Inclusion Criteria
- Patients suspected of having Kawasaki Disease (KD)
- ≥ 4 days since onset of fever

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

Principal Clinical Features
1. Mucositis – “strawberry tongue”
2. Nonpurulent conjunctivitis
3. Erythematous rash
4. Extremity changes – swelling/peeling
5. Cervical lymphadenopathy (≥ 1.5 cm diameter)

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

Evaluate for presence of principal clinical features

Laboratory Tests
- CBC + Diff
- CRP
- ESR
- Albumin
- ALT
- UA (microscopic)
- Red top tube to hold

Consider
- Blood culture
- Respiratory viral panel

Differential Diagnosis
- CRP ≥ 3.0 mg/dL and/or ESR ≥ 40 mm/hr
- CRP < 3.0 mg/dL and ESR < 40 mm/hr

Special Consideration
- If ED visit within 30 days of treatment for KD, evaluate for refractory KD with low threshold for treatment.

PHASE I (DIAGNOSIS)

<table>
<thead>
<tr>
<th>Presence of 2 or 3 principal clinical features</th>
<th>Presence of 4 or 5 principal clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 days of fever</td>
<td>Complete KD</td>
</tr>
<tr>
<td>5 to 10 days of fever</td>
<td>Suspected Incomplete KD</td>
</tr>
<tr>
<td>&gt; 10 days of fever</td>
<td>Complete KD</td>
</tr>
</tbody>
</table>

If diagnosis of KD is unclear, consider early Infectious Disease consult if diagnosis of KD is unclear.

Complete KD
- Order and initiate inpatient treatment as soon as diagnosis is made
- Order Echocardiogram and Electrocardiogram (if not done already) and Consult Cardiology and Infectious Disease

Suspected Incomplete KD

CRP ≥ 3.0 mg/dL and/or ESR ≥ 40 mm/hr
- Yes
- 2 or more Laboratory Findings:
  1. Anemia for age
  2. Platelet count of ≥ 450,000 after the 7th day of fever
  3. Albumin ≤ 3.0 g/dL
  4. Elevated ALT level
  5. WBC count of ≥ 15,000/mm³
  6. Urine ≥ 10 WBC/hpf
  OR
  Positive Echocardiogram
  (Call Cardiology to determine timing of Echocardiogram)

CRP < 3.0 mg/dL and ESR < 40 mm/hr
- No
- Discharge if Clinically Stable
  - Serial clinical and laboratory re-evaluation as outpatient if fevers persist
  - Echocardiogram if typical peeling occurs

For questions concerning this pathway, contact: KawasakiPathway@seattlechildrens.org
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Last Updated: June 2021
Next Expected Review: February 2023
**Kawasaki Disease Pathway v5.0: Management Phase**

**Inclusion Criteria**
- Complete KD or Incomplete KD diagnosis

**Echocardiogram** should be performed when the diagnosis of KD is considered, but unavailability or technical limitations should not delay treatment.

**PHASE II (MANAGEMENT)**

**Treatment**
- **High-dose IVIG**: 2 g/kg single infusion over 12 hours
- **Moderate-dose aspirin**: 30 to 50 mg/kg/day divided every 6 hours
- Verify Echocardiogram and Electrocardiogram have been done (repeat if abnormal per Cardiology)
- **Steroid use** as adjunct to primary treatment is controversial

**Document IVIG start time and completion time** (in Med Infusion Monitoring)

**Monitor for 36 hours after IVIG completion** (Fever may be related to IVIG)

**Fever between hour 24 and hour 36 after IVIG completion?**

- **Yes**
  - Fever defined as:
    - ≥ 38.5 °C for 1 reading
    - ≥ 38.0 °C for 2 readings at least 2 hours apart
  - Continue to monitor
  - Fever beyond 36 hours after IVIG completion
  - Refractory KD
  - Repeat Laboratory Tests
    - CBC + Diff
    - CRP
  - Management Options
    - Reassess differential diagnosis
    - Notify Cardiology and Rheumatology
    - Second dose of IVIG (2 g/kg)
    - Clinical judgment is needed to determine whether to consider additional/alternate therapies

