

Multisystem Inflammatory Syndrome in Children in the Critical Care Setting

Kristin Atlas, MSN, CPNP-AC, ACCNS-P

Jessica Strohm Farber, DNP, CPNP-AC

Kerry Shields, MSN, CPNP-AC

Ruth Lebet, PhD, RN, CCNS-P

BACKGROUND Multisystem inflammatory syndrome in children is a new syndrome that has been hypothesized to be connected with the COVID-19 pandemic. Children are presenting—likely after SARS-CoV-2 infection or exposure—with vague symptoms including fever, gastrointestinal distress, and/or rash.

OBJECTIVE To review what is currently known about multisystem inflammatory syndrome in children, including physiology, signs and symptoms, laboratory and imaging findings, treatment options, and nursing considerations in critical care settings.

METHODS This integrative review was conducted using the keywords *multisystem inflammatory syndrome in children*, *Kawasaki-like syndrome*, *COVID*, *COVID-19*, and *SARS-CoV-2*. Initially, 324 articles were found. All were screened, and 34 were included. Eight articles were added after hand-searching and weekly literature searches were conducted.

DATA SYNTHESIS Multisystem inflammatory syndrome in children is a newly identified syndrome, thus information on diagnosis, treatment, and outcomes is available but evolving. Many aspects of nursing care are important to consider with regard to this illness, including COVID precautions, physical assessments, medication administration, and timing of blood sampling for laboratory testing as well as other standard intensive care unit considerations. Providing anticipatory guidance and support to patients and their families is also important.

CONCLUSION Critical care nurses must remain informed about advances in the care of patients with multisystem inflammatory syndrome in children, as these patients are often seen in critical care environments because of their high risk of cardiovascular failure. (*Critical Care Nurse*. Published online October 18, 2021)

Since its onset, the COVID-19 pandemic has dramatically affected critical care in adult and pediatric populations and has provoked severe respiratory symptoms in adults.¹ It was not until April 2020 that medical teams in Europe noticed that the SARS-CoV virus might be affecting children differently when cohorts of children began presenting with vague symptoms such as fever, abdominal pain, and/or symptoms often seen with a Kawasaki disease–like rash.^{2,3} A connection to the SARS-CoV-2 virus was hypothesized when an increase in cases was observed several weeks after a rise in community virus infection rates.^{4,5} In May 2020, the Centers for Disease Control and Prevention (CDC) named this syndrome multisystem inflammatory syndrome in children (MIS-C).⁶ The syndrome is also

Table 1 Definitions of multisystem inflammatory syndrome in children

Centers for Disease Control and Prevention ⁶	World Health Organization ⁷	Royal College of Paediatrics and Child Health ⁸
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 exposure to a suspected or confirmed COVID-19 case within the 4 weeks before onset of symptoms	Children and adolescents aged 0-19 years with fever ≥ 3 days AND 2 of the following: • Rash or bilateral nonpurulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet) • Hypotension or shock • Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP) • Evidence of coagulopathy (by PT, PTT, elevated D-dimers) • Acute GI problems (diarrhea, vomiting, or abdominal pain) AND elevated markers of inflammation such as ESR, CRP, or procalcitonin AND no other obvious microbial cause of inflammation, including bacterial sepsis or staphylococcal or streptococcal shock syndromes AND evidence of COVID-19 (RT-PCR, antigen test, or serology positive) or likely contact with patients with COVID-19	A child presenting with persistent fever, inflammation (neutrophilia, increased CRP, and lymphopenia), and evidence of single-organ or multiorgan dysfunction (shock, cardiac, respiratory, renal, GI, or neurological disorder) with additional features, which might include children fulfilling full or incomplete criteria for Kawasaki disease; exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, and infections associated with myocarditis such as enterovirus; and positive or negative SARS-CoV-2 PCR test.

Abbreviations: CRP, C-reactive protein; ECHO, echocardiogram; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; NT-proBNP, N-amino terminal fragment of the prohormone brain natriuretic peptide; PT, prothrombin time; PTT, partial thromboplastin time; RT-PCR, reverse transcriptase–polymerase chain reaction.

^a Fever >38.0 °C for ≥ 24 hours or report of subjective fever lasting ≥ 24 hours.

^b Including, but not limited to, 1 or more of the following: elevated CRP, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, or interleukin 6; elevated neutrophils; reduced lymphocytes; and low albumin.

recognized and defined by the World Health Organization (WHO)⁷ and the Royal College of Paediatrics and Child Health⁸ (Table 1). Because MIS-C can mimic other

Authors

Kristin Atlas is a clinical nurse specialist in the infant transitional care unit, Children's Hospital of Philadelphia, and a clinical instructor for the undergraduate BSN program, University of Pennsylvania School of Nursing, Philadelphia, Pennsylvania.

Jessica Strohm Farber is a pediatric critical care nurse practitioner, Children's Hospital of Philadelphia, and program director of the pediatric acute care and neonatal nurse practitioner programs, University of Pennsylvania School of Nursing.

Kerry Shields is a pediatric acute care nurse practitioner in the pediatric intensive care unit and progressive care unit, Children's Hospital of Philadelphia, and associate program director of the pediatric acute care nurse practitioner program, University of Pennsylvania School of Nursing.

