, the procedure can be done as an atraumatic in-office treatment without general anesthesia.

**PDL treatment**

**MECHANISM**

The safety and efficacy of PDL treatment of PWS is explained by the principle of selective photothermolysis. The 595-nm wavelength of the PDL targets hemoglobin in the affected cutaneous blood vessels. Heat that is produced upon hemoglobin absorption of the laser energy results in photocoagulation and aggregation of red blood cells and subsequently necrosis of the vascular endothelial cells. Risk of collateral damage to surrounding cutaneous structures is limited by selection of a proper pulse duration that confines thermal injury to the targeted PWS vasculature.

**TIMING**

Optimal treatment of PWS with the PDL laser involves multiple sessions that are performed until there is no further improvement. Early initiation of PDL treatment has several benefits. Importantly, available evidence indicates that earlier treatment allows for optimal outcomes, including a greater response and lower risk of recurrence.8-11 Several factors may explain the better results that are achieved with earlier PDL treatment for PWS. Because skin thickness increases with age, penetration of the laser energy to its target—the hemoglobin in the PWS capillaries—is better in younger children. The blood in neonates also contains a greater proportion of erythrocytes, and young infants have relatively less melanin in the skin that can be a competing chromophore for absorbing the laser energy.12 In addition, changes that occur in PWSs with time (thickening, darkening, and increase in size) make achieving clearance more challenging.

Treatment in infancy also enables the laser procedure to be performed in office without general anesthesia. Because the treatment can be mildly uncomfortable—each laser pulse produces a sensation that has been likened to the feeling of a light rubber band snap or less—controversy exists over the best clinical setting for performing the procedure.13 Citing concerns over comfort and the need for the child to remain still, some laser surgeons advocate performing the treatment in an operating room with the child placed under general anesthesia. Treatment with this approach, however, is expensive and time consuming, and access to an operating room staffed by an anesthesiologist with specialized training in the care of pediatric patients may be limited.

Perhaps most importantly, the safety risks associated with the use of general anesthesia in children must be considered. As noted in a warning issued by the US Food and Drug Administration (FDA) in 2016, repeated or lengthy use of general anesthetic and sedation drugs in the care of pediatric patients may be limited.
children aged younger than 3 years may affect brain development. The warning was based on evidence from animal studies showing that exposure to general anesthetic and sedation drugs for more than 3 hours can cause widespread loss of nerve cells in the developing brain with resultant long-term negative effects on behavior or learning. In the warning, the FDA advised that consideration be given to delaying potentially elective surgery in young children where medically appropriate. Treatment of PWSs typically requires multiple treatments.

Because of the relative ease of holding babies immobile, infants can undergo PDL treatment for PWS without the need for general anesthesia (Figure). A paper published in the peer-reviewed literature described the positive findings from a retrospective cohort study of in-office PDL PWS treatment without general or topical anesthesia in children aged 1 year or younger. Jeon and colleagues’ medical record review identified 197 infants who were treated between 2000 and 2017. The study population was comprised of 73 (37%) boys and 124 (63%) girls. The mean age of first treatment was 3.4 months, and the earliest treatment was performed in a child who was aged just 5 days.

Approximately 75% of the children were treated for a facial lesion, and 91% of the children had light skin (Fitzpatrick phototypes I-III). Mean PWS size was 61 cm² with a range from 0.49 cm² to 600 cm². On average, the children underwent 10 treatments (range, 2 to 23). The mean treatment interval was 37 days, although the study authors recommended that patients return for treatment every 2 to 3 weeks because the more frequent interval seemed to accelerate the response and minimize the total number of treatments needed and the time until treatment was completed. Therefore, it enabled the opportunity to perform the sessions without general anesthesia and the likelihood that maximal clearing was achieved before the child entered school and risked becoming a target for teasing and bullying.

**Available evidence indicates that earlier treatment allows for optimal outcomes, including a greater response and lower risk of recurrence.**

Improvement in PWS was rated by 4 independent physicians who used a 5-point visual analog scale to compare before and after photographs. The Table summarizes the results that show near-complete to complete clearing was achieved in the majority of children.

### Outcomes of early in-office treatment

Many have reported on the success of PDL treatment for PWS in infants as an in-office procedure without general anesthesia (Figure). A paper published in the peer-reviewed literature described the positive findings from a retrospective cohort study of in-office PDL PWS treatment without general or topical anesthesia in children aged 1 year or younger. Jeon and colleagues’ medical record review identified 197 infants who were treated between 2000 and 2017. The study population was comprised of 73 (37%) boys and 124 (63%) girls. The mean age of first treatment was 3.4 months, and the earliest treatment was performed in a child who was aged just 5 days.

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### TABLE

**VISUAL ANALOG SCALE RATING OF PWS IMPROVEMENT**

<table>
<thead>
<tr>
<th>GRADE (% IMPROVEMENT)</th>
<th>N (% OF TOTAL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Complete (100%)</td>
<td>51 (25.9%)</td>
</tr>
<tr>
<td>4 Excellent (76%-99%)</td>
<td>81 (41.1%)</td>
</tr>
<tr>
<td>3 Good (51%-75%)</td>
<td>44 (22.3%)</td>
</tr>
<tr>
<td>2 Fair (25%-50%)</td>
<td>13 (6.6%)</td>
</tr>
<tr>
<td>1 Poor (0%-25%)</td>
<td>8 (4.1%)</td>
</tr>
</tbody>
</table>

*From Jeon H, et al.*

Consistent with reports favoring earlier treatment, Jeon and colleagues found that lesions that cleared completely had a smaller average size and required fewer treatments than those achieving less improvement. Although analyses of outcomes based on anatomic location showed that the best results were obtained when treating lesions on the first branch of the trigeminal nerve, the mean visual analog scale (VAS) grade was 3.65 in analyses of all lesions as well as for all
Patients often suffer with much more than the skin manifestation of atop- ic dermatitis (AD), or eczema. Children with AD who present to pedi atricians also may be more likely to experience decreased self-esteem, anxiety, bullying, and more, says ShaSha D. Jaquez, PHD, a pediatric psychologist at Dell Children’s Medical Center and assistant clinical professor of Psychiatry, Dell Medical School, University of Texas at Austin.

A tough road for kids with eczema

Researchers analyzing health status data from 92,649 noninstitutionalized children, aged 0 to 17 years, found a “striking association between mental health disorders and AD in the US pediatric population. The severity of the skin disease alters the strength of the association,” they wrote in a paper published in 2013 in the Journal of Allergy and Clinical Immunology.1

Researchers studying psychosocial problems in adolescents with eczema found that 15.5% of teenagers with current eczema reported suicidal ideation compared with 9.1% of those without eczema.2 Another finding from that study: Boys with current eczema were less likely to have had romantic relationships than those without, according to the study in the Journal of Investigative Dermatology.

In a study published in the Scandinavian Journal of Caring Sciences, researchers concluded that teasing, taunting, and bullying may represent an underappreciated source of psychologic morbidity in children and adolescents with eczema, acne, and psoriasis.3

Pediatric dermatologic disorders, including AD, impact self-esteem throughout childhood, according to a study published in the International Women’s Journal of Dermatology.4

“In addition to the surgical and medical management of these disorders, clinicians can also take an active role in the assessment and improvement of the psychosocial impact of these skin disorders,” those authors concluded.4

Pediatricians should be mindful that what they see with AD patients isn’t necessarily all that there is. They also should be cognizant about the risk for psychologic and social comorbidities, says Jaquez, who presented “Healing children one layer at a time: integration of Psychology in pediatric Dermatology,” in July during the Society for Pediatric Dermatology 44th Annual Meeting in Austin, Texas.

“The pediatrician or dermatologist who might be the first to identify the problems but doesn’t have time to focus on this during treatment should refer to a psychologist who is trained to focus on how to get the child to be [his/her] best self despite the medical condition that they have.”

—Sasha D. Jaquez, PHD

to Jaquez, see more than traditional outpatient mental health concerns, such as depression and anxiety.

“What sets child/adolescent psychologists and pediatric psychologists apart is that knowledge of medical conditions and working on multidisciplinary teams to address difficulties a child and family experience related to the medical condition, whether it is a diagnosable psychiatric condition or not,” Jaquez says. “This would include seeing patients for nonadherence; coping with and acceptance of a medical condition; behavior problems in younger children, which may affect their adherence; sleep problems; and

DERMATOLOGY

Healing both body and mind in atopic dermatitis

Children with atopic dermatitis (AD) will go to great lengths to hide their skin. Here’s how referring them to a pediatric psychologist can help them be their best self, even with AD.
Why

Establishing

HEALTHY ORAL CARE HABITS IN INFANTS is Imperative

It’s easy for new parents to overlook oral hygiene — but it’s just as easy for you to start a conversation about care and introduce a routine to keep young children healthy and smiling.

