Current Approach to the Evaluation and Management of Incomplete Kawasaki Disease in the Emergency Department

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Abstract: Kawasaki disease (KD) is one of the most common vasculitides of childhood and frequently presents to the emergency department. Although the diagnosis of KD is based on clinical criteria, children who do not fulfill the criteria but have sufficient supportive features of KD are diagnosed as having incomplete KD and warrant the same course of therapy as children with classic KD. The diagnosis of incomplete KD is challenging and requires a high index of suspicion. The purpose of this article is to review presenting features of incomplete KD and the diagnostic approach and management of children in the emergency department.

Key Words: Kawasaki disease, incomplete, atypical

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TARGET AUDIENCE

This CME activity is intended for all practitioners who care for pediatric patients presenting with possible Kawasaki disease, which may include pediatricians, general practitioners, pediatric emergency physicians, general emergency physicians, and pediatric intensive care physicians.

LEARNING OBJECTIVES

After completion of this article, the reader should be better able to:

1. Describe key presenting features of Kawasaki disease in the emergency department.
2. Identify diagnostic testing needed for children with incomplete Kawasaki disease in the primary care setting.
3. Explain clinical treatment strategies and their administration in children with incomplete Kawasaki disease.

Mucocutaneous lymph node syndrome was first reported by a Japanese physician, Dr. Kawasaki, in 1967. Subsequently, the syndrome became known as Kawasaki disease (KD).[1] KD is one of the most common vasculitides of childhood and affects the medium-sized muscular arteries, primarily coronary arteries. It is an acute systemic vasculitis that predominantly affects children younger than 5 years and is the leading cause of acquired heart disease in developed countries. Kawasaki disease typically presents as a self-limited febrile illness with up to 25% of patients developing coronary artery aneurysms, if untreated.[2] Timely treatment with intravenous immunoglobulin (IVIG) has been shown in clinical trials to reduce the risk of coronary artery aneurysms from 25% to 4%.[3,4]

The diagnosis of KD is based on syndrome recognition—a combination of clinical features supported by laboratory and/or echocardiographic findings. In cases when insufficient clinical criteria are present but echocardiographic abnormalities are found, the diagnosis can still be made. Patients who fulfill clinical criteria for KD are defined as having complete KD (also termed "classic" or "typical" KD), whereas those that do not fulfill all the criteria are referred to as having incomplete KD (also atypical KD).

Historically, there has been some confusion over the terms "incomplete" versus "atypical" KD. The American Heart Association (AHA) and the American Academy of Pediatrics (AAP) have recommended that the term "incomplete" is preferable over "atypical" because these patients lack sufficient clinical signs to fulfill the classic criteria but do not demonstrate atypical features.[5] The term "atypical Kawasaki disease" should be used to describe patients with features that are not generally seen in KD, such as renal complications.[5]

The range of presentations of KD to the emergency department (ED) is broad, and diagnosis is complicated by the lack of a criterion standard diagnostic test, a wide-ranging differential diagnoses, and the overlapping features with many acute (usually viral) infections. The challenge of diagnosis is amplified in patients who do not present with recognized diagnostic criteria which may result in diagnostic delays[6,7] and worse outcomes (higher rates of coronary aneurysms).[6,8–10]

Incomplete KD is an important diagnosis to consider in any infant or child with prolonged unexplained fever presenting to the ED, even if few principle features of KD are present. Improved recognition of these patients will reduce the number of patients with a delayed diagnosis and will increase the chance of administering timely treatment.

