Clinical Pathways

Kawasaki Disease and Incomplete Kawasaki Disease

Marta Neubauer, MD
Melissa Held, MD
Heather Tory, MD
Alex Golden, MD

Connecticut Children's

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

BEST CHILDREN'S HOSPITAL WOMEN'S CHOICE AWARD 2023

What is a Clinical Pathway?

An evidence-based guideline that decreases unnecessary variation and helps promote safe, effective, and consistent patient care.

Objectives of Pathway

- Standardize care of patients with Kawasaki Disease and Incomplete Kawasaki Disease
- Reduce the incidence of coronary artery aneurysms
- Reduce the time to IVIG treatment
- Reduce inpatient length of stay
- If steroids are used, reduce the incidence of refractory Kawasaki Disease

Why is Pathway Necessary?

- Kawasaki Disease is one of the most common vasculitides of childhood, and is the most common cause of acquired heart disease in children in developed countries
- Estimated annual incidence of 20 per 100,000 children younger than five years in the United States, and prevalence is higher in children of Japanese or East Asian descent
- Complications such as coronary artery aneurysms, myocardial dysfunction, and heart failure may develop and lead to significant morbidity and mortality
- Given the high risk of delayed diagnosis and/or treatment, it is imperative to standardize care to expedite recognition and timely treatment of Kawasaki Disease

Kawasaki Disease Clinical Features

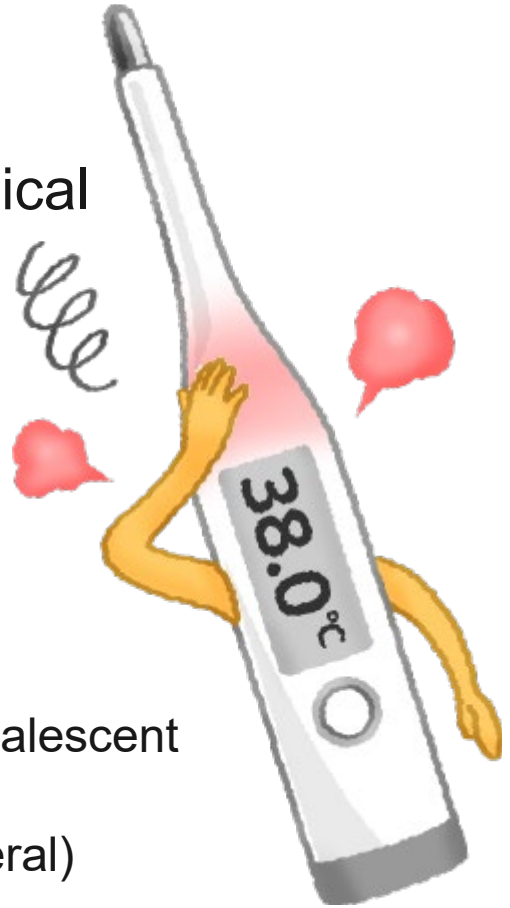
Fever for at least 5 days **and** *at least* 2/5 of the following clinical criteria

OR

Newly added

Fever for at least 4 days **and** *at least* 4/5 of the following clinical criteria:

- Bilateral bulbar non-exudative conjunctivitis
- Mucosal changes
  - Red, cracked lips
  - Strawberry tongue
  - Erythema of oral and pharyngeal mucosa
- Polymorphous Rash
- Extremity changes (swelling and/or erythema; peeling occurs in convalescent phase)
- Cervical lymphadenopathy of at least 1.5cm diameter (usually unilateral)



See the Kawasaki Pathway (page 1)

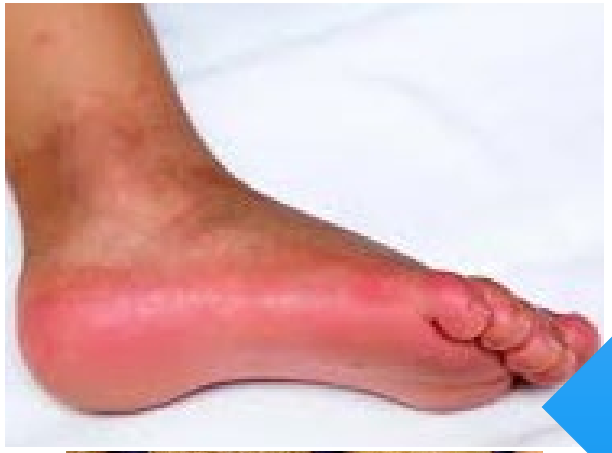
Kawasaki Disease Clinical Features

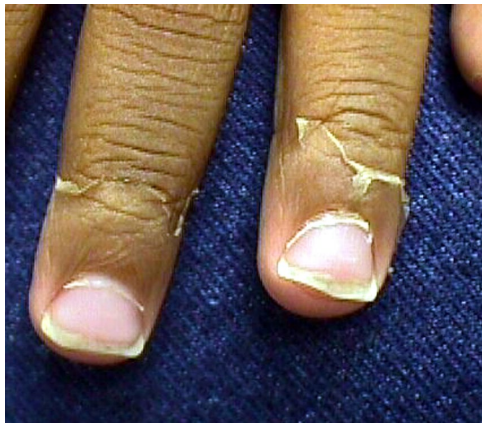
Conjunctivitis: Bilateral bulbar conjunctival injection without exudate

Oral Changes:

