STATE OF THE UNION

Mental Health
Pandemic mental health tips for pediatricians

Your Voice

Supporting At Risk Nurses & Families

Exergen Corporation Launches Nurse Support Program to Ensure Every Nurse Has Access to an Accurate Thermometer at Home to Protect Themselves and Their Families.

A series of new studies underscores the alarming toll that COVID-19 takes on frontline nurses and, ultimately, their families. The studies show that patient-facing nurses and their households have a three- and two-fold increased risk of COVID-19 hospitalization, respectively.

- Patient-facing nursing 3x
- Nurses are disproportionately affected among healthcare personnel
- Checking temperature only once is not sufficient

Accuracy backed by more than 80 peer-reviewed published studies.

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Q: What are the recommendations for back-to-school and back-to work temperature screenings?
A: Back to school and back to work recommendations from authorities on direct temperature screenings to be done at home.
- American Academy of Pediatrics Interim Guidance for School Re-entry
- Centers for Disease Control and Prevention (CDC)
- Occupational Safety and Health Administration (OSHA)

Q: How do circadian rhythms impact temperatures and assessments of temperatures?
A: Our internal biological clocks produce circadian cycles that vary throughout the 24 hours of each day. This causes body temperature to vary about 1.2°F (0.7°C) between lowest temperatures in the morning and highest temperatures in the evening. With fever, the circadian variation still occurs, but at higher temperatures. Accordingly, temperature assessments in the morning are low and will miss about half of the fevers. Temperature assessments in the evening are high and will detect all the fevers.

Q: When should temperatures be taken?
A: Twice daily. Before leaving for school or work in the morning, and at dinner time in the evening, if a fever is detected at either time, a medical care professional should be contacted immediately. Even if school or work is done on-line, it is important to check temperature twice daily for the health of the family.

Q: What makes thermometers accurate? What should we know about thermometer accuracy? How about No Touch Thermometers?
A: Published peer-reviewed clinical studies. Without such studies by medical professionals, there is no assurance of accuracy on children and adults in all settings. No Touch thermometers are well known to be inaccurate, with unavoidable errors of +/- 4 deg F. They have no published peer-reviewed clinical studies supporting their accuracy.

Q: What types of thermometers are recommended for use in schools and workplaces? For use by families?
A: Only those thermometers that are clinically accurate as demonstrated by published peer-reviewed clinical studies.

Q: Can you explain how a thermometer margin of error might guide the choice for a cut-off of fever?
A: Some attempts to use a lower cut-off for Covid-19 screening have been made due to the low readings of the no touch thermometers from their inaccuracies. These attempts have been unsuccessful in “improving” the no touch devices’ accuracies. A thermometer with accuracy backed by more than 80 published peer reviewed studies requires no adjustment to the medical standard cut-off for fevers.
STATE OF THE UNION ON COVID

Mental Health
Pandemic mental health tips for pediatricians

Your Voice
What a pediatrician learned about dyslexia from his daughter

Puzzler
A newborn boy with red lesions on his cheek

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Do your patients need winter supplements?

Dermatology
What you should know about terra firma-forme dermatosis

Best treatments for children
What’s new in testing
When will they get the vaccine?
The latest on MIS-C
YOU CAN’T PROTECT THEM FROM ADOLESCENCE

The persons depicted here are models used for illustrative purposes only.
BUT YOU CAN HELP PROTECT THEM FROM MenB

Help protect appropriate patients by vaccinating against MenB.

There are many threats out there, but MenB is one you can help prevent. CDC recommends MenB vaccination for adolescents not at increased risk, aged 16-23 years [preferred age 16-18 years], based on shared clinical decision-making.1 Start the conversation with your patients and their parents about the importance of vaccinating against MenB.

Recommend that your appropriate patients start the MenB vaccination series. Review what meningococcal disease is, as well as potential consequences, including death, and the rapid progression it may take.2,3

List the behavioral risk factors that can lead to contracting MenB. Emphasize the importance of series completion and schedule their second dose.

Are you doing all you can to help protect your appropriate patients from MenB? Learn more at VaccinateForMeningitis.com

Vaccination may not protect all recipients.

CDC=Centers for Disease Control and Prevention; MenB=meningococcal serogroup B.


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¹A skin protectant
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New Year’s Greetings!

It is hard to believe that 2021 has arrived. I am sure we all are happy to bid 2020 farewell and are looking forward to much more “normal” year in 2021. As the COVID-19 pandemic continues to surge across the country and stay-at-home orders, travel bans, and other restrictions remain in place, the Emergency Use Authorization of 2 COVID-19 vaccines brings a much welcomed glimmer of hope to obtaining some control over this pandemic. The start of large COVID-19 vaccine trials in children are planned for these next several months, with the hope of vaccine availability for children by the 4th quarter of 2021. This month’s issue has several “must read” articles:

- This issue’s cover story: The state of the union on COVID-19, which provides a comprehensive review of different aspects of COVID-19 in the pediatric population.
- The pandemic has fostered the exponential growth of social media outlets and the creation of many social media challenges, some of which present significant danger to a person’s health and well-being. The pediatric pharmacology article in this issue addresses the "Benadryl challenge" that is trending on TikTok and discusses the dangers of and treatment for this challenge.
- The pandemic has created nutritional challenges for persons of all ages. The nutrition article looks at the nutritional needs of children during the winter months and the importance of adequate vitamin D.

Best wishes for a peaceful, healthy, and happy New Year. As Oprah Winfrey states “Cheers to a New Year and another chance to get it right”. Please stay safe and well. And as always, I welcome your suggestions, comments, and questions.

With warmest regards,
Tina

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Editor’s View

Editor’s View

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To a new year, at last

Last month, *Time* magazine came out with a dramatic cover that garnered a lot of media buzz: The year 2020 was displayed in imposing black type and crossed out with a dramatic red “X,” the line underneath reading, “The worst year ever.” I suspect it also echoed the sentiments of many of us. Considering last year was ushered in with a calamitous pandemic and further punctuated by intense racial and political divides, I think it is fair to say that virtually all of us in the medical community will be glad to put the past year in our rearview mirrors and look ahead with a clean slate. And certainly, the clouds already seem to be lifting, with highly-touted vaccines now on the market to help eradicate COVID-19 and, hopefully, in the near future, multisystem inflammatory syndrome in children. And, while we are still uncertain when children aged 16 years and younger will be able to get vaccinated, medical authorities assure us that vaccine is coming, with trials including both pregnant women and children just starting. (You can read about where we are with children’s vaccinations and more in our cover story, “State of the union on COVID-19”).

Elsewhere, *Contemporary Pediatrics* as always, continues to offer you the latest news and case studies in pediatrics via our print and digital content, which includes podcasts, expert interviews with key opinion leaders, and more.

And, just so you know: we pay careful attention to what you tell us. Nearly 80 percent of you responded in our recent survey that you would like to see more content that covers updates on current pediatric guidelines. We now have a new navigation bar item for just that kind of information, so please visit our website (www.contemporarypediatrics.com) to check it out.

Finally: Here’s to a great 2021, filled with medical marvels and good health for everyone. Happy New Year!
Practitioners at a health center in Nova Scotia improved the time to antibiotics (TTA) for children with chemotherapy-induced febrile neutropenia (FN) by instituting a quality improvement project that included making many small and easy-to-implement changes to streamline the process.

Multiple potential delays (what the authors of a report on the project call “process wastes”) to TTA included patients’ waiting to be registered or for laboratory technicians, delayed central venous access device (CVAD) access, waiting for the absolute neutrophil count (ANC) to be reported, and delayed antibiotic orders. A multidisciplinary team sought to eliminate these wastes by laying out all stakeholders’ tasks to allow them to be executed in parallel, including nurse-initiated CVAD access and planned antibiotic administration no later than 45 minutes after triage. The authors reviewed how oncology patients who visited the emergency department (ED) with suspected FN were managed under a new streamlined process and compared these results with a baseline audit to evaluate improvements.

After the new process was initiated, 49 FN encounters in 26 patients took place during a 1-year period. The TTA significantly improved to a median of 59 minutes compared with the baseline of 99 minutes for patients with confirmed FN. In addition, the percentage of patients treated within 60 minutes rose from 12% to 47% and those treated within 90 minutes from 39% to 74%. The TTA was significantly shorter if the CVAD was accessed by a nurse to collect blood samples, with a median TTA of 55 minutes compared with 99 minutes when laboratory personnel collected them. The authors also determined that use of a standardized order set was associated with a median TTA of 55 minutes compared with 79.5 minutes without use of standardized order sets. Other positive changes included having families apply topical anesthetic en route to the ED, nurse-initiated steps, information to the electronic medical record, printing important orders with the initial ED package of paperwork, and setting a time limit for ANC returns before administering antibiotics (Geerlinks A, et al. Pediatr Emer Care. 2020;36[11]:509-514).

Shortening the time to initiating antibiotic therapy in these potentially septic patients is quite important. You do not have to follow all the steps the authors took and can adapt some for your own circumstances, but arranging a protocol at your local hospital should not be that difficult, and could have immense benefits.

Dr. Farber, section editor for Journal Club, is a pediatrician in Woodbridge, Virginia. Ms Freedman is a freelance medical editor and writer in New Jersey. The editors have nothing to disclose in regard to affiliations with or financial interests in any organizations that may have an interest in any part of these articles.
A 3-minute step test (3MST) is a valid and reliable way to assess the cardiopulmonary and functional capacity of healthy children, according to a comparison of 3MST with the 6-minute walking test (6MWT), a tool often used for this purpose.

Investigators in Brazil recruited 66 public school children aged from 7 to 11 years old for the comparative study. Participants performed the 3MST with a 20 cm-high wooden step, a nonslip surface, and no handrail. They were instructed to go up and down 24 times a minute, keeping pace with a metronome. The 6MWT was performed in a 30m long flat hallway, with the children instructed to walk as far as possible without running.

Comparisons between the 2 tests with regard to performance variables found that the 3MST was a safe and reproducible way to determine exercise tolerance in healthy children in this age group. Further, compared with the 6MWT, the 3MST is short, easy to perform, and requires less physical space (Teoxeora KB, et al. Acta Paediatr. 2020;109[11]:2354-2355).

THOUGHTS FROM DR FARBER

This test is easy enough to perform, requiring just a metronome and a step. I wish the authors had indicated what an abnormal result might be, so you may want to create your own norms. However, everyone they tested (including those who were obese) was able to complete the task so, at the least, a child who cannot complete the test warrants further evaluation before being cleared for participation in sports.

A study of a large, multistate primary care group of more than 77,000 children spanning multiple years found a significant association between positional skull deformity (plagiocephaly) and developmental delay. The retrospective analysis relied on electronic medical record data from 45 primary care sites during a 17-year period and included children aged 5 years or younger who were classified as having plagiocephaly if they were diagnosed by 12 months of age.

Of the 77,108 patients seen by 12 months, 2315 (3%) were diagnosed with plagiocephaly (median age of diagnosis, 3 months), with prevalence of the condition increasing over time from 0.1% in 2000 to a maximum of 6.2% in 2016. Patients with plagiocephaly were more likely than their peers to be male, white, have private insurance, have English as a primary language, and have a history of prematurity and abnormal tone and torticollis. Almost 9% of total patients had a developmental delay diagnosis, with 17.5% of the plagiocephaly group having such a diagnosis compared with 8.7% in the group without plagiocephaly. Further, plagiocephaly was independently associated with increased odds for any developmental delay, even after controlling for sociodemographic and clinical factors. As for specific delays, motor, language, social, and general delay—but not cognitive delay—were significantly more likely in the plagiocephaly group. In patients with both plagiocephaly and developmental delay, plagiocephaly generally was diagnosed before developmental delay, at a median age of 3 months and 15 months, respectively (Rohde JF, et al. J Dev Behav Pediatr. Epub ahead of print).