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Read more: contemporarypediatrics.com/oralcare
Helping kids accept their skin

Jaquez says she helps pediatric patients with AD to accept their skin. “I talk with kids all the time about how their skin is just different. It’s not that it’s bad. So, we practice how they can tell other people that,” she says. “Other children often are afraid to play with children that have AD because they’re afraid that it’s going to be contagious. So, we practice with the child and also the parent about how to educate others about what it is and that it’s not contagious.”

Jaquez also works with children and families to find things that they’re able to do and enjoy doing and encourages them to do those things. “If they’re able to accept their skin condition and that it’s going to ebb and flow in terms of flares, then we can find time that they’re able to do the things they enjoy doing,” she says.

Part of the work involves overcoming perceived barriers. If a child who likes to swim doesn’t think he or she can swim in public anymore, Jaquez will work with the child and family to find a way that the child can safely swim, without putting them in a situation where people are going to judge them for the way that their skin looks.

Pediatricians should be mindful that what they see with AD patients isn’t necessarily all that there is. They also should be cognizant about the risk for psychologic and social comorbidities. —Sasha D. Jaquez, PhD

Helping to destigmatize mental health

A big takeaway for pediatricians is that they should help to destigmatize mental health by helping families understand that AD and other diseases are stressful, and that just because there’s a referral to Psychology doesn’t mean that there’s a larger concern about mental health. Rather, they’re simply in a stressful situation, so it’s OK to have Psychology involved.

“Families fear what it means when they’re getting a referral to Psychology and can be very resistant to that. It helps when pediatricians talk about Psychology as part of the team versus ‘You’re getting a referral to Psychology,’ which often can have negative connotations,” Jaquez says. “Working together as a team we’re kind of able to peel away their layers and work toward healing the whole person.”

Dr. Jaquez has no conflicts to report.

For references, go to ContemporaryPediatrics.com/mind-body-healing-AD
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Clinical Roundup

**DERMATOLOGY**

**Food allergy: A trigger for atopic dermatitis?**

Recommendations for whether to test for and treat food allergy in the setting of atopic dermatitis have changed.

**LISSETTE HILTON**

Pediatricians might know that food allergy and atopic dermatitis (AD) often coexist. What they might not realize is that food allergy rarely is a primary cause of AD, or eczema, according to Pooja Varshney, MD, clinical assistant professor of Pediatrics at Dell Medical School at the University of Texas at Austin and a pediatric allergist at Dell Children’s Medical Center, Austin.

**Cow’s milk, hen’s egg, peanut, wheat, soy, tree nuts, fish, and shellfish are responsible for more than 90% of food allergy in children.**

Nearly 40% children with moderate- to-severe AD have immunoglobulin E- (IgE-) mediated food allergy.

Pediatricians should keep in mind that patients with AD, especially those with more severe disease, are likely to have or develop food allergy, according to Varshney, and it’s important to identify whether AD patients have food allergy with IgE-mediated symptoms, which is seen soon after eating foods. "Ask food allergy screening questions in children that have AD, certainly if it is moderate-to-severe," she says.

However, whether foods are actually triggering AD can be much harder to determine. A history of eczema flaring soon after ingestion of a food, either through the child’s diet or through the diet of a breastfeeding mother, is difficult to differentiate from the natural waxing and waning of AD disease.

What’s a pediatrician to do?

There isn’t much evidence to support eliminating foods from moms’ or children’s diets to help their eczema improve, and elimination diets have real risks, according to Varshney.

“The risk-to-benefit ratio is really changing. Recent studies have shown that elimination of foods from a child’s diet rarely improves AD and [a child] very well may have increasing risk of developing anaphylactic food allergy if he or she avoids a food unnecessarily. This is particularly true of a child who was previously able to eat the food without any immediate or anaphylactic symptoms,” Varshney says.

The recommendation to avoid unnecessary elimination diets is a paradigm shift in thinking, Varshney says. A recent guideline published by the National Institute of Allergy and Infectious Diseases (NIAID) helps guide pediatricians and others in the care of young children who have AD in how to introduce foods. The current NIAID guidelines help pediatricians identify patients that may most benefit from allergy evaluation, as well as guide patients at no or low risk for peanut allergy.

“I think a main take-home of the guidelines is if a baby has mild-to-moderate AD, we really do not need to test before food introduction. We really want these assessments and conversations to be happening early—at the 4- to 6-month well checks,” Varshney says. "In those infants who have severe AD, testing is recommended before giving the baby peanut. We really are looking to identify babies with severe AD or those who already have a food allergy, particularly to egg, as they are at highest risk of peanut allergy but also stand to benefit most from early introduction if not allergic. That’s when early
testing is suggested.”

Varshney also points pediatricians to a recent American Academy of Pediatrics (AAP) guideline looking specifically at nutritional interventions for prevention of atopic disease. The guideline reports no benefit from using hydrolyzed formulas or changing maternal diet for the development of allergy, according to Varshney. It’s a field that’s constantly evolving, she says.

The diagnosis of food allergy tends to be more reliable when it’s based on and guided by a thorough history and physical exam. Whereas allergy testing is useful to confirm IgE-mediated food allergy, it has its limitations. Food IgE panels are not recommended because they can result in misdiagnosis of food allergy, Varshney says.

There’s also unnecessary and potentially harmful testing going on. Varshney says some naturopathic and nontraditional providers utilize inappropriate or disproven testing, including food immunoglobulin G (IgG) panels and muscle testing. These tests are not recommended and often lead to unnecessary elimination diets. Pediatricians need to firmly but gently educate their patients about the pitfalls of such testing and risks of inappropriate elimination diets in children, she says.

Testing is most useful when pediatricians determine or suspect that a patient has an immediate or IgE-type food allergy, Varshney says.

“All patients with a suspected food allergy should be seen by a board-certified allergist trained in food allergy. Whether the pediatrician orders any blood testing or defers the full evaluation to the allergist is dependent on the physician. Consultation with an allergist allows for additional testing like skin prick testing, food challenge, as well as follow-up because we know that certain food allergies—particularly milk and egg—are commonly outgrown,” Varshney says. “Testing can help determine the course of a particular child’s food allergy. Peanut allergy is less commonly outgrown but is outgrown in about 20% of kids, so we do need to follow these kids.”

Pediatricians should recommend that patients with IgE-type food allergy strictly avoid the food until seeing the allergist and consider prescribing injectable epinephrine in case of a severe reaction.

Eczema and food allergy often coexist

Varshney says there are a few theories about why eczema and food allergy often coexist.

The idea of the “atopic march” is one. The theory describes the progression of allergic disease seen in many children who have allergies, starting with AD and food allergy early on. Then these children typically go on to develop other allergic conditions such as allergic rhinitis and allergic asthma.

Another idea has to do with sensitization through the skin. So, children with a defective skin barrier, which is a big part of AD, are more susceptible to allergens, including food allergens, that penetrate the skin and activate the immune system to develop an abnormal or allergic response to food.

Still other theories revolve around the thinking that these conditions aren’t actually a cause-and-effect but rather travel together, perhaps due to genetic predisposition.

“We know genetic abnormalities and certain mutations exist with both those conditions. So perhaps the conditions are just different expressions of a particular patient’s genetic predisposition to developing allergic disease,” Varshney says. “This is an active area of research looking at how early intervention for AD may reduce the rate of food allergy development.”

That includes ongoing research looking at whether starting treatments such as dupilumab early in life can help prevent or halt the atopic march, she says.

In the meantime, attention to the skin barrier with thick emollients and moisturizers is a low-cost and low-risk intervention that pediatricians can recommend early on. It might be an intervention to help prevent the atopic march for at-risk infants, according to Varshney, but that’s not yet clear.

For references, go to ContemporaryPediatrics.com/food-allergy-and-AD

Dr. Varshney discloses the following: Food Allergy Research and Education, clinical network grant, principal investigator and medical director; Aimmune, principal investigator; DBV Technologies, principal investigator.
Positive results from studies looking at pipeline treatments for common warts might give pediatricians hope that something simple and non-destructive would magically make warts disappear—never to return.

In June, for example, Verrica Pharmaceuticals (West Chester, Pennsylvania) announced Phase 2 trial results showing 51% of subjects achieved complete clearance of common warts when treated with VP-102, a topical solution of 0.7% cantharidin in a single-use applicator.\(^1\)

Although the trial suggests VP-102 was well tolerated with no serious adverse events, treating warts with cantharidin and other options brings up the old wart conundrum: Is treating warts worth the risk when most will vanish on their own and most treatments are only temporary? This is according to Bernard A. Cohen, MD, professor of Pediatrics and Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland.