Erythema and cracking of the lips, strawberry tongue, or erythema of oral and pharyngeal mucosa

Kawasaki Disease Clinical Features





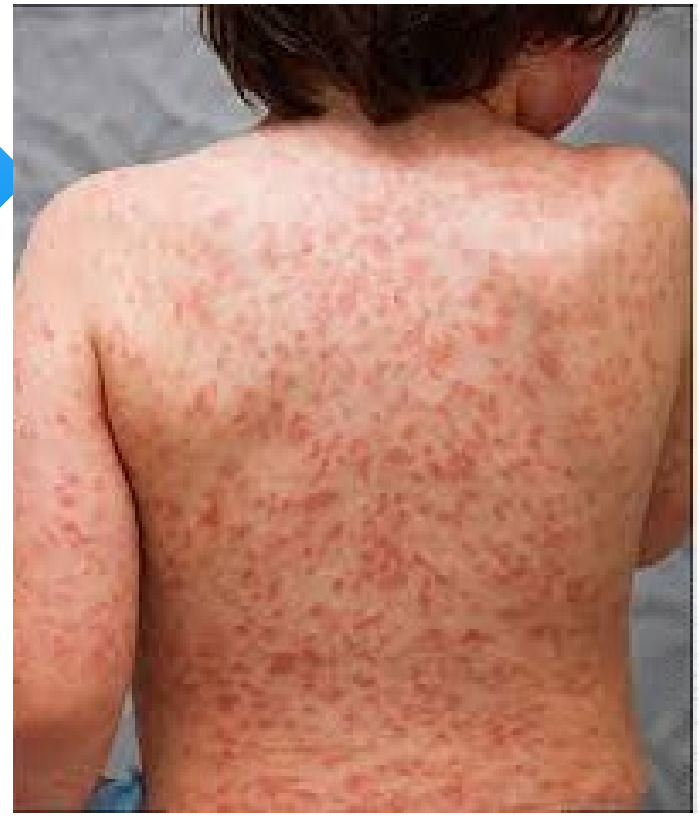
Extremity Changes:

Swelling and/or erythema; or desquamation in convalescent phase

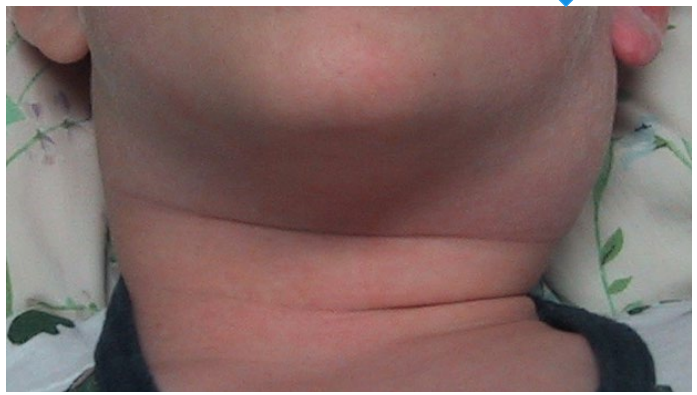
Rash:

Diffuse maculopapular rash

(There are many variations)



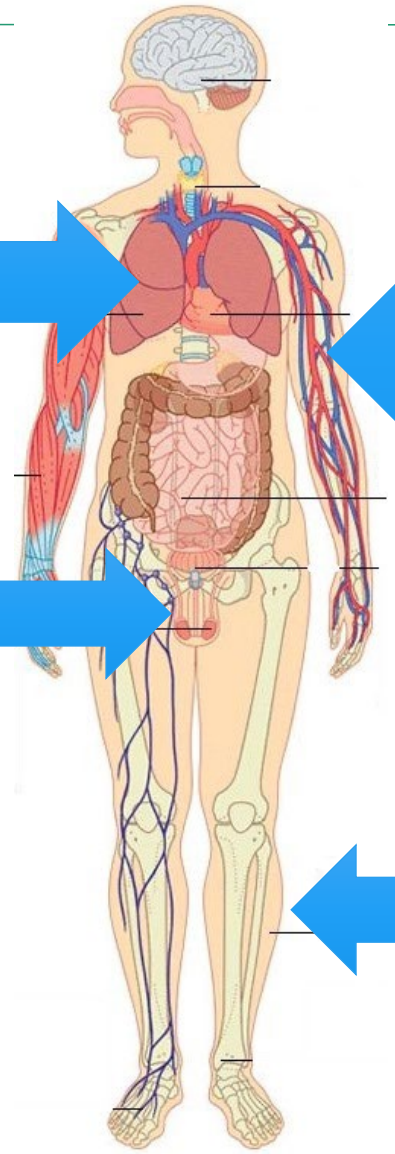
Cervical Lymphadenopathy: at least 1.5cm in diameter



Other Clinical Findings

Respiratory System:
- Peribronchial and interstitial infiltrates
- Pulmonary nodules

