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JUNE 2020

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COVID-19: The Impact on Pediatric Emergency Care

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Although there is still much that is not understood, experience with previous coronavirus outbreaks and available data on COVID-19 indicate a reduced propensity to affect children. Nonetheless, serious complications—although rare—are being seen in pediatric patients. This review, written with the emergency medicine clinician in mind, describes the epidemiology, clinical features, and management implications for COVID-19 in pediatric patients. It includes a discussion of multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19, as well as other aspects of the COVID-19 pandemic that are affecting children and families, such as poisonings, childhood immunizations, mental health, nonaccidental trauma, and neglect.



For up-to-date information on the management of COVID-19 patients in the emergency department, as well as associated resources, go to www.ebmedicine.net/COVID-19.

Introduction

Since the discovery of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the evolution of the current coronavirus disease 2019 (COVID-19) pandemic, there have been major disruptions to economic stability and healthcare infrastructure throughout the world. Early literature and media reports about COVID-19 presented this pandemic as mainly affecting older adults with underlying conditions. This review describes the epidemiology, clinical features, and management implications for COVID-19 in pediatric patients.

For more information on the management of adult patients with COVID-19 in the emergency department (ED), see the May 2020 issue of *Emergency Medicine Practice*, "Novel 2019 Coronavirus SARS-CoV-2 (COVID-19): An Overview for Emergency Clinicians," as well as additional COVID-19 resources, including translations, podcasts, and updates, available at www.ebmedicine.net/COVID-19

Critical Appraisal of the Literature

A literature search was conducted using PubMed, LitCovid (a compilation of publications related to COVID-19 that is curated by the National Library of Medicine), and medRxiv (a repository of preliminary work). Multiple searches were performed during the writing of this article, as the COVID-19 pandemic is still evolving. All searches used the terms *COVID-19 OR coronavirus AND pediatric OR infant OR child* to identify publications since December 2019 that address the epidemiology or clinical aspects of COVID-19 in children. Most of the publications were single case reports, small case series, or literature reviews. The bulk of these publications were from China. More recent publications, many from Italy and the United States, describe multi-system inflammatory symptoms in children, thought to be associated with COVID-19. Additional limited searches were performed if specific topics of interest were identified (eg, Kawasaki disease shock syndrome [KDSS]).

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Virology and Transmission

SARS-CoV-2 is a novel human coronavirus. There are now a total of 7 coronaviruses known to cause disease in humans. Other members of the family include severe acute respiratory syndrome-related coronavirus 1 (SARS-CoV-1), responsible for the 2003 outbreak in Hong Kong, and Middle East respiratory syndrome-related coronavirus (MERS-CoV), identified during an outbreak on the Arabian Peninsula in 2012. The other 4 human coronaviruses—HCoV-NL63, HCoV-229E, HCoV-OC43, and HCoV-HKU1—are responsible for milder disease in humans: upper respiratory infections, croup, bronchiolitis, and pneumonia.^{1,2}

SARS-CoV-2 likely originated in bats and then infected 1 or more mammal species sold at food markets in Wuhan, China.³ Transmission is primarily via direct inhalation of infected droplets produced when coughing or sneezing. Contact with mucosal surfaces of the eyes, nose, or mouth after touching surfaces contaminated with these respiratory droplets is another mode of transmission.^{4,5} While the virus has been found in stool samples of patients, transmission via the fecal-oral route is unclear.⁴ There is currently no evidence that SARS-CoV-2 passes vertically from mother to child.⁵ Close contact with people infected with SARS-CoV-2 is the main transmission route in children.⁶ Given that children may have only mild symptoms or be asymptomatic, they are less likely to be tested, and, therefore, children may be important in overall transmission patterns of the virus.⁷

Figure 1, page 4 presents a timeline of the COVID-19 pandemic, with a specific focus on pediatric patients.^{8,9}