Cohen and coauthors did a retrospective chart review of pediatric patients with common warts in an outpatient setting, published in 2015 in *Pediatric Dermatology*. Most of the 214 patients surveyed received some form of therapy, but it wasn’t clear that any form of treatment altered the course of their warts. The researchers found that warts resolved in 65% of children by age 2 years and in 80% by age 4 years, regardless of treatment.\(^2\)

The findings suggest that counseling without aggressive destructive treatment is reasonable for managing warts in most children, the authors concluded.\(^2\)

“The bottom line is we didn’t find anything that worked better than placebo,” Cohen says. “I think it’s very important for pediatricians to know that still, at this point, it is unclear if anything works better than placebo to make warts go away permanently.”

To best guide patients and families about whether to treat or not to treat warts, pediatricians should know about the natural history of common warts, according to Cohen.

Most important: Risk of serious complications from warts in otherwise healthy kids is negligible. Yet many treatments for warts are destructive and painful and are more likely to cause complications than the warts themselves, he says.

That’s not to say never treat

Still, Cohen notes that children’s quality of life can suffer when their warts are in places that are visible to others. “I’m not saying you should never treat warts. In fact, if I have patients who come in and the kids insist on it, we do a lot of conservative things,” he says.

Topical salicylic acid agents are among the first-line wart treatments Cohen recommends. He tells patients or parents to titrate the sali-
Salicylic acid to the point that it doesn’t hurt and children don’t overdo the treatment.

Years ago, Cohen would freeze, burn, and laser warts off, but says he isn’t a big fan of those options today.

“Occasionally I will use a nondestructive laser to make some of them smaller and less visible, but I do not do painful destructive things that could leave scars in children who cannot give consent themselves,” he says. “It’s important that pediatricians know there are palliative treatment options that are very conservative and not painful, which I think would be OK to do.”

When children are distraught about their warts, the goal is to recommend a nonpainful, not terribly destructive treatment to get the warts to dry out and shrink, while recognizing the chances of getting full resolution without recurrence is very low, according to Cohen.

“I had a kid the other day who came in and had one of these filamentous warts on the side of the nose. Everybody thinks they’ve got boogers in their nose falling out,” Cohen says. “I had the patient use a topical salicylic acid very gently to the point where it dries the wart, and I had the patient twist it and pull it off. It’ll probably come back but it might be a couple of weeks.”

Another option among nondestructive treatments is use of a topical retinoid. There are a number of over-the-counter products that Cohen says can make warts peel off a little bit, become flatter and subtler.

None of these have been shown to definitively make warts go away, but treating with salicylic acid, topical retinoid, or over-the-counter wart products might at least decrease wart size and visibility

There are also treatments that patients might have heard work but lack data to support that they do. Take garlic, for example. “What I tell people about garlic is it reduces the risk of it spreading among members of the same household if you wear garlic around your neck. Who wants to get near you if you have garlic around your neck?” Cohen says.

Pediatricians can lay the groundwork

Pediatricians are in a position when they understand the natural history of warts to advise parents and patients about whether to treat and how best to do it for optimal results.

Part of the care includes having a frank discussion with patients and parents about how today’s treatments haven’t been proven to be better than doing nothing and could carry risks. If patients or parents still insist on treatment, pediatricians could recommend safer options, Cohen says. “I do think pediatricians can play a big role here by counseling patients and treating them with conservative treatments early on, if needed,” Cohen says.

Where warts might be more of an issue and worthy of a referral to a pediatric dermatologist or dermatologist is when children have symptoms related to the warts, including pain, or if the warts are on places such as the head or neck.

Pediatricians who elect to treat sexually active pediatric patients who have genital warts should consider a product such as imiquimod or Condylox gel (podofilox).3 “I don’t routinely use these for genital warts in young children unless they have symptoms from the warts,” he says.

In the end, understanding limitations of wart treatment is key for pediatricians, according to Cohen.

“I do think warts are a rite of passage of childhood,” Cohen says. “If you look at warts, the peak presentation is probably 8 or 10 years and around 16 years. I’m not saying that adults don’t get them but many kids who have had them and have had them go away have had an immunologic response and are not going to get them as adults.”

About the pipeline

Cohen says there is some potential for wart products in clinical trials, including the cantharidin topical VP-102. Researchers studied subjects receiving VP-102 to day 84 with an additional period of follow-up through day 147.

“Secondary endpoints included the percent change from baseline in the number of treatable warts and VP-102 achieved a 51% reduction in the number of warts (28 of 55 warts) compared to baseline by Day 84,” according to Verrica Pharmaceutical’s press release. “The most frequently reported adverse events were application site reactions that are well known, reversible side effects related to the mechanism of action of can-

FIGURE 2 This 5-year-old girl had an irritating wart hanging from the left upper eye lid. It became inflamed and she picked it off several days later.
Infographics make educating parents about AD easier

For diseases such as atopic dermatitis (AD) that require complex care, colorful infographics take the guesswork out of patient education.

Kathleen A. Kent, DNP, APRN, CPNP-PC, and Carol Clark, DNP, APRN, FNP-BC, delivered a presentation at the National Association of Pediatric Nurse Practitioners’ 40th National Conference on Pediatric Health Care in March discussing the benefit of using infographics for educating patients and parents.

Whereas infographics are beneficial for almost any type of education, Kent and Clark note that they are particularly helpful when it comes to educating parents on managing complex conditions, including atopic dermatitis (AD).

AD is all too common

Twenty percent of children suffer from AD, and half of children with the condition report that it has a severely negative impact on their quality of life. Children with AD often suffer from depression anxiety, have activity restrictions attributed to the disease, and their families become financially burdened by the cost of care. Parents also become frustrated with managing the condition, which mostly affects very young children, because treatments are time consuming and the condition is fraught with frequent relapses. For providers, the condition is also frustrating because it’s complex to manage, guidelines for treatment are outdated, and it’s difficult for parents to comply with plans of care.

“A family with a child affected by AD spends considerable time, energy, and money to care for this disorder. The treatment success is directly linked to compliance,” Kent says. “To enhance compliance, parents need simplistic instructions with as few steps as possible.”

Wake Forest researchers studied several methods of teaching parents about the care of AD in children, Kent notes.

“Eczema action plans were found to be the most successful method over group education and extra office visits to teach parents the treatment plan,” she says. “However, the existing eczema action plans are all

One in 3 adults reads below an eighth-grade level and 14% of adults have below-basic health literacy.¹
text based, which is a challenge for most people but especially for those with low literacy.”

If it’s known that infographics improve comprehension, Kent says, it’s worth investigating whether applied infographic education-based tools can aid in the complex care of AD in children.

Part of the challenge in managing AD is that it often affects very young children, and this is also a demanding time in parenthood, Kent says. “These kids with significant skin disease are crabby and unhappy because of their skin. When kids don’t sleep, parents don’t either. There are many quality-of-life studies out there that demonstrate this connection,” she says. “Frustrated parents try many treatment plans that until recently were vastly different between providers.”

New national guidelines that utilize evidence-based practices were released in 2014 and should help providers get on the same page with treatment plans, she adds, but the nature of AD means that more complications are likely when it comes to care plans and management.

“Because the nature of AD, where it comes and goes, varies depending on the season and health of the child, which also varies, there are many relapses after a period of good skin. It can take up to 3 hours a day to provide skin care to these children, and parents are busy,” Kent says. “Without consistent use of medications and skin maintenance, the disease will flare.”

Infographics vs text-only handouts

The problem is that these complex care plans and the health literacy of the average parent don’t pair well.

One in 3 adults reads below an eighth-grade level, according to Kent’s research, and 14% of adults have below-basic health literacy.1 People are visual learners, Kent adds.

“It has been established in physiology textbooks and research that humans are visually wired and can more quickly process information when in a picture format over text.”

—Kathleen A. Kent, DNP, APRN, CPNP-PC

“More quickly process information when in a picture format over text,” Kent says. “When using pictorial tools in the office, information may be taught more efficiently, and the goal is that the patient’s understanding of the information is improved.”

It can help patients and providers to embrace this and use it to improve compliance and outcomes.

“We wanted to shine a light on health literacy in the United States and how this impacts care and outcomes,” Kent says of her research. “By using infographics for patient education, our goal is to reduce the health literacy barrier. Creating infographics is not difficult and the simpler the better.”