THOUGHTS FROM DR FARBER

You may hear about this study from worried parents. I understand why plagiocephaly could be associated with motor delay, but it is harder to account for other delays. I also note that the percentage of children with diagnosed delays seems high. In any case, most children with plagiocephaly will be developmentally normal. Follow them carefully, but you can reassure parents that their child likely will be fine.
Red papulonodule with central crusting on a neonate’s cheek

JULIA WITOWSKA, MS4; RACHEL SEHGAL, MD; BRIDGET BOYD, MD

A newborn boy born via normal vaginal delivery at 38.6 weeks gestation to a 33-year-old G5P2022 mother presented at birth with an asymptomatic 8-mm red, papulonodule with central crusting on the right cheek (Figure 1). Pregnancy had been complicated by maternal type 2 diabetes mellitus and obesity. Delivery was uncomplicated and the patient was otherwise healthy.

History
Mother was otherwise healthy and the pregnancy was uneventful. Medications that were used during the pregnancy included prenatal vitamins, insulin, ranitidine, and diphenhydramine. All antenatal ultrasounds, serologies, and labs were unremarkable. Mother reported no relevant personal or family history, specifically no history of herpes simplex virus (HSV) infection, other viral infections, leukemia/lymphoma, or immunodeficiencies.

Physical examination
Initial physical examination revealed a well appearing infant. The APGAR scales were 9, 9, and 9 at 1, 5, and 10 minutes respectively. Patient weighed 3485 grams, an appropriate weight for his gestational age. Vital signs were within normal limits upon delivery.

Skin examination revealed an asymptomatic, round, red, non-blanching, 8-mm firm papulonodule on the right cheek. The lesion had an erythematous base with no drainage or crusting on initial exam. Central crusting later developed on the first day of life. The patient did not appear bothered by the lesion. Physical exam...
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was otherwise unremarkable.

**Laboratory**
The patient received all routine neonatal labs. Hemoglobin and hematocrit levels were within normal limits. He required 2 oral glucose gels prior to glucose normalization. Metabolic screens were within normal limits.

At 24 hours of life, C-reactive protein and a complete blood count were drawn and returned with no abnormalities.

**Imaging and consultation**
Ultrasound of the lesion of the right cheek demonstrated a heterogeneous, hypoechoic lesion with no evidence of increased vascularity. Pediatric dermatology was consulted for further evaluation of the lesion and performed a biopsy that revealed Langerhans cells with surrounding inflammatory cells and eosinophils (Figures 2 and 3). A cutaneous proliferation of CD1a, CD68, and S100 positive cells was also confirmed via immunohistochemical staining (Figures 4 and 5). Fungal cultures, aerobe-anaerobe cultures, and an acid-fast bacilli culture were negative. These findings were typical of cutaneous Langerhans cell histiocytosis.

**Differential diagnosis**
The initial differential diagnosis included several infectious and non-infectious etiologies that could account for such a skin lesion (Table). Infantile hemangiomas were high on the differential, as these are the most common skin neoplasms presenting in infancy. Ultrasound imaging may demonstrate an increase in internal vascularity. Ultrasound of our patient on day 1 of life indicated no prominent internal vascularity, making the diagnosis of infantile hemangioma less likely. Moreover, the presence of a nodule at birth and uniform blanching erythema with central crusting would not be typical of a classic infantile or congenital hemangioma.

Langerhans cell histiocytosis (LCH) was another diagnosis considered as it has a variable clinical presentation. Manifestations of this hematologic disorder can range from single cutaneous lesions to multiple cutaneous lesions, and to a multi-organ disease. Skin involvement is present in 33% of patients and appearance can vary from dry scaly lesions to crusted vesicles and red papules. Biopsy confirms characteristic histologic and immunohistochemistry findings.

Biopsy is also critical to exclude other diagnoses such as congenital juvenile xanthogranuloma. This is a form of non-Langerhans cell histiocytosis which can present as subcutaneous masses with overlying skin changes, papules, or nodules that are erythematous at presentation and become yellow in color over weeks to months. These lesions vary from a few mm in diameter to over 3cm, and most commonly involve the head, neck, or trunk.

Leukemia cutis describes skin manifestations that arise as a result of an underlying leukemia. These le-
sions can also have a variable presentation including red or violet papules, plaques, nodules or hemorrhagic lesions. These lesions commonly appear after a diagnosis of leukemia has already been made, but may also appear before there is any involvement of the peripheral blood or any systemic symptoms arise. Approximately two-thirds of patients presenting with neonatal acute myeloid leukemia also present with skin lesions, but lesions may be limited to the skin and resolve without treatment. However, these patients usually have other findings including hepatosplenomegaly or a high systemic tumor burden. Confirmation of this diagnosis is also completed via skin biopsy.

Other potential etiologies include congenital sarcomas, such as rhabdomyosarcoma. These soft-tissue neoplasms can present as red or violaceous nodules if they metastasize to involve the skin. Additionally, extramedullary hematopoiesis, or a “blueberry muffin rash”, can also present as similar papules and nodules that can be the result of an underlying infection (often TORCH infections), hemolysis, or malignancy.

An infectious etiology also cannot be ruled out when a newborn presents with an abnormal skin lesion. Neonatal HSV needs to be considered due to the high morbidity and mortality rates associated with this infection. Patients with neonatal HSV usually present with clusters of vesicles localized to the skin, eyes or mouth. Failure to treat could lead to disseminated disease or spread to the central nervous system. Cutaneous lesions can also be the manifestation of infections caused by the other congenital TORCH infections, *Staphylococcus aureus*, Group A or B *Streptococcus*, and congenital candidiasis. Infection could suggest that there is an underlying immunodeficiency such as HIV, malignancy, or a white blood cell disorder. Our patient did not present with any risk factors for these conditions and lab values were reassuring. Additionally, the patient was not exposed to any risk factors that would alter the function of the immune system at this age including maternal illness, prematurity, immunosuppressive medications or inadequate prenatal care.

**Discussion**
Langerhans cell histiocytosis has an incidence of 2.6-8.9 cases per million amongst children aged younger than 15 years, and a median age of diagnosis of 3-4 years. This disorder is characterized by proliferation of CD1a, SI00, CD68, and CD207 myeloid dendritic cells and has a highly variable clinical presentation. Any organ system can be affected, thus requiring a comprehensive evaluation of affected patients. Commonly affected sites include the bone, skin, central nervous system, pulmonary, hematopoietic, and hepatobiliary systems.

Among patients diagnosed with LCH, 33% present with skin findings. Skin lesions usually present as ulcerated, red papules, as was seen in our patient, but may also appear pustular, vesicular, or petechial in nature. In infancy skin manifestations may also resemble other skin disorders such as erythema toxicum neonatorum, eczema, or seborrheic dermatitis. As a result, it is important to accurately diagnose this condition to ensure appropriate treatment.

A rare variant of LCH named con-
genital self-healing reticulocytosis has also been identified. This condition was first described by Hashimoto and Pritzker and presents at birth or within the first few weeks of life. Patients may present with brown to violaceous papules located anywhere on the body. As with classic LCH, these lesions can be single or multiple. It is thought that the true incidence of this variant is underreported because most of these lesions resolve without treatment within the first 3-4 months of life.  

Although children with lesions isolated to the skin usually have a good prognosis, patients with LCH who have isolated skin involvement also have an excellent prognosis, however, close observation is still required. In 40% of patients with similar isolated cutaneous findings progression to multi system disease or reactivation was observed.  

Management  
Initial evaluation of patients with LCH requires determining whether there is single or multisystem involvement. Recommended testing includes a complete blood count with differential, complete metabolic panel including liver function tests, and coagulation studies. Imaging assessment should include a skeletal survey, ultrasound of the liver and spleen, and chest radiography. Treatment can then be tailored to the individual patient and extent of their disease.  

Treatment for LCH is dependent on the site affected and the number of lesions. For patients presenting with isolated skin involvement, surgical resection can lead to cure. If lesions are multiple then topical corticosteroids are first line therapy, with second line agents including topical nitrogen mustard, oral thalidomide, and oral methotrexate. Additional studies need to be completed to further assess the efficacy of second line treatment options.  

If skin involvement is diffuse or there are signs of multisystem disease, a systemic steroid with vinblastine for 6-12 months is first-line treatment. For patients with organ involvement (spleen, liver, bone marrow) 6-mercaptopurine may also be added to this treatment regimen. Prognosis for patients who fail these first-line treatment options is typically poor, and salvage therapy is indicated in these situations. This includes treatments such as hematopoietic stem cell transplant or a combination of cladribine and cytarabine.  

Recent research has been investigating the use of therapies targeting BRAF-V600E mutations. Patients with this mutation are more likely to have higher risk LCH or have increased resistance to treatment. Vemurafenib, a BRAF inhibitor, has been shown to be efficacious, however further studies are required to determine appropriate dosing and duration of therapy.  

Current recommendations for follow up for patients treated for isolated skin findings include evaluation of the lesion every 2 to 4 weeks. This includes monitoring for any signs of progression to multisystem involvement. Once the skin lesions have resolved, follow-up is recommended every 6 months for at least 5 years.  

Patient outcome  
The cheek lesion was excised by pediatric dermatology and our patient was evaluated by the pediatric hematology-oncology service. Initial skeletal survey to assess for bone involvement showed a calvarial lesion suspicious for LCH. Follow up whole body positron emission tomography scan was completed and showed no findings of bone or other multisystem involvement. As a result, systemic therapy was not indicated as the cheek lesion was previously excised. It was determined that the patient likely had the congenital self-healing reticulocytosis variant of LCH. The patient continues to follow with serial skeletal surveys and labs, and remains in complete remission.  

Acknowledgements: The authors thank Dr Kumaran Mudaliar, MD; Dr Wendy Kim, DO; and Dr Natalie Kamberos, DO for their valuable contributions to this case.

COMMENTS? E-mail them to llevine@mjhlifesciences.com

For references, go to
ContemporaryPediatrics.com/papulonodule-neonate

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A pediatrician’s role in dyslexia: Where theory meets practice

A pediatrician in Colorado attempts to tackle the way literacy is taught so that his daughter—and others—who have dyslexia can get the help they need.

TODD R PORTER, MD, MSPH

Recent articles and position statements have been calling for pediatricians to view literacy as a developmental domain and to participate in screening for future literacy concerns as early as preschool age.1-4 As a pediatrician, I agree wholeheartedly with one article’s statement that “The development of reading proficiency in childhood is a public health issue.”1 There is robust evidence linking lack of reading proficiency with school failure, negative impact on meaningful employment, increased risk of involvement in the criminal justice and welfare systems, as well as mental health consequences of reduced self-esteem, anxiety, and depression. As pediatricians we should be aware of and attempt to modify all of these negative outcomes by helping to identify risk factors for future reading disabilities and referring our struggling readers for further evaluation and remediation if available.

Yet, is it really that simple? To help answer this question I would like to point out existing barriers that make executing these recent recommendations difficult if not near impossible. My perspective is based on my experiences as a community pediatrician who currently cares for mostly low-income Medicaid patients, many of whom come from non-English speaking households, as well as my experience being the parent of a now 10-year-old daughter with dyslexia. As a disclaimer, this perspective is based on the educational landscape in the state of Colorado where I live and may not be representative of other educational and health care systems.