Ruth Lebet is a nurse-scientist in the Center for Nursing Research and Evidence-Based Practice, Children's Hospital of Philadelphia, and lecturer, University of Pennsylvania School of Nursing.

Corresponding author: Kristin Atlas, MSN, CPNP-AC, ACCNS-P, Children's Hospital of Philadelphia, University of Pennsylvania School of Nursing, 1525 Ellsworth St, Philadelphia, PA 19146 (email: kristin12atlas@gmail.com).

To purchase electronic or print reprints, contact the American Association of Critical-Care Nurses, 27071 Aliso Creek Rd, Aliso Viejo, CA 92656. Phone, (800) 899-1712 or (949) 362-2050 (ext 532); fax, (949) 362-2049; email, reprints@aacn.org.

conditions commonly seen in intensive care units (ICUs), critical care nurses should be informed about this evolving body of knowledge.⁵ In this article, we review what is currently known about MIS-C, including epidemiology, physiology, signs and symptoms, laboratory and imaging findings, treatment options, and nursing considerations in critical care settings.

Methods

In conducting this review, we searched the PubMed, Scopus, and Web of Science databases as well as the websites of the CDC, WHO, and nationally ranked pediatric hospitals. We also reviewed alerts from professional organizations, including the Society of Critical Care Medicine, National Association of Pediatric Nurse Practitioners, and American Association of Critical-Care Nurses. We used Google and Google Scholar to conduct weekly broad searches for new material on this emerging entity, as many manuscripts were being published online ahead of print. Search terms included keywords and controlled vocabulary. However, controlled vocabulary for searching was limited because of the novelty of COVID-19. The following terms were used alone and in combination:

multisystem inflammatory syndrome in children, Kawasaki-like syndrome, COVID, COVID-19, SARS-CoV-2. Publications were included if they focused on MIS-C in pediatric patients. No restrictions were placed on study design or peer-review status. Publications without a focus on MIS-C or that were not published in English were excluded. All team members participated in screening and data abstraction. Electronic search strategies yielded 324 relevant publications after duplicates were removed. Review of all abstracts narrowed the search to 65 relevant publications. Thirty-four met inclusion criteria and were reviewed in full text. Forward citation searching and hand-searching reference lists from relevant publications identified an additional 8 articles.

Data Synthesis

Epidemiology

Multisystem inflammatory syndrome in children occurs predominantly in healthy children aged 1 to 14 years, with a median age of 9 years, and appears to be more prevalent in children with obesity.^{9,10} It disproportionately affects Latino and Black children, and there appears to be a male predominance. A retrospective surveillance study of the CDC database found that non-Hispanic Black children had more severe courses.¹¹ As of July 2021, more than 4000 cases have been reported in the United States, with a reported mortality rate of 0.85%.⁹ Although mortality is low, the long-term outcomes of MIS-C are unclear, with no distinct correlations between presentation features, laboratory test results, treatments, and risk of coronary artery abnormalities.²

Pathophysiology

The exact pathophysiology of MIS-C is currently unknown, but it has been hypothesized to be a postviral hyperinflammatory condition with multiorgan involvement.^{4,12} This hypothesis is supported by the observation that MIS-C rates typically increase approximately 4 weeks after COVID-19 case rates increase in the community.¹³ Children with MIS-C tend to have negative COVID-19 polymerase chain reaction (PCR) tests but positive serologic evidence indicating past infection.¹⁴ Those who do have positive PCR tests trend toward higher cycle threshold, indicating low viral load at the time of presentation.¹⁵ Several mechanisms have been proposed for the acquired postviral or acquired immune response to SARS-CoV-2. These include antibody or

T-cell recognition of self-antigens or viral antigens, immune complexes that activate inflammation, or viral superantigen sequences that activate immune cells.¹³ The proposed pathways all lead to proinflammatory cytokine secretion. These cytokines include interleukins (IL-6, IL-8) and tumor necrosis factor α , which can be measured on cytokine panels. The cytokines lead to increased inflammation and the multiorgan impairment seen in MIS-C.¹⁵ The interplay between virus, host, and genetic predisposition remains undetermined.

Presenting Signs and Symptoms

Children with MIS-C initially present with symptoms consistent with common childhood ailments. These include fever, fatigue, myalgia, headache, meningismus, emesis, diarrhea, abdominal pain, and rash.¹⁶ It is often the prolonged course of fever or gastrointestinal symptoms including inability to tolerate enteral intake that prompts families to seek medical care. Fever, gastrointestinal symptoms, and mucocuta-

aneous findings can be distinguishing features of MIS-C in the context of

known or suspected COVID-19 infection or exposure. There is no distinct pathognomonic rash for MIS-C, which can make it difficult to distinguish from other ailments. The rash has been described in case studies as nonpurulent conjunctivitis; oral mucosal changes including erythematous tongue and posterior oropharynx and dry, cracked lips; truncal or diffuse maculopapular rash; petechiae; and erythema and induration of limbs, including palms of hands and soles of feet.^{17,18} On physical examination, mucocutaneous lesions and conjunctival injections were associated with coronary artery abnormalities and less severe cardiac dysfunction.¹¹ Some children present with no rash, and few children present with all of the aforementioned symptoms.