EPIDEMIOLOGY AND PATHOGENESIS

The etiology of KD is unknown but several observations have implicated an infectious trigger—seasonal peaks in the winter and spring months, similar presentation to many infectious illnesses, and detection of concurrent infections in a significant proportion of patients diagnosed with KD.[11–13] In one study, respiratory viruses were detected in 42% of children with KD, and of these, half reported current upper respiratory symptoms. Rhinovirus and enterovirus were most commonly identified. Documented viral infection was not associated with unique presentation, laboratory findings, length of illness, response to IVIG, and development of coronary artery pathology.[13]

Some host genetics underlie the pathogenesis. A predisposition to KD appears to exist, because children of parents who have had KD have twice the risk of developing the disorder than the general population. Children with affected siblings have a tenfold higher risk.[14,15]

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The incidence of incomplete KD is not known. Epidemiologic data from Japan suggest that 10% to 20% of children diagnosed with KD did not fulfill the criteria for KD.[16,17] Incomplete presentations occur at any age[18,19] but are more likely to present in infants. The diagnosis of KD in an infant younger than 6 months in the ED is imperative because these patients are at high risk for developing coronary artery aneurysms.[20–23]

HISTORY AND PHYSICAL EXAMINATION

The diagnosis of classic KD is made by meeting the following criteria: daily fever persisting for 5 or more days (the day of fever onset is the first day of fever) in addition to at least 4 of the 5 principle clinical criteria (Table 1).[5] For a child who has unexplained fever for 5 or more days and less than 4 of the principle clinical features at time of ED presentation, the diagnosis of incomplete KD should be considered. It should be emphasized that principle features do not need to present all at the same time, and in many cases, some features may appear and abate before other features develop.[18] Hence, it is important to specifically inquire about the presence of principle criteria in the preceding 1 to 2 weeks.[18]

Fever, usually high spiking (above 102°F [39°C]), is the hallmark of KD. The other signs and symptoms that are seen in incomplete KD tend to parallel those seen in classic KD; however, the presence of fewer features—particularly the absence of oral mucosal changes and eye findings, makes the diagnosis more likely to be missed or delayed.[7] When compared, patients with incomplete KD were significantly less likely to have cervical lymphadenopathy and extremity changes.[19,24] Laboratory findings in complete and incomplete KD appear to be similar.[16,19,24] In the presence of few clinical criteria for KD, supportive laboratory abnormalities may increase the probability of an incomplete presentation.

The AHA and AAP have proposed a diagnostic algorithm to help identify patients who are at risk of developing coronary artery aneurysms and should receive treatment with IVIG.[18] Based on the algorithm, any child with 5 or more days of fever and 2 to 3 compatible clinical criteria, or any infant (0–6 months) with unexplained fever for 7 or more days (even in the absence of other features of KD), should be evaluated for suspected incomplete KD (see Diagnostic Testing below). Fever is frequently 102°F (39°C) or higher and minimally responsive to antipyretic medications.

TABLE 1. Criteria for the Diagnosis of Kawasaki Disease

Classic KD is diagnosed in the presence of fever for at least 5 days* together with at least 4 of the 5 following principle clinical features. In the presence of ≥4 principle clinical features, the diagnosis of KD can be made on day 4 of illness. Experienced clinicians who have treated many KD patients may establish diagnosis before day 4.

1. Erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa
2. Bilateral bulbar conjunctival injection without exudate
3. Rash: maculopapular, diffuse erythroderma, or erythema multiforme-like
4. Erythema and edema of the hands and feet in acute phase and/or periungual desquamation in subacute phase
5. Cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral

*Patients with fever at least 5 days and <4 principal criteria can be diagnosed with KD when coronary artery abnormalities detected by echocardiography or angiography.

However, intermittent fevers or lower temperature do not exclude the diagnosis.

The physical examination of patients with suspected KD involves a multisystem assessment. As a systemic vasculitis, any organ system can be affected. For principle KD features, similar to classic KD, the least likely feature to be present is cervical lymphadenopathy. Conjunctivitis is bilateral, classically spares the limbus, and is nonexudative. Rash typically occurs early in the course of illness and is often extensive. For infants and toddlers wearing diapers, the inguinal region should also be examined for the presence of rash or early desquamation. Almost any rash can be seen in KD, and the most common are maculopapular, morbilliform, scarlatiniform erythroderma, and targetoid.[18] Vesicular or bullous rashes are not generally seen and suggest an alternate diagnosis. For extremity changes, erythema of the palms and soles, sometimes accompanied by swelling, occurs early, whereas the desquamation of the fingers and toes generally occur late.[18] Oral mucosal changes can be quite striking with notable red vertically cracked lips and a strawberry tongue. Bleeding of the lips can also be seen.