The International Dyslexia Association defines dyslexia as “a specific learning disability that is...characterized by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties typically result from a deficit in the phonological component of language that is often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction.”5 Because learning to read requires explicit instruction, identification of such a difficulty in word level reading typically cannot occur until after the child receives formal instruction starting in kindergarten. Yet, as noted in a recent article on dyslexia, “Even after formal instruction begins, it takes some time for individual differences in word reading ability to clearly emerge.”6

Perhaps this is the reason why the diagnosis of dyslexia typically does not happen until the struggling reader is in second grade or later when the word level reading gap is well established and negative consequences are already underway.6,7 This leads to what is called the dyslexia paradox which speaks to the greater effectiveness of word level reading interventions when administered in kindergarten and first grade compared to the later grades when the diagnosis is typically made.7 Early identification therefore is crucial, which is why the authors of these recent articles exhort that I, as a pediatrician, should be screening my pre-k and kindergarten patients, but how?

To date I am unaware of a gold standard for screening preschool and kindergarten aged patients quickly and effectively during an office visit. Recent studies acknowledge that available screenings for this age are not scientifically validated or reliable.1 For this age group a pediatr-
cian is better served to look for risk factors that may consist of family history of reading or spelling problems in the parents as well as history in the child of speech language delay and difficulties in pre-literacy skills of rhyming and learning letter names and sounds (as found in a propagated dyslexia screener by Hugh Catts at https://reachevery-reader.gse.harvard.edu). Presence of these risk factors should raise concern about future literacy struggles yet do not definitively say that the child has dyslexia. For children aged 6 years and older, screeners such as the Colorado Learning Disabilities Questionnaire (CLDQ)6,9 have been validated yet still come with the caveat that it would not be “appropriate for clinicians to use the CLDQ in isolation to make categorical diagnostic or treatment decisions regarding a specific individual.”9 Moreover, studies correctly point out the limitations that screeners may face with respect to sensitivity, specificity, and the inherent risk of over identifying early typical readers who just need more time.6

My personal experience with the dyslexia paradox comes as a father of a dyslexic child. Our 10-year-old daughter was first pulled out for reading intervention in the first grade. Despite my pediatric training, I was ill-equipped to understand and evaluate what screening and interventions the school was providing her, and I trusted that the school would teach her how to read. By the middle of second grade, after 18 months of intervention without improvement, my pediatrician spidey-sense told me it was time to get her privately tested. She seemed to be on the wait to fail trajectory which occurs when “children at risk for dyslexia have to experience considerable failure before receiving appropriate intervention.”7 Wait to fail also represents a criticism of a failed multi-tiered system of supports (MTSS)8 where a dyslexic child experiences considerable failure because the applied Tier 1, Tier 2, or Tier 3 intervention does not meet their word level reading needs.5

The results of my daughter’s private testing revealed what I knew in my gut all along, she has dyslexia. We brought the 13-page evaluation to our school with lists of accommodations and recommended intervention expecting that all would now be fine. It wasn’t. The intervention provided her was ineffective (as it had been prior) and her teachers could not seem to accept that she had dyslexia. Not even an Individualized Education Plan (IEP) could grant us recommended modifications for her.

It was not until I listened to the eye-opening documentaries of Emily Hanford from American Public Media15-16 that the light bulb went on as to why her school was reacting this way. Many years ago, education abandoned the teaching of phonics for whole language and balanced literacy, which teaches our children to guess at words rather than decode them. What all children need, especially struggling readers, is systematic and explicit phonics that is based on the science of reading. Yet to my dismay, many teacher preparation programs still do not teach the science of reading. In fact, in Colorado, the largest teacher prep program was cited again by the State Board of Education for not teaching the science of reading to teachers in training.15 Perhaps this is why in 2019, state testing showed that only 41% of Colorado third graders were reading at grade level.16 Another likely reason for this failing score is because many Colorado elementary schools are not using reading curriculum approved by the Colorado Department of Education (CDE).17,18

What my dyslexic daughter needed was Structured Literacy, which can be found in the explicit multi-sensory scope and sequence approach of programs such as the Orton-Gillingham (OG) method. This was not available in her classroom, so we paid privately for twice weekly OG tutoring and moved her to a public charter school who used an approved CDE reading curriculum and required all K-3 teachers to be trained in Structured Literacy. The result has been life changing for my daughter’s mental health and reading proficiency.

However, I wish I can say that my low-income pediatric patients who are struggling readers and who are experiencing the behavioral and mental health consequences of school failure have had the same experience. Similar to my daughter’s wait to fail experience, the school may proceed slowly with MTTS that is not evidence based, relying on literacy assessment tools such as iReady19 and Istation20 that do not always provide important data on word level reading and oral reading fluency. One might think that such a response to intervention as-

IN 2019, STATE TESTING SHOWED THAT ONLY 41% OF COLORADO THIRD GRADERS WERE READING AT GRADE LEVEL.
assessments are the domain of the school. However, a recent medical journal article mentioned that pediatricians should become adept at interpreting and responding to these educational assessments and interventions. I believe this is out of the scope of a pediatrician’s practice and to circumvent this, I have relied on professional courtesy of qualified educational neuropsychologists and speech-language pathologists to interpret these for me.

For my patients who do have IEPs for their specific learning disability, their parents are typically not aware of the type of intervention the child receives or whether the school’s reading curriculum is supported by the science of reading. Even in the rare case I have been able to secure grant funding for a private evaluation that confirms dyslexia, the child’s school usually does not have qualified staff trained in Structured Literacy to remediate it. As the child’s pediatrician, there are few if any outside referral options for Structured Literacy reading intervention as not all speech language pathologists have received additional training in Structured Literacy nor do insurance payers typically reimburse reading intervention.

It is heartbreaking for me to see my patients year after year for their well-child exam and not know how to help them overcome all of these system barriers that prevent them from obtaining grade-level reading proficiency. Although privately funded programs like the Promise Project would be wonderful to have locally to provide free to low-cost identification and remediation for all children with significant reading deficiencies, parents and pediatricians must continue to advocate at the local and state level for continued educational reforms in teacher preparation programs and science-based reading curricula.

Clinically, pediatricians can attempt to screen their native English-speaking patients aged 6 years and older with literacy concerns with the validated online CLDQ-R screener during office visits. Additionally, they can equip parents with tools on how to assess what literacy block curricula the school is using so that they can more effectively advocate for their child’s needs as well as hold the school more accountable for compliance with evidence-based literacy instruction and intervention. One helpful tool is the “Literacy Dialogue Tool for Parents/Caregivers” produced by the Colorado statewide dyslexia parent advocacy group Colorado Kids Identified with Dyslexia in partnership with an educational consulting firm. Links to this tool as well as description of how it can be utilized by parents can be found in the referenced Chalkbeat article by Ann Schimke. As best as they are able, pediatricians should also attempt to educate themselves and parents of struggling readers on special education law with respect to the Individuals with Disabilities Education Act and section 1400(D)(1)(A) that defines access to a “free and appropriate education that emphasizes special education and related services designed to meet their unique needs and prepare them for further education, employment, and independent living.”

One reputable special education advocacy website is wrightslaw.com.

It cannot be overemphasized how effective grass roots advocacy and public attention can have on how school districts teach K-3 literacy. Just recently, thanks to successive articles on the discredited curriculum used by Colorado’s second largest school district (the district that had failed my daughter), district management recently announced that they will present a new literacy instruction plan to CDE that aligns with the board’s approved programs. Successes like this that push schools and school districts toward teaching the science of reading are within reach of parent and pediatric advocacy groups.

Finally, pediatricians also need to advocate for state legislation that requires insurance payers to cover evaluations as well as remediation for children with dyslexia given the preponderance of medical evidence of its neurobiological origin. Insurance coverage that provides access to early identification and remediation of dyslexia could mitigate the commonly associated physical and mental health consequences of stress, anxiety, depression, and suicide that later on results in great personal and economic costs.

My pediatrician spidey-sense told me it was time to get her privately tested.

COMMENTS? E-mail them to llevine@mh lifesciences.com

For references, go to ContemporaryPediatrics.com/pediatricians-role-in-dyslexia

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In the best of times, the treatment of attention-deficit/hyperactivity disorder (ADHD) is not always as easy as just following an algorithm, but the COVID-19 pandemic and the multitude of changes it has caused has added a wrinkle to this treatment. To offer some help, Contemporary Pediatrics® and its sister publication Psychiatric Times® offered a Viewpoint that examined the multidisciplinary approach needed to manage the condition, as well as to tackle the effects of COVID-19. It was led by Tim Wilens, MD, chief of Division of Child and Adolescent Psychiatry at Massachusetts General Hospital in Boston. He was joined by Ann Childress, MD, a practicing child and adolescent psychiatrist; Robert Findling, MD, a practicing child and adolescent psychiatrist; Harlan Gephart, MD, a pediatrician from Bellevue, Washington; and Dr Mark Wolraich, MD, a practicing developmental and behavioral pediatrician.

The Viewpoint opened with a discussion of the recent guidelines from the American Academy of Pediatrics, before moving on to discuss the screening process and comorbidities of the condition. Panel members discussed how pediatricians and child psychiatrists work together to diagnose ADHD and when psychiatry might be called in to work with the patient. A sizeable portion of the Viewpoint examined ADHD in the COVID-19 pandemic, launching with a discussion on using telemedicine to help families and children manage. The members also discussed unmet needs of children who have ADHD and the need it improve communication. Finally, they considered the future of treatment for ADHD, including nonstimulant medications.
The use of social media has proliferated the rate of information sharing with both significant benefits and concerns. What has emerged in the last decade have been Internet challenges that pose a significant risk to pediatric patients. Some of these include the cinnamon challenge in 2012, the Tide Pod challenge in 2016, and nutmeg challenge in 2020. Each resulted in serious morbidity amongst children. These challenges are spread rapidly through social media channels such as YouTube, Facebook, and TikTok.

TikTok is a social media platform where individuals view short videos that are curated to their interests based on TikTok’s algorithms. It began in 2017 in mainland China but proliferated rapidly to reach over 1 billion users worldwide. Some countries have engaged users on this platform for public health messaging. Vietnam created videos on TikTok during the initial phases of the COVID-19 pandemic focusing on mask wearing and avoiding touching one’s face. However, there has been a great deal of misinformation on TikTok during the pandemic as well. What is most important for pediatricians to know is that 32.5% of TikTok users are teenagers. These impressionable minds are likely to view and respond to various challenges.

In August of 2020, Johnson & Johnson, the makers of Benadryl, issued a warning about the “Benadryl challenge” following the death of a 15-year-old female who ingested a large amount of diphenhydramine. This challenge, made popular on TikTok, encourages the user to ingest large amounts of diphenhydramine to get high and record their responses. This resulted in numerous cases of diphenhydramine poisoning, with case first reported May of 2020. The US Food and Drug Administration issued a warning following the increase of these cases in September of 2020.