Criteria for admission to an ICU reflect institutional triage guidelines and include high risk of organ system failure. Children with MIS-C are at risk for cardiovascular failure, which may be noted on examination as tachycardia, poor perfusion including delayed capillary refill, activity intolerance, decreased urine output, inability to tolerate changes in fluid status, and respiratory distress, indicating possible cardiac failure.¹⁶ Abrams et al¹¹ reported that

Patients with MIS-C should be evaluated with a high index of suspicion, as they often look well initially but can decompensate rapidly.

Table 2 Laboratory values and imaging used for evaluation of multisystem inflammatory syndrome in children^{12,19-22}

	Evidence of inflammatory response	Evidence of cardiac dysfunction	Evidence of other organ dysfunction	Evidence of possible infection
Laboratory values	CBC with differential Neutrophils ↑ Lymphocytes ↓ Platelets ↓ C-reactive protein ↑ ESR ↑	Arterial or venous blood gas (metabolic acidosis) Lactate ↑	Complete metabolic panel Sodium ↓ Liver enzymes ↑ BUN ↑ Creatinine ↑	SARS-CoV-2 PCR and antibodies Respiratory viral panel Blood culture Urinalysis and urine culture Respiratory culture Cerebrospinal fluid studies
Tier 1				
Tier 2	PT/PTT/INR ↑ D-dimer ↑ Fibrinogen ↑ Ferritin ↑ Triglycerides ↑ LDH ↑ Cytokine panel ↑	Troponin ↑ BNP ↑		
Imaging		ECG: evaluate for myocardial strain ECHO: evaluate cardiac function and coronary artery abnormalities CXR: evaluate for cardiomegaly	CXR: evaluate for primary respiratory process Head CT: evaluate possible etiology for altered mental status or focal deficits EEG: evaluate possible etiology of altered mental status or focal deficits; evaluate for seizure activity	

Abbreviations: ↑, elevated; ↓, decreased; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; CBC, complete blood cell count; CT, computed tomography; CXR, chest radiograph; ECG, electrocardiogram; ECHO, echocardiogram; EEG, electroencephalogram; ESR, erythrocyte sedimentation rate; INR, international normalized ratio; LDH, lactate dehydrogenase; PCR, polymerase chain reaction; PT, prothrombin time; PTT, partial thromboplastin time.

ICU admission was associated with shortness of breath and abdominal pain. Critical care nurses may encounter MIS-C patients before ICU admission on rapid response or other ICU consultative teams. These patients should be evaluated with a high index of suspicion, as they often look well initially but can decompensate rapidly.¹⁸

Laboratory and Imaging Findings

Because MIS-C is a diagnosis of exclusion, laboratory studies and imaging are beneficial in not only quantifying the degree of inflammation and organ dysfunction present but also helping to exclude other potential causes of the presenting symptoms. Table 2 includes laboratory test results and imaging findings that are frequently obtained in a suspected case of MIS-C.^{12,19-22} Laboratory test results in MIS-C commonly associated with shock and ICU admission include elevated troponin, brain natriuretic peptide, D-dimer, C-reactive protein, and ferritin and decreased platelet and lymphocyte counts.¹¹

Treatment

Currently, there is no known definitive treatment for MIS-C. Supportive care, including ensuring adequate

hydration and fever control, is the criterion standard for mild to moderate presentations.^{23,24} For hospitalized patients, a variety of treatment options are available, generally offered in a tiered fashion.

The first tier of treatment includes intravenous immunoglobulin (IVIG) independently or in conjunction with steroid administration.^{25,26} Ouldali et al²⁷ analyzed independent IVIG administration versus a combination administration with steroids and suggested that the IVIG and steroid combination was more favorable. However, more research is needed to support this finding. If symptoms persist and laboratory values indicate an ongoing inflammatory response, interleukin antagonists such as anakinra and tocilizumab may be considered. Broad-spectrum antibiotics should be initiated during ongoing evaluation until a bacterial infection is conclusively excluded as the cause of the symptoms.²⁸

In addition to treating the active inflammatory process, antiplatelet and anticoagulation treatments are often initiated.²⁵ Because MIS-C causes systemic endothelial injury, these patients are at risk of developing thrombi.^{12,29} Additionally, when cardiac function is impaired, there

Table 3 Treatment options and consulting services for multisystem inflammatory syndrome in children^{4,12,20,25,31,34}

Focus	Treatment	Use	Consultants
Possible infection	Antibiotics (eg, ceftriaxone, cefepime, vancomycin, doxycycline, clindamycin)	Treatment of presumed bacterial infection until proven otherwise	Infectious disease
Inflammation	IVIG	Replacement of antibodies	Rheumatology
	Steroids (eg, methylprednisolone)	Suppression of immune response	
	Interleukin antagonists (eg, anakinra, tocilizumab)	Reduction of cytokine and acute phase reactant production	
Cardiac dysfunction	Vasoactive agents (eg, epinephrine, norepinephrine, dobutamine, dopamine, milrinone)	Increase contractility, chronotropy, and lusitropy on cardiac muscle and peripheral vessels in refractory shock and cardiogenic shock	Cardiology
Hypercoagulability	Anticoagulation and antiplatelet therapy (eg, enoxaparin, aspirin)	Treatment of known thrombus or prophylaxis	Hematology
End-organ failure	Mechanical ventilation	Treat primary pulmonary process or afterload reduction with left ventricular dysfunction	Critical care
	ECMO	Manage refractory cardiovascular collapse	

