



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Emerging and Re-emerging Infections in Children

COVID/ MIS-C, Zika, Ebola, Measles, Varicella, Pertussis ... Immunizations

Carol C. Chen, MD, MPH^{a,*}, Anne Whitehead, MD^b

KEYWORDS

- COVID-19 • Vaccine-preventable • Traveler • Emerging infections
- Re-emerging infections

KEY POINTS

- Although the disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) seems to be less common and less severe in children, it remains unclear what role pediatric populations play in the spread of the virus.
- The understanding of multisystem inflammatory syndrome in children associated with SARS-CoV-2 infection is continuing to evolve, and guidelines for evaluation and treatment may depend on local and institutional recommendations.
- Although they may be seen infrequently in the emergency department, it is essential that emergency providers be familiar with the presentation of vaccine-preventable illnesses in order to assist with identifying outbreaks in their communities.
- Emergency providers can play an important role in advocating for public health in the form of vaccine advocacy and education.
- While still rare, emergency providers must also consider nonendemic, mostly tropical infections in children presenting with fever who are recently returning from international travel.

INTRODUCTION

Emergency physicians often stand at the frontlines in the identification and management of outbreaks of emerging and re-emerging infectious diseases. As a specialty, emergency physicians must be prepared and adapt quickly to diseases whose

^a Department of Emergency Medicine, Division of Pediatric Emergency Medicine, University of California San Francisco, 550 16th Street, Box 0632, San Francisco, CA 94143, USA;

^b Department of Emergency Medicine, Division of Pediatric Emergency Medicine, Indiana University School of Medicine, 720 Eskenazi Avenue, FT 3rd Floor, FOB, Indianapolis, IN 46202, USA

* Corresponding author.

E-mail address: carol.chen@ucsf.edu

presentations may be unfamiliar or entirely novel. The novel coronavirus pandemic starting in 2019 has highlighted these important roles.

Children presenting to the emergency department with these novel and re-emerging diseases comprise a unique population, often with distinct presentations and specific vulnerabilities. As has been seen with the novel coronavirus causing COVID-19, the presentation and severity of illness may differ from that seen in adults. In the case of vaccine-preventable illnesses, children may be more susceptible to infection. It is vital that emergency providers be well-versed in the diagnosis and treatment of emerging and re-emerging infections. It is also important that they are armed with epidemiologic knowledge and tools to advocate for public health in their communities and beyond. The purpose of this article is to supply the emergency provider with this armamentarium.

COVID-19 IN CHILDREN

Incidence and Transmission

COVID-19, the disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has swept across the world since late 2019. Both in the United States and globally, the burden of disease has been much less in children (0–17 years) than in adults.^{1–3} Despite making up 22% of the population, children accounted for only 9.1% of COVID-19 cases in the United States as of November 2020 according to data from the Centers for Disease Control and Prevention (CDC).^{4,5}

In addition, fewer children are hospitalized with COVID-19, suggesting that they may have less severe illness than their adult counterparts.^{6,7} Similarly, children represent less than 0.3% of all confirmed deaths caused by the disease.⁵

It is still unclear whether children are able to transmit SARS-CoV-2 as easily and effectively as adults. More recent evidence suggests that children likely harbor the same viral load in their nasopharynx as adults and are just as likely to transmit the virus to household and close contacts.^{8–12}

Typical Presentation

Potential signs and symptoms of COVID-19 in children are nonspecific. Cough and fever are the most common, however, still less common than in adults.^{3,11} Rates of asymptomatic infection in children range from an estimated 16% to 45%.^{13,14} The table from an earlier study compares the symptomatology of 291 pediatric cases and 10,944 adult cases (**Table 1**).⁷

There is some evidence to suggest that children with certain underlying medical conditions such as obesity, asthma, and neurologic disease, and infants (<1 year) are at higher risk for developing severe disease if infected; however, it has also been noted that only half of hospitalized children with COVID-19 have an underlying medical condition.¹⁵

Testing for Severe Acute Respiratory Syndrome Coronavirus-2 and Implications

The CDC recommend nucleic acid or antigen testing to diagnose SARS-CoV-2 infection in children. Most academic institutions in the United States have developed protocols to guide practitioners on when to conduct testing; however, the CDC also provide some guidance on their website.³

Once a child is diagnosed with COVID-19, the question of when isolation can be discontinued often arises. For non-healthcare settings, the CDC recommend a cessation of isolation based on symptom guidelines. Recent evidence has shown that patients with mild-to-moderate illness remain infectious for up to 10 days after symptom onset,

Table 1
Table of signs and symptoms of COVID-19 disease in a sample of pediatric (<18 y) and adult patients