Infographics are most helpful for individuals with a reading level at or below the fourth-grade level, Kent and Clark noted in the presentation. The most effective infographics keep messages to 1- or 2-syllable words; use large and basic fonts such as 14-point Times New Roman; offer a simple message; avoid jargon; and use simple color combinations with plenty of white space. One important consideration, Kent adds, is to be sure that whatever graphic feature, icon, or symbol is used is widely known enough to represent a common concept or definition in one’s culture or society.

Another problem is, when it comes to developing infographics that can help, providers may not know where to start.

“There are so many infographic-maker websites available and it is important for a provider to find one that works with his or her needs and budget,” Kent suggests, adding that there are many uses beyond AD for visual aids. “There are many health-related infographics. I have seen them in public spaces like the subway and in public restrooms. I have seen topics like flu prevention, handwashing, and many other topics. Some of these are free to use and some will have copyrights, so it is important to know the difference.”

Kend says she hopes to help spread the message of the benefit that infographics can provide to clinicians.

“When we only have 15 minutes with a patient and family, time is squeezed to cover every aspect of well care,” she says. “It is a challenge to address other conditions, so using an infographic handout to reiterate the points made verbally in the office helps save time and improves education.”

REFERENCE

Paternal factors also affect children’s risk for AD

Pediatricians should consider family history of atopic dermatitis (AD) in both parents to help frame the risk for their offspring.

Maternal and paternal genetics, immune function, and socioeconomic factors influence atopic dermatitis (AD) risk in offspring, and whereas studies looking at how parents impact their children’s risk for the common skin disease tend to demonstrate a greater maternal influence, more studies are needed to examine how paternal genetics, lifestyle, and more might increase or decrease AD risk in their children, according to a review published in 2017 in *Dermatitis*.1

“There appears to be a larger maternal factor than paternal in many of the studies reviewed. For example, maternal smoking doubles the risk of AD development, but apparently not paternal. To a certain extent, fathers are ‘off the hook,’ but it is probably not that simple. Practical aspects such as recall bias in filling out the surveys could mean that paternal risk factors were overlooked, and some studies found evidence that if either parent has AD, the risk is increased in offspring,” says study author Peter A. Lio, MD, clinical assistant professor of Dermatology and Pediatrics, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

Socioeconomics, occupation, maternal/paternal lifestyle

Lio says there were 2 things that surprised him when doing research for the review.

“The first was that having a higher socioeconomic status is associated with a higher AD risk. This is interesting because many conditions seem to affect lower socioeconomic groups more, presumably for a number of health and lifestyle-related reasons,” Lio says. “The second was that higher education level in mothers was associated with a higher risk of AD. I have long felt that our AD patients seemed to be a particularly intelligent group, and this is a fascinating association.”

Maternal influence seems to outweigh paternal impact when it comes to educational differences. Data suggesting that parents with higher education levels were more likely than parents with low education levels to have kids with AD was statistically significant only for more educated mothers.1

Although research is lacking about whether fathers’ occupations impact their offspring’s AD risk, there is data suggesting that working pregnant women are more at risk of having children who develop AD than nonworking pregnant women.5

Maternal smoking, prenatally and postnatally, and maternal alcohol consumption during pregnancy both have been shown to increase AD risk in offspring. However, whether paternal smoking or alcohol consumption impact AD risk isn’t clear. One study showed that paternal alcohol consumption had no influence on AD risk in children.6

LISETTE HILTON
Greater clarity on the way?
The dream of “precision medicine” is finally starting to come into fruition, according to Lio.

“With new therapies such as targeted biologic medications for AD, we are beginning to more deeply understand the complex pathogenesis of the disease. Along with this, I am hopeful that we will be better able to tease out maternal and paternal factors and, perhaps most importantly, explain why they have the effects that they do on the children,” Lio says. “To some extent, this research is useful as it can also help guide mechanistic understanding of the disease, as well as allow for better counseling. Knowing that certain lifestyle issues like smoking and alcohol use can increase the risk of development of AD—a disease with significant morbidity and sometimes shocking associated costs—should help guide public policy programs to minimize such risks.”

In summary
Pediatricians should consider asking about family history of AD in both parents to help frame some of the risk, according to Lio.

“Reviewing the behaviors that are associated with increased risk such as alcohol use and smoking is probably important,” Lio says. “We also have some evidence that taking probiotics during pregnancy may decrease the risk of developing AD, and evidence that moisturizing daily starting in the newborn period may also decrease the risk of AD. Together, these may help identify higher-risk families and promote potentially helpful approaches to minimize disease.”

For references, go to ContemporaryPediatrics.com/paternal-factors-for-AD

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MS HILTON is a medical writer who has covered health and medicine for 25 years. She lives in Boca Raton, Florida. 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.

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All mothers should be tested for Group B Streptococcus (GBS) infections and treated with antibiotics during delivery if needed in order to prevent them from passing the infection on to their newborns, according to new guidance from the American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG).1

The guidance was published in Pediatrics, and is the newest update on GBS management in infants since 2010. The most common cause of neonatal sepsis is GBS, with symptoms beginning within a day or two of birth, according to the AAP. Routine screening of mothers before delivery, however, is more than 50% effective at preventing the disease, the report notes.

Mothers can be colonized with GBS without feeling sick in any way, but the disease can become very serious and quickly fatal for infants, according to the AAP.

“The AAP and the ACOG have together developed separate but aligned updated guidance on the prevention of, risk assessment for, and treatment of neonatal infection caused by GBS,” says Karen M. Puopolo, MD, PHD, chief of the Section on Newborn Medicine at Pennsylvania Hospital, associate professor of Pediatrics at the University of Pennsylvania Perelman School of Medicine, Philadelphia, and coauthor of the new guidelines. “These separate but aligned documents replace the consensus GBS prevention guidance published in 2010 by the Centers for Disease Control and Prevention (CDC).”

A new look at GBS
The updated guidance includes more information about the epidemiology of GBS, as well as current recommendations for antibiotics. The new guidelines include intrapartum administration of penicillin G as a first-line treatment; ampicillin or cefazolin as alternatives for neonatal onset of GBS; also, treatment of women at high risk for anaphylaxis from beta-lactam antibiotics with clindamycin and vancomycin.

The recommendations mirror those issued in recently updated guidance from the ACOG, including the recommendation to screen for GBS between 36 and nearly 38 weeks’ gestation. The major changes in the ACOG guideline, Puopolo says, are a revision in the optimal window for antenatal GBS and new recommendations on antibiotics timing and allergy testing for mothers. The AAP endorses the ACOG recommendations and adds new risk-assessment guidance for early onset GBS disease that move away from relying on lab testing toward more complete assessments.

“The major changes in the ACOG guideline are a revision in the optimal window for antenatal GBS and new recommendations on antibiotics timing and allergy testing for mothers.”1

—KAREN M. PUOPOLO, MD, PHD

for GBS screening to 36 to 37 (nearly 38) weeks’ gestation, we hope to optimize the identification of GBS-colonized women and impact the incidence of neonatal GBS early-onset disease that occurs among infants born to women who screened (false-ly) GBS negative,” Puopolo says.

She says allergy testing is also a big change, and that by advocating for formal penicillin allergy skin testing among pregnant women, the number of women who are unable to receive
Parents’ vaping harms their children with asthma

More parents vape to protect their kids from secondhand smoke, but it really doesn’t work that way.

RACHAEL ZIMLICH, RN, BSN

Adults with children—especially children with asthma—are turning to electronic cigarettes (e-cigarettes) in a misguided effort to reduce secondhand smoking exposure, but they really aren’t fully aware of the risks, according to a new report.

A research letter published in *JAMA Pediatrics* revealed that nationwide, 4.4% of adults used e-cigarettes between 2016 and 2017. An even higher number—4.9%—of adults with children vape, the research notes. The number climbs even more for parents of children with asthma, with 5.6% admitting to e-cigarette use at home.

Researchers note that e-cigarette users often consider the aerosols released by e-cigarettes to be harmless, but in reality, they contain a number of harmful compounds.

Jenny L. Carwile, SCD, MPH, and Kirsten Young, DO, of the Maine Medical Center, Portland, Abby F. Fleisch, MD, MPH, of the Maine Medical Center Research Institute, Scarborough, and Katherine A. Ahrens, PHD, MPH, of the Muskie School of Public Health at the University of Southern Maine, Portland, all coauthored the research letter.

“Pediatricians can share that the American Academy of Pediatrics (AAP) recommends that parents do not use e-cigarettes around children, particularly in cars and homes, and that smoke-free laws be expanded to e-cigarettes,” Carwile says.