Abbreviations: ECMO, extracorporeal membrane oxygenation; IVIG, intravenous immunoglobulin.

is a risk of clot formation due to blood stasis, especially when coronary artery abnormalities are present.¹²

If patients exhibit signs of multiorgan dysfunction or failure, mechanical ventilation, vasoactive support, and/or extracorporeal membrane oxygenation should be considered. Cardiac dysfunction is noted in many patients on presentation.² For example, in a study by Feldstein et al,⁵ 80% of the 186 studied patients were treated in the ICU, with 80% (or 149) of those patients having cardiovascular compromise. In studies by Belot et al³⁰ and Toubiana et al,³¹ 67% to 81% of patients required admission to the ICU. Torres et al³² reported that 59% of studied patients were admitted to intensive care. Other authors noted that many MIS-C patients would present with mild symptoms and then decompensate quickly, requiring ICU interventions.^{18,33}

Consulting Services

Because of the multiorgan involvement of this disease process, support from several specialty consultants, as delineated in Table 3, is needed when determining a treatment plan.^{4,12,20,25,31,34}

Nursing Implications

COVID-19 Considerations

Patients with suspected MIS-C should be considered COVID-19 PCR positive and assumed to be shedding virus until proven otherwise.²⁶ These children should be

placed in single-patient rooms during diagnostic evaluation, and staff members should don appropriate personal protective equipment. Many patients with MIS-C are found to have a negative COVID-19 PCR test result and may subsequently be treated with standard precautions based on CDC guidelines.³⁵ Cases of MIS-C must be reported to the local health department.³⁶

Physical Assessment

Isolation requirements may leave the critical care nurse as the consistent presence at the bedside and often the key individual responsible for identifying and reporting patient changes, particularly given that these children often experience rapid deterioration.¹⁸ Multisystem inflammatory syndrome in children is associated with various vital sign and physical examination abnormalities, including hypotension, respiratory distress or failure, neurological changes, and renal or hepatic insufficiency.^{25,37} These patients are at high risk for developing hemodynamic instability, cardiac dysrhythmias, pericardial effusion, coronary artery dilation, and shock.³⁸ Serial nursing assessments and hourly measurement of urinary output may assist in the early identification of evolving organ dysfunction, impending respiratory or neurological failure, or other similar changes. Nursing assessment is essential to identifying changes that guide therapy and evaluating the impact of therapies.

Diagnostic Laboratory and Imaging Studies

Patients with suspected MIS-C require laboratory studies to aid in the evaluation of severity of inflammation and rule out other plausible causes of symptoms, including sepsis.²⁵ The timing of the initial laboratory analysis is essential; in particular, the COVID-19 antibody study must be obtained before IVIG administration. Patient stability must be considered, as the care team determines the extent of evaluation. Optimally, patients will have a full evaluation before the initiation of therapies. However, in those with life-threatening presentations, it may be necessary to initiate treatment before completion of diagnostic laboratory studies. Many institutions and recommendations have stratified laboratory evaluation into tiers as shown in Table 2.^{12,19,22,25} In addition to initial laboratory evaluation, ICU patients with MIS-C require studies trended over time, particularly to follow cardiac function such as brain natriuretic peptide and troponin levels. Henderson et al²⁵ recommended that these laboratory results be monitored until they are normalized.

Imaging studies are also important to the diagnostic evaluation. Chest radiography may elucidate evidence of cardiac dysfunction, with findings including pleural effusions or cardiomegaly in addition to pulmonary findings such as consolidation or infiltrates.^{37,38} Echocardiography (ECHO) should be performed upon initial presentation,

with specific attention to function, the evaluation of pericardial effusion, and coronary arteries.

In addition to initial laboratory evaluation, patients with MIS-C require studies trended over time, particularly to follow cardiac function such as brain natriuretic peptide and troponin levels.

^{25,38} Repeat ECHO is recommended at intervals, with follow-up studies 7 to 14 days after the initial study and then 4 to 6 weeks after initial diagnosis.²⁵ Additional cardiac diagnostic procedures may be indicated in certain circumstances, such as cardiac computed tomography for patients with possible coronary artery aneurysm not well visualized by ECHO.

Activity Restriction

Patients with suspected or confirmed MIS-C are at risk for heart failure, hemodynamic compromise, and shock.^{37,38} These patients should remain on strict bed rest until ECHO can be performed to document function and establish medical stability. Activity may need

to be limited owing to risk of rapid decompensation and development of poor cardiac output.¹⁸ Patient-specific activity restrictions should be determined by the interdisciplinary team.

Dysrhythmia Monitoring

Children with MIS-C are at risk for conduction abnormalities, and electrocardiographic (ECG) anomalies are common.^{37,38} Recent evidence suggests that more than 50% of patients have abnormal ECG findings, including first-degree atrioventricular (AV) block with progression to second- or third-degree block in a subset of patients.^{37,39} In addition, prolonged QTc has been noted in some patients as well as nonspecific ST segment changes and ectopic atrial tachycardia.^{38,39} Some patients may not develop these conduction abnormalities initially, as first-degree AV block has been reported several days after the onset of initial symptoms.⁴⁰ Bedside cardiac monitoring by the critical care nurse with patient-specific, appropriate dysrhythmia filters maintained is essential for ongoing screening for rhythm abnormalities. Additionally, given the frequency of first-degree AV block, PR interval monitoring should be performed. Formal telemetry monitoring is indicated for these patients if conduction abnormalities are evident.³⁹ For patients in the ICU, serial ECG monitoring at least every 48 hours is recommended.²⁵