Sign/Symptom	Number (%) with Sign/Symptom	
	Pediatric	Adult
Fever, cough, or shortness of breath	213 (73)	10,167 (93)
Fever	163 (56)	7794 (71)
Cough	158 (54)	8775 (80)
Shortness of breath	39 (13)	4674 (43)
Myalgia	66 (23)	6713 (61)
Runny nose	21 (7.2)	757 (6.9)
Sore throat	71 (24)	3795 (35)
Headache	81 (28)	6335 (58)
Nausea/vomiting	31 (11)	1746 (16)
Abdominal pain	17 (5.8)	1329 (12)
Diarrhea	37 (13)	3353 (31)

Adapted from CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020. *MMWR*. 2020;69(14):422-426.⁷

and those with severe illness or those who are immunocompromised may be infectious for up to 20 days after symptom onset.¹⁶ Therefore, patients with COVID-like symptoms may discontinue isolation after at least 10 days from symptom onset as long as they have not had a fever for at least 24 hours, and other symptoms have improved.

For asymptomatic patients with COVID-19, it is recommended to discontinue isolation and other precautions 10 days after the date of the initial positive test.

Multisystem Inflammatory Syndrome in Children Associated with COVID-19

While most cases of COVID-19 are uncomplicated in children, an inflammatory syndrome similar, but not identical, in presentation to Kawasaki's Disease has been described in a small number of children. Multisystem inflammatory syndrome in children (MIS-C) is currently defined as any person under 21 years of age with unexplained fever (at least 38 °C for at least 24 hours), laboratory evidence of inflammation, and illness requiring hospitalization with involvement of at least 2 organ systems in the setting of current or recent SARS-CoV-2 infection.¹⁷ If infection cannot be confirmed by viral testing, a history of exposure to a suspected or confirmed case in the 4 weeks prior to symptom onset will also satisfy this last requirement. Laboratory findings that confirm inflammation include: elevated C-reactive protein, erythrocyte sedimentation rate, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, interleukin 6, or neutrophils, and reduced lymphocytes or albumin.

Clinical presentations of MIS-C may vary, but can include fever, abdominal pain, vomiting, diarrhea, rash, and mucocutaneous lesions. Severe cases may present with hypotension and shock.

In addition to the laboratory testing noted previously, patients with MIS-C are especially vulnerable to cardiac insult, leading many hospitals to also obtain an electrocardiogram, echocardiogram, cardiac enzymes, and a B-type natriuretic peptide.

Treatment for MIS-C is largely supportive and includes respiratory support, inotropic support, and fluid resuscitation. The American College of Rheumatology

has developed guidelines to assist practitioners with the evaluation of children suspected of having MIS-C (Fig. 1).¹⁸

RE-EMERGING VACCINE PREVENTABLE INFECTIONS

Over the past century, an emerging and expanding arsenal of childhood vaccines has changed the landscape of pediatric infectious diseases and emergencies. Illnesses once considered the bread and butter of pediatric practice have become for some physicians, distant memories, and for many physicians, entities seen only in textbooks. Unfortunately, the growing phenomenon of vaccine hesitancy and refusal has created growing populations of unvaccinated and undervaccinated children, and triggered outbreaks of eliminated and near-eliminated diseases in the United States. It has become imperative for emergency providers not only to have a working knowledge of these re-emerging diseases, but also to understand the role that they can take in addressing vaccine hesitancy and misinformation.