Diphenhydramine is a first-generation antihistamine, which was approved in 1946. It works as an antagonist at histamine and muscarinic receptors. The antimuscarinic effects largely constitute the agent’s abuse potential. Abuse with antimuscarinic agents dates back hundreds of years where natural antimuscarinics (atropine, scopolamine, etc.) were brewed in teas and ingested. Similarly, diphenhydramine abuse and toxicity are not novel. In 2018 over 21,500 exposures to diphenhydramine occurred in the United States in pediatric patients with only 23 deaths reported. The intent, however, has changed: Self-harm of all antihistamines in patients aged between 10-25 years have been significantly increasing in the United
The clinical effects of the agent are due to its antagonism of muscarinic receptors. The antimuscarinic toxidrome (sometimes referred to as the anticholinergic toxidrome) consists of tachycardia, dry mucous membranes, mydriasis, urinary retention, flushed skin, and delirium. Not all patients will present with the full toxidrome and a large proportion will present with delirium and mydriasis, but without tachycardia. The antihistaminic effects can cause sedation along with an increased risk of seizures. Additionally, diphenhydramine blocks sodium and potassium channels in the myocardium. This causes a widening of the QRS segment and prolongation of the QTc interval on an electrocardiogram, which can predispose patients to developing significant dysrhythmias. In a review of 13 years of poison center data on pediatric exposures, common effects were tachycardia, hallucinations, somnolence, agitation, and mydriasis. Seizures were uncommon, but still occurred in 5.5% of cases.

Treatment of diphenhydramine toxicity is largely supportive. Primary therapy involves the use of benzodiazepines to treat agitation or seizures. If patients have QRS segment prolongation, usual practice is to administer sodium bicarbonate as a bolus and possibly an infusion. Sodium bicarbonate works by presenting a bolus of Na+ to the myocardium to outcompete the blockade by diphenhydramine. Additionally, the HCО₃⁻ alkalinizes the serum which theoretically decreases diphenhydramine binding to the sodium channel as it becomes more un-ionized. The most specific therapy is physostigmine, which is a reversible inhibitor of acetylcholinesterase. This prevents the breakdown of acetylcholine, increasing the amount of acetylcholine in the synaptic cleft to compete with muscarinic receptor blockade. Physostigmine relieves delirium and agitation in approximately 75% of patients but does not affect length of stay. Use of physostigmine varies heavily based on provider comfort which has varied use depending on region. Important monitoring and evaluation include cardiac, respiratory, and a bladder scan to assess for urinary retention. A quiet room can help to reduce external stimuli and decrease agitation. Duration of treatment is dependent on the evolution of patient symptoms. Most patients resolve within 24 hours.

Conclusion
Pediatricians should screen for and discuss the risks from these challenges with their patients. The TikTok Benadryl challenge has resulted in at least one death and significant morbidity. Management includes early recognition of the signs and symptoms of antimuscarinic toxicity (altered mentation, tachycardia, dry mucous membranes, etc.) and providing supportive management with benzodiazepines, sodium bicarbonate, and physostigmine when necessary. Assistance is available by calling your local poison center 800-222-1222.

COMMENTS? E-mail them to llevine@mjh lifesciences.com

For references, go to ContemporaryPediatrics.com/benadryl-challenge

ANSWER 1 A. COVID-19
Cough, sore throat, and fatigue are symptoms that can be caused by either COVID-19 or flu, however, patients infected with COVID-19 are more likely to present with change in or loss of taste or smell.

ANSWER 2 A. True
Both COVID-19 and flu are transmitted from person-to-person mainly by respiratory droplets made when infected persons cough, sneeze, or talk. Compared to flu, however, transmission of COVID-19 has been more frequently associated with superspreading events and is more contagious among certain populations and age groups.

ANSWER 3 C. Blood clots
Both COVID-19 and flu can result in pneumonia, respiratory failure, sepsis, and cardiac injury, among others. Blood clots in the veins and arteries of the lungs, heart, legs, or brain as well as multisystem inflammatory syndrome in children are additional complications associated with COVID-19.

ANSWER 4 F. All of the above.
Length of illness (A) is important because after 5 days of symptoms, low antigen levels might lead to a false negative. Even if the antigen test is negative, the patient could have symptoms (B) consistent with SARS-CoV-2 infection and so would need follow-up testing. Type of employment (C) is an essential consideration as frontline workers or those who have regular contact with them might warrant confirmatory testing.

ANSWER 5 C. High specificity and sensitivity (both >95%)
Both rapid molecular assays (eg, PCR) and RIDT are CLIA-waived (A), have specificity of >95% (B), and can produce results in between 15-30 mins (D) (rapid molecular assays, 15-30 mins; RIDT, 10-15 mins). However, while RIDT have specificity of between 98% to 100% (depending on virus type) their sensitivity is very low (0%-33%) compared to rapid molecular assays.
It’s winter: are children getting enough Vitamin D?

How changing seasons affect children’s nutrition

LAIRD HARRISON

Most pediatricians have no trouble recommending healthy diets for their patients. However, as the days grow shorter and colder, children’s nutritional needs can change in ways that not everyone takes into account.

Exposed to less sunlight, children may not make enough vitamin D. Natural production of melatonin shifts. As everyone spends more time indoors, influenza and upper respiratory infections become more common. Fresh fruits and vegetables may be harder to find. And in 2020, the rising incidence of COVID-19 has added a new risk to consider.

Human beings evolved outdoors eating fresh foods, and vitamin D deficiency may have resulted from our switch to living indoors and eating processed food. Considerations about supplementation with this nutrient start before conception and continue throughout a lifetime.

It’s not clear yet whether supplementing the diets of breastfeeding mothers can provide adequate vitamin D to their infants. Due to the risk of skin cancer, the American Academy of Pediatrics (AAP) recommends against sun exposure for infants. That leaves vitamin D supplements given directly to the breastfeeding infant as the best option.

Children aged 1 year and older may get enough vitamin D in their diets. Natural sources of vitamin D in food include salmon (wild is better than farmed), canned sardines, canned tuna, canned mackerel, and shiitake mushrooms. Most milk and some other foods are fortified with this nutrient. If, however, children aren’t getting enough vitamin D through food, they may need supplements, especially in winter, says Dr. Cora Collette Breuner, professor of adolescent medicine at the University of Washington in Seattle, and a member of the American Academy of Pediatrics (AAP) Council on Integrative Health.

“In areas where there is not a lot of sunshine and children have a lactose intolerance or they’re super picky eaters, and they won’t consume milk or calcium-containing vegetables, or they don’t eat fish, what do you do in those families? I believe it’s appropriate to supplement vitamin D and calcium.”

There is little risk of over-supplementing with vitamin D, and the AAP recommends that children take a supplement of 400 IU/day of vitamin D within the first few days of life and continue throughout childhood.1 For formula-fed infants and older children who are consuming less than 32 ounces per day of vitamin D-fortified formula or milk, it also recommends a vitamin D supplement of 400 IU a day. For adolescents who do not get 600 IU of vitamin D per day through foods, it recommends a supplement containing that amount.1

The best documented consequence of vitamin D deficiency in children is rickets. Many studies have also linked the deficiency to an increased risk of respiratory tract infections including influenza, and even COVID-19. Although preliminary trials have suggested that vitamin D supplements can reduce the risk of some of these infections, the evidence is not yet strong enough to result in recommendations.2 The evidence for other supplements in preventing or treating respiratory tract infections has also not risen to the level where strong recommendations can be made, though the data for zinc is strong, Breuner says.

With less sunlight, patterns of natural melatonin production shift as well, Breuner says. This may be a consideration when children are taking melatonin for sleep disorders. Some research has explored the use of melatonin as a treatment for sea-
sonal affective disorder as well. However, the AAP currently recommends melatonin only as a short-term therapy for sleep disturbances while the underlying causes of the problem—such as poor sleep hygiene—are addressed.2

Pediatricians should investigate their patients’ lifestyle and supplements before making recommendations, Breuner says. “People self-medicate their children all the time,” she says. “They don’t know what to do to prevent their kids getting COVID, not getting enough sleep, not eating organic foods. Parents just throw up their hands and say, ‘We’ll give them a multivitamin and we’re good.’” In her experience, parents of children with complex medical needs are even more likely to use alternative or complementary medicine, typically without telling their pediatrician.

Parents may feel especially inclined to hand their kids a bottle of vitamins in the winter in northern latitudes, when the selection of fresh fruits becomes less appealing. The 2017-2018 National Health and Nutrition Examination Survey, showed that 23.8% of children and teenagers were taking multivitamins.3

The problem with this one-size-fits-all approach is that it doesn’t take into consideration what else a child may be consuming. Often children taking multivitamins still end up deficient in some nutrients while exceeding recommended levels of others. That’s why Breuner and the academy take a “less is more” approach when it comes to most supplements. Breuner also cautions against extrapolating from the research on adults. “The premise of pediatrics is they’re not little adults, so you can’t do that,” she says.

COMMENTS? E-mail them to llevine@mjlifesciences.com

For references, go to ContemporaryPediatrics.com/winter-are-children-getting-vitamin-D

Laird Harrison writes about science, health and culture. He is at work on a novel about alternate realities in physics. Visit him at www.lairdharrison.com or follow him on Twitter: @LairdH.

WIC and Without

WIC is a terrific program that provides free infant formula to families who struggle with food-insecurity. Although it is intended to serve as a supplemental program, it may unintentionally leave some families in need of additional help.

WIC covers 80% of an infant’s nutritional needs.1

That leaves a 20% gap for struggling families.

Families on WIC receive name brand formulas and may feel compelled to use those same (expensive) brands during that WIC gap. Regrettably, 27% of food-insecure families report stretching, diluting or limiting formula to make it last.2

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3Calculations based on September 2020 IRi Market Advantage annual retail sales data of national brand infant formula compared to store brand infant formula based on an average cost per week and average weekly usage of 1.5 pounds of powder.

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Pandemic pediatric tips for mental health

Lucia had begun to take school seriously in 8th grade but now, in 9th grade, she has become disheartened and says the teachers do not explain things well virtually. She does not like to show her face on camera and has begun to stay in her room, refusing to even eat dinner with the family. She keeps asking them to leave her alone. Her parents are worried. She just wants to play video games and play music in her room, and she has stopped seeing her best friend. The freshman guidance counselor called the parents to say she has missed more than half of the school days in the last week. The parents had no idea because they both work through the day online and assumed Lucia was participating in school virtually. They don’t know what to do.

The impact of the COVID-19 pandemic has hit home, school, work, and social life unlike any other acute change in our lifetime. Resulting isolation, loss of routine, limited social contact, grief, hardship, and stress have increased difficulties and further challenged youth. The deficiencies in our health care provision of mental health care for children have been further highlighted in the press and academic journals. What can those of us on the front lines caring for children do?

Devising an approach for health care workers to address mental health concerns in brief office visits may feel overwhelming. The sections below offer practical pandemic relief to help manage mental health concerns brought by families. During office visits, you can discuss the pillars of well-being by including these 10 priorities.

**Validation:** Since the pandemic hit, there have been a range of reasons for misery for everyone. Remind families that it is understandable that stress levels are high, and worrying is rampant. Parents and children face new stressors to navigate. Acknowledging this reality has potential benefit. Family environment, parenting practices, coping, and support influence psychological consequences on children. Parental mental health significantly impacts children, so remind parents that their own self care is important for their own and their children’s well-being. Help parents acknowledge how much their children are missing from their usual lives. School no longer includes the favorites of lunchtime chatting and playful recess interaction. Children are not likely having much opportunity online to solidify new friendships or flirt with a new crush. Their favorite activities are likely limited or on pause. Encourage parents to set aside time to devote their full focus on their children. Emotional support from parents can be protective.