Ventilation

Some patients with MIS-C will require intubation and mechanical ventilation owing to myocardial dysfunction or circulatory failure and, less commonly, to respiratory failure.²⁴ The role of the critical care nurse in preparing for hemodynamic compromise during the peri-intubation period is vital in maintaining patient safety. Because most patients with MIS-C experience left ventricular (LV) dysfunction, understanding both the role of mechanical ventilation in supporting LV function and the potential need for continued mechanical ventilation until LV function has been restored is essential.²⁴

Medication Administration Considerations

Understanding priorities in care, particularly in medication administration, is essential to the role of the critical care nurse. Intravenous immunoglobulin and corticosteroids are generally administered once initial laboratory test results are obtained.²⁵ Working with the medical team to ensure the timing of immunomodulatory therapies such

as IVIG and corticosteroids is properly coordinated is an important intervention for the ICU nurse to ensure certain laboratory tests are sent before medication administration to be useful in diagnosis. Recent evidence suggests that the combination of IVIG and methylprednisolone is associated with improved fever course, decreased severity of complications in the acute period, and reduced need for hemodynamic support, making the prompt administration of these medications a nursing priority.²⁷ Anaphylaxis, hemolysis, hypertension, pulmonary edema, and other adverse effects have been reported with IVIG.⁴¹

In addition to immunomodulatory therapies, broad-spectrum antibiotics for suspected sepsis are administered pending confirmation of the MIS-C diagnosis, typically after cultures have been obtained.²⁵ Vasoactive agents may be required to support cardiac function and provide hemodynamic support if there is evidence of poor ventricular function, hypotension, or hypoperfusion.^{37,38} Medications to initiate anticoagulation are also required given the prothrombotic state in MIS-C.²⁵

Prothrombotic State and Anticoagulation Impact

Children with MIS-C are generally in a prothrombotic state and at risk for thrombus formation.^{25,29} Any swelling or asymmetry in the extremities, changes in neurological examination findings, or other assessment findings that could be associated with hemorrhage or thrombus should be immediately reported to the medical team for further evaluation. Additionally, most children will have anticoagulation therapy instituted, creating a risk of bleeding.^{12,19-22,25}

Low-dose aspirin is initiated in patients without active bleeding, risk for hemorrhage, or thrombocytopenia during the acute phase and continued for a minimum of 4 weeks after diagnosis. Therapeutic anticoagulation with enoxaparin is recommended in the acute phase and extending until at least 14 days after hospital discharge in patients in whom a thrombus has been identified or those with depressed ejection fraction (<35%).²⁵

Vascular Access

Adequate vascular access must be maintained to support medication administration and frequent laboratory studies. A central venous catheter should be considered for any patient with altered cardiac function or shock necessitating vasoactive agents for hemodynamic support.³³ The timing of central venous catheter placement

must be balanced with consideration of the risk of thrombus formation for a patient in a prothrombotic state as well as the risk of bleeding in an anticoagulated patient. Placement of an arterial catheter for continuous hemodynamic monitoring and arterial blood specimen analysis may optimize care for patients with evidence of heart failure and/or shock.³³

Fluid Status

Patients with MIS-C require careful management of fluid status, particularly those with evidence of heart failure, hemodynamic compromise, or shock.²⁹ These patients will generally receive IVIG, which adds significant fluid volume; therefore, the rate of infusion and the total fluid volume must be carefully determined, as this volume may lead to hemodynamic compromise. Some patients with altered cardiac function may also require diuretics.²⁵ An appropriate fluid limit and strategies to minimize medication volumes should be discussed by the interdisciplinary team, with monitoring by the critical care nurse administering medications and fluids at the bedside.³³

Nutrition

As with all critically ill children, the early implementation of nutrition is necessary to consider in the care of the ICU patient with MIS-C. In accordance with current guidelines, enteral nutrition should be considered within 24 to 48 hours of ICU admission when feasible. For patients with impending respiratory failure, poor splanchnic perfusion, and

shock, enteral feeds may need to be avoided, and the appropriateness of enteral feeds should be con-

sidered by the multidisciplinary team. At a minimum, a multidisciplinary nutrition support team including a registered dietitian should be consulted early to determine a plan to deliver nutrition with attention to fluid restrictions, protein and energy requirements, and caloric needs.⁴²

Because MIS-C is a newly identified syndrome, knowledge of diagnosis, treatment, and outcomes is evolving. Critical care nurses must remain informed about advances in the care of children with MIS-C.