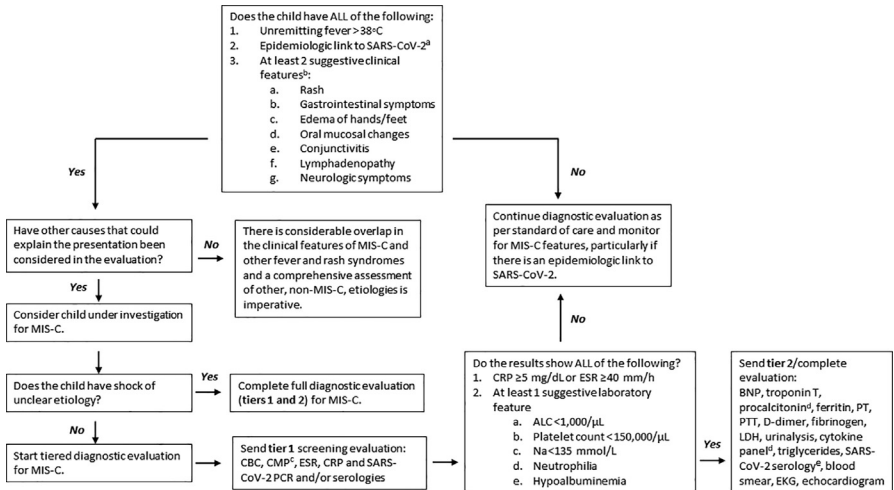


Fig. 1. Diagnostic pathway for MIS-C from the American College of Rheumatology. ^a An epidemiologic link to SARS-CoV-2 infection is defined as a child with any of the following criteria: positive SARS-CoV-2 polymerase chain reaction (PCR), positive SARS-CoV-2 serologies, preceding illness resembling COVID-19, or close contact with confirmed or suspected COVID-19 cases in the past 4 weeks. ^b Rash (polymorphic, maculopapular, or petechial, but not vesicular), gastrointestinal (GI) symptoms, (diarrhea, abdominal pain, or vomiting), oral mucosal changes (red and/or cracked lips, strawberry tongue, or erythema of the oropharyngeal mucosa), conjunctivitis (bilateral conjunctival injection without exudate), neurologic symptoms (altered mental status, encephalopathy, focal neurologic deficits, meningismus, or papilledema). ^c Complete metabolic panel: Na, K, CO₂, Cl, blood urea nitrogen (BUN), Cr, glucose, Ca, albumin, total protein, aspartate aminotransferase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), bilirubin. ^d Send procalcitonin and cytokine panel, if available ^e if not sent in tier 1 evaluation. If possible, send SARS-CoV-2 immunoglobulin G (IgG), immunoglobulin M (IgM), immunoglobulin A (IgA). (Adapted from Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology clinical guidance for pediatric patients with multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 and hyperinflammation in COVID-19. Version 1. *Arthritis Rheumatol.* 2020;72(11):1791-1805; with permission.¹⁸)

Vaccine Hesitancy and Refusal

The role of vaccines in reducing pediatric morbidity and mortality is indisputable and well-studied. Prior to the introduction of the measles vaccine in the 1960s, measles caused an estimated 2 million annual deaths globally.¹⁹ By 2000, endemic measles had been eliminated from the United States, and global rates had dropped by 80% by 2016.^{20,21} Since the introduction of the varicella vaccine, varicella-related hospitalizations and deaths have dropped by over 95%. Although the incomplete effectiveness of the pertussis vaccine makes eradication of this disease difficult, studies suggest a significant protective effect.^{21,22}

In recent years, there have been a growing number of families demonstrating vaccine hesitancy and vaccine refusal, most commonly related to concerns about vaccine safety. Many cite the Wakefield case series, which falsely claimed an association between childhood vaccines and autism. Despite the debunking and retraction of the article and its findings, many parents have a misunderstanding that the association truly exists. In the case of near-eliminated diseases, communities have no recent memory of the impact and complications associated with these diseases, and may therefore underestimate the importance of prevention. As a result, philosophic exemption rates in many communities have risen in recent years, and with them, have come significant outbreaks of vaccine-preventable disease. One of the most compelling examples has been the measles virus, which caused only 63 illnesses in the United States in 2010, but caused 1282 illnesses 9 years later in 2019.²³ Cases occurred largely in the unvaccinated, and many outbreaks occurred within unvaccinated or poorly vaccinated communities.

It is therefore essential that emergency providers have familiarity with these re-emerging diseases and an understanding of the public health role they can play in discussing vaccines with their patients and families.

Measles

Transmission

Measles is a highly contagious viral illness caused by the paramyxovirus measles morbillivirus. It is spread by aerosolized particles and respiratory droplets, which belies the importance of isolation for suspected patients. Ideally, patients with symptoms suspicious for measles would be kept out of the waiting rooms whenever possible, either by immediate rooming, or use of an alternate, isolated waiting area. Unfortunately, measles tends to have a very high reproductive number, with each infected individual infecting an average of 9 to 18 others in a nonimmune community.¹⁹ A 1990 study documenting an outbreak in an almost entirely unvaccinated church community in Philadelphia demonstrated an attack rate of 91% in children aged 5 to 14 years and 94% in children aged 1 to 4 years.²⁴

Typical presentation

Measles has an average incubation of 12.5 days after exposure, and patients are considered contagious from 4 days before, until 4 days after the appearance of the rash. The typical progression of symptoms begins with fever, cough, coryza, and conjunctivitis. Patients often suffer significant malaise, which serves as the inspiration for the term *measly*. Two to 3 days after the onset of symptoms, small bluish-white Koplik spots appear in the oral mucosa. Three to 5 days after the onset of symptoms, the typical measles rash appears. Macules and papules tend to start on the head, particularly the face and behind the ears, before spreading down to the trunk and extremities. Recovery typically occurs within 1 week of rash onset. Rash may be less prominent, or nonexistent, in the immunocompromised.