Genitourinary:
- Urethritis
- Hydrocele
- Orchitis

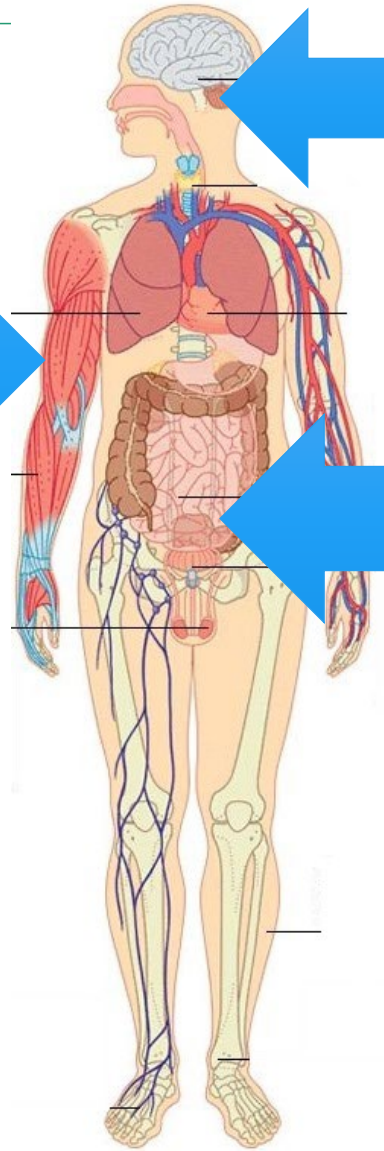


Cardiovascular System:
- Decreased LV ejection fraction (85% patients, generally transient
- Myocarditis (50-70% patients), pericarditis, shock
- Valvular dysfunction (25% patients), typically mitral valve
- Aneurysms of non-coronary arteries
- Peripheral gangrene
- Aortic root enlargement
- Small pericardial effusion
- EKG changes (prolonged PR interval, low voltage, non-specic ST and T wave changes

Skin:
- Erythema and induration at a previous BCG vaccine site

Other Clinical Findings

Musculoskeletal System:
- Arthritis, arthralgia (arthrocentesis will show aseptic purulent fluid with WBCs 125,000 to 300,000 per mm^3 but normal glucose)



Nervous System:
- Irritability/Encephalopathy
- Aseptic meningitis in about 30% of kids
- Transient Facial nerve palsy
- Temporary Sensorineural hearing loss in 1 of 5 kids; rarely permanent

Gastrointestinal:
- Abdominal pain, diarrhea, vomiting
- Hepatitis, jaundice
- Pancreatitis
- Gallbladder hydrops
- Splenomegaly is NOT seen in Kawasaki

Diagnosis: Incomplete Kawasaki

- Presentation of KD is not always classic
- Children who should be further evaluated for incomplete KD include:
  - Children with at least 5 days of fever, but have *only* 2 or 3 clinical signs of KD, **or**
  - Infants with fever for 7 days or more with no identified source

See the Incomplete Kawasaki Pathway (page 2)

This is the Kawasaki Disease Clinical Pathway.

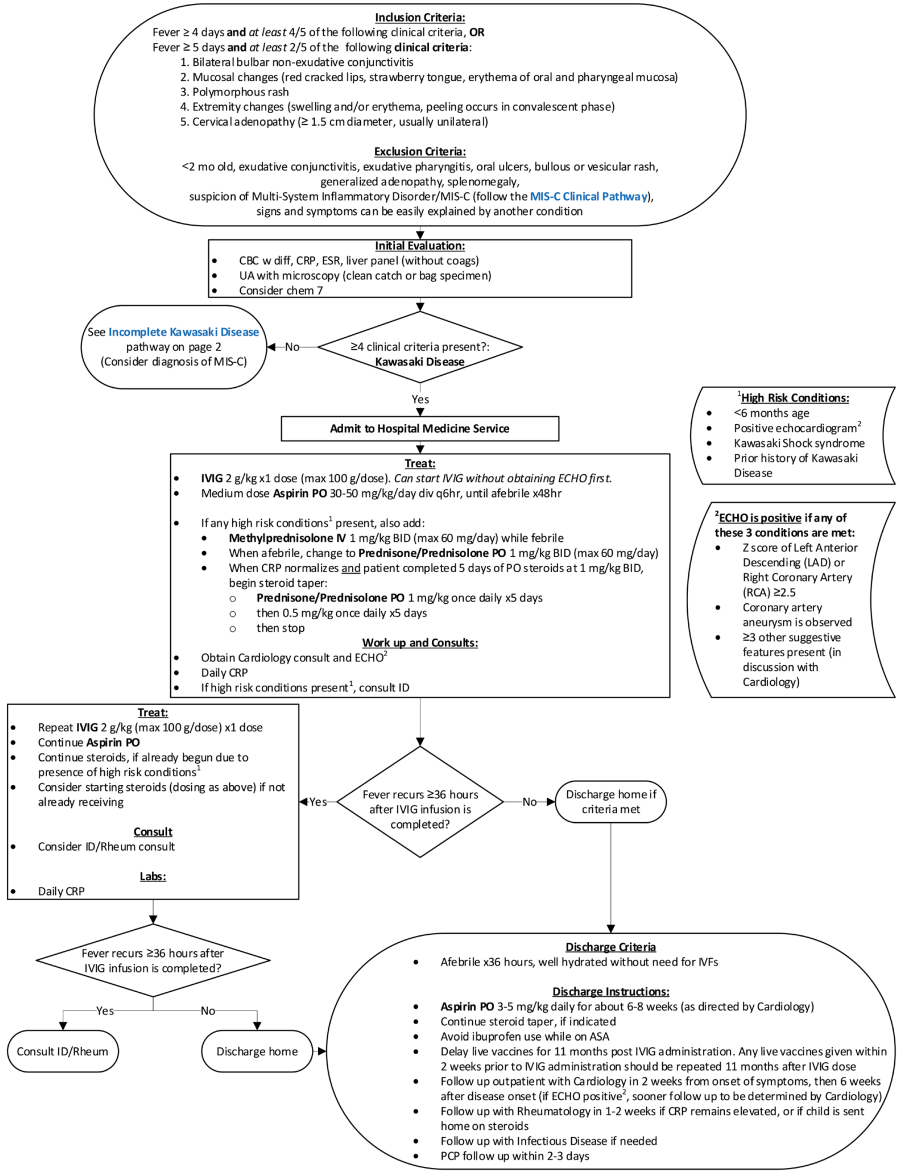
It is comprised of Kawasaki disease (page 1), and Incomplete Kawasaki disease (page 2).