Family and Sibling Support

The critical care nurse should provide anticipatory guidance to the family. A recent review article by Shields

Table 4 Outpatient follow-up and anticipatory guidance

Follow-up service	Clinical issue	Time frame
Primary care provider	Well-child care Immunizations (after IVIG or blood products) PICS	24-48 hours after discharge ¹²
Cardiology	Heart failure (including left- and right-sided dysfunction, myocarditis, coronary artery abnormalities)	Guidance from ACR ²⁵ : Repeat ECHO a minimum of 7-14 days and 4-6 weeks after presentation Consideration of ECHO 1 year after MIS-C diagnosis with cardiac abnormalities Consideration of cardiac MRI 2-6 months after diagnosis for children with significant or persistent left-sided heart dysfunction Interim guidance from AAP ²⁶ : Outpatient pediatric cardiology follow-up 2-3 weeks after discharge Myocarditis: cardiology-directed restriction and/or release for vigorous activities Guidelines for Kawasaki disease ⁴⁴ : Repeat ECHO 1-2 weeks and 4-6 weeks after treatment for uncomplicated course
Hematology	Hypercoagulability Therapeutic drug monitoring	Guidance from ACR ²⁵ : Length of treatment dependent on presence of coronary artery abnormalities, continued heart failure with low ejection fraction, or documented thrombosis
Gastroenterology	Inflammatory bowel surveillance	No published guidance ⁴⁵
Rheumatology	Therapeutic drug monitoring (if treated with steroids or biologic agent)	No published guidance
Immunology Infectious disease	Monitoring of laboratory values	No published guidance
Neurology	Cerebral edema Neuroirritability	No published guidance
Critical care follow-up programs	PICS	No published guidance

Abbreviations: AAP, American Academy of Pediatrics; ACR, American College of Rheumatology; ECHO, echocardiography; IVIG, intravenous immunoglobulin; MIS-C, multisystem inflammatory syndrome in children; MRI, magnetic resonance imaging; PICS, post-intensive care syndrome.

et al⁴³ specifically addresses potential resources for both parents and other caregivers. With an understanding of the “typical” trajectory of MIS-C patients, the critical care nurse can guide families in supporting the child as well as creating a plan to meet the needs of the family. Hospital visitation is typically limited in the era of COVID-19, creating additional stressors and challenges for the patients and their caregivers.

Patients with MIS-C are often treated by members of various subspecialty services on the basis of organ dysfunction, creating a need for the critical care and advanced practice nurse to have a role not only in coordination of care for these services but also in helping the family to understand the role of each consulting team, the recommendations of each service, and the eventual need for

multispecialty follow-up, as described in Tables 3 and 4.^{4,12,20,25,26,31,34,44,45} In a study by Penner et al,⁴⁶ systemic inflammation was found to be resolved at 6-month multidisciplinary follow-up examination, which is encouraging. Anticipatory guidance about the potential sequelae of ICU hospitalization, including post-intensive care syndrome (PICS), is also necessary.

Post-Intensive Care Syndrome

Patients with MIS-C requiring ICU admission are at risk for PICS. The symptoms include ICU-acquired weakness, cognitive dysfunction, and mental health difficulties that may linger after hospitalization. These symptoms may occur not only for the child but also for the family and may be associated with posttraumatic stress disorder.⁴⁷

In children, this condition may affect school performance as well.⁴⁸ Critical care nurses have a significant role in ICU interventions to prevent PICS or mitigate its impact on patients and their families.

Conclusion

As COVID-19 confirmed cases and potential exposures continue to have a global impact, it is essential to understand MIS-C in the pediatric population, especially because it can initially mimic other common pediatric illnesses but evolve into cardiovascular failure resulting in ICU admission. As the constant and consistent presence at the bedside, the critical care nurse plays a key role in the assessment and treatment of patients with this complex disorder and is instrumental in coordinating care provided by members of multiple specialty services. Balancing multiple medications, maintaining an appropriate fluid balance to support cardiovascular stability, monitoring response to therapies, and helping the family understand the treatment plan and illness trajectory are key responsibilities of the critical care nurse.

Because MIS-C is a newly identified syndrome, knowledge of diagnosis, treatment, and outcomes is evolving. It is imperative that critical care nurses remain informed about advances in the care of children with MIS-C. Furthermore, it is crucial that critical care nurses contribute to this growing body of knowledge through accurate documentation of patient assessment and response to therapies in the medical record, participating in pathway development, and contributing to multidisciplinary research. **CCN**

Financial Disclosures
None reported.

See also

To learn more about pediatric care in the critical care setting, read “Improving Collaborative Decision-making in the Pediatric Setting” by Manolis Small in *AACN Advanced Critical Care*, 2019;30(2):189-192. Available at www.aacnconline.org.