Diagnosis

The diagnosis of measles can be made based on clinical picture alone; however, testing can be of particular public health importance. Confirmation of suspected cases via testing can be important in identifying and addressing outbreaks, and often the identification of a laboratory confirmed case can trigger health department involvement. Typically, testing includes nasopharyngeal and/or throat swabs for reverse transcriptase polymerase chain reaction (RT PCR) testing, as well as serum testing for IgM. Both tend to be most sensitive if collected within 3 days of rash onset.²³

Treatment

As is so often the case with viral illnesses, the mainstay of treatment for measles is supportive care. There is some evidence from endemic areas to suggest that vitamin A supplementation may play a role in reducing morbidity and mortality,²⁵ however, this may not be the case for patient populations being seen in North American emergency departments, where vitamin A deficiency may be less common. Recommendations for supplementation in mild disease vary, but all severely ill and/or hospitalized children should receive 2 consecutive daily doses of vitamin A. No specific antiviral therapies exist for the treatment of measles.

Complications/concerns

Case fatality rates for measles vary significantly depending on the underlying health and socioeconomic status of the affected population, from 0.01% in high-resource countries to 5% in low-resource countries, and even higher in displaced populations.¹⁹ Significant morbidity and mortality can arise from secondary bacterial infection, most commonly pneumonia. Measles keratoconjunctivitis is a significant cause of blindness worldwide. Measles is also associated with 3 distinct clinical conditions that are potentially neurologically devastating and at times fatal: acute disseminated encephalomyelitis (ADEM) days to weeks following infection, measles inclusion body encephalitis (MIBE) months following infection, and subacute sclerosing pan encephalitis (SSPE) years following infection. Measles infections in pregnant patients can result in maternal or fetal death. Young children and the immunocompromised tend to have higher mortality and more severe illness.

Varicella

Transmission

Varicella zoster virus is the cause of 2 distinct illnesses: varicella (chicken pox), the primary infection and largely a childhood illness, and zoster (shingles), the reactivation of the varicella zoster virus. Many, but not all practicing physicians likely experienced a case of varicella personally in childhood, but many of these same physicians have rarely or never seen the disease in practice. Vaccination became available in 1995, and cases and complications of the disease have dropped precipitously since its introduction.^{26–28} Both vaccine and infection tend to confer lifelong immunity. Although vaccination has a relatively high rate of failure of seroconversion, breakthrough cases are infrequent and tend to be associated with more mild disease.^{29,30} Varicella is a highly contagious illness, like measles, with both droplet and aerosol spread. Attack rates for unvaccinated close contacts are estimated to be around 70%.²⁹ Isolation of suspected cases as soon as possible is recommended, again, with attention placed to waiting room procedures.

Typical presentation

The typical chicken pox rash is often, but not always, preceded by several days of prodromal symptoms that include fever, malaise, nausea, and headache. Rash develops roughly 10 to 21 days following exposure.³¹ Macules and papules are an early

manifestation, subsequently taking on the proverbial dew drop on rose petal appearance. These first appear on the trunk, then spread to the extremities and head. Papules become pustules within 12 to 72 hours, then scabs. Pruritic lesions appear in crops, and patients will typically have several hundred lesions in various stages.³⁰ The number of lesions is often significantly lower in vaccinated breakthrough cases.³²

Diagnosis

The diagnosis of varicella can be made based on clinical presentation, but as is the case with measles, it can be helpful to confirm the diagnosis of this vaccine-preventable illness via laboratory testing. This can be done via serologic testing of a serum sample, and/or sampling of vesicular fluid or scabs for PCR testing.

Treatment

For low-risk children with mild disease, treatment is aimed at symptom relief and prevention of secondary bacterial infections. Antihistamines, lotions, and baths can help with itching. Trimming fingernails can be important to keep children from inadvertently causing secondary cellulitis through scratching. It is imperative that aspirin be avoided to prevent Reye syndrome.

Acyclovir should be considered in some patients. In low-risk groups (eg, healthy young children), acyclovir may reduce the number of lesions and days of fever, but is not associated with less itching or fewer complications, so is generally not recommended.³³ High-risk patients (eg, immunocompromised, chronic lung disease, chronic skin disorders, chronic aspirin or steroid therapy, individuals over age 12) should receive acyclovir. Those who are significantly immunocompromised or with severe disease should receive intravenous acyclovir.³⁰

Anti-varicella immunoglobulin is also used in some hospitalized populations such as pregnant patients, some young infants, and the immunocompromised.

Complications/concerns

Those who have memory of childhood varicella infections may mistakenly categorize it as a benign infection. Complications run from the relatively minor, such as acute otitis media and cellulitis, to severe, which include pneumonia, encephalomyelitis, myocarditis, and death. Case fatality is about 1 in 60,000, but may be as high as 36% for the immunocompromised, and up to 30% for infants of infected mothers in the immediate peripartum period, which is why these groups are typically treated prophylactically with immunoglobulin, and if ill, intravenous acyclovir.³⁰ Acute cerebellar ataxia is one of the more common complications, and while it is typically self-limited, it can result in weeks to months of symptoms.