Although the study did not compare the effects of second-hand smoke in traditional cigarettes versus e-cigarettes, Carwile says there are a number of known harmful chemicals in the vapors from e-cigarettes, and more research is needed to determine the long-term effects of secondhand exposures to these chemicals.

“Other studies have shown that many people consider e-cigarette aerosols to be harmless water vapors, and in many cases do not have household rules about not using e-cigarettes in cars or homes,” Carwile says. “We hope that providers and patients will be more aware of potential health risks of secondhand e-cigarette use in children, and limit use around children as recommended by the AAP and other groups.”

The researchers used data from the 2016 and 2017 US Behavioral Risk Factor Surveillance System to survey adults on e-cigarette use, but the study did not investigate what leads adults to use e-cigarettes or what effect inhaling vapors from e-cigarettes might have on children. Still, the research letter suggests that some parents might be turning to e-cigarettes in order to spare their children from being exposed to secondhand smoke from traditional cigarettes. Only about one-fifth of e-cigarette users with children limit vaping in their homes or vehicles, the paper notes.

**Vaping causes harmful exposure as well**

Another recent report, published in *Pediatrics* on e-cigarette use around children, reveals that whereas most users of both traditional and e-cigarettes have smoke-free home poli-
A new study of 2 million children from 5 countries has determined that one’s inherited genetics contribute nearly 80% of the risk for developing autism spectrum disorders (ASDs), according to Swedish researchers.

The study population was comprised of children born between January 1, 1998, and December 31, 2011, and researchers followed them until they reached age 16 years. In this entire group, 22,156 children were diagnosed with ASDs. After examining genetic outcomes among family members, maternal effects, and environments, the researchers estimated the heritability of autism to be approximately 80%. There were only modest differences in the heritability rate among the 5 countries.

In a companion editorial in the same issue, several autism and psychiatry experts said years of research have disproportionately implicated environmental factors and parental influences as affecting the incidence of autism.

The new study authors suggest it’s now time to recognize how family history might contribute heavily to a child’s risk of developing ASD, and to be observant for early signs of autism as they present so that interventions can begin as early as age 2 years. Expectant parents who are aware of a family history of autism might consider genetic counseling, one researcher noted.

The researchers also point out that more work needs to be done to identify specific genes, alone or in combination with potential environmental and familial factors, that contribute to autism spectrum disorder and in which specific ways.

“For references, go to ContemporaryPediatrics.com/vaping-and-asthma

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MENTAL/BEHAVIORAL/DEVELOPMENTAL HEALTH

Autism could be inherited

Researchers suggest that genetics are a major contributing factor to developing autism spectrum disorder.

"[T]he American Academy of Pediatrics recommends that parents do not use e-cigarettes around children and that smoke-free laws be expanded to e-cigarettes."
—Jenny L. Carwile, SCD, MPH

The report suggests that clinicians must do more to identify parents who use tobacco products and educate them on the dangers of second-hand exposure. Specifically, the Clinical Effort Against Secondhand Smoke Exposure (CEASE) interventions, designed to help providers identify and educate parents, was suggested, as well as the need for broadened tobacco control recommendations.

For references, go to ContemporaryPediatrics.com/vaping-and-asthma

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The researchers also point out that more work needs to be done to identify specific genes, alone or in combination with potential environmental and familial factors, that contribute to autism spectrum disorder and in which specific ways.
Obesity might increase risk of MS for certain children

Overweight/obesity in some kids could affect their risk of multiple sclerosis (MS) as well as the effectiveness of treatment.

A new study from Germany highlights another reason to fight childhood obesity: to reduce the risk of developing pediatric multiple sclerosis (MS) as well as protect the efficacy of first-line treatment for the disease.

Researchers used medical records and the database at the Center for Multiple Sclerosis in Childhood and Adolescence in Göttingen, Germany. The sample included 453 children with relapsing/remitting pediatric MS who had a body mass index (BMI) measurement that had been taken within 6 months of the MS diagnosis. Disease onset occurred between April 28, 1990, and June 26, 2016, and the average disease duration was 38.4 months. The BMIs were compared with BMI data from another 14,747 controls pulled from a nationwide child health survey.

Of the 453 children in the study, 306 were girls. The average age at diagnosis was 13.7 years. One hundred twenty-six of the children were either overweight or obese and obesity was linked to a statistically significant 2-fold odds of MS for both boys and girls, with girls having slightly higher odds than boys (girls: odds ratio [OR], 2.19; 95% confidence interval [CI], 1.5-3.1; \( P \leq .001 \); vs boys: OR, 2.14; 95% CI, 1.3-3.5; \( P = .003 \)).

When compared with nonoverweight MS patients, children with MS who were obese/overweight were found to have significantly more relapses while on first-line treatments such as interferon beta and glatiramer acetate, with an annualized relapse rate of 1.29 versus 0.72, respectively. Obese patients with MS were also more likely to be using second-line treatment than their nonoverweight counterparts, 56.8% versus 38.7%, respectively.

The researchers concluded that obesity appears to be associated with an increased risk of pediatric MS and that obese children with MS may not do well with first-line medications. They stated that altered pharmacokinetics are the likely factor in treatment response and that adjusting the dose according to BMI while helping the child achieve a healthy weight could improve therapy responses.

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[The researchers concluded] that adjusting the dose [of first-line medication] according to BMI while helping the child achieve a healthy weight could improve therapy responses.

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**METABOLIC DISORDERS**

**Obesity might increase risk of MS for certain children**

Overweight/obesity in some kids could affect their risk of multiple sclerosis (MS) as well as the effectiveness of treatment.

MIRANDA HESTER, EDITOR

A new study from Germany highlights another reason to fight childhood obesity: to reduce the risk of developing pediatric multiple sclerosis (MS) as well as protect the efficacy of first-line treatment for the disease.

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**REVISIT RECENT PUZZLERS**

**Sudden neutropenia and emesis in an SGA infant**
A newborn with prenatally diagnosed intrauterine growth restriction is transferred to the nursery for evaluation of significant blood-tinged emesis.

ContemporaryPediatrics.com/puzzler-0819

**Massive splenomegaly in a 6-year-old girl**
The patient presents to the emergency department with nonbilious vomiting and diffuse abdominal pain and for evaluation of a large abdominal mass.

ContemporaryPediatrics.com/puzzler-0719

**Fever and neck swelling in a teenaged girl**
A previously healthy 15-year-old female complains of right-sided neck swelling, pain, decreased range of motion, and fever and sore throat that have persisted for 3 days.

ContemporaryPediatrics.com/puzzler-0619
Children’s hospital addresses AYA patients’ cancer care needs

An innovative program helps adolescents and young adults (AYAs) hospitalized with cancer to cope with their disease and navigate their journey through treatment and beyond.

LISETTE HILTON

Nick Meza was 17 years old when doctors delivered the life-changing news that he had acute lymphoblastic T-cell leukemia. Halfway through his senior year in high school, Meza would spend the foreseeable future at the Hyundai Cancer Institute at Children’s Hospital of Orange County (CHOC), California.

Meza says he felt like an outsider, at first. “Every time a child life specialist would come in, they’d bring you a coloring book or a puzzle. They didn’t have anything focused for older kids,” Meza says.

A positive person by nature, Meza still struggled with why cancer happened to him. He says the whole situation stunk. However, he didn’t have anyone going through the same thing or to talk with who was about the same age.

Things changed at CHOC in the middle of Meza’s 3 years of inpatient and outpatient cancer treatment. Children’s Hospital of Orange County started offering activities aimed at engaging teenagers and young adults. First it was simply a competition to encourage adolescents and young adults, known as AYAs, to get out of bed and walk the halls. Today, CHOC offers an assortment of social and educational activities through its Richard C. and Virginia A. Hunsaker AYA Oncology Child Life Program (Figure 1).

Meza, who at 23 is in remission and studies mechanical engineering and robotics at Embry-Riddle Aeronautical University in Prescott, Arizona, is among the developers, leaders, and mentors of CHOC’s AYA program.

About AYA oncology patients
Cancer incidence among AYAs is increasing, according to a recent editorial in *Cancer.*

In that editorial, CHOC oncologist Jamie Frediani, MD, says that research in the last 15 to 20 years has revealed that adolescents have not had the same survival gains seen in the pediatric patients younger than age 12 years or older adults.

“There has been a lot of interest in the community at looking at this particular cohort of patients of adolescents to young adults, defined as from 15 to 39 years of age. It incorporates the wide range of oncologic malignancies that happen during the time frame,” Frediani tells *Contemporary Pediatrics.*
Whereas the reasons for the lower survival among AYA cancer patients is multifactorial, a large part is psychosocial, according to Frediani.