OTHER CLINICAL FEATURES

Other clinical features have also been reported with KD. Extreme irritability is frequently observed and is most likely due to aseptic meningitis.[25] Gastrointestinal involvement is common and may present as abdominal pain, diarrhea, hepatitis, and gallbladder hydrops. Joint pain (arthralgia or arthritis) is reported in up to 15% of the patients.[26,27]

Coronary artery involvement is a prominent complication in KD; however, cardiac illness may also present as myocarditis, valvulitis, and pericarditis. Cardiovascular shock is a rare but important presentation of KD and should be recognized early by the ED provider (see below).[28–30] Noncardiac arterial aneurysms can also occur and axillary, brachial, and femoral artery aneurysms might be palpable on physical examination.

KD SHOCK SYNDROME

In rare cases, KD can present with hemodynamic instability and shock, referred to as KD shock syndrome (KDSS), and recognition by the ED provider is prudent. The syndrome was formally defined by Kanegaye et al[29] in 2009 as systolic hypotension for age, a sustained decrease in systolic blood pressure from baseline of 20%, or clinical signs of poor perfusion. The incidence of KDSS is estimated to be around 7%.[29,30] Kawasaki disease shock syndrome is associated with significant inflammation in laboratory findings, greater risk of coronary artery abnormalities, mitral regurgitation, and prolonged myocardial dysfunction, as well as a higher risk for IVIG resistance.[29] One recent study reported a 6.8% mortality rate in children diagnosed with KDSS.[31] Misdiagnosis of KDSS at initial presentation is frequent, with one study reporting that 39% of KDSS cases were not diagnosed as having KD at the time of admission, the most common initial diagnosis being septic shock.[32] Children who present with KDSS may require initiation in the ED of inotropic support and should be transferred to a pediatric intensive care unit for close monitoring until stable. Intravenous immunoglobulin should be administered as soon as KDSS is recognized. Steroids in conjunction with IVIG are also frequently used in these patients.[31,33]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for KD is broad and includes infections (bacterial or viral), toxin-mediated syndromes (staph scalded skin syndrome and toxic shock syndrome), and hypersensitivity reactions (Stevens-Johnson syndrome, drug reactions, acrodynia)

and systemic-onset juvenile idiopathic arthritis. In general, the clinical presentation of children with KD is considered more severe, compared with children with viral infections, and typically, there is additional evidence of systemic inflammation.[34] Common viruses like adenovirus can present with very similar mucocutaneous changes to KD. However, extremity changes and unilateral neck swelling are less common with adenoviral disease.[35] More than 30% of children with typical KD also have evidence of a concomitant infection; hence, evidence of a concurrent infection does not necessarily preclude the diagnosis of KD.[12]

DIAGNOSTIC TESTING

Laboratory Investigations

There are no specific diagnostic tests for KD. However, several laboratory investigations may provide support for the diagnosis. Laboratory tests should reflect systemic inflammation manifested as elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), an elevated white count with leukocytosis, and commonly anemia. Thrombocytosis is characteristic, usually in the second week of illness. The presence of thrombocytopenia may herald the onset of rare complications of KD including disseminated intravascular coagulation or macrophage activation syndrome. Other laboratory abnormalities that support the diagnosis of KD include elevations of serum transaminases, gamma glutamyl transpeptidase, bilirubin, and hypoalbuminemia. Sterile pyuria may also be present.

CARDIAC IMAGING

Children with suspected incomplete KD should have echocardiography early on in the evaluation of their disease. However, when a diagnosis of KD has been made, treatment should not be delayed and echocardiography can be done mid-treatment.