We will be reviewing each component in the following slides.

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

If a patient presents with clinical suspicion for Kawasaki Disease (KD), the initial management is a thorough history and physical exam to determine if any clinical criteria are present.

Screening labs should be done.
★ Chem 7 can now be considered for screening.

If a patient matches criteria for KD then you proceed with the main pathway.

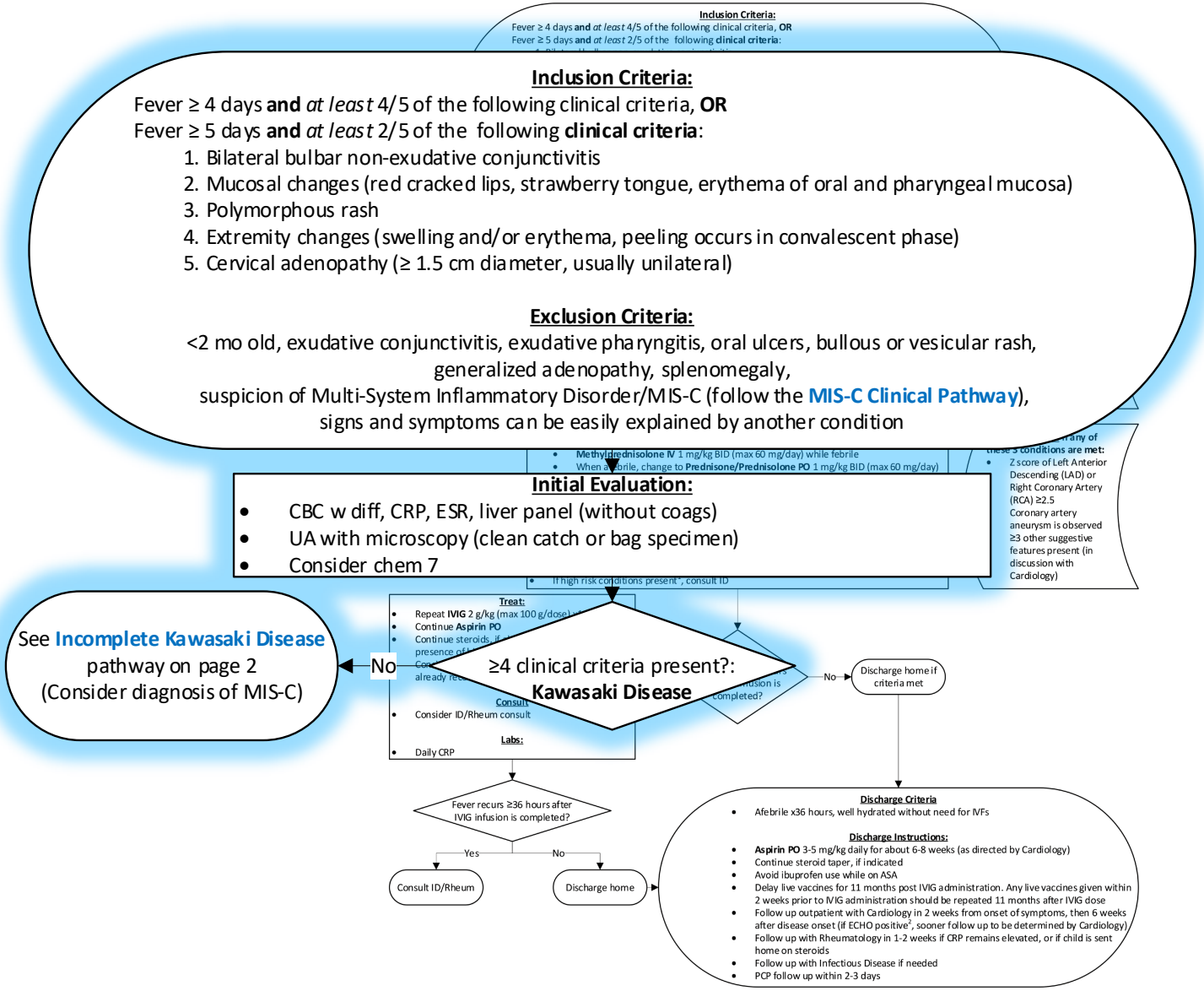
If they do not meet criteria for full KD then go to the Incomplete Kawasaki Disease Pathway

→ See the Incomplete Kawasaki Disease Pathway in later slides

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Kawasaki Disease

If a patient is identified as meeting criteria for Kawasaki Disease, treatment should not be delayed while the work up continues (ECHO, consults, etc.).