“We’re meeting these patients at very critical junctures in their lives. They’re in the process of graduating high school, starting a career, or starting a family,” she says. “Putting cancer in that environment undoes all of that. It takes them away from school. It takes them away from peer groups. It takes them away from a job, career, their family. The loss of hair and the change the body undergoes—the not feeling well. Dating isn’t quite as ripe.”

That’s one piece of the AYA cancer puzzle. Another is their cancer tends to be different, Frediani says. “The actual biology of adolescent cancer and young adult cancer seems to be different than our pediatric and adult population. Just simply their age is often a prognostic factor as to whether or not their cancer is treatable. We know that they have a higher burden of side effects compared to the pediatric population. They have AYA-specific side effects that for whatever reason seem to be worse in this particular population,” Frediani says.

Studies suggest that AYAs treated on pediatric protocols have better outcomes at pediatric versus adult hospitals.

—Jamie Frediani, MD

Children’s Hospital of Orange County and other cancer centers in the United States, including the Moffit Cancer Center in Tampa, Florida, are focusing on AYA cancer care from different angles, including research. Adolescents and young adults tend to enroll much less frequently in clinical trials, according to Frediani.1

Studies also suggest that AYAs treated on pediatric protocols, particularly in diseases such as leukemia, have better outcomes at pediatric versus adult hospitals, Frediani points out.1,2 That could be in part because pediatric hospitals might have more experience in the more aggressive therapies often used in young patients, she says.

Therapy aside, pediatric and adult oncology hospitals should try to address AYAs’ tremendous psychosocial burden. Programs should focus on the psychosocial well-being of teenagers and young adults during treatment and beyond that includes helping them take ownership of their disease; helping them understand what’s going on; and providing the opportunity to make friends with peers in the hospital, Frediani says.

Adolescent and young adult cancer patients are often withdrawn. “It took me maybe close to a month to get one of my friends from the program interested in going to one of the events,” Meza said. “The first event he attended was the Halloween party. He was kicking himself in the butt for not going after that. I think the security of knowing there are other people who have been through something similar at this hospital, it helped him feel a little more comfortable in his situation.”

AYA program elements

The CHOC program focuses on AYA cancer patients aged between 14 and 26 years, according to Kara Noskoff, CHOC child life specialist. The CHOC staff noticed that was the age group that really struggled socially, felt depressed and isolated, and wasn’t engaged in their care. “They weren’t leaving their rooms,” Noskoff said.

Noskoff meets CHOC AYA oncology patients when they’re diagnosed to assess how they’re coping. She helps
them navigate their journey through treatment and beyond. “A lot of our patients focus on all the things their doctor tells them they can’t do. I’m focusing on all the things they can do,” she says.

Noskoff will bring in a music therapist if patients like or want to make music. She’ll use the hospital’s onsite studio if patients are interested in graphic design, videography, or photography. For patients who want to continue their studies online, Noskoff can bring in a tutor.

Today, AYA beds at CHOC are mixed in with other age groups. Although the hospital is considering a separate AYA wing, Noskoff says the majority of AYA patients have told her that they like being near the little ones—whether it’s to encourage them through their journey or be encouraged.

“Several of them have said they were in their darkest moments when they were lying in the bed, curled up with the lights off, and someone opens their door, and in that split second they see a 3-year-old riding down the hall on a tricycle with a parent chasing them with the IV pole. In that moment they realize if those children can do it, they can too,” Noskoff says.

It’s important, however, to have AYA-only areas. “That’s a key component to building these programs. Even if you don’t have a whole ward or unit that’s just for young adults, having that space that they can go to be with other people their age is really crucial to building that support group,” Noskoff says.

Programs specifically for AYA patients don’t have to be elaborate, Meza says. “We just set up board games, have pizza or some other kind of food, and just hang out and enjoy each other’s company,” he says.

Other events take more planning, especially if they’re off-site. The CHOC staff and oncology patient leaders have planned prom nights, barbecues to honor patients’ siblings, a holiday party, drumming circles, and much more (Figure 2).

Children’s Hospital of Orange County offers AYA cancer patients education events every other month to address their specific concerns, such as how therapy might affect their sex lives, long-lasting adverse effects, and about survivorship.

“We just did a career resource expo where we brought in people from the community who talked about resumes and they got to practice interviewing. A few of them walked away with interviews lined up. It was a safe space for them to build that confidence again,” Noskoff says.

The CHOC staff also take about 25 patients and former patients on a yearly retreat to help hone their leadership skills. “One of the big things they told us was they want to give back. That is shown in a couple of ways. One, they want to be at the bedside when these patients are diagnosed. They want to be able to meet the young adults, meet the teenagers, be a friend, be somebody that they can text if they’re having a bad day,” Frediani says.

“A lot of our patients focus on all the things their doctor tells them they can’t do. I’m focusing on all the things they can do.”

—Kara Noskoff, CHOC child life specialist

The CHOC AYA cancer community addresses grieving and loss when one of their friends doesn’t make it through treatment. “We have grief sessions where we get to express our feelings and be close to the people that were close to the person. We can do drum circles, write down our
thoughts," Meza says.

Noskoff says CHOC plans to track the program’s outcomes and quality-of-life measures. The hospital has tracked patient satisfaction, which has improved since the AYA program started. Patient attendance has also grown, multiplying since the program started in 2015. Today’s holiday party attracts roughly 100 patients.

Words of AYA wisdom
Pediatricians should realize that young adults are not old children and they’re not little adults, according to Frediani. “I think we get into the most trouble when we try to treat them as kids or adults. They’re not really there yet. They don’t have the maturity adulthood brings. They’re also not the carefree 5-year-old,” she says.

Providers shouldn’t be put off when these young adults seem angry, closed off, or unwilling to engage, Noskoff says. “Those are the exact patients that do need us. They’re very protective over their emotions because they don’t want to burden anyone. They’re much more aware of the severity of their illness and the impact that it has. They’re fearful for their lives. They’re grieving the loss of their friends and the life that they had. Getting these patients to participate and be part of this community takes time,” she explains.

Paying attention to the specific needs of AYA cancer patients matters, according to Meza. “The program improves quality of life at the hospital. I’ve seen it firsthand through mentoring patients and experienced it firsthand,” he says.

Frediani, who started working at CHOC about 2 years ago when the AYA program was well underway, says she has no doubt the program helps teenagers and young adults better cope and contributes to better outcomes.

“My hope is in the next 10 years we’ll have the data to prove it,” she says.

For references, go to ContemporaryPediatrics.com/AYA-cancer-care

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Pediatricians are being asked by parents about treating their children with cannabidiol (CBD) products obtained via local shops, online sellers, and national pharmacy chains. As many parents are using CBD regularly, it is likely that children are being given these products without pediatricians’ endorsement, convinced by the national media and word of mouth that they are both safe and effective for conditions such as anxiety, sleep problems, and pain.

The purpose of this article is to examine the evidence relating to the safety and therapeutic benefit of CBD for pediatric patients, and to offer suggestions how pediatricians should respond to queries from parents regarding its use.

Cannabis: CBD and THC content
Cannabis contains over 100 different chemicals identified as cannabinoids. The major psychoactive component in cannabis is delta-9-tetrahydrocannabinol (THC), which produces euphoria, changes in perception and mood, as well as an increase in appetite. In contrast, CBD alone produces sedation, without the psychoactive effects associated with THC.1

Marijuana consists of the dried flowers, leaves, and stems of the female cannabis plant and contains between 3% to 20% THC. Different subspecies of cannabis contain different ratios of THC to CBD, with the highest ratios in Cannabis sativa and the lowest in Cannabis indica.2 “Hemp” is a term used to classify varieties of cannabis with 0.3% or less of THC and is the source of most CBD products available commercially. Cannabidiol is sold for inhalation by smoking or vaping; ingestion via a spray, pill, oil, or tincture; as a CBD-infused edible; or to be used topically as a cream or balm.

Delta-9-tetrahydrocannabinol exerts its effects by binding to 2 cell membrane receptors called the cannabinoid type 1 (CB1) receptor and type 2 (CB2) receptor. Cannabinoid type 1 receptors are mainly concentrated in brain tissues and CB2 receptors are found in immune and hematopoietic cells. Through its effects on these receptors, THC affects pain, perception, anxiety, learning, memory, and motor control.