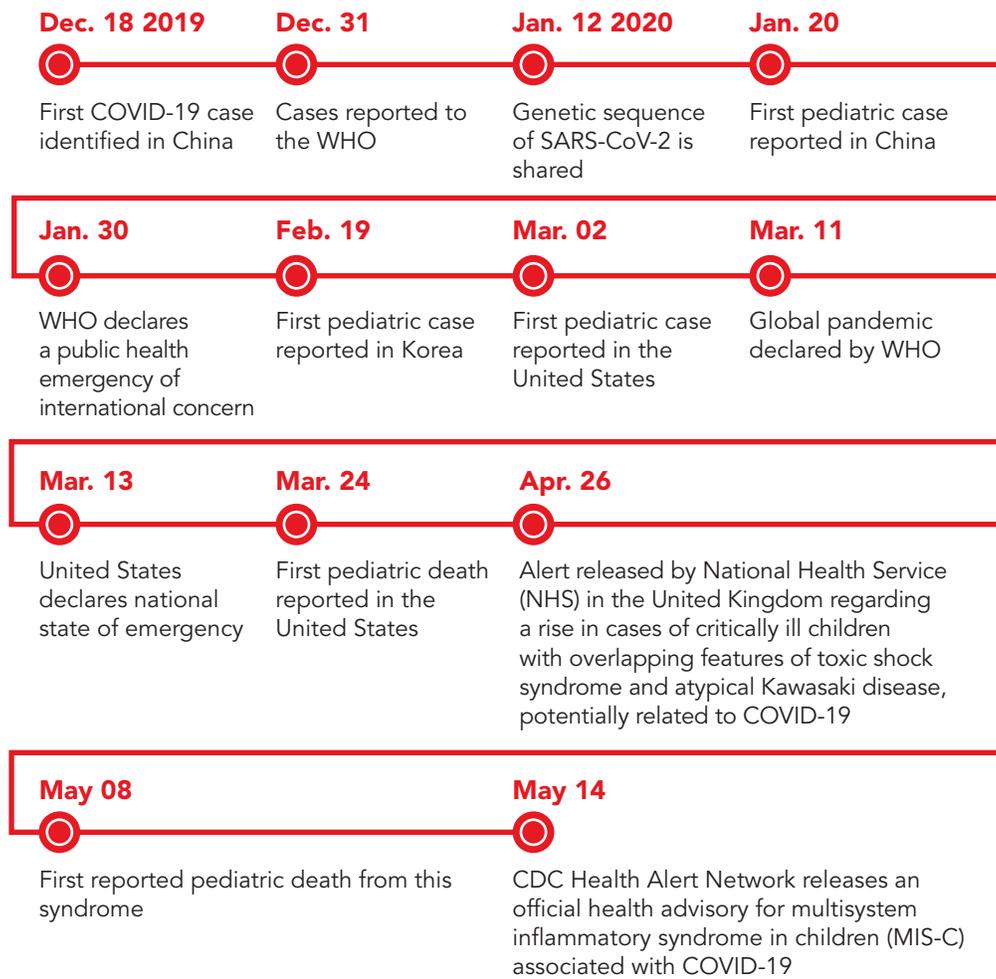
Epidemiology

The current count of confirmed cases and deaths from COVID-19 worldwide can be found at the website of the [Johns Hopkins Coronavirus Resource Center](#). As of May 20, 2020, the United States had the highest numbers of cases (32%) and deaths (29%).¹⁰

Experience with previous coronavirus outbreaks indicates that there is a reduced propensity for these viruses to affect children. Of the patients infected during the 2003 SARS-CoV-1 outbreak, only 6.9% were children, and there were no mortalities in patients aged < 18 years. Additionally, children experienced a milder form of the disease.¹¹ In the MERS-CoV outbreak in 2012, only 2% of cases were children.¹²

Table 1, page 4 summarizes pediatric COVID-19 statistics from various countries.¹²⁻¹⁹ **Table 2, page 5** lists current theories that support the phenomenon of milder disease in children.^{2,11,20-26}

Figure 1. Timeline of the Impact of the COVID-19 Pandemic on Pediatric Patients^{8,9}



Abbreviations: CDC, United States Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WHO, World Health Organization.

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Table 1. Pediatric COVID-19 Statistics in Selected Countries

Country	Cases in Children As a Percent of All Cases
Australia ¹³	2.4 (as of May 3, 2020)
China ¹⁴	2.2 (as of Feb 11, 2020)
United States ^{15,16}	2.3 (as of May 5, 2020)
Italy ^{17,18}	1.2 (as of Mar 20, 2020)
Norway ¹²	3.3 (as of Mar 20, 2020)
Spain ¹⁹	0.8 in Madrid region (as of Mar 16, 2020)

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Table 2. Theories Regarding Susceptibility of Children to COVID-19

Factor	Theory
ACE2 receptor	The ACE2 receptor is necessary for viral entry into cells. ^{11,20,23,24} The development, function, or activity of this protein might be less in children. ^{2,20} ACE2 receptors are upregulated in those with COPD or hypertension, which may partially explain more serious disease in those with comorbid conditions. ²⁴
Role of other viruses	Children are susceptible to a wide variety of viral illnesses. Presence of these viruses on epithelial surfaces can limit infection of SARS-CoV-2 through competition. ²⁵ Also, cross-reactive antibodies resulting from other viral infections, including non-SARS coronaviruses, may be partially protective against SARS-CoV-2. ^{20,26}
Reduced exposures	Children may have fewer opportunities than adults to be exposed to the virus or to those with COVID-19. ^{2,11,22} Additionally, compared to adults, children have had less lifetime exposure to toxins such as cigarette smoke and air pollution, factors which may affect the health of an individual's epithelium. ¹¹
Aging of the immune system	Natural involution of the thymus over time leads to a decline in circulating naïve T cells. Due to this normal process, immune systems in adults are less able to be adaptive than those of children. ²¹
Innate versus adaptive immune system	The innate immune system, which acts earlier than the adaptive immune response, is more active in children, and may prevent more serious illness. ^{20,22,26}
Inflammation	There is evidence that the levels of various proinflammatory cytokines are higher in adults. This may mean that adults experience a more pronounced inflammatory response than children with a similar exposure to SARS-CoV-2. ²³

Abbreviations: ACE2, angiotensin-converting enzyme 2; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Risk Factors for Severe Illness

Data from the United States, China, and Italy reveal that adults with underlying conditions such as diabetes, hypertension, chronic obstructive pulmonary disease, coronary artery disease, cerebrovascular disease, and chronic renal disease, as well as smokers, are at higher risk of severe illness or death from SARS-CoV-2.²⁷ In children, available data regarding the influence of age or comorbidities on severe disease is limited by sample size, although preliminary research suggests an association. The United States Centers for Disease Control and Prevention (CDC) reported that, of 295 children hospitalized with COVID-19, 77% had 1 or more underlying medical conditions.¹⁵ A study of 46 pediatric COVID-19 intensive care unit admissions found that 83% of patients had "significant pre-existing comorbidities."²⁸ Another study found that cardiac, hematologic, neurologic, and oncologic diagnoses were more common in hospitalized children with COVID-19 compared to nonhospitalized children with the disease.²⁹ In both of these studies, a pre-existing diagnosis of asthma was not associated with risk of hospitalization or need for critical care.^{29,30} Studies following cohorts of patients with chronic diseases or those receiving immunosup-

pressive therapy have shown that patients with COVID-19 typically have a mild course.^{31,32} It is possible that young age is a factor that protects against severe effects of COVID-19, even in the presence of chronic disease. More research involving children is needed to understand the interaction between chronic diseases and SARS-CoV-2/COVID-19.

Clinical Presentation

The incubation period of SARS-CoV-2 ranges from 2 to 14 days, with most patients developing symptoms 3 to 7 days after exposure.³³ Overall, children are more likely than adults to be asymptomatic or present with mild disease.^{34,35} The symptoms of COVID-19 overlap with many other pediatric viral infections and can include fever, cough, congestion, sore throat, fatigue, vomiting, and diarrhea. Patients with moderate disease typically have respiratory signs and symptoms: shortness of breath, chest tightness, and/or hypoxemia. These symptoms can progress to acute respiratory distress syndrome.