For young children, obtaining a good quality echocardiogram can be challenging, especially when a child is irritable. The ED provider should weigh the risks and potential benefit for sedation to obtain optimal visualization of the coronary arteries.[36] According to the algorithm proposed by the AHA, any child with persistent unexplained fever for 5 or more days with 2 to 3 clinical features of KD (or any infant with persistent unexplained fever for 7 or more days without other features of KD) should undergo laboratory testing in the ED setting. If the ESR and/or CRP are elevated, and other laboratory findings do not warrant treatment, cardiology should be consulted for echocardiography. An abnormal echocardiogram in the presence of ongoing inflammation warrants treatment with IVIG regardless of whether other supportive features are present. It is important to note that in the majority of cases, coronary artery dilatation will not be detected during the first week of illness, so normal echocardiography in that early period does not rule out the diagnosis of KD.[18]

MANAGEMENT

Children diagnosed with incomplete KD are managed in a similar fashion to children with complete KD. Some children present acutely unwell, including in cardiogenic shock. Initial stabilization in the ED, in face of potential abnormal vital signs or cardiogenic shock, remains a priority in management of children with suspected KD.

Treatment with IVIG (at 2 g/kg) should be started once the diagnosis has been established. The majority of randomized studies of IVIG in KD have evaluated its use within the first 10 days of fever.[3,37–40] Even if the presentation is beyond 10 days of illness, treatment may still be warranted. Children who present after 10 days of illness but who still have evidence of systemic inflammation (elevated ESR and/or CRP) along with ongoing unexplained fever or coronary artery abnormalities should receive treatment with IVIG.

Acetylsalicylic acid (ASA) has been routinely used in conjunction with IVIG in the treatment of KD with insufficient evidence to the value of this therapy for prevention of coronary artery abnormalities.[41] Acetylsalicylic acid should be used with IVIG at a moderate (30–50 $mg \cdot kg^{-1} \cdot d^{-1}$) to high dose (80–100 $mg \cdot kg^{-1} \cdot d^{-1}$) until the patient is afebrile. Subsequently, ASA should continue at a low-dose (3–5 $mg \cdot kg^{-1} \cdot d^{-1}$) until the child has had a follow-up echocardiogram at 6 to 8 weeks posttreatment. At moderate to high doses, ASA has an anti-inflammatory effect, although at low doses, it exerts an antiplatelet effect that coincides with the thrombocytosis often seen during the second or third week of illness. Long-term ASA may be indicated for children who develop coronary abnormalities.

The role of corticosteroids in the treatment of KD continues to be a source of controversy. Several randomized trials and a meta-analysis have shown that the addition of corticosteroids to standard treatment reduced the rate of coronary artery abnormalities.[42] The meta-analysis included 9 studies, 6 of which were prospective randomized controlled studies. The combined rates of coronary artery abnormalities were 6.3% versus 18% (odds ratio, 0.3; 95% confidence interval, 0.18–0.5; $P < 0.001$) for the IVIG plus corticosteroid groups compared to the IVIG alone, respectively.[42] The corticosteroid regimens used were highly varied, ranging from one dose of 30 mg/kg of intravenous methylprednisolone to 15 days of 2 mg/kg of prednisolone. Because the majority of studies are from Japan and included patients that were considered at a high risk for IVIG treatment failure, the AHA recommends the addition of a course of corticosteroids to standard IVIG and ASA be considered for treatment of high-risk patients with KD.[18] Existing scoring systems for determining risk of IVIG resistance that were developed using data from children from Asia fail to show the same predictive qualities in non-Asian populations.[43–47] Some of the clinical features associated with risk of IVIG resistance include a young age (<12 months), low albumin, thrombocytopenia, fever less than 4 days, low sodium, and elevated transaminases.[48–50]

COMPLICATIONS

Diagnosis of KD may be delayed if clinical criteria are not fulfilled or recognized in a timely manner.[51] Reports from the 1990s suggested a very high mortality rate (up to 41%) for children with incomplete KD.[52] The delay in diagnosis has been further complicated in younger children, especially under 6 months of age where diagnostic criteria are less likely to be met and incidence of coronary arteritis is higher.[53]