In contrast, CBD has no effect on CB1 and CB2 receptors and exerts its sedative activity by affecting numerous other neurotransmitters. It also has been demonstrated to reduce the euphoric effects of THC by inhibiting its effects on the CB1 and CB2 receptors and modulating the metabolism of THC.2

To date, the US Food and Drug Administration (FDA) has approved only one CBD medication, Epidiolex, for treatment of refractory seizures in patients aged 2 years and older with Lennox-Gastaut syndrome or Dravet syndrome. Epidiolex, approved just last year, is synthetic CBD and contains no THC. Extensive clinical trials with this drug have been conducted and results provide significant insight regarding its benefits.
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CBD & AUTISM

I have been asked by parents several times regarding the use of a cannabidiol (CBD) product to calm their aggressive autistic children when other medications, including risperidone, sertraline, fluoxetine, and others have not been effective. It would be tempting to recommend CBD/THC products to help parents in this regard, but my concerns about safety as well as efficacy have dissuaded me from doing so. Although 3 observational studies of autistic children with medication containing both CBD and THC show promise for controlling aggressive behavior in these patients, there have been no randomized clinical trials showing CBD’s efficacy and safety for autistic patients. Over the next few years, I anticipate new recommendations are likely to be issued by the US Food and Drug Administration and medical organizations, regarding prescribing CBD medications for autistic children.

—Andrew J Schuman, MD, FAAP

The same survey also found that 37% reported using CBD for relaxation or stress/anxiety reduction, 24% for joint pain, 11% for recreation, and 10% as a sleep aid. In addition, 40% of users obtained CBD from cannabis dispensaries, 34% from retail stores, and 27% from online sellers with the remainder from unspecified outlets. The most popular forms were infused edibles (35%), drops or sprays (30%), and vaping devices (30%).

What the Epidiolex trials reveal

In controlled trials, Epidiolex was administered to pediatric patients aged 2 years and older with Lennox-Gastaut syndrome or Dravet syndrome in a dosage range of 5 to 20 mg/kg/day. The drug reduced the frequency of seizures by 36% to 41% compared with a reduction of 14% to 16% seen in patients receiving placebo. According to the package insert, adverse effects seen in at least 10% of Epidiolex-treated patients included elevated liver enzymes, somnolence, decreased appetite, diarrhea, fatigue, sleep problems, and malaise. An increase in suicidal ideation was also seen.

The trials also showed that Epidiolex interfered with the metabolism of many drugs including propofol, bupropion, morphine, clobazam, lorazepam, and phenytoin. The incidence of dose-related liver transaminase elevations were seen in 13% of

Medical cannabinoids in pediatric patients

Wong and Wilens published a systematic review of medical cannabinoids in pediatric patients in 2017. Of 2743 citations examined to identify the evidence base of cannabinoids for children and adolescent patients, they identified 22 studies meeting inclusion criteria. They found sufficient evidence that THC-derived products are effective for chemotherapy-induced nausea as well as CBD for epilepsy. They also reported insufficient evidence for cannabinoids for spasticity, Tourette syndrome, neuropathic pain, and posttraumatic stress disorder. They advocated for further research regarding CBD and THC, given that recreational cannabis has potential psychiatric and neurocognitive adverse effects, including lower intelligence quotient scores, deficits in memory, psychomotor performance, and attention.

CBD and the marketplace

In spite of warnings issued by the FDA (see “Current status of FDA-approved cannabis or cannabis-derived compounds” below), many Americans are using CBD, convinced that it is effective for anxiety, pain, and sleep problems. It is even being used for cancer treatment, arthritis, and mood disorders, in place of or in addition to prescribed medications. It is no surprise that CBD is growing in popularity, as 22% of adolescents and young adults use marijuana regularly and 22 million Americans use marijuana at least once per month.

Cannabidiol is poised to be a multibillion-dollar industry in the United States over the next few years. What is most disconcerting is that many online sellers are promoting the use of CBD-infused gummies to calm overactive and “fussy” children and CBD-infused oils are now being sold as a teething remedy for infants. We don’t know how many children receive CBD on a regular or sporadic basis.

A recent Harris Poll survey of 2000 Americans indicated that 7% of those surveyed use CBD regularly. Another survey of over 4000 CBD users performed by Consumer Reports revealed some interesting findings:

- 26% of those surveyed have tried CBD at least once in the past 2 years.
- 14% use it daily.
- 47% used CBD preparations to replace over-the-counter medications.
- 30% used it to supplement their regular medications.
- 22% used CBD to replace their medications entirely.

and adverse effects. More on this in a moment.

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The same survey also found that 37% reported using CBD for relaxation or stress/anxiety reduction, 24% for joint pain, 11% for recreation, and 10% as a sleep aid. In addition, 40% of users obtained CBD from cannabis dispensaries, 34% from retail stores, and 27% from online sellers with the remainder from unspecified outlets. The most popular forms were infused edibles (35%), drops or sprays (30%), and vaping devices (30%).

What the Epidiolex trials reveal

In controlled trials, Epidiolex was administered to pediatric patients aged 2 years and older with Lennox-Gastaut syndrome or Dravet syndrome in a dosage range of 5 to 20 mg/kg/day. The drug reduced the frequency of seizures by 36% to 41% compared with a reduction of 14% to 16% seen in patients receiving placebo. According to the package insert, adverse effects seen in at least 10% of Epidiolex-treated patients included elevated liver enzymes, somnolence, decreased appetite, diarrhea, fatigue, sleep problems, and malaise. An increase in suicidal ideation was also seen.

The trials also showed that Epidiolex interfered with the metabolism of many drugs including propofol, bupropion, morphine, clobazam, lorazepam, and phenytoin. The incidence of dose-related liver transaminase elevations were seen in 13% of
patients treated with Epidiolex compared with 1% in placebo-treated patients, and extreme elevations were much more common in patients taking other seizure medications. The package insert for Epidiolex cautions that bilirubin levels and liver function tests should be obtained prior to starting treatment, and at 1 month, 3 months, and 6 months, as well as at 1 month following a dosage change.

**Takeaway**
The Epidiolex trials provide evidence that CBD in appropriate dosages can be effective for refractory seizures in children with either Lennox-Gastaut syndrome or Dravet syndrome. Epidiolex may prove to be a useful antiepileptic drug for refractory seizures in other conditions as well. However, Epidiolex’s adverse effect profile is significant, and although some trials were as long as 2 years, the long-term effects of Epidiolex are not known.

**What’s in CBD products: a cautionary tale**
Most CBD sold to consumers is hemp derived and contains small quantities of THC, usually less than 0.3%. However, depending on the strain used to prepare the product, some CBD preparations will contain a higher content of THC, of the order of 1.5% to 3%.

In researching this article, I made some interesting observations relating to commercial CBD products. Many CBD products are labeled with claimed health benefits including reducing pain, facilitating sleep, and reducing stress and anxiety. Many also display that they are preservative free and rich in vitamins. Online shops that cater to CBD users usually contain more information regarding the CBD content and many display the chemical analysis of the hemp used to manufacture the product, displaying the CBD and THC percentages by weight.

**OTHER INTERESTING OBSERVATIONS:**
- CBD gummies contain from 25 mg to 50 mg CBD per candy, so it would only take a few gummies per day to reach the dosages associated with Epidiolex use that produce the adverse effects listed above—and no one tests children or adults using CBD regularly for liver enzyme elevations!
- An interesting study was published 2 years ago in which researchers...

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**CURRENT STATUS OF FDA-APPROVED CANNABIS OR CANNABIS-DERIVED COMPOUNDS**

There is much controversy regarding the use of marijuana for medical conditions and the regulations surrounding both cannabis and cannabidiol (CBD) products are both confusing and nuanced.

As of this writing, cannabis and commercial CBD products have not been approved by the US Food and Drug Administration (FDA) for use in patients as they are concerned about safety and efficacy. Many state legislatures have sidestepped the FDA, permitting the use of marijuana and CBD for medical conditions with physician “approval.” There are now 33 legal “medical marijuana” states and Washington, DC; 10 legal recreational marijuana states and Washington, DC; and 17 states with “medical CBD” laws.

Last December, the Agricultural Improvement Act of 2018 was signed into law, which removed cannabis from the Controlled Substances Act. Previously, cannabis was a Schedule I drug, defined as drugs with no accepted medical use and high abuse potential, a category that includes heroin, ecstasy, peyote, and lysergic acid diethylamide (LSD). Congress, however, preserved the FDA’s authority to regulate cannabis and cannabis derivatives under the Federal Food Drug and Cosmetic Act and the Public Health Service Act.

