Kawasaki Disease Diagnosis Pathway
Evidence Based Outcome Center

EXCLUSION CRITERIA
Complicating existing diagnoses:
- Hematologic
- Immunologic
- Rheumatic diseases
- Major Chronic inflammatory/immunologic diseases
- Significant congenital heart disease
- Infectious disease(s)
- Active uveitis
- Suspected systemic JIA with active systemic features

Not exclusive to these diagnosis review Differential Diagnosis.

GUIDELINE INCLUSION CRITERIA
Patients with symptoms concerning for possible Kawasaki Disease
- Prolonged febrile illness (>5 days) in a patient with any of the principle clinical features of Kawasaki Disease
- Patient exam with 4 or 5 principal clinical features and fever <5 days
- Prolonged fever in an infant <6 months without any principle clinical features

Order Diagnostic Labs:
- Complete blood count
- Complete metabolic panel
- Erythrocyte sedimentation rate
- C-reactive protein
- Urine analysis
- Gold/Yellow Top for additional workup

Consistent with Kawasaki Disease

YES
ADMIT patient to hospital
MANAGE OFF-PATHWAY

NO
Discuss with infectious diseases specialist

Previously treated for Kawasaki Disease

NO
MEETS CLASSIC DIAGNOSTIC CRITERIA FOR KAWASAKI DISEASE

YES
ADMIT patient to hospital
Classic Kawasaki Disease Management Pathway

NO
Assess Patient for Other Possible Clinical and Laboratory Findings

-AND-
Discuss with infectious diseases specialist

Consistent with Kawasaki Disease

NO
Review differential diagnosis
Manage OFF-PATHWAY

YES
ADMIT patient to hospital
MANAGE OFF-PATHWAY

1

Kawasaki Disease Diagnostic Criteria:
Prolonged febrile illness ≥5 days

-AND-
Presentation of four or more of the following symptoms meets classic criteria, if the patient presents with two or three symptom consider incomplete Kawasaki Disease:
1. bilateral conjunctival congestion
2. changes in lips and oral cavity: reddening of lips, strawberry tongue, diffuse injection of oral pharyngeal mucosa
3. polymorphous exanthema
4. changes in peripheral extremities: reddening of palms and soles, indurative edema (initial stage), membranous desquamation from fingertips (convalescent stage)
5. acute non-purulent cervical lymphadenopathy

For questions concerning this pathway, Click Here
Last Updated November 2, 2016
GUIDELINE INCLUSION CRITERIA

Patients with symptoms concerning for possible Kawasaki Disease
- Prolonged febrile illness (>5 days) in a patient with any of the principle clinical features of Kawasaki Disease
- Patient exam with 4 or 5 principal clinical features and fever <5 days

ICU Criteria

YES

Treatment:
- Intravenous immunoglobulin (IVIG) 2 g/kg single infusion per Protocol
- AND
- High dose aspirin: Dosing table

Order echocardiogram (ECHO) for day after completion of IVIG course

Kawasaki Disease Echocardiogram Pathway

Normal ECHO

YES

Persistent or recrudescent fever 36 hours after IVIG treatment

DISCHARGE CRITERIA

- Afebrile 36-48 hours after treatment
- Clinical Criteria:
  - C-reactive protein trending down
  - Normal heart rate
  - Patient irritability stable
  - Able to tolerate oral medication

YES

Aspirin Maintenance (Step-Down) Dosing
Continue Aspirin until directed to stop by Cardiologist

Complete Kawasaki Disease Action Plan
Discharge Education
Follow-up Schedule:
- Cardiology Clinic Visit 2-3 weeks after discharge
- Infectious Disease Clinic Visit 2-3 weeks after discharge

Discharge with Medication

NO

EXCLUSION CRITERIA

Atypical/Incomplete Kawasaki Disease
Kawasaki Disease with complicating morbidities
Recurrent/Refractory Kawasaki Disease
Pre-existing medications that modulate immune response
Complicating existing diagnoses:
- Hematologic
- Immunologic
- Rheumatic diseases
- Major Chronic inflammatory/immunologic diseases
- Significant congenital heart disease
- Infectious disease(s)
- Active uveitis
- Suspected systematic JIA with active systemic features

Not exclusive to these diagnosis review Differential Diagnosis.