Speak privately to your patients...
Teach families the myriad ways the pandemic is increasing stress for many by reviewing how stress occurs in the following conditions:3

- When a circumstance is NEW.
- When an event is UNPREDICTABLE as to when or how it may occur.
- When competence is being THREATENED (challenged/threatened).
- When lack of control forces SURRENDER of your autonomy.4

Despite current times meeting all of the above criteria, there is reason for optimism. A study among 381 undergraduate students (age range: 17–24, mean: 20.16, SD = 1.46 years) suggested that active coping strategies predicted life satisfaction during the 2003 Beijing SARS epidemic, whereas the number of stressors and use of avoidant coping strategies predicted psychological symptoms.5

Present this pandemic crisis as an opportunity to learn and support well-being.

**Routine:** Because unpredictability contributes to stress, a schedule does much to regulate our daily lives and contribute to a sense of stability. Recommend families maintain consistent routines for wake up, bathing, meals, exercise, designated screen time, unwind time, and sleep. Suggest schedules be discussed collaboratively with children emphasizing what is healthy and within reason. Instead of hours, speak in minutes about their available time after school of 180-360 minutes depending on grade and homework prior to bedtime. The reason? To children, 120 minutes of screen time sounds like a lot compared to 20 minutes for sitting with family for meals.

**Sleep:** Emphasize what you already know about the importance of sleep’s effect on physical health, appetite, mood, and coping ability. This may be the simplest but most powerful intervention you can suggest, as so many parents do not realize how significantly inadequate sleep affects a child’s functioning. Advise families on good sleep hygiene.7

**Screen Time:** Watching or scrolling through the media makes us even more anxious. An excess of news and visual images about a traumatic event can create symptoms of post-traumatic stress disorder and negative health effects that remain years later, according to research by University of California at Irvine’s Roxy Silver, PhD, and others.8 Turn off the background news. Monitor Internet safety. Encourage families to view the Netflix documentary, “The Social Dilemma,” because it provides a convincing argument to limit internet use.

**Movement:** Sedentary scores have shot up during the pandemic. Our brains are programmed to move...
and when we don’t it’s not good for our mind or body. Children in school are recommended to get 60 minutes of exercise daily. Encourage parents to keep their children active. Websites online offer creative indoor options such as “indoor and at home exercises for kids” at childrens.com.

6 Pursue mastery/achievement: Suggest families identify a new skill/hobby or activity to learn or do together. Learn sign language, paint a room, create questions to share with family at meals, create homemade gift surprises, play board games, learn to cook, teach the pets new tricks, make posters of passionate beliefs for windows, listen to audiobooks together, or start sharing a daily high and low.

7 Acts of kindness: Research supports the link between altruistic behavior and increased health and well-being. Do something that makes someone’s day better. A surprise sticky note, help with cleaning up dinner, call a relative who is alone during the pandemic, bake cookies for neighbors, write a letter to a favorite teacher, volunteer online.

8 Mindfulness Anyone interested can learn this skill with simple, brief, regular practice. Help your patients understand that their goal is not to empty their minds of thought but to become aware of their sensations, emotions, and thoughts so they can use that self-awareness for their own benefit. There is evidence supporting benefits on mood, cognition, and symptoms including pain and associated with depression and anxiety. There are many options for learning, and countless easy and practical ways to incorporate mindfulness into a daily routine.

9 Socialize: Social isolation and loneliness can contribute to worsening of mental health. It’s a human need. Urge families to prioritize social meet ups while keeping safety in mind. Meeting outdoors wearing masks and socially distancing can still allow kids to see each other at a park, for a walk, in the yard, on a deck or porch. Even a prearranged consistent Zoom connection for your child and a friend has value. A limited group of contacts by designating a pod within which to socialize could be considered. Reiterate Centers for Disease Control and Prevention guidelines, handwashing, and testing options to maintain safe activities.

10 Find joy: Encourage parents to initiate the daily practice of noticing 3 positive moments of the day and share them with family. Create opportunities to enjoy time together. Noticing and appreciating daily pleasures can help improve mood.

CONCLUSION
In every mental health diagnosis that by definition is causing impairment and/or significant suffering, whether mild, moderate, or severe, evidence supports inclusion of psychotherapy in the treatment plan. Especially in pediatrics, this may include parental guidance and intervention. When conditions are severe, a combination of psychotherapy and medications provides the best outcome across conditions. For anxiety and depression-related conditions that cause moderate impairment, consider adding Selective Serotonin Reuptake Inhibitors medication if needed to help them engage in therapy, if they have persistent issues despite evidence-based therapy, or they are unable or refuse currently to access therapy.

Finally: As caregivers, our role is to both support well-being and address common reactions during these historic threats. Additionally, we must remain vigilant and prepared to initiate treatment when challenges have progressed into significant impairment and suffering.

COMMENTS? E-mail them to llevine@mjhlife.com

For resources, references, and more information, go to ContemporaryPediatrics.com/pandemic-tips-mental-health

Dr Man is a pediatrician at Mind Body Seven, a mental health and wellness practice in Brooklyn, New York.
It is now 2021, and our understanding of the novel coronavirus first reported in Wuhan, China in December 2019 has drastically expanded due largely to the extensive number of individuals who have been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) worldwide, as well as those who have exhibited symptoms of disease from this virus (COVID-19). Currently, the increase in incidence throughout the country is significantly impacting our health care system capacity. Whereas children in general have been reported to experience less disease from infection with SARS-CoV-2, the nationwide surge in cases has led to an increase in pediatric hospitalizations, as well as cases of multisystem inflammatory syndrome in children (MIS-C). Despite a growing number of cases throughout the United States, we have greatly improved our understanding of infection control measures to curb transmission, have better access to personal protective equipment (PPE), and have improved testing availability to aid in mitigating transmission. We must now reduce community, household, and workplace transmission to relieve the strain that an ill and reduced workforce is having on the health care system.

What we know right now: SARS-CoV-2 infection in children
Due to variation in public health reporting, accurate numbers of SARS-CoV-2 infected pediatric patients are a challenge to obtain. However, available data show a consistent increase in pediatric patients that tested positive for SARS-CoV-2 over the past year, and particularly the past several months. As of November 19, 2020, the American Academy of Pediatrics/Children’s Hospital Association (AAP/CHA) Children and COVID-19: State Data Report1 reported 1,183,609 cumulative child cases, representing 11.8% of total cases reported and 1572.6 cases per 100,000 children. Fifty-seven percent of these cases were reported since September 2020.

Despite climbing numbers of pediatric SARS-CoV-2 infections, children continue to be proportionally less affected by infection than adults. Although children represent about 22% of the United States population, they represent only 1.8% of total hospitalizations related to SARS-CoV-2.1 The scope of asymptomatic infections in children is challenging to fully represent due to the retrospective nature of current reports, but estimates range between 5% and 35%.2,3 Children presenting to care with symptoms and subsequently diagnosed with SARS-CoV-2 infection most commonly have fever or cough.2-4 There is variation in representation of other complaints, including pharyngitis, rhinorrhea, congestion, headache, or gastrointestinal (GI) complaints. Children with some underlying medical conditions (obesity, asthma or chronic lung disease, and immunosuppression) are at greater risk for severe illness from SARS-CoV-2 infection.5,7 This does not, however, discount...
infectious disease

the potential for healthy children to develop severe disease or require hospitalization. Although rates of severe illness due to SARS-CoV-2 are generally lower in children than adults, a hyperinflammatory syndrome associated with SARS-CoV-2 infection has been identified as MIS-C. As of December 9, 2020, 23 of these cases in the United States resulted in death. More than 75% of reported cases of MIS-C occurred in children of Hispanic/Latino or Black, non-Hispanic reported race/ethnicity and the average age was 8 years. The most common symptoms reported for children with MIS-C include GI complaints (abdominal pain, vomiting, diarrhea), rash, and conjunctival injection. Whereas some MIS-C patients may present with symptoms overlapping with Kawasaki disease or toxic shock syndrome, multiple case series of patients with MIS-C demonstrate clear differences between these patients, including age distribution, prominence of GI symptoms, the degree of multisystem organ involvement, and cardiogenic shock with myocardial dysfunction. Multiple studies are ongoing to better understand the pathophysiology of this inflammatory syndrome.

Infection prevention in community and health care settings

Understanding of SARS-CoV-2 transmission has increased exponentially throughout the pandemic. Basic concepts of infection prevention such as wearing face coverings/masks, hand hygiene, not working when ill, and social distancing have proved to be of the utmost importance for the health care setting and for the public, including our patients and their families. Although children who cannot remove their mask in case of an emergency or those with sensory sensitivities should not use face coverings, children aged as young as 2 years can learn to don them when out in public or at school. The epidemiologic curve in relation to social distancing and masking guidance over the past 10 months supports the use of these infection prevention methods. Additionally, household contact with an individual with SARS-CoV-2 is a risk factor for transmission, likely due to individuals exposing one another than older children. Age-based schooling recommendations may therefore be an appropriate consideration, with greater emphasis on the ability of younger school-aged children to continue in-person learning even if this cannot be maintained in older age groups.

In the health care setting, use of negative pressure rooms, PPE, social distancing, environmental cleaning with focus on high touch surfaces, and hand hygiene decrease the likelihood of transmission of SARS-CoV-2 between patient and provider. Nosocomial transmission is likely more associated with lack of PPE particularly during prolonged exposure and/or performing aerosol-generating procedures (AGP) without the recommended PPE. Transmission dynamics of SARS-CoV-2 to date support transmission via direct or indirect contact with secretions, respiratory droplets, or fomites unless a procedure is being performed that may generate aerosol. Use of a face mask and eye protection has been shown to reduce risk of transmission. Face masks prevent large droplets from being breathed in, but also to prevent any viral secretions from going out. However, if an AGP is being performed, a respirator (eg, N95 respirator) should be employed to keep generated aerosols from being inhaled. The Infectious Diseases Society of America has published a table of AGPs to aid in decision making around PPE use. It is yet unclear whether SARS-CoV-2 can be spread through aerosol other than those generated by medical procedures, though the transmission dynamics of this virus does not match those of known airborne infections such as measles or varicella. Implementation of these infection prevention and control principles has the potential to reduce transmission.

Fatigue from using PPE and laxity with social distancing have more recently become real concerns.

In the hospital setting, use of PPE and/ or performing aerosol-generating procedures (AGP) is often required to keep transmitted pathogens from being inhaled. PPE is intended to protect the provider. Nosocomial transmission is more common in settings with lack of PPE particularly during prolonged exposure and/or performing aerosol-generating procedures (AGP) without the recommended PPE.

