Kawasaki Disease (KD)

Emergency Department

Nationwide Children's — When your child needs a hospital, everything matters.

Center for Clinical Excellence

Patient with ≥ 4 days of fever

Patients with > 4 principal features and 3-4 days of fever

Other Clinical Features

Clinical features usually NOT associated with KD

Principle Clinical Features

- Bilateral nonexudative conjunctival injection
- Erythema/cracking of lips, strawberry tongue, erythema oral mucosa
- Erythema or swelling of distal extremity or periungual desquamation
- Rash
- Cervical adenopathy (≥ 1.5 cm), usually unilateral

Not all features need to be present at the same time.

Document features photographically, when possible

How many principle clinical features present

- 0-1 → ≤ 6 months old with fever ≥ 7 days?
  - No → **Unlikely KD** — **Consider alternate diagnoses** → Discharge if Clinically Stable — Follow up with PCP
  - Yes → **Possible Incomplete KD** — Obtain Labs*
- 2-3 → **Possible Incomplete KD** — Obtain Labs*
- 4-5 → **Complete KD** — Obtain Labs* → **Admit to ID** — *For patients with hemodynamic instability, discuss admission to ICU and echo in ED vs ICU*

*** Lab Tests:**

- CBC + Diff
- CRP/ESR
- Albumin
- ALT
- UA (microscopic)
- Red top tube to hold
- Blood culture
- Respiratory viral panel

CRP ≥ 3.0mg/dL **OR** ESR ≥ 40mm/hr

- Yes → **Consider Incomplete KD** → **Admit to ID**
- No → **Discharge if Clinically Stable**

A respiratory viral infection should not be used to exclude a diagnosis of KD

Discharge if Clinically Stable

Follow-up for any of the following:

- **Fever persists > 24 hours after evaluation**
- **Peeling of the fingers and toes occurs**
- **Total fever duration is ≥ 7 days**

Evaluation to include:

- **Repeat laboratory evaluation***
- **Inpatient echocardiogram if indicated**

Principle Clinical Features of KD

Fever:
- Typically high spiking and remittent.
- Spontaneous resolution of fever after 7 days should **not** be regarded as evidence that the diagnosis of KD has been excluded.

Conjunctival injection:
- Often begins shortly after fever and spares the limbus.
- Not typically associated with tearing or discharge.
- Anterior uveitis may be present by slit-lamp exam.
- Subconjunctival hemorrhage/punctate keratitis occasionally observed.
- Conjunctival injection that begins in one eye and then becomes bilateral is more typically associated with adenovirus infection.

Hand/feet swelling/changes:
- Erythema of the palms and soles and firm sometimes painful induration of the hands or feet often occur in the acute phase.
- Desquamation of the fingers and toes (around the nailbed, “periungual”) occurs only 2-3 weeks after fever onset and may extend to palms/soles.

Rash:
- Scarlatiniform, erythema multiforme-like, urticarial or micro-pustular.
- Usually extensive, primarily involving the trunk and extremities with accentuation in the groin.
- *KD rashes are typically NOT bullous, vesicular or petechial.*

Oral mucosal changes:
- Erythema, dryness, fissuring, cracking, bleeding or peeling of the lips.
- A “strawberry tongue” with erythema and prominent fungiform papillae may be present.
- *KD does NOT typically present with oral ulcers and/or pharyngeal exudate.*

Lymphadenopathy:
- This is the least common of the principal clinical features.
- Lymph node swelling is usually unilateral, > 1.5 cm in diameter, and confined to the anterior cervical triangle.

Other Clinical Features

McCrindle et al. Diagnosis, treatment, and long term management of Kawasaki disease. American Heart Association. Circulation. 2017;135:e927-e999.

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Definition & Diagnosis

Kawasaki disease (KD) is an acute, self-limited febrile illness of unknown etiology typically affecting children under the age of 5 years, though it can affect older children. KD is the most common cause of acquired heart disease in children in developed countries.

The highest risk period for coronary aneurysm is the first 6 weeks after diagnosis when the coronary artery dilation can occasionally expand to aneurysm, leading to thrombosis and rupture with ischemia, arrhythmia, and even sudden death.

With treatment, the majority of cardiac findings will resolve.

Definitions:

- **COMPLETE** presentation is defined as:
  - Fever of ≥ 4 days and at least 4 of 5 principal clinical features (conjunctival injection, oropharyngeal changes, unilateral cervical lymphadenopathy, hand/feet changes, and/or rash).
  - *In the presence of > 4 principal clinical features, particularly when redness and swelling of the hands and feet are present, the diagnosis may be made with only 4 days of fever, and for an experienced clinician rarely at day 3 of fever.*

- **INCOMPLETE** presentation is defined as one of the following:
  - Fever of ≥ 4 days and 2-3 principal features in those ≥ 6 months WITH elevated inflammatory markers and ≥ 3 supplemental lab criteria
  - Fever of any duration in any age child with documented coronary artery abnormalities (coronary diameters normalized to height and weight with calculated Z score of ≥ 2.5) with 2-3 cardinal features of the disease.
  - Fever in infants ≤ 6 months with fever of 7 or more days duration, evidence of systemic inflammation and no other explanation for the illness. These infants may have none of the principal clinical features of KD.