Furthermore, with incomplete KD, and delayed onset of treatment with IVIG, coronary artery lesions are more likely to develop.[54]

DISPOSITION

Children with incomplete KD require admission for IVIG therapy and for ongoing close monitoring. Observation units (up to 24-hour admission) in most EDs are not appropriate for such admission because of the limited capacity to provide intense monitoring. However, treatment should not be delayed because of admission to a busy ward, and effort should be made to start IVIG therapy in the ED setting, if protocols offer this option. Echocardiography by an operator skilled in pediatric evaluation of coronary arteries must be done as soon as possible after the diagnosis is made, and serial echocardiography examinations may be needed.

It is anticipated that the majority of children will recover from KD without any long-term sequelae. However, approximately 4% to 5% will develop coronary aneurysms despite standard therapy, and this has implications for long-term cardiac morbidity and requirement for anticoagulation.[3,4,55]

CONCLUSIONS

The diagnosis of incomplete KD should be considered in the ED in any infant or child with prolonged unexplained fever, fewer than 4 of the principal clinical findings, and compatible laboratory and/or echocardiographic findings.

REFERENCES

1. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of the fingers and toes in children. *Arerugi*. 1967;16:178–222.
2. Kato H, Sugimura T, Akagi T, et al. Long-term consequences of Kawasaki disease. A 10- to 21-year follow-up study of 594 patients. *Circulation*. 1996;94:1379–1385.
3. Newburger JW, Takahashi M, Burns JC, et al. The treatment of Kawasaki syndrome with intravenous gamma globulin. *N Engl J Med*. 1986;315: 341–347.
4. Terai M, Shulman ST. Prevalence of coronary artery abnormalities in Kawasaki disease is highly dependent on gamma globulin dose but independent of salicylate dose. *J Pediatr*. 1997;131:888–893.
5. Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the committee on rheumatic fever, endocarditis and Kawasaki disease, council on cardiovascular disease in the young, American Heart Association. *Circulation*. 2004;110:2747–2771.
6. Anderson MS, Todd JK, Glode MP. Delayed diagnosis of Kawasaki syndrome: an analysis of the problem. *Pediatrics*. 2005;115:e428–e433.
7. Minich LL, Sleeper LA, Atz AM, et al. Delayed diagnosis of Kawasaki disease: what are the risk factors? *Pediatrics*. 2007;120:e1434–e1440.
8. Wilder MS, Palinkas LA, Kao AS, et al. Delayed diagnosis by physicians contributes to the development of coronary artery aneurysms in children with Kawasaki syndrome. *Pediatr Infect Dis J*. 2007;26:256–260.
9. Witt MT, Minich LL, Bohnsack JF, et al. Kawasaki disease: more patients are being diagnosed who do not meet American Heart Association criteria. *Pediatrics*. 1999;104:e10.
10. Koren G, Lavi S, Rose V, et al. Kawasaki disease: review of risk factors for coronary aneurysms. *J Pediatr*. 1986;108:388–392.
11. Son MBF, Newburger JW. Kawasaki Disease. *Pediatr Rev*. 2018;39:78–90.
12. Benseler SM, McCrindle BW, Silverman ED, et al. Infections and Kawasaki disease: implications for coronary artery outcome. *Pediatrics*. 2005;116:e760–e766.
13. Turnier JL, Anderson MS, Heizer HR, et al. Concurrent respiratory viruses and Kawasaki disease. *Pediatrics*. 2015;136:e609–e614.
14. Onouchi Y. Molecular genetics of Kawasaki disease. *Pediatr Res*. 2009;65 (5 Pt 2):46R–54R.
15. Hata A, Onouchi Y. Susceptibility genes for Kawasaki disease: toward implementation of personalized medicine. *J Hum Genet*. 2009;54:67–73.
16. Fukushige J, Takahashi N, Ueda Y, et al. Incidence and clinical features of incomplete Kawasaki disease. *Acta Paediatr*. 1994;83:1057–1060.