ADMIT to PICU MANAGE OFF-PATHWAY
Consider consult with infectious diseases, hematology, rheumatology, and cardiology

MANAGE OFF-PATHWAY
Consult with infectious diseases and Cardiology

MANAGE OFF-PATHWAY
Consult with Infectious Diseases and Cardiology for management

I

PICU Criteria:
- Hypotension or any other signs of hemodynamic instability
- Known or developed cardiac complications requiring monitoring and intervention

For questions concerning this pathway, Click Here
Last Updated November 2, 2016
### (1) Other clinical and laboratory findings:

<table>
<thead>
<tr>
<th>Cardiovascular:</th>
<th>Gastrointestinal:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Congestive heart failure, myocarditis, pericarditis,</td>
<td>• Diarrhea, vomiting, abdominal pain</td>
</tr>
<tr>
<td>valvular regurgitation</td>
<td>• Hepatic dysfunction</td>
</tr>
<tr>
<td>• Coronary artery abnormalities</td>
<td>• Hydrops of gallbladder</td>
</tr>
<tr>
<td>• Aneurysms of medium-size noncoronary arteries</td>
<td></td>
</tr>
<tr>
<td>• Raynaud's phenomenon</td>
<td></td>
</tr>
<tr>
<td>• Peripheral gangrene</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Musculoskeletal system:</th>
<th>Genitourinary system:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Arthritis, arthralgia</td>
<td>• Urethritis/meatitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Central Nervous System</th>
<th>Other findings:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Irritability</td>
<td>• Anterior uveitis (mild)</td>
</tr>
<tr>
<td>• Aseptic meningitis</td>
<td>• Desquamating rash in groin</td>
</tr>
<tr>
<td>• Sensorineural hearing loss</td>
<td></td>
</tr>
</tbody>
</table>

### (2) Laboratory findings in Kawasaki Disease

- Normal or elevated WBC with predominance of neutrophils
- Elevated ESR (> 40 mm/h) and/or CRP (> 3 mg/dL)
- Anemia for age
- Albumin < 3 mg/dL
- Hyponatremia
- Thrombocytosis (platelets > 450,000 /mm³)
- Sterile pyuria (> 10 WBC/hpf)
- Elevated serum transaminases with or without elevated serum GGT or bilirubin
- CSF pleocytosis
- Leukocytosis in synovial fluid (WBC > 15,000 /mm³)

### (3) Differential Diagnosis for Kawasaki Disease

- Viral infections (adenovirus, EBV, enterovirus)
- Scarlet fever
- Staphylococcal scalded skin syndrome
- Toxic Shock syndrome
- Bacterial cervical lymphadenitis
- Drug hypersensitivity reactions
- Stevens-Johnson Syndrome
- Juvenile idiopathic arthritis
- Rocky Mountain spotted fever
- Leptospirosis
- Mercury hypersensitivity reaction
Kawasaki Disease Management – Echocardiogram Pathway
Evidence Based Outcome Center

Non-sedated Criteria
Patients who are developmentally and emotionally mature enough to cooperate with echocardiogram. Have demonstrated cooperation during previous interactions with medical personnel. Should be capable of lying still and cooperating for 30 minutes.

Perform non-sedated echocardiogram
-AND-
Document findings (LINK)

Adequate ECHO

YES

NO

Minimal-sedated Criteria
Patients who demonstrate a mild degree of apprehension or mildly limited capacity to cooperate with 30 minute procedure.

Administer intra-nasal midazolam
DOSE: 0.2 – 0.5 mg/kg | Max dose = 7.5 mg

Perform minimal-sedated echocardiogram
-AND-
Document findings (LINK)

Adequate ECHO

YES

NO

Sedated Criteria
Patients who have demonstrated a clear inability to cooperate with medical procedures.

Manage patient with Pediatric Guidelines for Analgesia, Anxiolysis, Amnesia & Sedation and Seton Sedation Policy

Perform sedated echocardiogram
-AND-
Document findings (LINK)

YES

NO

Cardiologist evaluate ECHO & Document findings (Link)

For questions concerning this pathway, Click Here
Last Updated November 2, 2016
This action plan is your “checklist” to make sure you and your child are prepared after your recent hospitalization for Kawasaki Disease. You should complete this form along with your care team before you leave the hospital.

- I received patient information packet on Kawasaki disease
  - No anomaly/aneurysm
  - Possible coronary anomaly/aneurysm

- Our first **Cardiology Clinic** visit will be in 2-3 weeks:
  - Date of visit: ____________________________
  - Provider: ________________________________
  - Phone number for office contact: ________________

- Our first **Infectious Disease Clinic** visit is in 2-3 weeks:
  - Date of visit: ____________________________
  - Provider: ________________________________
  - Phone number for office contact: ________________

- At my child’s first visits, the Cardiology and Infectious Disease Teams will arrange for future follow-up visits.

- I understand my child is to continue aspirin until instructed to stop by the cardiologist seen outside the hospital (Aspirin usually continues for 6-8 weeks).