McCrindle et al. Diagnosis, treatment, and long term management of Kawasaki disease. American Heart Association. Circulation. 2017;135:e927-e999.

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Diagnostic Pearls

In the infant ≤ 6 months of age, prolonged fever and irritability may be the only clinical manifestations of Kawasaki disease (KD), and these children are at high risk of developing coronary artery abnormalities.

In a child with clinical findings compatible with classic KD, the detection of respiratory viruses such as respiratory syncytial virus, metapneumovirus, coronaviruses, parainfluenza viruses, or influenza viruses does not exclude the diagnosis of KD.

In children with some clinical features of KD and a positive rapid test or culture for group A streptococcus who do not improve after 24 to 48 hours of effective antibiotic therapy (streptococcal carriers), the diagnosis of KD should be again considered.

McCrindle et al. Diagnosis, treatment, and long term management of Kawasaki disease. American Heart Association. Circulation. 2017;135:e927-e999.

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Clinical Features Usually NOT Associated with KD

- **Features generally NOT consistent with KD:**
  - Exudative conjunctivitis
  - Exudative pharyngitis
  - Oral ulcerations
  - Splenomegaly
  - Vesiculobullous or petechial rashes
  - Acute lymphadenitis in which radiologic imaging reveals a sole node, especially with purulence

- Patients with adenovirus infections typically have conjunctival injection which begins mono-ocular and then becomes bilateral within 24-48 hours and is associated with EITHER tearing or exudate

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Other Clinical Features

Neurologic:

- **Common:**
  - Extreme irritability exceeding that observed in other febrile illnesses
  - Aseptic meningitis
- **Less common:**
  - Transient peripheral facial nerve palsy
  - Sensorineural hearing loss

Cardiovascular:

- **Common:**
  - Myocarditis
  - Inflammation of the pericardium, myocardium, endocardium including valves, and coronary arteries
- **Less Common:**
  - Arrhythmias
  - A shock-like picture, including myocardial dysfunction, valvar dysfunction (MR > TR > AR) and pericardial effusion

Gastrointestinal:

- **Common:**
  - Hepatitis
  - Diarrhea
  - Vomiting
  - Abdominal pain
  - Gallbladder hydrops
- **Less common:**
  - Pancreatitis
  - Jaundice

Genitourinary:

- **Common:**
  - Urethritis
- **Less common:**
  - Hydrocele
  - Phimosis

Musculoskeletal:

- First week of illness:
  - Arthralgia/arthritis involving small interphalangeal joints and large weight bearing joints
- Second-third week of illness:
  - Predominantly large weight bearing joints, especially knees and ankles (If aspirated, joint fluid may look purulent with a WBC count of 125,000-300,000/mm^3, normal glucose, negative Gram stain and culture)

Respiratory:

- Peribranchial and interstitial infiltrates on chest X-ray; nodular infiltrates occur rarely

Other:

- Prolonged fever and cervical lymphadenitis unresponsive to antibiotic therapy. Imaging can reveal cluster of lymph nodes.
- Prolonged fever and retropharyngeal or parapharyngeal phlegmon unresponsive to antibiotic therapy.
- Erythema and induration at the site of previous vaccination with bacille Calmette-Guerin.
- Macrophage Activation Syndrome: disseminated intravascular coagulopathy, cytopenia, thrombosis.

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Differential Diagnoses

Differential Diagnoses

- Viral infections (EBV, adenovirus, enterovirus, measles)
- Staphylococcal scalded skin syndrome
- Streptococcal toxin-mediated disease
- Drug hypersensitivity reactions including Stevens-Johnson syndrome
- Systemic onset juvenile idiopathic arthritis
- Rocky Mountain spotted fever
- Leptospirosis
- **Macrophage Activation Syndrome**
- **MIS-C** (Especially if known exposure to or known illness with COVID-19 in last month)

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Macrophage Activation Sydrome

2004 HLH/MAS diagnostic criteria, which includes 5 of the following 8 findings:

- Persistent fever > 38.5°C
- Splenomegaly
- Peripheral blood cytopenia, with at least two of the following: hemoglobin < 9 g/dL (for infants < 4 weeks, hemoglobin < 10 g/dL); platelets < 100,000/microL; absolute neutrophil count < 1000/microL
- Hypertriglyceridemia (fasting triglycerides > 265 mg/dL) and/or hypofibrinogenemia (fibrinogen < 150 mg/dL)
- Ferritin > 500 ng/mL (many consider a ferritin > 3000 ng/mL as more indicative of HLH)
- Hemophagocytosis in bone marrow, spleen, lymph node, or liver not diagnostic and not recommended at this time
- Low or absent NK cell activity newer literature with recommendations to not use this criteria due to the nature of the testing
- Elevated soluble CD25 (soluble IL-2 receptor alpha) two standard deviations above age-adjusted laboratory-specific norms

MAS patients are off pathway. Consult Rheumatology.

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Metrics

Pathway Goal

- **Evidence based standardized diagnostic approach to patients suspected or confirmed with Kawasaki disease with the timely initiation and escalation, if necessary, of treatment to promote optimal patient outcomes.**

Quality Measures

Outcome Metrics

- ED LOS
- ED Admission rate

Process Metrics

- Pathway EPIC tool utilization

Balancing Metrics

- ED and hospital readmission, all cause, 7 and 30 day

Pathway Team & Process

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Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associates with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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