17. Nakamura Y, Yashiro M, Uehara R, et al. Epidemiologic features of Kawasaki disease in Japan: results of the 2007–2008 nationwide survey. *J Epidemiol*. 2010;20:302–307.
18. 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:e927–e999.
19. Manlhiot C, Christie E, McCrindle BW, et al. Complete and incomplete Kawasaki disease: two sides of the same coin. *Eur J Pediatr*. 2012;171: 657–662.
20. Yeom JS, Woo HO, Park JS, et al. Kawasaki disease in infants. *Korean J Pediatr*. 2013;56:377–382.
21. Yanagawa H, Tuohong Z, Oki I, et al. Effects of gamma-globulin on the cardiac sequelae of Kawasaki disease. *Pediatr Cardiol*. 1999;20:248–251.
22. Burns JC, Wiggins JW Jr., Toews WH, et al. Clinical spectrum of Kawasaki disease in infants younger than 6 months of age. *J Pediatr*. 1986;109: 759–763.
23. Chang FY, Hwang B, Chen SJ, et al. Characteristics of Kawasaki disease in infants younger than six months of age. *Pediatr Infect Dis J*. 2006;25: 241–244.
24. Yellen ES, Gauvreau K, Takahashi M, et al. Performance of 2004 American Heart Association recommendations for treatment of Kawasaki disease. *Pediatrics*. 2010;125:e234–e241.
25. Dengler LD, Capparelli EV, Bastian JF, et al. Cerebrospinal fluid profile in patients with acute Kawasaki disease. *Pediatr Infect Dis J*. 1998;17: 478–481.
26. Baker AL, Lu M, Minich LL, et al, Pediatric Heart Network Investigators. Associated symptoms in the ten days before diagnosis of Kawasaki disease. *J Pediatr*. 2009;154:592–595.e2.
27. Gong GW, McCrindle BW, Ching JC, et al. Arthritis presenting during the acute phase of Kawasaki disease. *J Pediatr*. 2006;148:800–805.
28. Gatterre P, Oualha M, Dupic L, et al. Kawasaki disease: an unexpected etiology of shock and multiple organ dysfunction syndrome. *Intensive Care Med*. 2012;38:872–878.
29. Kanegaye JT, Wilder MS, Molkara D, et al. Recognition of a Kawasaki disease shock syndrome. *Pediatrics*. 2009;123:e783–e789.
30. Dominguez SR, Friedman K, Seewald R, et al. Kawasaki disease in a pediatric intensive care unit: a case-control study. *Pediatrics*. 2008;122: e786–e790.
31. Gamez-Gonzalez LB, Murata C, Munoz-Ramirez M, et al. Clinical manifestations associated with Kawasaki disease shock syndrome in Mexican children. *Eur J Pediatr*. 2013;172:337–342.
32. Ma L, Zhang YY, Yu HG. Clinical manifestations of Kawasaki disease shock syndrome. *Clin Pediatr (Phila)*. 2018;57:428–435.
33. Luca NJ, Yeung RS. Epidemiology and management of Kawasaki disease. *Drugs*. 2012;72:1029–1038.
34. Sundel RP. Kawasaki disease. *Rheum Dis Clin N Am*. 2015;41:63,73, viii.
35. Song E, Kajon AE, Wang H, et al. Clinical and virologic characteristics may aid distinction of acute adenovirus disease from Kawasaki disease with incidental adenovirus detection. *J Pediatr*. 2016;170:325–330.
36. Margossian R, Lu M, Minich LL, et al. Predictors of coronary artery visualization in Kawasaki disease. *J Am Soc Echocardiogr*. 2011;24:53–59.
37. Furusho K, Kamiya T, Nakano H, et al. High-dose intravenous gammaglobulin for Kawasaki disease. *Lancet*. 1984;2:1055–1058.
38. Newburger JW, Takahashi M, Beiser AS, et al. A single intravenous infusion of gamma globulin as compared with four infusions in the treatment of acute Kawasaki syndrome. *N Engl J Med*. 1991;324: 1633–1639.
39. Durongpisitkul K, Gururaj VJ, Park JM, et al. The prevention of coronary artery aneurysm in Kawasaki disease: a meta-analysis on the efficacy of aspirin and immunoglobulin treatment. *Pediatrics*. 1995;96:1057–1061.
40. Oates-Whitehead RM, Baumer JH, Haines L, et al. Intravenous immunoglobulin for the treatment of Kawasaki disease in children. *Cochrane Database Syst Rev*. 2003;2003:CD004000.
41. Baumer JH, Love SJ, Gupta A, et al. Salicylate for the treatment of Kawasaki disease in children. *Cochrane Database Syst Rev*. 2006:CD004175.