Cardiology consults will be routine, and ECHO may wait until the morning if patient admitted overnight

Inclusion Criteria:

Fever ≥ 4 days **and** *at least* 4/5 of the following clinical criteria, **OR**
Fever ≥ 5 days **and** *at least* 2/5 of the following **clinical criteria**:

1. Bilateral bulbar non-exudative conjunctivitis
2. Mucosal changes (red cracked lips, strawberry tongue, erythema of oral and pharyngeal mucosa)
3. Polymorphous rash
4. Extremity changes (swelling and/or erythema, peeling occurs in convalescent phase)
5. Cervical adenopathy (≥ 1.5 cm diameter, usually unilateral)

Exclusion Criteria:

<2 mo old, exudative conjunctivitis, exudative pharyngitis, oral ulcers, bullous or vesicular rash, generalized adenopathy, splenomegaly, suspicion of Multi-System Inflammatory Disorder/MIS-C (follow the MIS-C Clinical Pathway), signs and symptoms can be easily explained by another condition

Initial Evaluation:

- CBC w diff, CRP, ESR, liver panel (without coags)
- UA with microscopy (clean catch or bag specimen)
- Consider chem 7

≥4 clinical criteria present?: **Kawasaki Disease**

Yes

Admit to Hospital Medicine Service

Treat:

- **IVIG** 2 g/kg x1 dose (max 100 g/dose). *Can start IVIG without obtaining ECHO first.*
- Medium dose **Aspirin PO** 30-50 mg/kg/day div q6hr, until afebrile x48hr

- If any high risk conditions[1] present, also add:
  - **Methylprednisolone IV** 1 mg/kg BID (max 60 mg/day) while febrile
  - When afebrile, change to **Prednisone/Prednisolone PO** 1 mg/kg BID (max 60 mg/day)
  - When CRP normalizes and patient completed 5 days of PO steroids at 1 mg/kg BID, begin steroid taper:
    - **Prednisone/Prednisolone PO** 1 mg/kg once daily x5 days
    - then 0.5 mg/kg once daily x5 days
    - then stop

Work up and Consults:

- Obtain Cardiology consult and ECHO[2]
- Daily CRP
- If high risk conditions present[1], consult ID

No → ≥4 clinical criteria present?: **Kawasaki Disease**

Yes → Admit to Hospital Medicine Service

Incomplete Kawasaki Disease pathway on page 2 (Consider diagnosis of MIS-C)

Treat:

- **IVIG** 2 g/kg x1 dose (max 100 g/dose). *Can start IVIG without*
- Medium dose **Aspirin PO** 30-50 mg/kg/day div q6hr, until af
- If any high risk conditions[1] present, also add:
  - **Methylprednisolone IV** 1 mg/kg BID (max 60 mg/day) w
  - When afebrile, change to **Prednisone/Prednisolone PO**
  - When CRP normalizes and patient completed 5 days of P

Work up and Consults:

- Obtain Cardiology consult and ECHO[2]
- Daily CRP
- If high risk conditions present[1], consult ID

aneurysm is observed
- ≥3 other suggestive

Work up outpatient with Cardiology in 2 weeks from onset of symptoms, then 6 weeks after disease onset (if ECHO positive[2], sooner follow up to be determined by Cardiology)

- Follow up with Rheumatology in 1-2 weeks if CRP remains elevated, or if child is sent home on steroids
- Follow up with Infectious Disease if needed
- PCP follow up within 2-3 days

[1]High Risk Conditions:

- < 6 months age
- Positive echocardiogram[2]
- Kawasaki Shock syndrome
- Prior history of Kawasaki Disease

[2]ECHO is positive if any of these 3 conditions are met:

- Z score of Left Anterior Descending (LAD) or Right Coronary Artery (RCA) ≥2.5
- Coronary artery aneurysm is observed
- ≥3 other suggestive features present (in discussion with Cardiology)

CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

Connecticut Children's

Kawasaki Disease

Treatment consists of IVIG and medium dose Aspirin

Goals of therapy are to:

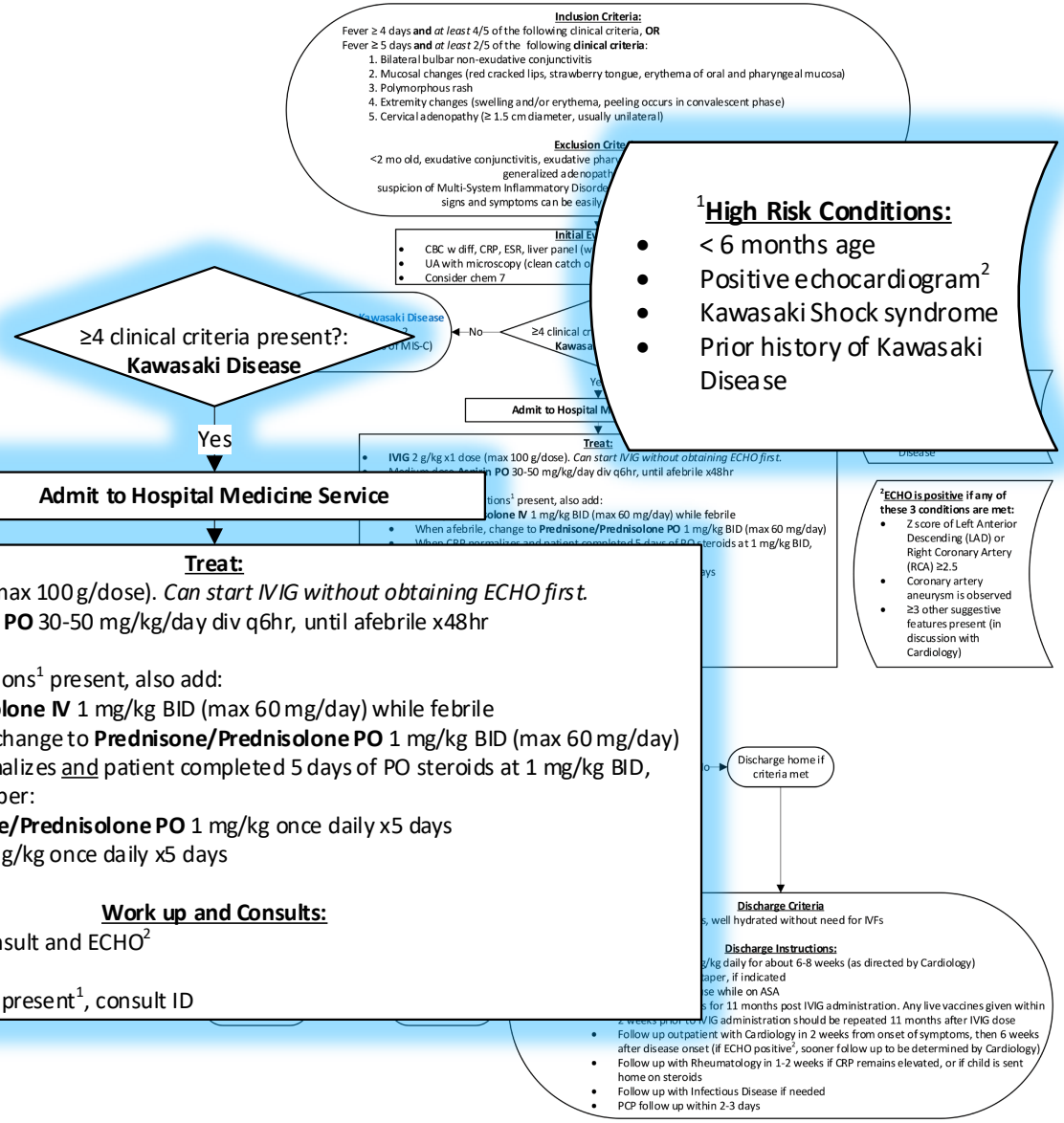
1. reduce the systemic inflammatory process
2. prevent coronary artery abnormalities
3. if coronary artery abnormalities are present, then to minimize the peak dimension and any clots

If a patient has any high risk characteristics, consult with Infectious Diseases and consider adding steroids with a taper

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

CLINICAL PATHWAY:

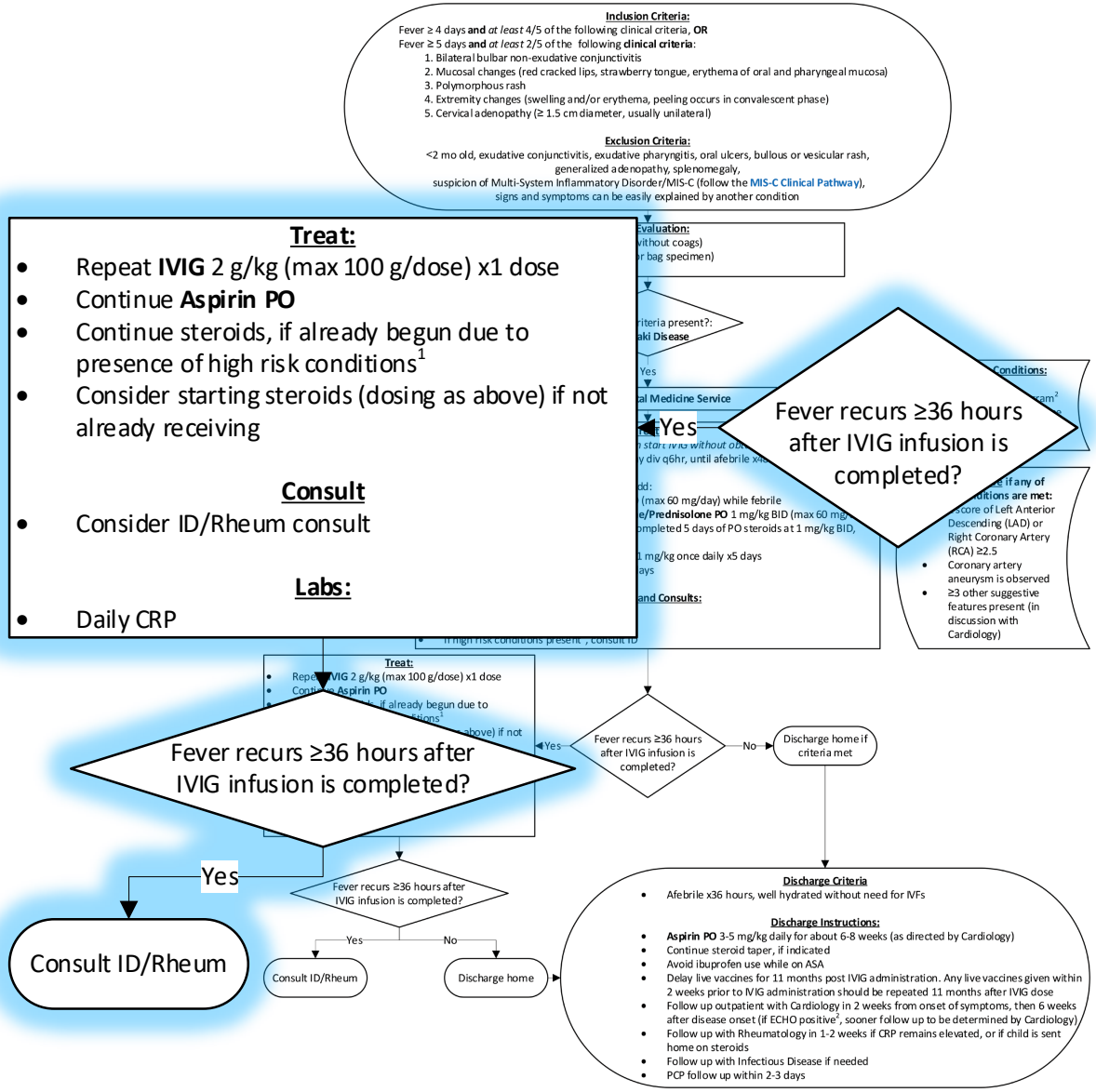
Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Kawasaki Disease