Frequency data on presenting symptoms mainly exist in small case series from China. In those studies, fever was the most common symptom (57%-100%), followed by cough (45%-100%). Less common symptoms included rhinorrhea, sore throat, headache, diarrhea, and dyspnea.^{8,9} In one study of 171 children who tested positive for SARS-CoV-2, 23% had no symptoms.³⁶

Taste and smell dysfunction or loss has been shown to be associated with COVID-19, with up to 88% of COVID-19 patients in one study reporting these symptoms.⁸ There are no publications that describe the frequency of these symptoms in the pediatric population.

Skin findings in patients with COVID-19 can range from petechiae to papulovesicular rashes to diffuse urticaria and can be confused with rashes of non-COVID-19 conditions.³⁷ These rashes typically appear early in the course of COVID-19 and are thought to be secondary to viral replication or circulating cytokines.³⁸ Chilblains are painful or itchy swellings of the toes and fingers, caused by small-vessel inflammation from repeated exposure to cold. Chilblain-like lesions are being reported in patients with COVID-19. **(See Figure 2, page 7.)** These lesions are more often found in older children and adolescents and tend to appear later in the course.³⁸ The pathophysiology is still unknown, but the symptoms are typically mild and the lesions resolve without treatment.³⁹

Figure 2. Chilblain-like Lesions in Pediatric Patients With COVID-19



Reprinted from David Andina, Lucero Noguera-Morel, Marta Bascuas-Arribas, et al. Chilblains in children in the setting of COVID-19 pandemic. *Pediatric Dermatology*. 2020;10.1111/pde.14215. <https://doi.org/10.1111/pde.14215>, with permission from John Wiley & Sons Ltd.

Neonates and infants with COVID-19 may be asymptomatic or may present with fever, with or without mild cough and congestion. Case reports from China and the United States demonstrate that COVID-19 should be considered in the evaluation of the youngest of pediatric patients, even with minimal symptoms or with fever as the only sign.⁴⁰⁻⁴⁶ A case report from New York City described a 6-month-old boy with fever, cough, and episodes of upward gaze, stiffening, and decreased responsiveness. The evaluation showed that the patient was positive for SARS-CoV-2 without evidence of bacterial infection. This case highlights the broad spectrum of presenting symptoms in neonates and infants and suggests consideration of SARS-CoV-2 in the evaluation of patients with acute events, especially those without classic infectious COVID-19 symptoms.⁴⁷

COVID-19–associated coagulopathy is described as “common” in adult patients with COVID-19, and it is responsible for thrombotic complications including deep vein thrombosis, pulmonary embolism, ischemic stroke, cerebral venous sinus thrombosis, myocardial infarction, and peripheral arterial occlusion.⁴⁸ Highly abnormal D-dimers have been associated with higher thrombosis rates in adult patients with COVID-19.⁴⁸ Emergency clinicians must be aware that signs and symptoms of arterial and/or venous thrombosis might be related to underlying COVID-19, even in the absence of typical symptoms. Also, in patients with confirmed COVID-19, subtle signs of these thrombotic conditions need prompt evaluation. Although there are no publications focused on this phenomenon in pediatric patients, the emergency clinician should consider treatment and/or prophylaxis of thrombosis in the management of children with COVID-19.

Multisystem Inflammatory Syndrome in Children (MIS-C)

Recent media attention has focused on pediatric patients presenting with a multisystem inflammatory syndrome, the clinical presentation of which overlaps with Kawasaki disease (KD), toxic shock syndrome, and severe sepsis.⁴⁹ In late April 2020, the National Health Service (NHS) in the United Kingdom, followed by the New York City Department of Health and Mental Hygiene, released alerts of increasing cases of pediatric patients with symptoms of fever, gastrointestinal symptoms, and signs of shock.^{50,51} Some—but not all—of these patients tested positive for SARS-CoV-2. Many had evidence of cardiac inflammation, with or without coronary arterial dilation.⁴⁹ Since those initial reports, the Royal College of Paediatrics and Child Health, the CDC (see Table 3), and the World Health Organization have all released initial case definitions for this entity. While slightly different, they all include the presence of fever, elevated inflammatory markers, and manifestations of effect on more than one organ system. While there are other names for this syndrome, this article will use the CDC term, multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19.

Table 3. CDC Case Definition for MIS-C

Criteria

- An individual aged < 21 years presenting with fever^a, laboratory evidence of inflammation^b, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥ 2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic, or neurological); **AND**
- No alternative plausible diagnoses; **AND**
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms

^aFever > 38.0°C for ≥ 24 hours, or report of subjective fever lasting ≥ 24 hours

^bIncluding, but not limited to, 1 or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes, and low albumin

Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

Abbreviations: CDC, United States Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Source: United States Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). 2020.

Available at: <https://emergency.cdc.gov/han/2020/han00432.asp>

It is currently not known whether MIS-C is the same entity as KDSS, a condition described well before the current COVID-19 pandemic. Patients with KDSS meet the clinical criteria for KD but also show a sustained decrease ($\geq 20\%$) in normal systolic blood pressure for age or have signs of poor

perfusion.⁵² Research on KDSS has shown that the diagnosis may not be evident at the onset. In one case series, shock developed at a mean of 6 days after illness onset.⁵³ In another series, 39% of patients eventually diagnosed with KDSS were not recognized as having a diagnosis of KD at presentation.⁵⁴ Compared to patients with KD, those with KDSS tend to be older, have significantly higher inflammatory markers, and a higher rate of cardiac involvement,^{52,54,55} and they may develop laboratory evidence of coagulopathy.⁵² Because the levels of interleukin (IL)-6, IL-10, and interferon (IFN)-gamma are significantly elevated in KDSS, one author proposed that these levels be used to distinguish the 2 entities.⁵⁵ Several studies have documented significant rates of resistance to intravenous immunoglobulin (IVIG)—the usual treatment for KD—among their series of KDSS patients.⁵²⁻⁵⁴