42. Chen S, Dong Y, Yin Y, et al. Intravenous immunoglobulin plus corticosteroid to prevent coronary artery abnormalities in Kawasaki disease: a meta-analysis. *Heart*. 2013;99:76–82.

43. Arslanoglu Aydin E, Ertugrul I, Bilginer Y, et al. The factors affecting the disease course in Kawasaki disease. *Rheumatol Int*. 2019;39:1343–1349.

44. Fabi M, Andreozzi L, Corinaldesi E, et al. Inability of Asian risk scoring systems to predict intravenous immunoglobulin resistance and coronary lesions in Kawasaki disease in an Italian cohort. *Eur J Pediatr*. 2019;178: 315–322.

45. Loomba RS, Raskin A, Gudausky TM, et al. Role of the Egami score in predicting intravenous immunoglobulin resistance in Kawasaki disease among different ethnicities. *Am J Ther*. 2016;23:e1293–e1299.

46. Sleeper LA, Minich LL, McCrindle BM, et al, Pediatric Heart Network Investigators. Evaluation of Kawasaki disease risk-scoring systems for intravenous immunoglobulin resistance. *J Pediatr*. 2011;158:831–835.e3.

47. Song R, Yao W, Li X. Efficacy of four scoring systems in predicting intravenous immunoglobulin resistance in children with Kawasaki disease in a children's hospital in Beijing, North China. *J Pediatr*. 2017;184: 120–124.

48. Kobayashi T, Inoue Y, Takeuchi K, et al. Prediction of intravenous immunoglobulin unresponsiveness in patients with Kawasaki disease. *Circulation*. 2006;113:2606–2612.

49. Egami K, Muta H, Ishii M, et al. Prediction of resistance to intravenous immunoglobulin treatment in patients with Kawasaki disease. *J Pediatr*. 2006;149:237–240.

50. Sano T, Kurotobi S, Matsuzaki K, et al. Prediction of non-responsiveness to standard high-dose gamma-globulin therapy in patients with acute Kawasaki disease before starting initial treatment. *Eur J Pediatr*. 2007;166: 131–137.

51. Sittiwangkul R, Pongprot Y, Silvilairat S, et al. Delayed diagnosis of Kawasaki disease: risk factors and outcome of treatment. *Ann Trop Paediatr*. 2011;31:109–114.

52. Levy M, Koren G. Atypical Kawasaki disease: analysis of clinical presentation and diagnostic clues. *Pediatr Infect Dis J*. 1990;9:122–126.

53. Genizi J, Miron D, Spiegel R, et al. Kawasaki disease in very young infants: high prevalence of atypical presentation and coronary arteritis. *Clin Pediatr (Phila)*. 2003;42:263–267.

54. Qiu H, He Y, Rong X, et al. Delayed intravenous immunoglobulin treatment increased the risk of coronary artery lesions in children with Kawasaki disease at different status. *Postgrad Med*. 2018;130:442–447.

55. Michihata N, Matsui H, Fushimi K, et al. Guideline-concordant treatment of Kawasaki disease with immunoglobulin and aspirin and the incidence of coronary artery aneurysm. *Clin Pediatr (Phila)*. 2015;54:1076–1080.

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CME EXAMINATION
November 2020

Please mark your answers on the ANSWER SHEET.