IVIG treatment may be repeated for a second dose if the patient's fever recurs ≥36 hours after the IVIG infusion is completed.

Consider Infectious Disease and/or Rheumatology consults at any point, particularly if the patient's fever recurs ≥36 hours after the 2nd IVIG infusion is completed.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

Kawasaki Disease

Discharge can be considered once a patient is fever free for 36 hours and well hydrated.

Low dose Aspirin is continued on an outpatient basis as directed by Cardiology.

If patient is discharged on steroids, they should follow up with Rheumatology.

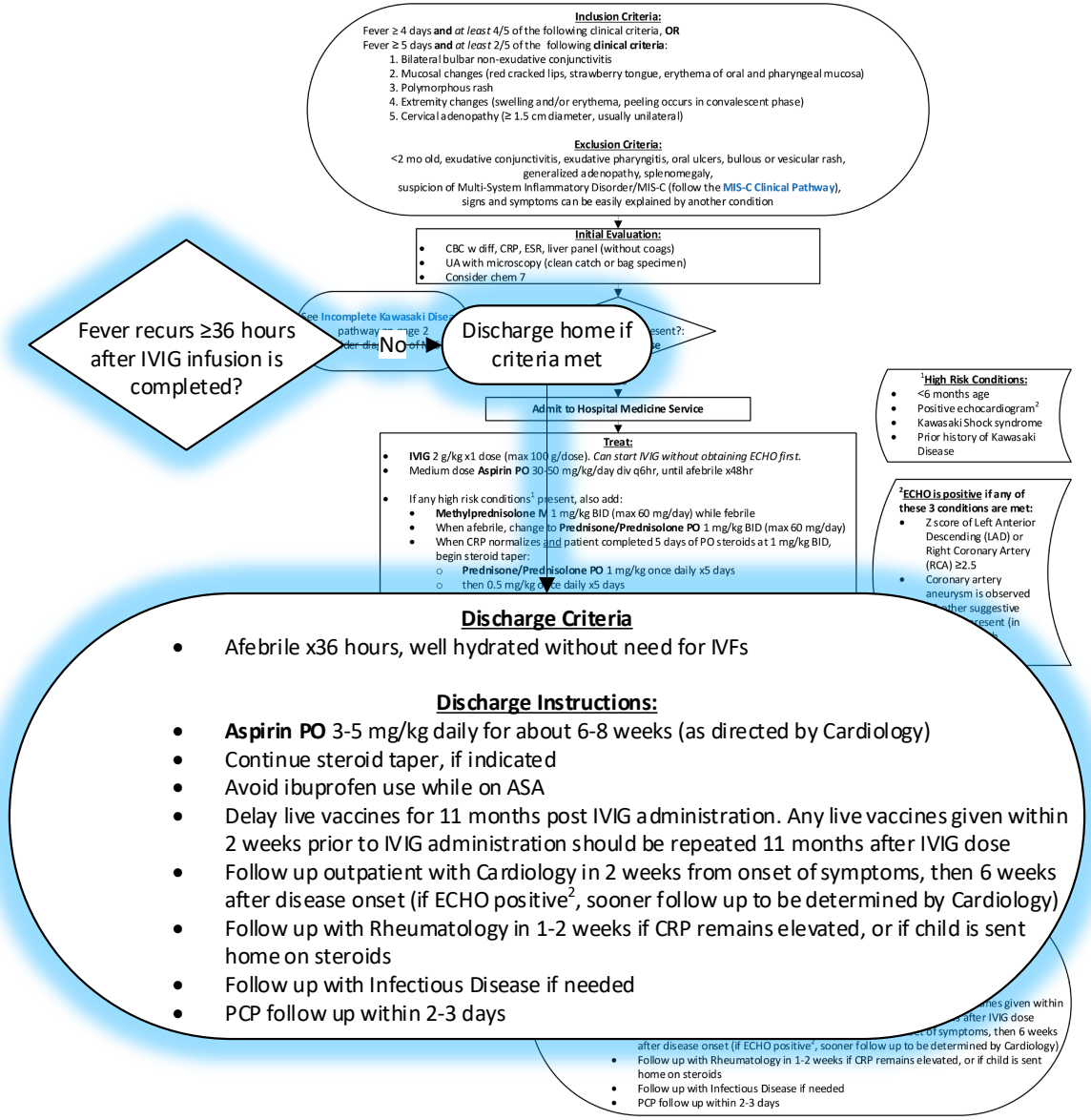
Parental education prior to discharge is imperative

- Emphasize the importance of continuing Aspirin and/or steroids as directed, delaying live vaccines, and following up with necessary services.