Pertussis

Incidence and transmission

Pertussis is the respiratory illness caused by the gram-negative aerobic bacteria *Bordetella pertussis*. Despite the availability of the pertussis vaccine in its whole cell and acellular forms since the 1940s and 1990s respectively, pertussis remains endemic throughout the world. Neither form of the vaccine, nor prior infection, confer lifelong immunity, and spread can be perpetuated by those with waning immunity. There are roughly 20 to 40 million cases worldwide yearly, with cyclical spikes in cases every 3 to 5 years.³⁴ The largest peak in the United States in recent years took place in 2012, with over 48,000 cases.³⁵

Typical presentation

Often described as the 100-day cough, pertussis moves through 3 phases over the course of weeks to months. During the catarrhal stage, which lasts 1 to 2 weeks,

symptoms are difficult to distinguish from a typical viral upper respiratory infection with runny nose, fever, and mild cough. The more characteristic whooping cough develops during the paroxysmal stage, with typical bursts of 5 to 10 coughs followed by a whoop, or in some cases, a period of apnea. Cough is severe enough that post-tussive emesis, subconjunctival hemorrhages, petechiae, and even seizures are not uncommonly seen; however, between the bouts of coughing, patients often breathe comfortably and can seem well. At week 6, the disease moves into the convalescent stage of illness, where cough is less severe and frequent, but may linger for weeks or even months.³⁶

Diagnosis

Although characteristic features can be helpful, there is no 1 symptom or set of symptoms pathognomonic for pertussis.³⁷ It can be extremely difficult to distinguish the disease from the myriad of other respiratory illnesses that bring children to the emergency department, so it is important to maintain a high index of suspicion, especially in more vulnerable populations such as young infants. The recommendation for suspected cases of pertussis is PCR testing from nasal swab or aspirate. Chest radiographs can be helpful in determining the presence of a secondary bacterial pneumonia or other complication, but these are typically normal or have nonspecific findings.³⁴

Treatment

Although antibiotics are often prescribed to patients with confirmed or suspected pertussis, it is important to recognize that antibiotics do not alter the course of illness. The primary role of antibiotics in pertussis is to prevent infectivity of affected individuals, and to prevent infection in exposed individuals. Clarithromycin, azithromycin, or erythromycin is recommended within 3 weeks of cough onset.³⁵ Close contacts, particularly high-risk individuals such as young infants, should be prescribed antibiotics within 3 weeks of initial exposure if possible. Treatment for symptomatic patients is largely supportive.

Complications/concerns

Severe pertussis is a significant cause of morbidity and mortality, particularly in young infants under 6 months of age. This group has the highest mortality, of roughly 1%, and 80% of those who die of pertussis are under 1 year of age.³⁶ Rib fracture, pneumothorax, and intracranial hemorrhage are potential complications during this stage, and can even cloud the clinical picture in infants as abuse mimics. Although the apnea many infants experience can be very concerning to physicians and families alike, and is likely associated with morbidity, it is not the cause of death in severe pertussis. Hypotension and organ failure account for much of the mortality in young infants with severe disease.³⁸

THE PUBLIC HEALTH ROLE OF EMERGENCY PROVIDERS IN VACCINE-PREVENTABLE ILLNESS

The emergency physician plays 2 key public health roles in vaccine-preventable illness. Recognition of cases to inform public health authorities is of the utmost importance. Emergency physicians are often the frontline in identifying outbreaks and other patterns of emergence. The emergency provider can also play a role in directly addressing vaccine hesitancy and refusal. Vaccine hesitancy in particular has potential to decrease or disappear during the early years of parenthood,³⁹ and it seems likely that both repeated physician education and increased familiarity with vaccines may play a role in this. Although the emergency department can be a difficult setting for rapport-building, a thoughtful discussion may be successful in reducing hesitancy in parents and other caregivers. Recommended techniques include nonconfrontational

language, recognition of parental free will, open and honest exchange of information, discussion of vaccination risks, and personal anecdotes. It can be effective to confirm that the provider and his or her family are vaccinated and believe in the safety and efficacy of vaccines.^{20,40,41} It is also likely that as frontline providers working with emerging diseases, emergency providers may play an important role in dissemination of new vaccines when available.

EMERGING AND RE-EMERGING INFECTIONS TO CONSIDER IN THE RETURNING TRAVELER

Although most emergency providers already have an established framework to manage children presenting with fever, such children who have recently returned from international travel pose additional challenges. While still rare, one must also consider nonendemic, mostly tropical infections in these patients, and involve infectious diseases colleagues where appropriate.