I understand the following symptoms should make me worry. If any of the following are present, I will contact the Infectious Disease Doctors at 512-628-1820:
  - Fever over 100.4°F
  - Conjunctivitis (redness of the eyes)
  - Red lips and mouth
  - Rash
  - Unusual irritability
  - Swelling of hands or feet
  - Vomiting

- I understand live virus vaccines like the measles vaccine or the chicken pox vaccine should not be given to my child for 11 months after treatment with IVIG for Kawasaki Disease

- I understand that children on aspirin and their families should receive the influenza vaccination.
### Initial (Acute) Phase Dosing Recommendation:

80-100 mg/kg/day divided Q6H

<table>
<thead>
<tr>
<th>Weight Range</th>
<th>Dose</th>
<th>Total Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>++++</td>
<td>2.9</td>
<td>Individualized Weight Based Dosing</td>
</tr>
<tr>
<td>3 (108 mg/kg)</td>
<td>3.9</td>
<td>81 mg (1 tab) Q6H 324</td>
</tr>
<tr>
<td>4 (101 mg/kg)</td>
<td>4.9</td>
<td>101.25 mg (1.25 tabs) Q6H 405</td>
</tr>
<tr>
<td>5 (97 mg/kg)</td>
<td>5.9</td>
<td>121.5 mg (1.5 tabs) Q6H 486</td>
</tr>
<tr>
<td>6 (108 mg/kg)</td>
<td>7.9</td>
<td>162 mg (2 tabs) Q6H 648</td>
</tr>
<tr>
<td>8 (101 mg/kg)</td>
<td>9.9</td>
<td>202.5 mg (2.5 tabs) Q6H 810</td>
</tr>
<tr>
<td>10 (97 mg/kg)</td>
<td>11.9</td>
<td>243 mg (3 tabs) Q6H 972</td>
</tr>
<tr>
<td>12 (95 mg/kg)</td>
<td>13.9</td>
<td>283.5 mg (3.5 tabs) Q6H 1134</td>
</tr>
<tr>
<td>14 (93 mg/kg)</td>
<td>15.9</td>
<td>324 mg (4 tabs) Q6H 1296</td>
</tr>
<tr>
<td>16 (101 mg/kg)</td>
<td>19.9</td>
<td>405 mg (5 tabs) Q6H 1620</td>
</tr>
<tr>
<td>20 (97 mg/kg)</td>
<td>23.9</td>
<td>486 mg (6 tabs) Q6H 1944</td>
</tr>
<tr>
<td>24 (95 mg/kg)</td>
<td>27.9</td>
<td>567 mg (7 tabs) Q6H 2268</td>
</tr>
<tr>
<td>28 (93 mg/kg)</td>
<td>31.9</td>
<td>648 mg (8 tabs) Q6H 2592</td>
</tr>
<tr>
<td>32 (91 mg/kg)</td>
<td>35.9</td>
<td>729 mg (9 tabs) Q6H 2916</td>
</tr>
<tr>
<td>36 (90 mg/kg)</td>
<td>39.9</td>
<td>810 mg (10 tabs) Q6H 3240</td>
</tr>
<tr>
<td>40</td>
<td>++++</td>
<td>Individualized Weight Based Dosing</td>
</tr>
</tbody>
</table>

### Maintenance (Step-Down Dosing Recommendation):

3-5 mg/kg/day

<table>
<thead>
<tr>
<th>Weight Range</th>
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</tr>
</thead>
<tbody>
<tr>
<td>++++</td>
<td>3.9</td>
<td>Individualized Weight Based Dosing</td>
</tr>
<tr>
<td>4 (10 mg/kg)</td>
<td>13.9</td>
<td>40.5 mg (1/2 tab) Qday 40.5</td>
</tr>
<tr>
<td>14 (5.8 mg/kg)</td>
<td>++++</td>
<td>81 mg (1 tab) Qday 81</td>
</tr>
</tbody>
</table>

- Aspirin 81 mg tablets may be crushed/chewed and mixed with flavoring for immediate single dose administration. Aspirin 81 mg tablets CANNOT be compounded into a suspension for multi-dose administration.
- Aspirin 325 mg tablets are enteric coated (EC) and CANNOT be crushed or chewed.
- Substitution with 325 mg tablets may be considered for patients on high doses and patients able to tolerate swallowing tablets whole.
- Maximum daily dose = 4000 mg/day or 120 mg/kg/day, whichever is less.
- Long term, high dose aspirin therapy puts children at increased risk for Reye’s syndrome.
For questions concerning this pathway, Click Here

Last Updated November 2, 2016

Kawasaki Disease
Principles of Echocardiographic Assessment
Evidence Based Outcome Center

- **Primary aim**
  - Identify coronary artery involvement, pericarditis, and/or myocarditis

- **Timing of echocardiography**
  - Uncomplicated Kawasaki
    - At time of diagnosis
    - Two-three weeks
    - Six to eight weeks
  - Complicated Kawasaki
    - At minimum, should adhere to echocardiography timing for uncomplicated Kawasaki
    - Increased frequency of imaging may be necessary and should be determined by clinical provider