In addition to Epidiolex, the CBD-only drug discussed in the article, the FDA has approved Marinol and Syndros, which contain the active ingredient dronabinol, a synthetic THC for treatment of anorexia associated with AIDS patients and nausea in adult and pediatric cancer patients who have not responded to antiemetics. Cesamet is another synthetic carbenoid, nabilone, with a structure similar to THC, and is FDA approved for treating nausea and vomiting associated with cancer chemotherapy in patients aged 18 years and older for whom other antiemetics are not effective. Sativex is an oromucosal spray contacting THC and CBD in a 1:1 ratio that is used overseas for treating pain associated with multiple sclerosis and is under consideration by the FDA for use in the United States.

—Andrew J Schuman, MD, FAAP
analyzed purchased CBD products from shops and online sellers, finding that many were labeled incorrectly.12

- Between 2017 and 2018, Utah reported 52 cases of poisoning from ingestion of CBD oil that produced symptoms that included hallucinations, nausea, vomiting, seizures, and loss of consciousness.11

- Last year, there were 518 CBD poisonings reported by the American Association of Poison Control Centers, and as of May 31 of this year there have been 492 poisonings reported.

What to tell parents: one pediatrician’s perspective
As you can see from the previous discussion, CBD has only been shown to be an effective therapy for refractory seizures associated with 2 uncommon medical conditions. For the duration of the trials, CBD was well tolerated but adverse effects were frequent. Cannabidiol has not been studied adequately via randomized clinical trials for medical problems for which CBD distributors claim significant benefit, including anxiety, attention-deficit/hyperactivity disorder (ADHD), pain, inflammation, and sleep disorders. Although many individuals report symptomatic improvement from CBD, only randomized controlled trials can exclude the placebo effect as being responsible for the results observed by consumers.12

Marijuana’s former Schedule I status hampered research regarding cannabinoids. Currently, there are now more than 100 ongoing clinical trials regarding the use of CBD products for conditions that include refractory seizures, anxiety, and cannabis abuse disorder (clinicaltrials.gov; key word: cannabidiol). In the near future, we will have more clinical data upon which to base our advice. Meanwhile, the FDA and many states are at odds regarding the legality of CBD products, so for the time being individuals can buy and vendors can sell products without fear of prosecution. (See “Current status of FDA-approved cannabis or cannabis-derived compounds,” page 43.)

I would encourage pediatricians to ask parents if they are using CBD to treat their children for autism, anxiety, or ADHD. In my experience, many adolescents do not acknowledge using marijuana, but according to the statistics above, 1 in 5 do. If parents are giving CBD in addition to prescribed medication, this situation may complicate and confound treatment. Parents of children with ADHD who are not responding optimally to their prescribed medications may be tempted to medicate or supplement with CBD as it is inexpensive and universally available. So, too, with aggressive children with autism who are not doing well on prescribed medications. (See “CBD and autism,” page 42.)

In my opinion, it would be inappropriate and irresponsible for pediatricians to encourage the use of CBD until more studies are available, particularly regarding its long-term safety, and it is endorsed for specific conditions by the FDA.

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“Many online sellers are promoting the use of CBD-infused gummies to calm overactive and ‘fussy’ children.”
—ANDREW J SCHUMAN, MD, FAAP

REFERENCES
vessels of the head and neck occur in approximately 40% of patients. Intracranial arterial anomalies localize to the same side as the facial IH. The presence of hypoplastic or progressively narrowing cerebral blood vessels increases the risk of arterial ischemic stroke, typically manifesting as hemiplegia and/or seizures.4 The most common structural brain anomaly in PHACE is unilateral cerebellar hypoplasia, but various cystic malformations of the posterior fossa, such as Dandy-Walker malformation, can be associated.

Cardiac, aortic arch, and brachiocephalic anomalies also are fairly common in PHACE. The prevalence of congenital heart disease can range from 41% to 67%.5 Aberrant subclavian arteries are common in PHACE syndrome. Therefore, when evaluating for coarctation of the aorta, the 4-extremity blood pressure assessment for a gradient between the upper and lower extremities may not be accurate.

Congenital anomalies of the eye may involve the posterior or anterior segment. Posterior segment anomalies are part of the major diagnostic criteria and include persistent fetal vessels, “morning glory” disc, peripapillary staphyloma, and optic nerve hypoplasia. Anterior segment anomalies are minor diagnostic criteria, including coloboma, iris hypoplasia, cataracts, sclerocornea, and iris hypoplasia.5

Management
Propranolol is now first-line therapy for complicated IH but should be used cautiously in PHACE syndrome. If possible, imaging studies of the head and neck should be performed prior to initiation of oral propranolol to evaluate the severity of cervical and cerebral arteriopathy and cardiac anomalies. Blood pressure fluctuations may increase the risk for ischemic stroke. Therefore, starting at the lowest effective dose and titrating the dose slowly is recommended. In high-risk patients, initiation of propranolol may be performed in the inpatient setting. Pediatric dermatologists or other specialists in cutaneous vascular anomalies typically lead propranolol titration.5

Patients with mid- to high-risk arterial anomalies require daily aspirin for ischemic stroke prophylaxis.2 Pediatric neurology can guide prophylaxis recommendations and provide close neurologic follow-up.

Patient outcome
Parents of this particular patient reported normal development and denied seizures, cyanosis, or feeding concerns. An MRI of the head and neck confirmed temporal and intraorbital hemangioma with hypoplasia of the left optic nerve (Figure 2). Additionally, hypoplasia of the left cerebellum was noted as well as several dysplastic and hypoplastic intracranial arteries on the affected

Cardiac, aortic arch, and brachiocephalic anomalies also are fairly common in PHACE. The prevalence of congenital heart disease can range from 41% to 67%.5
Because of the relative ease of holding babies immobile, infants can undergo PDL treatment for PWS without the need for general anesthesia. Despite the ability to achieve good results regardless of PWS location, guarantees about the outcome are never given, and when the PWS is below the elbow or knees, the family is informed about the potential for less improvement when treating birthmarks here.

Post-treatment sequelae
Transient purpura and mild swelling are the most common adverse effects of PDL treatment for PWS. These reactions generally persist for 4 to 7 days. Skin pigmentary changes are possible, but the risk is limited by selection of appropriate laser settings, use of photoprotection, and, in patients with darker skin, extending the interval between treatment sessions. The researchers encountered no cases of scarring or permanent pigmentary changes in their study of 197 children who were aged 1 year or younger when starting PDL treatment for PWS.18

Conclusion
Treatment of PWSs with the PDL can be initiated within the first few days after birth as an in-office procedure. This approach to early intervention may relieve parental anxiety about the baby’s appearance, avoids exposing the child to the risks of general anesthesia, and enables the best cosmetic outcome with fewer sessions. Therefore, it reduces the likelihood that a child born with a PWS will experience the psychosocial morbidity that can be the most significant complication of these lesions.

Help with referrals to a specialist with experience treating PWSs in infants and children can be obtained through the Vascular Birthmarks Foundation (https://birthmark.org/) and the American Society for Dermatologic Surgery (www.asds.net/).
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Segmental hemangioma on a newborn’s face

PUNEET TUNG, DO; JENNIFER SCHOCH, MD

A healthy 5-week-old girl presents for evaluation of rapidly growing, flat-topped red papules on the left side of her face (Figure 1).

Discussion

PHACE syndrome consists of posterior fossa brain malformation, hemangiomas of the face, arterial anomalies, cardiac anomalies, and eye abnormalities. It is primarily a cutaneous condition with many congenital anomalies. The term PHACE(s) is sometimes used when there are additional ventral developmental defects such as sternal cleft and/or subumbilical raphe, neither of which was present in this patient.

A complete and thorough physical exam should be performed at initial patient presentation to evaluate for developmental anomalies, eye anomalies, and midline defects. Initial workup also includes a head and neck magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA) and echocardiogram. If cardiac abnormalities are identified, a cardiac MRI/MRA is recommended to characterize the arch and brachiocephalic anatomy.

A large segmental facial infantile hemangioma (IH) should raise concern for the possibility of PHACE syndrome. Infantile hemangiomas must be distinguished from port wine stains: IH are faintly present or absent at birth, and then grow quickly in the first 2 months of life; in contrast, port wine stains typically are readily apparent at birth and do not grow quickly. Infantile hemangiomas may begin as more of a purplish bruise-like lesion or telangiectasias with surrounding pallor and then develop their characteristic cherry-red color in the first weeks of life. Port wine stains may begin as a pink-red patch and develop a deeper red hue with time.

The segmental IH of PHACE comprises 1 or more of 4 segments: frontotemporal, maxillary, mandibular, and/or frontonasal. Patients with PHACE may have subglottic airway hemangiomas and are at risk for airway obstruction. For this reason, MRA of the neck should be performed in addition to brain imaging.

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