Ebola

Ebola virus disease is caused by Ebolavirus, a member of the family that also contains Marburg virus. The disease mainly occurs in Central Africa and Sudan; however, outbreaks have also occurred in other parts of Africa and Asia. Symptoms, most commonly fever, malaise, headache, anorexia, vomiting and diarrhea, typically occur 6 to 12 days after exposure. Significant hemorrhagic complications are rare, with severe dehydration potentially leading to shock being the most frequent complication. Transmission occurs through bodily fluids of infected persons. As treatment is largely supportive, the most important first step in evaluating a patient with suspected Ebola virus disease is to assess the likelihood of exposure then initiate infection control measures in any child with a suspected exposure within 21 days of symptom onset.⁴² Diagnostic testing with RT-PCR can be coordinated with local health authorities.

Zika

Zika virus is a flavivirus transmitted by mosquitoes. Cases have been reported across several continents, making it an important consideration in travelers.^{43,44} Only about 20% of those infected will develop symptoms, most commonly fever, pruritic rash, arthralgias of the hands and feet, and nonpurulent conjunctivitis, and fortunately complications and death are rare.^{45,46} The CDC have concluded that infection with Zika virus during pregnancy causes microcephaly and other fetal brain defects, so this must be taken into account when evaluating female patients of child-bearing age. In general, testing for Zika is only recommended in symptomatic pregnant women with recent travel to high-risk areas; however, please see the CDC Web site for specific testing recommendations (<https://www.cdc.gov/zika/hc-providers/testing-guidance.html>).

Dengue and Chikungunya

Dengue virus is another flavivirus transmitted by mosquitoes. It presents as 3 distinct clinical syndromes recently reclassified by the World Health Organization (WHO) as dengue without warning signs, dengue with warning signs, and severe dengue. Most infected children are either asymptomatic or develop only mild disease. Typical presentation includes fever with rash, headache, and nausea and vomiting, with abdominal pain, mucosal bleeding, ascites, pleural effusions, and hepatomegaly considered warning signs. Severe disease includes significant plasma leakage or bleeding and evidence of end-organ damage. A small proportion of patients, typically children or young adults, will experience a systemic vascular leak syndrome that could lead to shock; this usually

occurs around day 3 to 7 of illness.⁴⁷ Chikungunya disease can present similarly and is transmitted by the same vector; however, joint swelling, which is more prominent in patients with chikungunya, can help to distinguish between the 2 diseases. Treatment for both is supportive, with patients suspected of having severe dengue needing close monitoring; in these patients neither corticosteroids nor empiric blood transfusions have been found to be effective.⁴⁸ In patients with severe dengue and shock, specific treatment recommendations have been provided by the WHO.^{49,50}

Malaria

Finally, malaria should be considered in any child with fever returning from an endemic area, as children are at risk of becoming severely ill if infected with the *Plasmodium falciparum* species. The clinical presentation of malaria in children has a broad range from asymptomatic to severe illness. Typical symptoms include fever, cough, vomiting, diarrhea, and headache. The presence of any of the following complications indicates severe malaria and requires urgent intervention: coma or altered level of consciousness, inability to sit up or drink, convulsions, hemoglobin less than 5 g/dL, respiratory distress, glucose less than 45 mg/dL, or jaundice.⁵¹ Cerebral malaria is also a form of severe malaria and is usually characterized by a change in behavior, confusion, drowsiness, altered consciousness, and weakness. If suspected, thin and thick blood smears can be used to diagnose malaria; rapid diagnostic tests are typically only available in endemic areas. The treatment of malaria depends on the pathologic species, the severity of disease, patient factors, and the area in which the infection was obtained, which usually dictates drug resistance. Specific guidance on treatment from the CDC can be found at https://www.cdc.gov/malaria/diagnosis_treatment/treatment.html.

SUMMARY

The role of the emergency provider lies at the forefront of the recognition and treatment of novel and re-emerging infectious diseases in children. Familiarity with disease presentations that might typically be considered rare, such as vaccine-preventable and nonendemic illnesses, is essential in identifying and controlling outbreaks. Rare and novel diseases often affect children differently than the rest of the population in various ways. As has been seen thus far in the novel coronavirus pandemic, susceptibility, severity, transmission, and disease presentation can all have unique patterns in children. Emergency providers also have the potential to play a public health role in emerging and re-emerging infectious disease by using lessons learned from the phenomena of vaccine hesitancy and refusal.

CLINICS CARE POINTS

- As the understanding of the disease caused by SARS-CoV-2 in children continues to evolve rapidly, frequent review of updated guidelines published by local health departments and the CDC are strongly recommended.
- It is important to have a plan for immediate appropriate isolation of children with suspected emerging and re-emerging infections to protect others in the emergency department who may be nonimmune and/or at high risk for severe disease.
- Pediatric infectious disease consultation should be considered in cases of suspected re-emerging vaccine preventable illnesses in children to assist with proper testing, reporting, and identification of those patients who need more aggressive management.
- Strongly consider admission for young infants with suspected pertussis (those under 3 months), as mortality is highest in this group.