The first case series of MIS-C from the United Kingdom described 8 patients with fever, rash, conjunctivitis, edema, extremity pain, and significant gastrointestinal symptoms. All patients had fluid-refractory shock requiring vasopressors. There were minimal respiratory symptoms. Four of the children had family exposure to SARS-CoV-2, but none tested positive (via polymerase chain reaction testing) during their inpatient stay. Two children tested positive for SARS-CoV-2 after discharge. The majority of patients had some element of cardiac dysfunction with elevated inflammatory markers and troponins.⁵⁶

A recent publication from Bergamo, Italy compared 19 patients who presented with Kawasaki-like illness before the pandemic to 10 patients who presented with the illness since the pandemic started.⁵⁷ The patients seen since the start of the outbreak were older (average age of 7.5 years vs 3 years). Half had incomplete features of KD. Non-Kawasaki signs and symptoms included diarrhea, meningeal signs, and clinical signs of hypoperfusion. The majority exhibited neutrophilia, hyponatremia, hypertriglyceridemia, elevated erythrocyte sedimentation rate (ESR), and elevated levels of C-reactive protein (CRP), ferritin, and pro-BNP (B-type natriuretic peptide). Only 2 had nasal swabs positive for SARS-CoV-2. Those 2 patients and 6 others (total of 8 of 10 patients) had positive serologies. Five of 10 patients had positive chest x-rays. Six of 10 patients had abnormal echocardiography.

Knowledge about MIS-C, and its relationship to KD, is evolving. Fever, gastrointestinal symptoms, and signs and symptoms of KD (rash, conjunctivitis, oral erythema, extremity changes) have been well documented. Many patients present with clinical signs of hypoperfusion or hypotension, but this extreme presentation seems to be less frequent. Laboratory findings indicate evidence of inflammation. Cardiac markers (troponin, BNP) are typically

elevated. Echocardiography is frequently abnormal. It is distinct from KD in that patients with MIS-C tend to be older than those with classic KD.

While MIS-C is temporally related to the SARS-CoV-2 pandemic, it may not be specific to this virus, but rather a clinical manifestation of hyperinflammation that appears weeks after exposure to the virus, as evidenced by negative nasal swabs but positive serologies.^{56,57} As KD and KDSS were described before the pandemic, it may be that different viruses or families of viruses can activate this hyperinflammatory response in children, not just SARS-CoV-2. There may be factors specific to each child, yet to be determined, that play a role in this process. What we know about SARS-CoV-2 and its relationship to MIS-C will continue to be elucidated by ongoing worldwide research efforts.

Differential Diagnosis

The diagnosis of COVID-19 does not completely rule out other infections. It is reported that children have a higher likelihood than adults of co-infection with bacteria or other viruses.²⁴ Therefore, the differential diagnosis of patients with signs and symptoms of respiratory distress should include other respiratory viruses (respiratory syncytial virus, influenza, parainfluenza, adenovirus, metapneumovirus) and bacterial pneumonia, including that caused by *Mycoplasma* and *Chlamydia*.⁵⁸ Of patients presenting with shock-like syndrome, it is important to consider KDSS, toxic shock syndrome, bacterial sepsis, and myocarditis.

Diagnostic Studies

Laboratory Studies

Laboratory abnormalities in adults with COVID-19 are described by other authors.^{59,60} In children with COVID-19, information regarding laboratory findings initially came from single-center studies out of China. Given the low numbers of pediatric patients sick with COVID-19, the numbers of patients in these studies are small, and the laboratory findings are not typically classified by severity of illness. In a study of 9 patients, children had normal or decreased white blood cell (WBC) counts, elevated levels of creatine kinase myocardial band (CK-MB) and transaminases, and normal levels of CRP, procalcitonin (PCT), ESR, and IL-6.⁶¹ In another study of 36 children, WBC count was lower and PCT, D-dimer, and CK-MB levels were higher in moderate cases compared with mild cases.³⁴ Patients with cardiac involvement were shown to have some combination of elevated levels of troponin, BNP, and CK-MB.¹¹

A recent study from New York City compared 2 groups of children with COVID-19 who were admitted to the hospital. Researchers found that ad-

mission to a critical care unit was associated with lower platelet counts and higher CRP, PCT, and BNP compared to those admitted to inpatient floors.³⁰

Patients with MIS-C all had evidence of inflammation with abnormal values of some combination of CRP, ESR, fibrinogen, PCT, D-dimer, ferritin, lactate dehydrogenase, IL-6, neutrophils, lymphocytes, and albumin. Additionally, they can present with—or develop—acute kidney injury, transaminitis, anemia, thrombocytopenia, hypertriglyceridemia, proteinuria, coagulopathy, and evidence of cardiac dysfunction (abnormal levels of troponin, BNP, or CK-MB).^{62,63}

Viral Testing

Reverse transcription-polymerase chain reaction (RT-PCR) is the current reference standard for diagnosis of COVID-19. The virus can be detected in respiratory secretions, blood, urine, and stool.⁵⁸ The occurrence of cross-reactivity with other pathogens and the unknown timing of antibody production after illness onset are considerations that make the role of serology testing unclear.⁶⁴ Antibody testing is not recommended for diagnosis of acute disease, but serologic testing probably reflects past SARS-CoV-2 infection, especially when testing for acute disease is negative. This serology is an important tool in determining the relationship of COVID-19 to MIS-C.

Since the start of the pandemic, the United States Food and Drug Administration (FDA) has released emergency use authorizations to commercial laboratories and academic medical centers for both acute viral and serologic tests. The viral testing landscape continues to evolve.

The current CDC recommendations for priorities for testing are listed in **Table 4**.

Table 4. Priorities for COVID-19 Testing (Nucleic Acid or Antigen)

High Priority

- Hospitalized patients **with** symptoms
- Healthcare facility workers, workers in congregate living settings, and first responders **with** symptoms
- Residents in long-term care facilities or other congregate living settings, including prisons and shelters, **with** symptoms

Priority

- Persons **with** symptoms of potential COVID-19 infection, including: fever, cough, shortness of breath, chills, muscle pain, new loss of taste or smell, vomiting or diarrhea, and/or sore throat
- Persons **without** symptoms who are prioritized by health departments or clinicians, for any reason, including but not limited to: public health monitoring, sentinel surveillance, or screening of other asymptomatic individuals according to state and local plans

Source: United States Centers for Disease Control and Prevention. Evaluating and testing persons for coronavirus disease 2019 (COVID-19). 2020. Available at: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-criteria.html>

Diagnostic Imaging

Chest X-Ray

Chest x-rays should be considered in children with hypoxemia or respiratory distress.⁴ Adult studies have shown that chest x-ray findings can include consolidations and ground-glass opacities, typically in the periphery and lower lung zones.⁴ Pleural effusion is uncommon.⁵⁸ The types of findings and their location are likely the same for pediatric patients.