Current Approach to the Evaluation and Management of Incomplete Kawasaki Disease in the Emergency Department, *Morishita and Goldman*

1. Kawasaki disease predominantly affects:
   a. Infants
   b. School age children
   c. Children younger than 5 years
   d. Children younger than 2 years
   e. Teenagers

2. The risk of developing coronary artery aneurysms in untreated Kawasaki disease is:
   a. 1%
   b. 5%
   c. 10%
   d. 25%
   e. 50%

3. All of the following are criteria for the diagnosis of Kawasaki disease except:
   a. Bilateral conjunctivitis
   b. Fever for 4 days
   c. Cervical lymphadenopathy
   d. Rash
   e. Edema of the hands and feet

4. Any child with persistent unexplained fever for 5 or more days with 2 to 3 clinical features of KD should:
   a. Receive IVIG
   b. Undergo laboratory testing
   c. Should be observed until further clinical features appear
   d. Should have an urgent ECHO
   e. Should be admitted to hospital for observation

5. Children diagnosed with incomplete KD should have the following treatment:
   a. IVIG 1 g/kg
   b. IVIG 2 g/kg
   c. Moderate to high-dose ASA only
   d. Oral corticosteroids only
   e. Close monitoring until diagnosis of complete KD can be made

ANSWER SHEET FOR THE *PEDIATRIC EMERGENCY CARE* CME PROGRAM EXAM November 2020

Please answer the questions on page 542 by filling in the appropriate circles on the answer sheet below. Please mark the one best answer and fill in the circle until the letter is no longer visible. To process your exam, you must also provide the following information:

Name (please print): _____

Street Address _____

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Specialty _____

1. (A) (B) (C) (D) (E)
2. (A) (B) (C) (D) (E)
3. (A) (B) (C) (D) (E)
4. (A) (B) (C) (D) (E)
5. (A) (B) (C) (D) (E)

Your completion of this activity includes evaluating them. Please respond to the following questions below.

Please rate this activity (1 - minimally, 5 - completely)	1	2	3	4	5
Was effective in meeting the educational objectives	○	○	○	○	○
Was appropriately evidence-based	○	○	○	○	○
Was relevant to my practice	○	○	○	○	○

Please rate your ability to achieve the following objectives, both before this activity and after it:
1 (minimally) to 5 (completely)

	Pre					Post				
	1	2	3	4	5	1	2	3	4	5
1. Describe key presenting features of Kawasaki disease in the emergency department.	○	○	○	○	○	○	○	○	○	○
2. Identify diagnostic testing needed for children with incomplete Kawasaki disease in the primary care setting.	○	○	○	○	○	○	○	○	○	○
3. Explain clinical treatment strategies and their administration in children with incomplete Kawasaki disease.	○	○	○	○	○	○	○	○	○	○

How many of your patients are likely to be impacted by what you learned from these activities?

○ <20% ○ 20%–40% ○ 40%–60% ○ 60%–80% ○ >80%

Do you expect that these activities will help you improve your skill or judgment within the next 6 months? (1 - definitely will not change, 5 - definitely will change)	1	2	3	4	5
	○	○	○	○	○

How will you apply what you learned from these activities (mark all that apply):

- In diagnosing patients ○
- In monitoring patients ○
- In educating students and colleagues ○
- As part of a quality or peformance improvement project ○
- For maintenance of board certification ○
- To consider enrolling patients in clinical trials ○
- In making treatment decisions ○
- As a foundation to learn more ○
- In educating patients and their caregivers ○
- To confirm current practice ○
- For maintenance of licensure ○

Other _____

Please list at least one strategy you learned from this activity that you will apply in practice:

Please list at least one change you will make to your practice as a result of this activity:

Did you perceive any bias for or against any commercial products or devices?	Yes	No
	○	○

If yes, please explain:

How long did it take you to complete these activities? _____ hours _____ minutes

What are your biggest clinical challenges related to pediatric emergency care?

[ ] Yes! I am interested in receiving future CME programs from Lippincott CME Institute! (Please place a check mark in the box)

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