- In children who have recently returned from international travel, clinicians must also consider nonendemic, mostly tropical infections, and involve their infectious diseases colleagues where appropriate.

DISCLOSURE

C.C. Chen has no commercial or financial conflicts of interest. A. Whitehead has no commercial or financial conflicts of interest.

REFERENCES

1. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus disease 2019 case surveillance — United States, January 22–May 30, 2020. *MMWR* 2020;69(24):759–65.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020; 323(13):1239–42.
3. COVID-19 Information for pediatric healthcare providers.. 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html>. Accessed November 3, 2020.
4. Quick facts: United States.. 2020. Available at: <https://www.census.gov/quickfacts/fact/table/US/AGE295219#AGE295219external> icon. Accessed November 3, 2020.
5. Demographic Trends of COVID-19 cases and deaths in the US reported to CDC.. 2020. Available at: https://covid.cdc.gov/covid-data-tracker/?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates%2Fcases-in-us.html#demographics. Accessed November 3, 2020.
6. Kim L, Whitaker M, O'Halloran A, et al. Hospitalization rates and characteristics of children aged <18 years hospitalized with laboratory-confirmed COVID-19 – COVID-NET, 14 states, March 1–July 25, 2020. *MMWR* 2020;69(32):1081–8.
7. CDC COVID-19 Response Team. Coronavirus disease 2019 in children — United States, February 12–April 2, 2020. *MMWR* 2020;69(14):422–6.
8. Sargent TH, Muller WJ, Zheng X, et al. Age-related differences in nasopharyngeal severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) levels in patients with mild to moderate coronavirus disease 2019 (COVID-19). *JAMA Pediatr* 2020; 174(9):902–3.
9. Park YJ, Chloë YJ, Park O, et al. Contact tracing during coronavirus disease outbreak, South Korea, 2020. *Emerg Infect Dis* 2020;26(10):2465–8.
10. Szablewski CM, Chang K, Brown MM, et al. SARS-CoV-2 transmission and infection among attendees of an overnight camp – Georgia, June. *MMWR* 2020; 69(31):1023–5.
11. Laws RL, Chancey RJ, Rabold EM, et al. Symptoms and transmission of SARS-CoV-2 Among Children—Utah and Wisconsin, March–May 2020. *Pediatrics* 2020;147(1). e2020027268.
12. Gilliam WS, Malik AA, Shafiq M, et al. COVID-19 transmission in US Child Care Programs. *Pediatrics* 2020;147(1). e2020031971.
13. Assaker R, Colas A, Julien-Marsollier F, et al. Presenting symptoms of COVID-19 in children: a meta-analysis of published studies. *Br J Anaesth* 2020;125(3):e330–2.
14. Poline J, Gaschignard J, Leblanc C, et al. Systematic SARS-CoV-2 screening at hospital admission in children: a French prospective multicenter study. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1044>.

15. COVIDView. Key updates for Week 43, Ending October 24, 2020.. Available at: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcovid-data%2Fcovidview.html. Accessed November 3, 2020.
16. Discontinuation of isolation for persons with COVID-19 not in healthcare settings.. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/disposition-in-home-patients.html>. Accessed November 3, 2020.
17. Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C).. Available at: <https://www.cdc.gov/mis-c/hcp/>. Accessed November 3, 2020.
18. Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology clinical guidance for pediatric patients with multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2 and hyperinflammation in COVID-19. Version 1. *Arthritis Rheumatol* 2020;72(11):1791–805.
19. Moss WJ. Measles. *Lancet* 2017;390:2490–502.
20. Dreisinger N, Lim CA. Resurgence of vaccine-preventable disease: ethics in the pediatric emergency department. *Pediatr Emerg Care* 2019;35(9):651–3.
21. Phadke VK, Bednarczyk RA, Salmon DA, et al. Association between vaccine refusal and vaccine-preventable diseases in the United States: a review of measles and pertussis. *JAMA* 2016;315(11):1149–58.
22. Zerbo O, Bartlett J, Goddard K, et al. Acellular pertussis vaccine effectiveness over time. *Pediatrics* 2019;144(1). e20183466.
23. Measles Cases and Outbreaks. National Center for Immunization and Respiratory Diseases. Available at: <https://www.cdc.gov/measles/cases-outbreaks.html>. Accessed October 31, 2020.
24. Rodgers DV, Gindler JS, Atkinson WL, et al. High attack rates and case fatality during a measles outbreak in groups with religious exemption to vaccination. *Pediatr Infect Dis J* 1993;12(4):288–91.
25. D'Souza R, D'Souza RR. Vitamin A for treating measles in children. *Cochrane Database Syst Rev* 2001;(2):CD001479.
26. Staat MA, Meinen-Derr J, Welch T, et al. Varicella-related hospitalization and emergency department visit rates, before and after introduction of varicella vaccine, among white and black children in Hamilton County, Ohio. *Pediatrics* 2006;117(5):e833–9.
27. Davis MM, Patel MS, Gebremariam A. Decline in varicella-related hospitalizations and expenditures for children and adults after introduction of varicella vaccine in the United States. *Pediatrics* 2004;114(3):786–92.
28. Seward JF, Watson BM, Peterson CL, et al. Varicella disease after introduction of varicella vaccine in the United States, 1995-2000. *JAMA* 2002;287(5):606–11.
29. Seward JF, Zhang JX, Maupin TJ, et al. Contagiousness of varicella in vaccinated cases: a household contact study. *JAMA* 2004;292(6):704–8.
30. Blair RJ. Varicella zoster virus. *Pediatr Rev* 2019;40(7):375.
31. Freer G, Pistello M. Varicella-zoster virus infection: natural history, clinical manifestations, immunity and current and future vaccination strategies. *New Microbiol* 2018;41(2):95–105.
32. Gershon AA. Varicella-zoster virus infections. *Pediatr Rev* 2008;29(1):5.
33. Klassen TP, Belseck EM, Wiebe N, et al. Acyclovir for treating varicella in otherwise healthy children and adolescents. *Cochrane Database Syst Rev* 2001;(2):CD002980.
34. Nee P, Weir E, Vardhan M, et al. Could this be whooping cough? *Emerg Med J* 2018;35(10):639–42.