During the pre-symptomatic period and lack of use of face coverings within the household, multiple studies have shown that transmission via direct or indirect contact with secretions, respiratory droplets, or fomites unless a procedure is being performed that may generate aerosol. Use of a face mask and eye protection has been shown to reduce risk of transmission. Face masks prevent large droplets from being breathed in, but also to prevent any viral secretions from going out. However, if an AGP is being performed, a respirator (eg, N95 respirator) should be employed to keep generated aerosols from being inhaled. The Infectious Diseases Society of America has published a table of AGPs to aid in decision making around PPE use. It is yet unclear whether SARS-CoV-2 can be spread through aerosol other than those generated by medical procedures, though the transmission dynamics of this virus does not match those of known airborne infections such as measles or varicella. Implementation of these infection prevention and control principles has the potential to reduce transmission.
control strategies can mitigate transmission of SARS-CoV-2 between health care personnel and patients if they are followed.20 Fatigue from using PPE and laxity with social distancing have more recently become real concerns and problems. Universal mask use and social distancing guidelines have been adopted within many health care settings, yet transmission among health care workers has become a new challenge when mask use is inconsistent. A recent Cochrane Review reported that a key facilitator to adherence to infection prevention guidelines among medical personnel was understanding the rationale behind the guide-

### TABLE: CONSIDERATIONS FOR TREATMENT OF ACUTE SARS-COV-2 INFECTION (COVID-19)

<table>
<thead>
<tr>
<th></th>
<th>HYDROXYCHLOROQUINE23</th>
<th>REMDESIVIR21</th>
<th>BAMLANIVIMAB21</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FDA Approval</strong></td>
<td>EUA issued March 2020</td>
<td>FDA approved for patients:</td>
<td>EUA issued November 2020</td>
</tr>
<tr>
<td></td>
<td>EUA revoked June 15, 2020</td>
<td>≥12 years AND ≥40 kg</td>
<td>≥12 years AND ≥40 kg</td>
</tr>
<tr>
<td></td>
<td>NOT RECOMMENDED FOR USE</td>
<td>Under EUA for patients:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.5 kg to &lt;40 kg OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;12 years and ≥3.5 kg</td>
<td></td>
</tr>
<tr>
<td><strong>Mechanism of action</strong></td>
<td>Increases endosomal pH, inhibiting fusion of SARS-CoV-2 to the host cell membrane</td>
<td>Binds viral RNA-dependent RNA polymerase to inhibit viral replication</td>
<td>Neutralizing monoclonal antibody; targets receptor-binding domain of SARS-CoV-2 spike protein; block entry into host cells</td>
</tr>
<tr>
<td><strong>Indication(s) for use</strong></td>
<td>N/A</td>
<td>Hospitalized patients requiring supplemental oxygen</td>
<td>Non-hospitalized patients with mild to moderate COVID-19 who are at high risk* for progressing to severe disease and/or hospitalization</td>
</tr>
<tr>
<td></td>
<td>Hospitalized adults and adolescents weighing ≥50 kg</td>
<td>Administer with or without dexamethasone adjunct therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 1: 800 mg PO once</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 2 through completion: 400 mg PO once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Length of therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4–7 days of total treatment, based on clinical evaluation</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dosing and administration</strong></td>
<td>Patients ≥12 years old and ≥40kg (FDA approved)</td>
<td>Length of therapy (either group):</td>
<td>700 mg IV once within 10 days of symptom onset</td>
</tr>
<tr>
<td></td>
<td>Day 1: 200 mg IV</td>
<td>5 days for patients not requiring mechanical ventilation or ECMO (may be extended to up to 10 days if not improved)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 2 through completion: 100 mg IV</td>
<td>10 days for patients requiring mechanical ventilation or ECMO</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patients ≤3.5kg to &lt;40 kg or &lt;12 years old (EUA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 1: 5 mg/kg IV once</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Days 2 through completion: 2.5 mg/kg once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adverse effects</strong></td>
<td>Prolonged QTc, hepatitis, hypoglycemia, hemolysis, GI symptoms (eg, nausea)</td>
<td>GI symptoms (eg, nausea), elevated transaminases, increased prothrombin time, hypersensitivity reactions</td>
<td>Hypersensitivity reactions, GI symptoms (eg, nausea), dizziness</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Not recommended if eGFR is &lt;30 mL/min</td>
<td></td>
<td>None</td>
</tr>
<tr>
<td><strong>Recommended monitoring</strong></td>
<td>CBC, transaminase levels, renal function, blood glucose, baseline ECG</td>
<td>Renal function, transaminase levels</td>
<td>Clinically monitor patients during infusion and observe patients for at least 1 hour after infusion is complete</td>
</tr>
</tbody>
</table>

*High risk patients (defined by EUA) for bamlanivimab:  
- Age ≥12 years with one of the following: BMI ≥35, chronic kidney disease, diabetes mellitus, immunosuppressive disease, currently receiving immunosuppressive treatment  
- Age 12 to 17 years with one of the following: BMI ≥85th percentile for age and gender based on CDC growth charts, sickle cell disease, congenital or acquired heart disease, neurodevelopmental disorders, medical-related technological dependence, (eg, tracheostomy, gastrostomy, or positive pressure ventilation not related to COVID-19), asthma or a reactive airway or other chronic respiratory disease requiring daily medication for control  
- Age ≥55 years with one of the following: cardiovascular disease, hypertension, chronic obstructive pulmonary disease/other chronic respiratory disease  
- Age ≥65 years
showed a mild influenza season, 22 it the Southern Hemisphere have within the winter respiratory virus SARS-CoV-2 pandemic, we are now burnout in health care. In the coming months as we face PPE fatigue and tant approach to take in the coming is therefore likely the most impor-

cacy. In parallel, an EUA was grant-
due to insufficient data to show effi-
COVID-19 and revoked in June 2020
droxychloroquine for treatment of

gained Use Authorization (EUA) was

strides in understanding COVID-19,
mitigating spread, treating the virus
and its sequelae, and connecting sci-
ents to advance our knowledge of
this virus and how to combat it.

Where are we now?
There have been many successes and
many “educational moments” in our
journey through the SARS-CoV-2
pandemic. The speed with which our
large health care and public health
systems, as well as our governments
and communities, have had to mobi-
lize and adapt to continually new in-
formation is tremendous. Early in the
pandemic, focus was primarily on
creating protocols and gaining better
understanding of the virus and its dy-
amics. We have confirmed that pub-
lic health and infection control mea-
ures can positively impact infection
rates. Our concern in the health care
setting has shifted from acquisition
of SARS-CoV-2 from our patients to
its acquisition from coworkers, com-
munity, or household members.

In the coming months, we will be
challenged with continuing to care for
the growing number of patients
with SARS-CoV-2 and increasing
rates of hospitalization, as well as
managing distribution of new vac-
cines. We will still encounter school
 closures, be challenged with our
patients’ and colleagues’ mental
health, and continue to seek preven-
tative care. However, looking back
over the past 11 months, it is evi-
dent that we have made tremendous
strides in understanding COVID-19,
mitigating spread, treating the virus
and its sequelae, and connecting sci-
ents to advance our knowledge of
this virus and how to combat it.
Examining the efficacy of flu shot in preventing severe flu

The influenza vaccine has been recommended as a key way to reduce severe influenza in children. An investigation examines how effective the 2018-2019 vaccine was in preventing hospitalization and emergency department visits. MIRANDA HESTER, EDITOR

The influenza vaccine is recommended every year as a way to reduce hospitalizations and emergency department visits linked to influenza. A report in Pediatrics offers a look at how well the 2018-2019 influenza vaccine worked in reducing both. During the season, the influenza A(H1N1)pdm09 peaked in the initial part of the season and the antigenically drifted influenza A(H3N2) had a peak later in the season.

The investigators used molecular assays to test children aged 6 months to 17 years who had acute respiratory illness for influenza at 7 pediatric hospitals. Parental report, provider records, and state immunization information systems were used to determine the vaccination status for inpatient children. Parental report was used for the vaccination status of children in the emergency department.

There were 1792 inpatient children with 226 patients testing positive for influenza: 47% for influenza A(H3N2), 36% for A(H1N1)pdm09, 9% for A (not subtyped), and 7% for B viruses. In the 1944 children in the emergency department, 420 children tested positive for influenza: 48% for influenza A(H3N2), 35% for A(H1N1)pdm09, 9% for A (not subtyped), and 7% for B viruses. The researchers found that vaccine effectiveness against any influenza-related hospitalization was 41% (95% CI, 20% to 56%). When looking at the 2 influenza types, the effectiveness was for 41% (95% CI, 11% to 61%) for A(H3N2), and 47% (95% CI, 16% to 67%) for A(H1N1)pdm09. Overall vaccine effectiveness against influenza-related emergency department visit was 51% (95% CI, 38% to 62%) and when broken across the 2 influenza types, 39% (95% CI, 15% to 56%) against A(H3N2), and 61% (95% CI, 44% to 73%) against A(H1N1)pdm09.

The investigators concluded that their research provides timely, necessary evidence of the benefit of vaccinating children for influenza to reduce the hospitalizations and emergency department visits. They noted that the data offers key information on vaccine efficacy in preventing severe influenza. They also noted that the vaccine was highly effective in reducing hospitalizations and visits by 40% to 60%, even in a season when the virus had experienced antigenic shift.

COMMENTS? E-mail them to mhester@mjhlifesciences.com

Nebulized magnesium in the ED
A new report looks at whether nebulized magnesium could impact hospitalizations due to asthma

Ear exams and hearing loss
A talk with Dr Andrew Schuman on ear exams, hearing loss, and when to refer to audiology.

Cancers trending up among young adults
A new report looks at certain cancer trends in teenagers and young adults.

For reference, go to bit.ly/2Ju5RhR
You are asked to evaluate a healthy 7-year-old boy with an asymptomatic brown “dirt-like” rash on the anterior neck (Figure 1). It has progressed over the last 2 months and does not clear with routine bathing and aggressive scrubbing by his mother with soap and water.

After wiping with 70% isopropyl alcohol in the office, the brown pigment readily disappeared and mild erythema secondary to rubbing was noted confirming the diagnosis of Terra firma-forme dermatosis (Figure 2).

**Terra firma-forme dermatosis**

**Diagnosis**

Terra firma-forme dermatosis (TFFD) is an acquired, benign, idiopathic dermatosis first described by Duncan and his colleagues in 1987. The name is derived from the Latin phrase ‘terra firma’ which refers to ‘dry land’. It is a rare type of keratinization disorder characterized by an asymptomatic brownish gray or black dirt-like patch that cannot be removed with soap and water and cleansers, but needs wiping with isopropyl alcohol or ethyl alcohol. The highest prevalence was found among prepubertal children (88.6%) with an average age of onset of 10.4 ±7.5 years, ranging from 3 years to 72 years.1 Commonly, the skin on the trunk and neck was involved, about a quarter of all patients showed involvement of the extremities, and in less than 3% over the head. Most of the lesions are solitary: however, in about 30% several lesions were found. It is often underreported.

Exact etiopathogenesis is not well understood. It is believed that the lesions arise as a result of a delay in the maturation of keratinocytes, with melanin retention and a sustained accumulation of sebum, sweat, corneocytes, and microorganisms in regions in which the skin is more sensitive to trauma and hygiene measures are less rigorous (neck, navel, flanks) leading to insufficient exfoliation and the formation of a highly adhesive, compact dirt like scale.2 It explains the hyperkeratosis and hyperpigmentation clinically seen in TFFD.

Histopathological examination, rarely required, shows prominent lamellar hyperkeratosis with whorls, keratotic plugging of follicular orifices, keratin globules in the stratum corneum, papillomatosis, and sharp invaginations between the papillae, increased melanin pigment in the basal layer, and minimal lymphocytic liquefaction. A Fontana-Masson stain shows focally increased melanin pigment in the basal layer of the
epidermis. Periodic acid Schiff stain revealed a few vellus hair shafts with pityrosporum spores. Parakeratosis is not observed.

Terra firma-forme dermatosis is characterized by accumulation of hyperpigmented, hyperkeratotic and verrucous scale and/or crusts. Rarely palpable verrucous or papillomatous plaques, reticulated patches, and mild focal scaling have been observed.

Dermoscopy shows large, polygonal, plate-like, brown scales in a mosaic, cobblestone, or tie like pattern interrupted in furrows. Diagnosis can be confirmed by rubbing the lesion with an alcohol-soaked pad or cotton ball, which results in resolution of the lesions. This is known as the skin modified by alcohol rubbing test.

Dermatosis neglecta typically affects individuals of any age with neglected hygiene. The brownish, hyperkeratotic, verrucous crusts and corn flake-like scales, often symmetrical, result from progressive accumulation of sebum, cellular debris, keratin, sweat, and exogenous impurities. Lesions can be removed with soap and water or an alcohol swab or cotton ball. Histopathologically shows lamellar hyperkeratosis without any whorled hyperkeratosis.