Computed Tomography

At the start of the pandemic, clinicians in China were using computed tomography (CT) as a diagnostic tool for children. While not recommended for routine use (due to concerns regarding exposure to radiation), this practice has provided information about pediatric-specific CT findings in patients with COVID-19.⁶⁴ As in adults, asymptomatic children may have abnormal findings on CT.^{65,66} The most frequent findings on CT are ground-glass opacities, mostly in the periphery or posterior lungs.⁶⁷ Pediatric patients are less likely to have bilateral disease and typically have fewer and smaller lesions than adults, perhaps due to milder disease.⁶⁸ In critical patients, early findings can progress to increasing size and number of lesions, multilobar involvement, and larger consolidations.⁶⁹

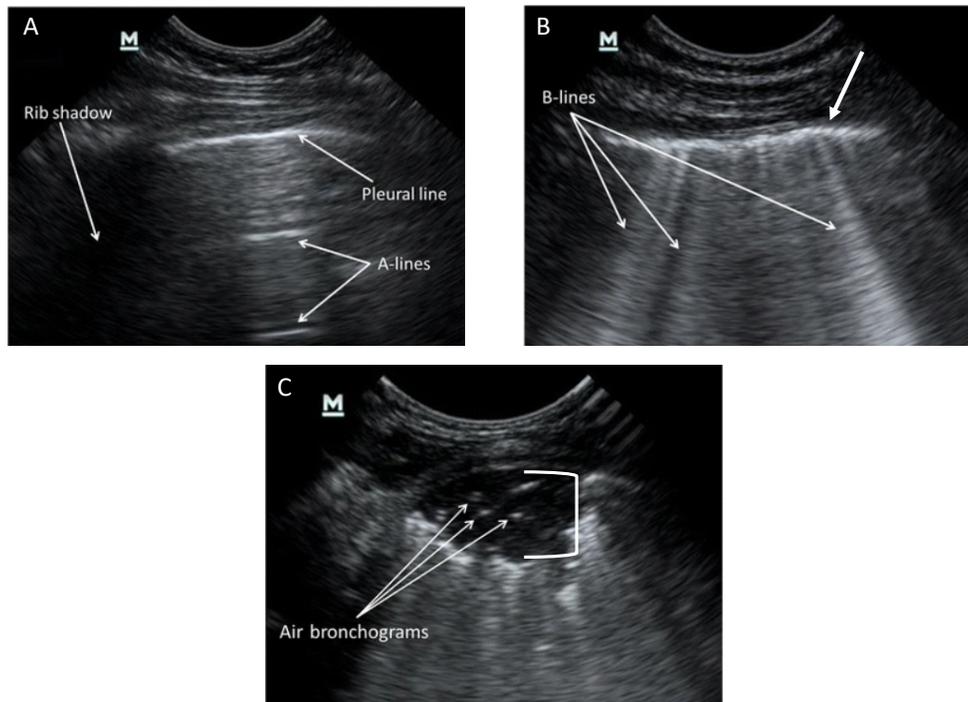
Ultrasound

Using ultrasound to diagnose lung disease in patients with COVID-19 has multiple benefits: minimizing radiation exposure, reducing patient movement within the hospital, minimizing medical device contamination, and minimizing healthcare worker exposure. Studies have shown that in the setting of COVID-19, lung ultrasound findings correlate with CT results.⁷⁰ At one pediatric center, the use of a wireless transducer (used by the examining clinician) paired with a tablet (outside the room) has minimized healthcare worker exposure and safely minimized the use of chest x-ray and CT in the evaluation of these patients.^{71,72} Patients with COVID-19 show a range of abnormalities on ultrasound that are similar to those found in adults: irregular or thickened pleural lines, scattered or confluent B lines, and consolidations.^{59,73} **Figure 3, page 13** depicts these abnormalities in a pediatric patient. **Figure 4, page 14** demonstrates the correlation of ultrasound findings with worsening lung disease.

Management

Carlotti and colleagues list the 4 principles of the management of children with COVID-19 as: (1) early identification, (2) early isolation, (3) early diagnosis, and (4) early treatment.⁵⁸ Application of these principles includes screening for risk factors for COVID-19 before entry into the clinical space, expediting room placement into a private room, use of appropriate per-

Figure 3. Pediatric Lung Ultrasound Findings



- A: Normal pediatric lung. Smooth, hyperechoic pleural line and A-lines (normal reverberation artifacts of the pleural line).
- B and C: Abnormal findings that can be seen in pediatric COVID-19 respiratory disease.
- B: Irregular pleural line (arrow), multiple B-lines.
- C: Subpleural consolidation (bracket) with air bronchograms. The pleural line (top of the bracket) is hypoechoic. Multiple B-lines.