35. 2019 Provisional pertussis surveillance report. National Center for Immunization and Respiratory Diseases. Available at: <https://www.cdc.gov/pertussis/downloads/pertuss-surv-report-2019-508.pdf>. Accessed October 12, 2020.
36. Snyder J, Fisher D. Pertussis in childhood. *Pediatr Rev* 2012;33(9):412–20.
37. Ebell MH, Marchello C, Callahan M. Clinical diagnosis of *Bordetella pertussis* infection: a systematic review. *J Am Board Fam Med* 2017;30(3):308–19.
38. Cherry JD. Pertussis in young infants throughout the world. *Clin Infect Dis* 2016; 63(suppl_4):S119–22.
39. Henrikson NB, Anderson ML, Opel DJ, et al. Longitudinal trends in vaccine hesitancy in a cohort of mothers surveyed in Washington State, 2013–2015. *Public Health Rep* 2017;132(4):451–4.
40. Hamborsky J, Kroger A. Epidemiology and prevention of vaccine-preventable diseases, E-Book: the Pink Book. Washington, D.C: Public Health Foundation; 2015.
41. Badur S, Ota M, Ozturk S, et al. Vaccine confidence: the keys to restoring trust. *Hum Vaccin Immunother* 2020;16(5):1007–17.
42. Ebola (Ebola virus disease).. Available at: <https://www.cdc.gov/vhf/ebola/diagnosis/index.html>. Accessed November 6, 2020.
43. Hamer DH, Barbre KA, Chen LH, et al. Travel-associated Zika virus disease acquired in the Americas through February 2016: a GeoSentinel analysis. *Ann Intern Med* 2017;166(2):99–108.
44. Armstrong P, Hennessey M, Adams M, et al. Travel-associated Zika virus disease cases among U.S. Residents—United States, January 2015–February 2016. *MMWR* 2016;65(11):286–9.
45. Zika virus.. Available at: <https://www.cdc.gov/zika/hc-providers/preparing-for-zika/clinicalevaluationdisease.html>. Accessed November 6, 2020.
46. LaBeaud AD. Zika virus infection: an overview. In: Baron EL (Deputy Ed.), *UptoDate*. 2020. Available at: https://www.uptodate-com.ucsf.idm.oclc.org/contents/zika-virus-infection-an-overview?search=zika&source=search_result&selectedTitle=1~105&usage_type=default&display_rank=1. Accessed November 6, 2020.
47. Kalayanarooj S, Vaughn DW, Nimmannitya S, et al. Early clinical and laboratory indicators of acute dengue illness. *J Infect Dis* 1997;176(2):313–21.
48. Dengue.. Available at: <https://www.cdc.gov/dengue/healthcare-providers/treatment.html>. Accessed November 6, 2020.
49. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. New edition. Geneva: World Health Organization; 2009.
50. WHO Regional Office for Southeast Asia. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded version. New Delhi: World Health Organization, SEARO Technical Publication Series; 2011.
51. World Health Organization. Pocket book of hospital care for children: guidelines for the management of common childhood illnesses. 2nd edition. Malta: World Health Organization; 2013.