- **Optimization of overall image assessment (improving quality and resolution)**
  - Plan for possible sedation in children between 12mo-3yrs
  - Use highest possible frequency transducer
  - Use cine loops/still frame images in conjunction with color Doppler imaging
  - Reduce two-dimensional gain and compression
  - Use low Nyquist limit to optimize visualization of normal diastolic coronary flow

- **Echocardiographic report content**
  - Coronary arteries
    - Visualization and location of coronary arteries
    - Presence and description of coronary abnormalities
    - Summary comment in conclusions about presence/absence of coronary involvement
  - Valvular function
  - Biventricular systolic function
  - Presence of pericardial effusion
  - Presence of pleural effusions

- **Coronary artery assessment**
  - Should be performed in multiple imaging planes
  - Optimal views to attain imaging of each coronary should be attempted (see page 2)
  - Method of measurement (see page 3)
    - Inner edge to inner edge of the vessel wall and not measured at the level of normal branching
  - Descriptions of coronaries should use specific descriptive terms (see page 3)

- **Additional resources** (page 4-5)
  - Normal coronary artery diameters with mean and standard deviation
  - Additional information about Kawasaki
  - Atypical Kawasaki-Echocardiographic Assessment

- **References** (page 8)
Optimal Views to Image Coronary Arteries

- Left main coronary artery (LMCA):
  - parasternal short axis at level of aortic valve
  - parasternal long axis toward PA
  - subcostal left ventricular long axis

- Left anterior descending (LAD):
  - parasternal short axis at level of aortic valve
  - parasternal long axis toward PA
  - parasternal short axis of left ventricle

- Left circumflex (LCx):
  - parasternal short axis at level of aortic valve
  - apical 4-chamber in MV AV groove

- Right coronary artery (RCA):
  - proximal segment:
    - parasternal short axis at level of aortic valve
    - parasternal long axis toward the TV
    - subcostal coronal projection of RVOT
    - subcostal short axis at level of AV groove
  - middle segment:
    - parasternal long axis of left ventricle toward TV
    - apical 4-chamber
    - subcostal left ventricular long axis
    - subcostal short axis at level of AV groove
  - distal segment
    - apical 4-chamber (inferior)
    - subcostal atrial long axis (inferior)

- Posterior descending artery (PDA):
  - apical 4-chamber (inferior)
  - subcostal atrial long axis (inferior)
  - parasternal long axis (inferior tangential) imaging
  - posterior interventricular groove
Method of Measurement (inner-to-inner)

- Left main coronary artery (LMCA)
  - Measure in the mid-position, distal to the flaring often seen near the aortic orifice and before the first bifurcation
- Left anterior descending (LAD)
  - Measure distal to the bifurcation and before the first marginal branch
- Right coronary artery (RCA)
  - Measure in the relatively straight section of artery just after the initial rightward turn from the anterior facing sinus of Valsalva

Coronary Descriptors

-Specific terminology should be used to describe coronary abnormalities seen in patients with Kawasaki disease in order to improve interoperator reliability between reports
- Main features of coronary artery involvement:
  - Dilatation (intra-luminal diameter Z-score of ≥ 2.5mm)
    - Ectatic:
      - Uniform: dilated long segment
      - Segmented: multiple dilatations joined by normal or stenotic areas
    - Lack of tapering of the distal coronary vessel
  - Perivascular brightness
  - Aneurysm formation
    - Fusiform: spindle-shaped, gradual tapering from normal to dilated segment
    - Saccular: spherical, acute transition from normal to dilated segment
Normal Coronary Diameters

-Mean and prediction limits for 2 and 3 SDs for size of LAD (A), proximal RCA (B), and LMCA (C) according to body surface area for children <18 years old. Adapted from de Zorzi, Newburger, J. W. et al. Pediatrics 2004;114:1708-33.
Additional Information about Kawasaki

- Common sites of coronary involvement (from highest to lowest frequency):
  - Proximal LAD
  - Proximal RCA
  - LMCA
  - LCx
  - Distal RCA
  - Junction of RCA and PDA

- Risk stratification of aneurysms
  - Smaller aneurysms/fusiform aneurysms have greater chance of resolution
  - Distal coronary artery aneurysms tend to regress more rapidly than proximal aneurysms

- Cardiovascular disease
  - History of Kawasaki disease may increase risk for adult cardiovascular disease
  - Studies show abnormal vascular endothelial function, intimal thickness and abnormal lipid profiles
EBOC Project Owner: Kenneth Shaffer, MD

Approved by the Kawasaki Disease Evidence-Based Outcomes Center Team

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