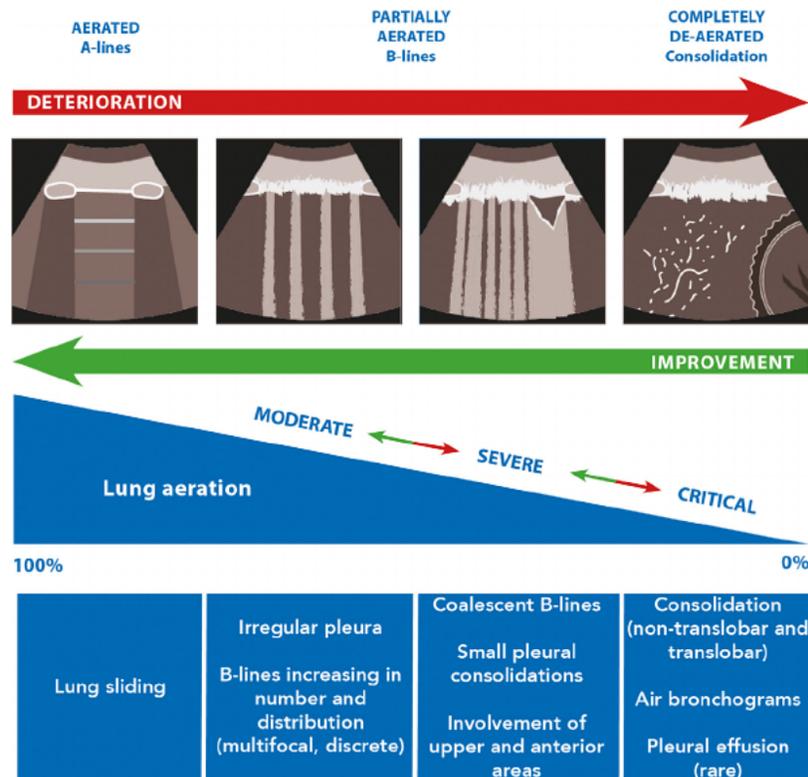
Source: Jacob A. M. Stadler, Savvas Andronikou, and Heather J. Zar. Lung ultrasound for the diagnosis of community-acquired pneumonia in children. *Pediatric Radiology*. 2017;47(11):1412-1419. <https://doi.org/10.1007/s00247-017-3910-1> Used under the Creative Commons Attribution 4.0 International License. <http://creativecommons.org/licenses/by/4.0/>

sonal protective equipment by clinicians, viral testing to confirm diagnostic suspicion, and supportive care as indicated by the clinical scenario.

Supportive care is the overarching concept for management of COVID-19, with focus on addressing fever, pain, and fluid status, as well as the cardiac and respiratory condition of the patient. The approach to the provision of this care, especially for those with respiratory insufficiency, has changed during this pandemic, but the overall goals of minimizing the spread of infection between patients and minimizing healthcare worker exposure to possible infection are at the heart of these new concepts. For more information on these altered approaches, see "The Impact of COVID-19 on the Practice of Pediatric Emergency Medicine," available at: www.ebmedicine.net/COVID-PEMP

Antibiotics should be used in patients with evidence of secondary bacterial infection and/or those who are critically ill, but their use is not routinely indicated.⁵⁸ Corticosteroids may have a role in specific clinical situations

Figure 4. Correlation of Ultrasound Findings With Worsening Lung Disease



Reprinted from M. J. Smith, S. A. Hayward, S. M. Innes, et al. (2020), Point-of-care lung ultrasound in patients with COVID-19 – a narrative review. *Anaesthesia*. 2020;10.1111/anae.15082. <https://doi.org/10.1111/anae.15082>, with permission from John Wiley & Sons Ltd.

(eg, in patients with acute heart failure).⁷⁴ While there is no indication for corticosteroids during initial ED management, there should be no concern for their use to treat specific indications in patients with COVID-19, such as bronchospasm for those with pre-existing asthma.^{58,75}

Although clinical guidelines are still evolving, initial ED management of MIS-C should include broad-spectrum antibiotics, fluid resuscitation, and/or vaso-pressors for circulatory support. Diagnostic studies should be used to evaluate for signs of involvement of a wide variety of organ systems. Subsequent management of critically ill patients, as well as those with mild symptoms, can be informed by input from pediatric specialists in cardiology, infectious disease, rheumatology, and hematology, regarding the various aspects of inflammation, cardiac involvement, and coagulopathy.

Pharmacologic Therapies

Nonsteroidal Anti-inflammatory Drugs

Anecdotal reports suggested that nonsteroidal anti-inflammatory drugs (NSAIDs) should not be used for pain or fever in patients with COVID-19. This was due to concern that NSAIDs cause upregulation of angiotensin-converting enzyme 2 (ACE2) receptors in human cells, thus providing more receptors for viral binding and potentiating severe disease. To date,

no reports or studies have linked NSAID use with severe or worsening COVID-19,⁷⁶ and there is no formal recommendation that medications like ibuprofen be avoided.

Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers

Children with chronic disease such as heart failure, hypertension, kidney disease, or diabetes may routinely take angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs). There is a theoretical concern that these medications may increase ACE2 receptor expression and may increase the likelihood of contracting COVID-19 or having a worse course.⁷⁶ This is not proven in humans, nor has it been studied in the setting of COVID-19.⁷⁷ In fact, it may be true that SARS-CoV-2 causes the downregulation of ACE2 expression, such that ACEIs and ARBs are being investigated as potential treatments to mitigate organ injury.⁷⁷ There has been no formal guidance issued to recommend stopping these medications, especially given the possible risk to the patient by withdrawing a standing medication.⁷⁶

Antiviral Medications

On May 1, 2020, the FDA issued an emergency use authorization for remdesivir for the treatment of suspected or laboratory-confirmed COVID-19 in adults and children hospitalized with severe disease. No other specific treatments have been approved by the FDA, but many are being used for the sickest of patients, based on evidence obtained from use in previous coronavirus outbreaks (SARS-CoV-1, MERS-CoV) or clinician familiarity with medications used for other indications in pediatric medicine. Antiviral medications and other immune-modulating treatments should be considered only for the sickest hospitalized patients, as most patients improve with supportive care. They may be appropriate for patients who are critically ill with COVID-19 but should be considered on a case-by-case basis, with special consideration given to the presence of clinical trials evaluating their efficacy and safety. Pediatric infectious disease specialists should be consulted before their use.⁷⁸

Other Agents

Other agents being studied for treatment of COVID-19 include favipiravir, galidesivir, ribavirin, interferon beta, and monoclonal antibodies to SARS-CoV-2. Since stabilization is the focus of emergency medicine in the care of these severely ill children, treatments under investigation may not necessarily be initiated in the ED setting, but are more appropriate for the inpatient services managing patient care. However, it is important for the emergency clinician to be informed of the range of treatments under investigation. See **Table 5, page 16** for a list of possible treatments for COVID-19.^{1,6,64,76,78-82}