**No**

**Transition to Low-dose Aspirin**
- Whichever comes first: at discharge OR if not ready for discharge, when afebrile for 48 hours
- 3 to 5 mg/kg once per day

**Discharge Criteria**
- Patient afebrile for at least 12 hours before discharge
- Patient received 6-week supply of low-dose aspirin
- Cardiology consult and Echocardiogram completed
- Cardiology follow-up and Echocardiogram scheduled in 2 weeks
- Patient received inactivated flu vaccine if in season
- Family received education materials regarding fever monitoring

**Patients with initial coronary artery z-score ≥ 2.5 should be considered for intensified initial treatment in consultation with Cardiology**

**Do not give ibuprofen or other NSAIDs while on aspirin**

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Principal Clinical Features

Not all features need to be present at the same time

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
Differential Diagnosis

The differential diagnosis includes other infectious and noninfectious conditions, including the following:

- Measles
- Other viral infections (eg, adenovirus, enterovirus)
- Staphylococcal and streptococcal toxin-mediated diseases (eg, scarlet fever and toxic shock syndrome)
- Drug hypersensitivity reactions, including Stevens Johnson syndrome
- Systemic onset juvenile idiopathic arthritis
- With epidemiologic risk factors:
  - Rocky Mountain spotted fever or other rickettsial infections
  - Leptospirosis
- Meningococcemia

Viral and bacterial infections can have symptoms that overlap with KD and should be considered and treated.

A respiratory viral infection should not be used to exclude a diagnosis of KD.
Special Consideration (> 10 days of fever)

If greater than 10 days since fever onset
AND
Presence of 2 to 5 principal clinical features
THEN

- It is reasonable to administer IVIG to children presenting after the 10th day of illness (ie, in whom the diagnosis was missed earlier) if they have either persistent fever without other explanation or coronary artery abnormalities together with ongoing systemic inflammation, as manifested by elevation of ESR or CRP (CRP >3.0 mg/dL)
  [LOE: Guideline: Class IIa, Level of Evidence B (McCrindle, 2017)]
- IVIG generally should not be administered to patients beyond the tenth day of illness in the absence of fever, significant elevation of inflammatory markers, or coronary artery abnormalities
  [LOE: Guideline: Class III, Level of Evidence C (McCrindle, 2017)]

High suspicion for KD in patients ≤ 12 months of age with onset of fever ≥ 7 days and without other clinical criteria for KD
Steroid Use

Steroid use as adjunct to primary treatment is controversial

Recommendations for adjunctive therapies for primary treatment:

- **Single-dose pulse methylprednisolone should not be administered with IVIG as routine primary therapy for patients with KD**
  [LOE: Guideline: Class III, Level of Evidence B (McCrindle, 2017)]

- **Administration of a longer course of corticosteroids (eg, tapering over 2–3 weeks), together with IVIG 2 g/kg and ASA, may be considered for treatment of high-risk patients with acute KD, when such high risk can be identified in patients before initiation of treatment**
  [LOE: Guideline: Class IIb, Level of Evidence B (McCrindle, 2017)]

Careful consultation with Cardiology
Additional/Alternate Therapies

Clinical judgment is needed to determine whether to consider additional/alternate therapies

- [LOE: Guideline: Class IIb, Level of Evidence B (McCrindle, 2017)]
  - High-dose pulse steroids (usually methylprednisolone +/- subsequent course and taper of oral prednisone)
  - Longer (eg, 2–3 weeks) tapering course of prednisolone or prednisone, together with IVIG 2 g/kg and ASA

- [LOE: Guideline: Class IIb, Level of Evidence C (McCrindle, 2017)]
  - Infliximab
  - Cyclosporine if second IVIG infusion, infliximab, or a course of steroids has failed
  - Monoclonal antibody therapy (except TNF-α blockers), cytotoxic agents, or (rarely) plasma exchange if second IVIG infusion, infliximab, or extended course of steroids has failed
Approved by the CSW Kawasaki Disease Pathway team for go-live on February 28, 2018

CSW Kawasaki Disease Pathway Team:

Cardiology, Owner
Michael Portman, MD

Rheumatology, Stakeholder
Matthew Basiaga, DO, MSCE

Emergency Medicine, Team Member
Elaine Beardsley, MN, ACCNS-P, CPEN

Rheumatology, Stakeholder
Kristen Hayward, MD, MS

Hospital Medicine, Team Member
Katie Kazmier, MD

Emergency Medicine, Stakeholder
Russ Migita, MD

Pharmacy, Stakeholder
Jennifer Rasiah, PharmD

Hospital Medicine, Stakeholder
Suzanne Sundermann, MD

Hospital Medicine, Literature Reviewer
Sarah Zaman, MD

Clinical Effectiveness Team:

Consultant
Sara Vora, MD, MPH

Project Manager
Ivan Meyer, PMP

Clinical Nurse Specialist
Rebecca Engberg, RN, BSN, CPN

CE Data Analyst
Nate Deam

CIS Informaticist
Mike Leu, MD

CIS Fellow
Reza Sadeghian, MD

CIS Analyst
Maria Jerome

Librarian
Peggy Cruse, MLIS

Program Coordinator
Kristyn Simmons

Executive Approval:

Sr. VP, Chief Medical Officer
Mark Del Beccaro, MD

Sr. VP, Chief Nursing Officer
Madlyn Murrey, RN, MN

Surgeon-in-Chief
Bob Sawin, MD

Retrieval Website:  http://www.seattlechildrens.org/pdf/Kawasaki-Disease-Pathway.pdf

Please cite as:

Return to Diagnosis Phase  Return to Management Phase
This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children’s. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94.):

Quality ratings are downgraded if studies:
- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are upgraded if it is felt that:
- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Guideline – Recommendation is from a published guideline that used methodology deemed acceptable by the team.

Expert Opinion – Our expert opinion is based on available evidence that does not meet GRADE criteria (for example, case-control studies).

**Quality of Evidence:**
- 🌟🌟🌟🌟 High quality
- 🌟🌟🌟 Moderate quality
- 🌟🌟 Low quality
- 🌟ΟΟΟ Very low quality

Guideline
Expert Opinion
Summary of Version Changes

- **Version 1.0 (2/28/2018):** Go live.
- **Version 2.0 (4/27/2018):** Changed warning in Management Phase to state, “Do not give ibuprofen or other NSAIDs while on aspirin.”
- **Version 3.0 (12/6/2019):** Added warning in Management Phase to state, “Patients with initial coronary artery z-score ≥ 2.5 should be considered for intensified initial treatment in consultation with Cardiology.”
- **Version 4.0 (5/19/2020):** Added warning in Diagnosis Phase to state, “Due to reports of PMIS, would send COVID-19 serology for all patients with confirmed or suspected KD.”
- **Version 5.0 (6/15/2021):** For Diagnosis Phase, removed warning for PMIS (MIS-C), added warning to state, “If ED visit within 30 days of treatment for KD, evaluate for refractory KD with low threshold for treatment,” and updated warning for “High suspicion for KD” to ≤ 12 months.
Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

However, in view of the possibility of human error or changes in medical sciences, neither the authors nor Seattle Children’s Healthcare System nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such information.

Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.
Search Methods, Kawasaki Disease Pathway, Clinical Standard Work

Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian, Peggy Cruse. Searches were performed in July, 2017. Queries were run in the following databases: Medline (Ovid platform), Cochrane Database of Systematic Reviews (Ovid platform), Embase (embase.com), National Guideline Clearinghouse (guideline.gov), TRIP (tripdatabase.com), and Cincinnati Children’s Evidence-Based Care Recommendations (cincinnatichildrens.org/service/anderson-center/evidence-based-care/recommendations). Medline and Embase strategies used controlled subject headings, along with text words to capture literature on Kawasaki disease (Mucocutaneous Lymph Node Syndrome). A synthesis-level evidence filter was applied to Kawasaki results to capture higher-level evidence syntheses. All retrieval was limited to English language and papers published from 2000 to July 2017.

Peggy Cruse, MLIS
October 25, 2017

Identification

306 records identified through database searching
0 additional records identified through other sources

Screening

246 records after duplicates removed

246 records screened
233 records excluded

Eligibility

13 records assessed for eligibility

4 full-text articles excluded,
1 did not answer clinical question
2 did not meet quality threshold
1 outdated relative to other included study

Included

9 studies included in pathway

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535