Confluent and reticulated papillomatosis (CARP): CARP is an acquired ichthyosis-form dermatosis characterized by persistent, asymptomatic, dark, scaly macules and patches that tend to be confluent in the center and reticulated at the periphery and localized predominantly on the trunk. The lesions are red to brown, slightly verrucous papules on chest, back, neck, chin, arms, axillae. It may respond to topical therapy with topical calcipotriol or retinoids but responds best with oral doxycycline.

Post-inflammatory hyperpigmentation also known as post inflammatory melanosis, develops as a sequela of a variety of insults to the skin, such as atopic dermatosis, acne vulgaris, trauma, chemical/physical injuries. It presents as hyperpigmented macules /patches in the preceding inflammatory dermatosis or injury. The color tends to be tan to light brown if the excess pigment is within the epidermis. If the excess pigment is in the dermis, the color is usually blue or dark gray.

Acanthosis nigricans consists of dark, velvety thickening of the skin, usually on the nape and sides of the neck, as well as the Axillae and inner thighs. The lesions typically present in a symmetric fashion. There is no melanin deposition. Rather, the pigmentation is mainly due to hyperkeratosis. The condition is most commonly caused by obesity, metabolic syndrome, diabetes mellitus. The hyperpigmentation or dust cannot be removed by washing with soap and water or alcohol swab or cotton ball.

The condition of TFFD can be treated by forceful rubbing with gauze immersed into 70% isopropyl alcohol/ethanol alcohol to remove the lesions, which is diagnostic and therapeutic too. This procedure possibly determines protein denaturation, interfering in the cell metabolism and diluting lipoprotein membranes, thus avoiding blood tests and skin biopsies. Mild inflammation, erythema, stinging like sensation are reported after vigorous rubbing of repeated applications. The skin should be washed with soap and water after using alcohol, considering the possible symptoms of intoxication as drowsiness, lethargy, respiratory depression, mucosal irritation and others, especially in children. Other keratolytic agents like salicylic acid 5%/20% in alcohol base, 30% Urea, 12% Ammonium lactate showed similar efficacy after application for 2 weeks on the affected area, without any irritation/erythema. Moisturizing the affected skin is important to prevent xerosis after regular treatments with isopropyl alcohol. Recurrence is unusual after proper treatment. Rare recurrences can also be treated weekly with alcohol wipes or topical keratolytic agents.

Our patient
At follow-up 3 months later there were no signs of recurrent pigmentation, and he did not require any cleaning with alcohol wipes.

COMMENTS? E-mail them to llevine@mjhlifesciences.com

TAKE HOME POINTS:
- The skin condition known as TFFD is underdiagnosed and underreported, but easily treatable.
- In the differential diagnosis of hyperpigmented and hyperkeratotic lesions, TFFD should be kept in mind to avoid unnecessary diagnostic testing, biopsies, or referrals to endocrinology/dermatology.
- Primary care physicians should be aware of this condition, dermatoscopic features and isopropyl alcohol wipe test for prompt diagnosis and treatment.
- Primary care physicians should reassure adolescents and family members that this is a benign and treatable condition to reduce anxiety.

Dr Guntreddi is a pediatric hospitalist at Sanford Medical Center in Bemidji, Minnesota.
Dr Vasudevan Nair is a pediatrician at Sutter Amador Hospital in Jackson, California.
Dr Nirujogi is a family medicine resident, Tower Health, Reading, Pennsylvania.
Dr Theell is an ECFMG certified physician currently applying for residency from Franklin, Pennsylvania.

For references, go to ContemporaryPediatrics.com/tt firma-forme-dermatosis
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1. This test has not been FDA cleared or approved. This test has been authorized by FDA under an EUA for use by authorized laboratories. This test has been authorized only for the detection and differentiation of nucleic acid of SARS-CoV-2 from multiple respiratory viral and bacterial organisms. This test is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bb-3(b)(1), unless the authorization is terminated or revoked sooner.

2. For use with the CLIA-waived BioFire® FilmArray® 2.0 EZ configuration.

Atopic Dermatitis (AD) Is More Than Lesions and Itchy Skin

AD is a chronic, recurring, systemic, immune-mediated disease driven in part by persistent type 2 inflammation and characterized by eczematous skin lesions and pruritus.1-3 Common lesional symptoms, reported to occur at least 5 days per week by more than 50% of adults with uncontrolled moderate-to-severe AD in one study, include bleeding, cracking, flaking, and dry, rough skin (FIGURE 1).4 Itch is the most common and persistent burden, and patients with uncontrolled moderate-to-severe AD may experience frequent, extended periods of itch (BOX 1). Itch is one of the most important symptoms that we ask about. Rather than focusing on BSA involvement or physical signs of AD, I focus on whether or not a child has persistent itching throughout their day and night. These things play a role in whether a patient may be appropriate for referral to a dermatologist. I also consider the patient’s history of failed prior treatments.

BOX 1

Itch, as Reported by Adults With Uncontrolled Moderate-to-Severe AD (N=380)4

86%  Daily presence of itch
61%  Severe or unbearable itching
>60%  Itch≥12 hours/day

BOX 2

Consensus Definition of Moderate-to-Severe AD3,9

- A minimum involvement of 10% body surface area (BSA) or, regardless of BSA:
  - Individual lesions with moderate-to-severe features
  - Involvement of highly visible areas or those important for function (e.g., neck, face, genitalia, palms, and/or soles)
- Significantly impaired quality of life (QOL)

Dr. Abramovits: The first question I ask my patients is, “How bad is your itch?” Then, I assess the affected area (or areas) for erythema, excoriations, and lichenification and consider the race/ethnicity of the patient.

Dr. Oquendo: Itch is one of the most important symptoms that we ask about. Rather than focusing on BSA involvement or physical signs of AD, I focus on whether or not a child has persistent itching throughout their day and night. These things play a role in whether a patient may be appropriate for referral to a dermatologist. I also consider the patient’s history of failed prior treatments.
Both Patients and Caregivers Experience Burdens of AD

Significant disease burdens are reported by both patients and caregivers, and it is noteworthy that these burdens can be unpredictable. In a survey of 2002 caregivers and patients with moderate-to-severe AD, patients experienced 8–10 flares per year, each lasting approximately 15 days. On average, these patients spend approximately one-third of each year in flare. However, the burden extends beyond the immediate symptoms: >50% of patients and caregivers of each year in flares are. However, the burden extends beyond the immediate symptoms: >50% of patients and caregivers think about the next flare even during remission.19 Caregivers report additional concerns, as shown in BOX 3.11

Q: How do the unpredictability and chronicity of AD affect your management strategies? How do you discuss the unpredictability and chronicity of AD with patients and caregivers?

Dr. Oquendo: Sometimes, you start with emollients every time the patient’s skin feels dry. I inform the parents that this treatment strategy will be ongoing for 3 to 4 months before reducing the number of applications per day over time, depending on the response. A lot of the parents are flabbergasted by the amount of work that AD management entails.

Dr. Abramovits: My patients have often been to primary care physicians or pediatricians like Dr. Oquendo. I explain to patients that I try to help them be able to manage their symptoms by prescribing proper treatments and advising them on how to avoid known triggers. I recommend medications that might either minimize the severity of AD symptoms or help reduce the occurrence of flares per year. I tell patients not to believe myths claiming that AD will “outgrow the disease” or that it definitely disappear over a certain period of time, or that it can be cured by the time the child reaches adolescence.

AD Persistence Is Unpredictable

Although estimates vary, based on survey, census, and claims database analyses, it has been suggested that approximately 13 million people age 6 years and older have AD,12-15 and, of these, approximately 2.3 million have moderate-to-severe AD that remains uncontrolled despite being treated.12,16-18 Although it is often believed that AD will “outgrow,” persistence is unpredictable and approximately 20% of children with AD will have persistent disease.19-21

Q: What factors do you see that might suggest that AD may persist in a patient? How do you discuss disease persistence with patients and caregivers?

Dr. Abramovits: I tell them that the severity of AD symptoms waxes and wanes—do not expect the ideal situation. Be prepared that you might need to address this condition for a long time. You must take care of your skin for many years to come because there are triggers out there that can appear at any time. For some patients, AD can be seasonal (e.g., tied to pollen or weather changes). For others, AD can be constantly triggered, which may require continuous management of the disease. It’s important to note that a relapse of AD symptoms can occur at any moment.

Dr. Oquendo: Like Dr. Abramovits mentioned, I inform them that AD may need to be managed for many years to come. In my experience, some of the predictor values are severity and extent of disease, family history, atopic disease history (e.g., asthma, allergic rhinitis), and even the presence of keratosis pilaris. If the patients identify with these predictor values, I inform them that this disease may be lifelong.

Diagnosis Relies on Clinical Features

Consensus recommendations have been proposed that may be useful in clinical practice, which classify clinical findings of AD into “essential,” “important,” and “associated” features. The essential and important features are listed in TABLE 1.

Q: In your experience, what factors most often play a role in referral of AD patients to specialists?

Dr. Oquendo: I refer to a dermatologist if a patient presents with extensive skin involvement that may warrant systemic treatment. Another factor is unresponsiveness to conventional treatments. The last factor involves parents. In my experience, parents seek second opinions and may be less hesitant to start certain treatments when they are able to consult with a specialist.

Dr. Abramovits: Family doctors and pediatricians manage a very significant number of AD patients. When complications are noted or even predicted, they should consider referring. Essentially, it is a lack of response to topical therapies that may warrant referrals. Earlier referrals may lead to improved outcomes for some patients with AD.23,24

Referral to Specialized Care May Be Considered for Appropriate AD Patients

Many patients with mild AD are able to control their disease with basic skin care, including use of moisturizers, and avoidance of irritants. When symptoms remain uncontrolled, patients may have moderate-to-severe AD.3,22

CONSIDERATIONS FOR REFERRAL3,22-24

- Patient has moderate-to-severe AD
- Patient has refractory AD
- Conventional therapies fail to provide sufficient improvement
- AD involves the face or skin folds
- A comorbidity is present
DUPIXENT® (dupilumab): Revolutionizing AD Indication

DUPIXENT is indicated for the treatment of patients aged 6 years and older with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. DUPIXENT can be used with or without topical corticosteroids.25

Important Safety Information

CONTRAINDICATION

DUPIXENT is contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.25

Warnings and Precautions

Hypersensitivity: Hypersensitivity reactions, including generalized urticaria, rash, erythema nodosum, anaphylaxis and serum sickness or serum sickness-like reactions, were reported in <1% of subjects who received DUPIXENT in clinical trials. If a clinically significant hypersensitivity reaction occurs, institute therapy and discontinue DUPIXENT.25

Conjunctivitis and Keratitis: Conjunctivitis and keratitis occurred more frequently in atopic dermatitis subjects who received DUPIXENT. Conjunctivitis was the most frequently reported eye disorder. Most subjects with conjunctivitis or keratitis recovered or were recovering during the treatment period. Advise patients to report new onset or worsening eye symptoms to their healthcare provider.25

Reduction of Corticosteroid Dosage: Do not discontinue systemic, topical or inhaled corticosteroids abruptly upon initiation with DUPIXENT. Reductions in corticosteroid dose, if appropriate, should be gradual and performed upon initiation with DUPIXENT. Reductions in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy.25

Atopic Dermatitis Patients With Comorbid Asthma: Advise patients not to adjust or stop their asthma treatments without consultation with their physicians.25

Parasitic (Helminth) Infections: It is unknown if DUPIXENT will influence the immune response against helminth infections. Treat patients with pre-existing helminth infections before initiating therapy with DUPIXENT. If patients become infected while receiving treatment with DUPIXENT and do not respond to anti-helminth treatment, discontinue treatment with DUPIXENT until the infection resolves.25

Please see additional Important Safety Information throughout.