Table 5. Possible Treatments for COVID-19

Medication	Reasoning for Use/Comments
Remdesivir	<ul style="list-style-type: none"> • Experience with treatment of Ebola virus disease^{76,78} • Blocks RNA replication by blocking action of viral RNA-dependent RNA polymerase^{76,78}
Chloroquine/ hydroxychloroquine	<ul style="list-style-type: none"> • Approved for certain indications in children⁷⁸ • Combination with azithromycin can increase the likelihood of QT prolongation^{76,78} • These medications are associated with increased in-hospital mortality and risk of new ventricular arrhythmia in adults⁸² • Inhibits viral entry into human cells, inhibition of viral binding via the ACE2 receptor^{1,78} • Need to closely monitor patients with glucose-6-phosphate dehydrogenase deficiency⁷⁸
Lopinavir-ritonavir	<ul style="list-style-type: none"> • Protease inhibitor • Currently used for pediatric human immunodeficiency virus⁷⁸ • Experience from SARS-CoV-1 and MERS-CoV outbreaks^{76,80} • Nonrandomized trials show benefit in adults^{1,78}
Interferon alpha	<ul style="list-style-type: none"> • Inhibits viral entry into cells, promotes proliferation of cytotoxic T cells⁶ • Studies from China show benefits in prevention of shortened disease duration and reduction of viral load in bronchiolitis; viral pneumonia; upper respiratory infections; and hand, foot, and mouth disease⁶ • Recommended for treatment of children in China⁸⁰ • Available in China and elsewhere as nebulization or nasal spray^{6,64}
Tocilizumab	<ul style="list-style-type: none"> • Monoclonal antibody that blocks IL-6 • Used in systemic juvenile idiopathic arthritis • Insufficient evidence for use in patients with COVID-19⁷⁶
Convalescent plasma	<ul style="list-style-type: none"> • Source of antibodies to SARS-CoV-2 • Used successfully in SARS-CoV-1 and MERS-CoV outbreaks⁷⁹ • Timing of administration, dosing for children, and identification of neutralizing antibodies still under investigation⁷⁹
Intravenous immunoglobulin	<ul style="list-style-type: none"> • Polyclonal antibodies, with potential for protective antibodies against SARS-CoV-2⁷⁶
Anakinra	<ul style="list-style-type: none"> • IL-1 receptor antagonist that was approved in 2001 in the United States for use in rheumatic arthritis; IL-1 is a proinflammatory cytokine⁸¹ • It has been used with success in the treatment of intravenous immunoglobulin-resistant Kawasaki disease⁸¹

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease 2019; IL, interleukin; MERS-CoV, Middle East respiratory syndrome-related coronavirus; RNA, ribonucleic acid; SARS-CoV-1, severe acute respiratory syndrome-related coronavirus 1; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Disposition and Outcomes

Data from the CDC as of March 16, 2020 found that 2% to 3% of pediatric patients with positive SARS-CoV-2 testing required hospitalization.⁸³ As of March 30, hospitalization rates for children were 0.3/100,000 in patients aged 0 to 4 years and 0.1/100,000 in patients aged 5 to 17 years.⁸⁴ Of pediatric patients who are hospitalized with COVID-19, the percent admitted to an intensive care unit range from 9.7% to 28.3%.^{19,29,30} Reports from China show that 1.8% to 8% of children hospitalized with COVID-19 require

intubation.⁸ At the time of this publication, there had been relatively few reported cases of pediatric deaths attributed to COVID-19. As of May 20, 2020, the National Center for Health Statistics reported 88 COVID-19–related deaths among those aged ≤ 25 years. A minority of those deaths (16%) occurred among those aged ≤ 15 years.¹⁶

Special Considerations for Pediatric Patients During the COVID-19 Pandemic

Poisonings

Data from the National Poison Data System shows that there were 45,550 calls to poison centers related to exposure to cleaners and disinfectants from January to March 2020. Compared to data during the same time period in 2018 and 2019, this represents a 16% and 20% increase in call volume, respectively. The highest number of these exposures occurred in children aged < 5 years. Bleaches accounted for the largest percentage of the increased cases, followed by non–alcohol-based disinfectants and hand sanitizers. The increase in call volume occurred at the beginning of March, similar in timing to the start of stay-at-home orders and cleaning supply shortages nationwide.⁸⁵ These data highlight the importance of anticipatory guidance for parents on home safety, focused on prevention of exposures to potentially toxic substances.

Mental Health and Violence

The existence of the pandemic, with its resultant social distancing, stay-at-home orders, school closures, and widespread economic disruption has created a myriad of stressors separate from individual health status. These situations can create environments conducive to increased rates of mental health conditions, substance use, suicide, nonaccidental trauma, and neglect.^{86,87} ED staff and clinicians need to understand this relationship and have a low threshold for probing family dynamics and sources of stress.

It is known from previous public health emergencies that violence against children increases with school closures.^{88,89} Caregivers may not understand that oppositional behavior and limit-testing are normal reactions of children to changes in routine, stress, or uncertainty.⁹⁰ Parents' own stress or anxiety may prevent them from caring for children adequately or appropriately.⁹¹ When schools are closed, children have less exposure to external oversight, and the largest source of reports to child protective services is silenced.^{90,92} Additionally, there is evidence that alcohol sales have increased since the start of the pandemic, with rising use in the home setting, due to closures of restaurants and bars.⁹³ These factors can exacerbate an already stressful situation, leading to a situation in which children are at increased risk for nonaccidental trauma or neglect.