References

1. Most ZM, Hendren N, Drazner MH, Perl TM. Striking similarities of multisystem inflammatory syndrome in children and a myocarditis-like syndrome in adults: overlapping manifestations of COVID-19. *Circulation*. 2021;143(1):4-6. doi:10.1161/CIRCULATIONAHA.120.050166
2. Davies P, Evans C, Kanthimathinathan HK, et al. Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. *Lancet Child Adolesc Health*. 2020;4(9):669-677. doi:10.1016/S2352-4642(20)30215-7
3. Dove ML, Jaggi P, Kelleman M, et al. Multisystem inflammatory syndrome in children: survey of protocols for early hospital evaluation and management. *J Pediatr*. 2021;229:33-40. doi:10.1016/j.jpeds.2020.10.026
4. Chiotos K, Bassiri H, Behrens EM, et al. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: a case series. *J Pediatric Infect Dis Soc*. 2020;9(3):393-398. doi:10.1093/pids/piaa069
5. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in U.S. children and adolescents. *N Engl J Med*. 2020;383(4):334-346. doi:10.1056/NEJMoa2021680
6. Centers for Disease Control and Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). CDC Health Alert Network Archive. Published May 14, 2020. Accessed March 31, 2021. <https://emergency.cdc.gov/han/2020/han00432.asp>
7. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Published May 15, 2020. Updated May 17, 2020. Accessed March 31, 2021. <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>
8. Royal College of Paediatrics and Child Health. Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19. Published May 1, 2020. Accessed March 31, 2021. <https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf>
9. Centers for Disease Control and Prevention. Health department-reported cases of multisystem inflammatory syndrome in children (MIS-C) in the United States. Published March 3, 2021. Accessed March 31, 2021. <https://www.cdc.gov/mis-c/cases/index.html>
10. Godfred-Cato S, Bryant B, Leung J, et al. COVID-19-associated multisystem inflammatory syndrome in children—United States, March–July 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(32):1074-1080. doi:10.15585/mmwr.mm6932e2
11. Abrams JY, Oster ME, Godfred-Cato SE, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. *Lancet Child Adolesc Health*. 2021;5(5):323-331. doi:10.1016/S2352-4642(21)00050-X
12. Chiotos K, Corwin D, Sartori L, et al. Emergency department, ICU, and inpatient clinical pathway for evaluation of possible multisystem inflammatory syndrome (MIS-C). Published May 2020. Updated March 2021. Accessed March 25, 2021. <https://www.chop.edu/clinical-pathway/multisystem-inflammatory-syndrome-mis-c-clinical-pathway>
13. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis*. 2020;20(11):e276-e288. doi:10.1016/S1473-3099(20)30651-4
14. Tang Y, Li W, Baskota M, et al. Multisystem inflammatory syndrome in children during the coronavirus disease 2019 (COVID-19) pandemic: a systematic review of published case studies. *Transl Pediatr*. 2021;10(1):121-135. doi:10.21037/tp-20-188
15. Pouletty M, Borocco C, Ouldali N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. *Ann Rheum Dis*. 2020;79(8):999-1006. doi:10.1136/annrheumdis-2020-217960
16. Rubens JH, Akindele NP, Tschudy MM, Sick-Samuels AC. Acute COVID-19 and multisystem inflammatory syndrome in children. *BMJ*. 2021;372:n385. doi:10.1136/bmj.n385
17. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem inflammatory syndrome in children in New York State. *N Engl J Med*. 2020;383(4):347-358. doi:10.1056/NEJMoa2021756
18. Waltuch T, Gill P, Zinns LE, et al. Features of COVID-19 post-infectious cytokine release syndrome in children presenting to the emergency department. *Am J Emerg Med*. 2020;38(10):2246.e3-2246.e6. doi:10.1016/j.ajem.2020.05.058
19. Kache S, Schwenk H, Mathew R, et al. Multisystem inflammatory syndrome in children (MIS-C) pathway. Updated October 6, 2020. Accessed March 25, 2021. [https://med.stanford.edu/content/dam/sm/school/documents/rambam/Saraswati_Multisystem%20Inflammatory%20Syndrome%20in%20Children%20\(MIS-C\).pdf](https://med.stanford.edu/content/dam/sm/school/documents/rambam/Saraswati_Multisystem%20Inflammatory%20Syndrome%20in%20Children%20(MIS-C).pdf)
20. Parker R, Schlott H, Schneider J, et al. Clinical pathway: multisystem inflammatory syndrome in children (MIS-C) clinical pathway. Updated February 17, 2021. Accessed March 25, 2021. <https://www.connecticutchildrens.org/wp-content/uploads/2021/02/MIS-C-02.17.21-with-new-vanc-protocol.pdf>
21. Kazmier K, Albert J, de la Morena M, et al. COVID-19 pathway. Updated December 2020. Accessed March 25, 2021. <https://www.seattlechildrens.org/pdf/covid-19-pathway.pdf>
22. Children's Minnesota. Clinic guideline for suspected MIS-C management. Updated February 2021. Accessed March 25, 2021. <https://www.childrensmn.org/Departments/infectioncontrol/pdf/mis-c-clinical-guideline.pdf>
23. Soma VL, Shust GF, Ratner AJ. Multisystem inflammatory syndrome in children. *Curr Opin Pediatr*. 2021;33(1):152-158. doi:10.1097/MOP.0000000000000974
24. Whittaker E, Bamford A, Kenny J, et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally

- associated with SARS-CoV-2. *JAMA*. 2020;324(3):259-269. doi:10.1001/jama.2020.10369
25. Henderson LA, Canna SW, Friedman KG, et al. American College of Rheumatology clinical guidance for multisystem inflammatory syndrome in children associated with SARS-CoV-2 and hyperinflammation in pediatric COVID-19: version 1. *Arthritis Rheumatol*. 2020;72(11):1791-1805. doi:10.1002/art.41454
 26. American Academy of Pediatrics. Multisystem inflammatory syndrome in children (MIS-C) interim guidance. Critical updates on COVID-19/COVID-19 interim guidance. Published May 2020. Updated February 10, 2021. Accessed March 31, 2021. <https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/multisystem-inflammatory-syndrome-in-children-mis-c-interim-guidance>
 27. Ouldali N, Toubiana J, Antona D, et al. Association of intravenous immunoglobulins plus methylprednisolone vs immunoglobulins alone with course of fever in multisystem inflammatory syndrome in children. *JAMA*. 2021;325(9):855-864. doi:10.1001/jama.2021.0694
 28. Kohn-Loncarica G, Fustiñana A, Díaz-Rubio F, et al. Recommendations for the initial management of multisystem inflammatory syndrome temporally related to COVID-19, in children and adolescents. *Arch Argent Pediatr*. 2020;118(6):e514-e526. doi:10.5546/aap.2020.eng.e514
 29. Hennon TR, Penque MD, Abdul-Aziz R, et al. COVID-19 associated multisystem inflammatory syndrome in children (MIS-C) guidelines; a Western New York approach. *Prog Pediatr Cardiol*. 2020;101232. doi:10.1016/j.ppedcard.2020.101232
 30. Belot A, Antona D, Renolleau S, et al. SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 March to 17 May 2020. *Euro Surveill*. 2020;25(22):2001010. doi:10.2807/1560-7917.ES.2020.25.22.2001010
 31. Toubiana J, Poirault C, Corsia A, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. *BMJ*. 2020;369:m2094. doi:10.1136/bmj.m2094
 32. Torres JP, Izquierdo G, Acuña M, et al. Multisystem inflammatory syndrome in children (MIS-C): report of the clinical and epidemiological characteristics of cases in Santiago de Chile during the SARS-CoV-2 pandemic. *Int J Infect Dis*. 2020;100:75-81. doi:10.1016/j.ijid.2020.08.062
 33. Magowan N, Darcy J, Mosiello A, Gomes C, Miller N. Navigating through the uncharted territory of multisystem inflammatory syndrome in children (MIS-C): what the pediatric clinical nurse must know. *Pediatr Nurs*. 2020;46(6):273-277.
 34. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet*. 2020;395(10239):1771-1778. doi:10.1016/S0140-6736(20)31103-X
 35. Centers for Disease Control and Prevention. Clinical questions about COVID-19: questions and answers. Updated March 4, 2021. Accessed March 31, 2021. https://www.cdc.gov/coronavirus/2019-ncov/hcp/faq.html?CDC_AA_refVal=https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-faq.html#Testing,-Isolation,-and-Quarantine-for-Persons-Who-Have-Recovered-from-Previous-SARS-CoV-2-Infection
 36. Centers for Disease Control and Prevention. Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C). Updated March 4, 2021. Accessed March 31, 2021. <https://www.cdc.gov/mis-c/hcp/index.html>
 37. Ramcharan T, Nolan O, Lai CY, et al. Paediatric inflammatory multisystem syndrome: temporally associated with SARS-CoV-2 (PIMS-TS): cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. *Pediatr Cardiol*. 2020;41(7):1391-1401. doi:10.1007/s00246-020-02391-2
 38. Valverde I, Singh Y, Sanchez-de-Toledo J, et al. Acute cardiovascular manifestations in 286 children with multisystem inflammatory syndrome associated with COVID-19 infection in Europe. *Circulation*. 2021;143(1):21-32. doi:10.1161/CIRCULATIONAHA.120.050065
 39. Dionne A, Mah DY, Son MBF, et al. Atrioventricular block in children with multisystem inflammatory syndrome. *Pediatrics*. 2020;146(5):e2020009704. doi:10.1542/peds.2020-009704
 40. Choi NH, Fremed M, Starc T, et al. MIS-C and cardiac conduction abnormalities. *Pediatrics*. 2020;146(6):e2020009738. doi:10.1542/peds.2020-009738
 41. Immune globulin. Pediatric and Neonatal Lexi-Drugs Online. Lexicomp. Wolters Kluwer Health, Inc. Updated November 2020. Accessed March 31, 2021. <http://online.lexi.com>
 42. Mehta NM, Skillman HE, Irving SY, et al. Guidelines for the provision and assessment of nutrition support therapy in the pediatric critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition. *JPEN J Parenter Enteral Nutr*. 2017;41(5):706-742. doi:10.1177/0148607117711387
 43. Shields K, Atlas K, Farber JS, Lebet R. Multisystem inflammatory syndrome in children: a review. *Am J Nurs*. 2021;121(5):26-37. doi:10.1097/01.NAJ.0000749756.12090.63
 44. McCrindle BW, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a scientific statement for health professionals from the American Heart Association. *Circulation*. 2017;135(17):e927-e999. doi:10.1161/CIR.0000000000000484.
 45. Miller J, Cantor A, Zachariah P, Ahn D, Martinez M, Margolis KG. Gastrointestinal symptoms as a major presentation component of a novel multisystem inflammatory syndrome in children that is related to coronavirus disease 2019: a single center experience of 44 cases. *Gastroenterology*. 2020;159(4):1571-1574.e2. doi:10.1053/j.gastro.2020.05.079
 46. Penner J, Abdel-Mannan O, Grant K, et al. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study. *Lancet Child Adolesc Health*. 2021;5(7):473-482. doi:10.1016/S2352-4642(21)00138-3
 47. Davidson JE, Hopkins RO, Louis D, Iwashyna TJ. Post-intensive care syndrome. Published 2013. Accessed March 25, 2021. <https://www.sccm.org/MyICUCare/THRIVE/Post-intensive-Care-Syndrome>
 48. Rodriguez-Rubio M, Pinto NP, Manning JC, Kudchadkar SR. Post-intensive care syndrome in paediatrics: setting our sights on survivorship. *Lancet Child Adolesc Health*. 2020;4(7):486-488. doi:10.1016/S2352-4642(20)30170-X