DUPIXENT Helps Repair the Skin by Specifically Targeting a Key Source of Type 2 Inflammation

Unlike topical and oral corticosteroids, DUPIXENT targets a source of underlying inflammation to proactively treat AD. Not an immunosuppressant or a steroid, DUPIXENT is the first and only dual inhibitor of IL-4 and IL-13 receptor signaling.25

5 Pivotal AD Clinical Studies With More Than 2700 Patients

DUPIXENT has been studied in 3 pivotal trials in adults and 1 pivotal trial in adolescents with uncontrolled moderate-to-severe AD, and 1 pivotal trial in children with uncontrolled severe AD (TABLE 2).25-29 DUPIXENT was initially approved for adults in 2017, with subsequent approvals for adolescents in 2019 and for children in 2020.25,30,31

Assessments in the clinical trials included the Investigator’s Global Assessment (IGA), the Eczema Area and Severity Index (EASI), and peak pruritus numerical rating scale (NRS),

Table 2. DUPIXENT AD Pivotal Trials25-29

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Patients</th>
<th>Duration</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADULT Monotherapy (2 Trials)a</td>
<td>1379 patients (age ≥18 years)</td>
<td>16 weeks</td>
<td>DUPIXENT 300 mg Q2W SC vs placebo SC</td>
</tr>
<tr>
<td>ADULT Concomitant TCSb</td>
<td>740 patients (age ≥18 years)</td>
<td>52 weeks</td>
<td>DUPIXENT 300 mg Q2W SC + TCS vs placebo SC + TCS</td>
</tr>
<tr>
<td>ADOLESCENT Monotherapyc</td>
<td>251 patients (age 12-17 years)</td>
<td>16 weeks</td>
<td>DUPIXENT 200/300 mg Q2W SC based on weight</td>
</tr>
<tr>
<td>CHILDREN Concomitant TCSd</td>
<td>387 patients (age 6-11 years)</td>
<td>16 weeks</td>
<td>DUPIXENT 300 mg Q4W SC + TCS/200 mg Q2W + TCS based on weight</td>
</tr>
</tbody>
</table>

Q2W=once every 2 weeks; Q4W=once every 4 weeks; TCS=topical corticosteroid.
a Patients with moderate-to-severe disease as defined by Investigator’s Global Assessment (IGA) score ≥3 on a scale of 0-4, Eczema Area and Severity Index (EASI) score ≥16 on a scale of 0-72, and disease body surface area (BSA) ≥10%.
b All patients received concomitant TCS for lesional areas; in the monotherapy trials, patients who required rescue treatment with topical TCS were classified as nonresponders.
c Patients with severe disease as defined by IGA score 4 on a scale of 0-4, EASI score ≥21 on a scale of 0-72, and disease BSA ≥10%.
d Patients with body weight <60 kg or with baseline weight of <30 kg received an initial dose of 200 mg on Day 1, followed by 100 mg Q2W from Week 2 to Week 14, and subjects with baseline weight of ≥30 kg (200 mg Q2W from Week 2 to Week 14). In analyses by prespecified baseline weight strata, optimal doses for efficacy and safety were: 15 kg to <30 kg (300 mg Q4W); subjects with baseline weight of <30 kg received an initial dose of 200 mg on Day 1, followed by 200 mg Q2W from Week 2 to Week 14. In analyses by prespecified baseline weight strata, optimal doses for efficacy and safety were: 15 kg to <30 kg (300 mg Q4W); ≥30 kg (200 mg Q2W).
e Q4W dosing was also studied in a randomized treatment arm, but no additional benefit was seen over Q2W dosing.

Table 3. Assessments12,25-29,32,34,35

<table>
<thead>
<tr>
<th>Scale</th>
<th>Assessment</th>
<th>Score Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGA</td>
<td>Global severity</td>
<td>0 (“clear skin”) to 4 (“severe disease”)</td>
</tr>
<tr>
<td>EASI</td>
<td>Lesion extent and severity</td>
<td>0-72 (≥21 indicates severe disease)</td>
</tr>
<tr>
<td>Peak Pruritus NRS</td>
<td>Patient-reported itch</td>
<td>0 (“no itch”) to 10 (“worst imaginable itch”)</td>
</tr>
</tbody>
</table>

Table 4. Baseline Disease Severity12,35,36

<table>
<thead>
<tr>
<th>Select Baseline Characteristics</th>
<th>ADULT Monotherapy and Concomitant TCS (N=2119)</th>
<th>ADOLESCENT Monotherapy (N=251)</th>
<th>CHILDREN Concomitant TCS (N=397)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean disease duration (years)</td>
<td>28</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Patients with IGA score 4 (%)</td>
<td>48</td>
<td>54</td>
<td>99</td>
</tr>
<tr>
<td>Mean EASI score</td>
<td>33</td>
<td>36</td>
<td>38</td>
</tr>
<tr>
<td>Peak pruritus NRS (weekly average)</td>
<td>7</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Mean BSA (%)</td>
<td>55</td>
<td>57</td>
<td>58</td>
</tr>
</tbody>
</table>
which are summarized in Table 3. Baseline disease severity in adults, adolescents, and children is shown in Table 4. Clinically Meaningful Itch Relief and Skin Clearance in Patients Aged 6 Years and Older

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>ADULT Monotherapy</th>
<th>ADULT Concomitant TCS</th>
<th>ADOLESCENT Monotherapy</th>
<th>Children Concomitant TCS (Severe AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IGA 0 or 1 (%)</td>
<td>37*</td>
<td>9</td>
<td>39*</td>
<td>12</td>
</tr>
<tr>
<td>Secondary:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EASI-75 (%)</td>
<td>48*</td>
<td>13</td>
<td>69*</td>
<td>23</td>
</tr>
<tr>
<td>Secondary:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak pruritus NRS (%)</td>
<td>38*</td>
<td>11*</td>
<td>59*</td>
<td>20*</td>
</tr>
</tbody>
</table>

Table 5. Clinical Efficacy in Adults, Adolescents, and Children at Week 16

Long-Term Safety Profile Across All Age Groups Studied

The most common adverse reactions, occurring in ≥1% of adult patients through Week 16, are shown in Table 7. The safety profile in children and adolescents through Week 16 was similar to that in adults with AD. In addition, the 52-week safety profile of DUPLEXTON + TCS in adults was generally consistent with the Week 16 adult safety profile. In children and adolescents, as observed in an open-label extension study, the safety profile of DUPLEXTON through Week 52 was consistent with that seen in adults with AD.

Q: How do you consider the long-term safety profile with adults, adolescents, and children?

Dr. Abramovits: It is very important. When patients ask questions regarding the time course of symptom resolution with DUPLEXTON and length of treatment, I review the chronicity of AD and how DUPLEXTON’s long-term safety profile plays a role in whether I make an individualized recommendation for that patient. We take it one step at a time, and I reevaluate the patients periodically.

As shown, 75% of children receiving DUPLEXTON + TCS achieved at least a 75% improvement in lesion extent and severity at Week 16 vs 27% of children receiving placebo + TCS. The time courses of improvements in itch and in lesion extent and severity in children are displayed in Figure 2. Post hoc analyses revealed that some adult and adolescent patients who did not achieve the primary endpoint (Table 8). As shown, 75% of children receiving DUPLEXTON + TCS achieved at least a 75% improvement in lesion extent and severity at Week 16 vs 27% of children receiving placebo + TCS. The time courses of improvements in itch and in lesion extent and severity in children are displayed in Figure 2. Post hoc analyses revealed that some adult and adolescent patients who did not achieve the primary endpoint

Table 6. Post Hoc Analysis of Adult and Adolescent Patients Not Achieving the Primary Endpoint

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>DUPLEXTON*</th>
<th>Placebo</th>
<th>Endpoint</th>
<th>DUPLEXTON*</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean percent change (LSM) in EASI from baseline</td>
<td>49%</td>
<td>11%</td>
<td>Mean percent change (LSM) in EASI from baseline</td>
<td>55%</td>
<td>21%</td>
</tr>
</tbody>
</table>

Limitations of analysis: The analysis was imbalanced, as there were more patients not achieving the primary endpoint in the placebo group than the DUPLEXTON groups. No adjustments were made for multiple comparisons; therefore, no definite conclusions may be drawn. Two imputation methods were implemented: (1) post baseline last observation carried forward (LOCF), with consideration of last value prior to rescue medication (data shown above), and (2) observed values, disregarding use of rescue medication. In analyses of adolescent patients, continuous outcomes were analyzed using multiple imputation and analysis of covariance with treatment, with randomization strata and relevant baseline values included in the model.

Figure 2. Time Course of Improvements in Itch and Lesion Extent and Severity in Children

(i.e., IGA 0 or 1 at Week 16 with at least a 2-point improvement from baseline) had changes in other validated measures (Table 8). As shown, 75% of children receiving DUPLEXTON + TCS achieved at least a 75% improvement in lesion extent and severity at Week 16 vs 27% of children receiving placebo + TCS. The time courses of improvements in itch and in lesion extent and severity in children are displayed in Figure 2. Post hoc analyses revealed that some adult and adolescent patients who did not achieve the primary endpoint

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Q: How do you consider the long-term safety profile with adults, adolescents, and children?

Dr. Abramovits: It is very important. When patients ask questions regarding the time course of symptom resolution with DUPLEXTON and length of treatment, I review the chronicity of AD and how DUPLEXTON’s long-term safety profile plays a role in whether I make an individualized recommendation for that patient. We take it one step at a time, and I reevaluate the patients periodically.

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The recommended dosing is shown in FIGURE 4.25

Q: How do you address concerns of patients and caregivers about injections or treatment with a biologic?

Dr. Abramovits: You focus patients on the reduction of symptoms they may see vs the fact that it’s an injection.

Dr. Oquendo: Patients always ask, “Is there a non-injection, oral medication?” We do discuss options. Although every patient is different, I share patient stories as examples to help guide other patients.

Important Safety Information (con’t)25

DRUG INTERACTIONS: Avoid use of live vaccines in patients treated with DUPIXENT.

USE IN SPECIFIC POPULATIONS

- Pregnancy: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to DUPIXENT during pregnancy. Healthcare providers and patients may call 1-877-311-8972 or go to https://mothertobaby.org/ongoing-study/dupixent/ to enroll in or obtain information about the registry.

Available data from case reports and case series with DUPIXENT use in pregnant women have not identified
a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Human IgG and IgA levels are known to cross the placental barrier; therefore, DUPIXENT may be transmitted from the mother to the developing fetus.

• **Lactation:** There are no data on the presence of DUPIXENT in human milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for DUPIXENT and any potential adverse effects on the breastfed infant from DUPIXENT or from the underlying maternal condition.

Please see accompanying Full Prescribing Information

**Summary**

• The burden of AD extends beyond visible signs and symptoms and affects caregivers as well as patients; AD is unpredictable and is associated with high disease burden for both patients and caregivers.

• Because AD is a chronic, relapsing, systemic inflammatory disease, it may require continuous, long-term management in moderate-to-severe cases. In addition, AD management may include referral to a specialist for appropriate patients.


17. Data on file. Sanofi; Bridgewater, NJ.