Children and caregivers with psychiatric diagnoses may have difficulty accessing care due to concerns about overloaded hospitals or difficulty navigating telemedicine appointments. Regular medication or therapy maintenance appointments may be deferred and medications might not be refilled on schedule, leading to interruption in treatment.⁹⁴ One study found 25% of Chinese college students had symptoms of anxiety secondary to the pandemic.⁹⁵ In a survey of Chinese primary students during school closures, 23% disclosed depressive symptoms and 17% reported anxiety symptoms.⁹⁶ A survey of pediatric oncology patients in Italy showed that these patients feel that the pandemic is dangerous, and they are afraid of catching the virus and having severe complications. They are also aware of their family's concern for their health, which can provoke anxiety.⁹⁷ **Table 6** summarizes some COVID-19–related factors that can increase stress on children and their families.^{91,98-101}

Table 6. Factors That Can Increase Stress on Children and Their Families^{91,98-101}

General factors

- Uncertainty about the future
- Inadequate information
- Overwhelming media coverage
- Exposure to stress/anxiety of others

Economic factors

- Food insecurity
- Housing insecurity
- Loss of health insurance
- Family financial loss

Health-related factors

- Fear for family who are frontline workers
- Irregular sleep
- Poor diet and exercise
- Death or illness of family members
- Opioid and alcohol abuse

Results of school/work closures, stay-at-home orders, and social distancing

- Changes to daily routine
- Social isolation/boredom
- Lack of personal space
- Cyber-based violence
- Reduced access to community support programs
- Reduced access to reproductive health services
- Reduced access to mental health resources

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Childhood Immunizations

Recent information has been released showing a decline in childhood immunizations during the pandemic. The data have shown a decrease in the proportion of children who are up-to-date on vaccinations for their age, as well as a decrease in the number of vaccine doses administered, compared to previous time periods.¹⁰² This is not a surprising consequence of stay-at-home orders. Telemedicine visits can be used for well-child visits

during this time, but immunizations require an in-person visit to the pediatrician's office.

There is a potential for outbreaks of vaccine-preventable illnesses if there is not a concerted effort to update delayed vaccines. Emergency clinicians should reinforce with triage staff and trainees the importance of asking about and documenting vaccine status in each patient. Vaccine delays should be considered when formulating differential diagnoses.

SARS-CoV-2 Vaccine

As SARS-CoV-1 and SARS-CoV-2 have similar viral structures and use the same ACE2 receptor for cell entry, the lessons learned during the 2003 SARS-CoV-1 outbreak in Asia are informing current vaccine development initiatives.³ The main target for vaccine development is the surface spike glycoprotein (S-protein) that is necessary for viral entry into human cells.¹ Similar to influenza, coronaviruses are likely to rapidly mutate, a fact that may complicate vaccine development.¹

Summary

Our understanding of COVID-19 in children is evolving. Given our knowledge of previous coronavirus outbreaks, it is not surprising that children fair better than adults in terms of severity of illness. Limited data available thus far show that the majority of children present with fever and respiratory symptoms. But, as in adults, there are a wide variety of presentations, including severe illness. Clinical presentations may be primarily cardiac, gastrointestinal, hematologic, or neurologic in nature. The recently described MIS-C seems most related to a hyperinflammatory state triggered by SARS-CoV-2. Our understanding of this syndrome will surely evolve in the months to come. From the ED perspective, care of pediatric patients with COVID-19 is primarily supportive, and may require consultation with other pediatric specialty services. The pandemic has had a multitude of unintended effects on patients and families. Continued mental health screening of all pediatric emergency department patients is important, as they are likely affected by the pandemic whether or not their viral test is positive.

Key Points

- Most children with COVID-19 are asymptomatic or present with mild disease. Fever and cough are the most frequent symptoms.
- Skin findings are nonspecific, but can range from petechiae to papulovesicular rashes to diffuse urticaria. Chilblain-like lesions are sometimes seen.
- The differential diagnosis of mild COVID-19 includes typical respiratory

- viruses and bacteria that cause upper respiratory tract infections and bacterial pneumonia.
- MIS-C presents with fever, evidence of inflammation, and multiorgan involvement.
 - Chest x-rays and CT scans can show ground-glass opacities or small consolidations, mostly in the periphery or posterior lungs. Lung ultrasound, which may be more appropriate for patients in isolation, can show irregular or thickened pleural lines, scattered or confluent B lines, and consolidations.
 - Most patients can be managed with supportive care. Management of MIS-C should involve various pediatric subspecialists.
 - There is insufficient evidence to support routine use of any antiviral medications or other immune-modulating treatments in children. Studies involving these medications are ongoing.
 - A variety of non-virus-related concerns have arisen secondary to social distancing, stay-at-home orders, and school closures: increased calls to poison control, negative effects on the mental health of patients and families, exacerbations of mental health disorders, and increased concern for nonaccidental trauma and child neglect.

Resources

COVID-19, Pediatric Patients

- [AAP News: COVID-19 Outbreak](#)
- [AAP: Critical Updates on COVID-19](#)
- [ACEP: COVID-19 & Pediatric Patients](#)
- [CDC: Information for Pediatric Healthcare Providers](#)
- [Pediatric Emergency Medicine Database](#)
- [Red Book Online \(AAP\): SARS-CoV-2](#)

COVID-19, All Patients

- [ACEP COVID-19 Field Guide](#)
- [ACEP: COVID-19](#)
- [CDC: COVID-19](#)
- [Internet Book of Critical Care \(IBCC\): COVID-19](#)
- [Johns Hopkins University Coronavirus Resource Center](#)
- [National Institutes of Health: COVID-19 Treatment Guidelines](#)
- [Pan American Health Organization \(PAHO\): COVID-19](#)
- [Rebel EM: COVID-19](#)
- [WHO: COVID-19 Pandemic](#)

For Patients and Families

- [CDC: COVID-19/Helping Children Cope](#)
- [CDC: Talking with children about Coronavirus Disease 2019](#)
- [HealthyChildren.org \(AAP\): COVID-19 patient information](#)
- [National Child Traumatic Stress Network](#)
- [Childhelp National Child Abuse Hotline: 800-4-A-CHILD](#)
- [National Domestic Violence Hotline: 800-799-7233](#)
- [National Suicide Prevention Lifeline: 800-273-8255](#)
- [National Parent Hotline: 855-427-2736](#)

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study is included in bold type following the references, where available. The most informative references cited in this paper, as determined by the authors, are noted by an asterisk (*) next to the number of the reference.

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