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

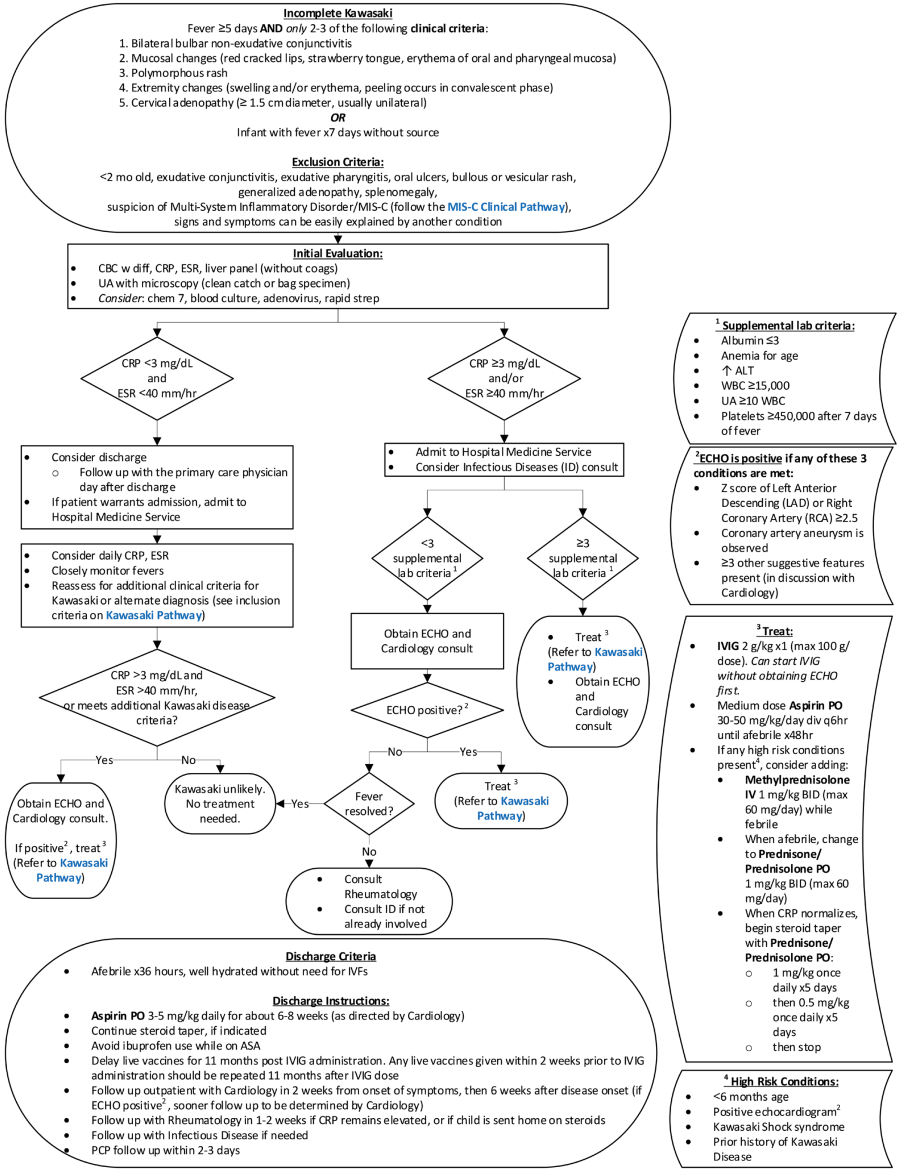
LAST UPDATED: 05.17.24

This is the Incomplete Kawasaki Disease Clinical Pathway.

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

Connecticut Children's

Incomplete Kawasaki Disease

If a patient meets criteria for incomplete Kawasaki Disease, the initial lab work done on presentation is used to guide further work up and possible treatment as necessary.

CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Incomplete Kawasaki

Fever ≥5 days **AND** *only* 2-3 of the following **clinical criteria**:

1. Bilateral bulbar non-exudative conjunctivitis
2. Mucosal changes (red cracked lips, strawberry tongue, erythema of oral and pharyngeal mucosa)
3. Polymorphous rash
4. Extremity changes (swelling and/or erythema, peeling occurs in convalescent phase)
5. Cervical adenopathy (≥ 1.5 cm diameter, usually unilateral)

OR

Infant with fever x7 days without source

Exclusion Criteria:

<2 mo old, exudative conjunctivitis, exudative pharyngitis, oral ulcers, bullous or vesicular rash, generalized adenopathy, splenomegaly, suspicion of Multi-System Inflammatory Disorder/MIS-C (follow the MIS-C Clinical Pathway), signs and symptoms can be easily explained by another condition

Hospital Medicine Service

Initial Evaluation:

- CBC w diff, CRP, ESR, liver panel (without coags)
- UA with microscopy (clean catch or bag specimen)
- *Consider*: chem 7, blood culture, adenovirus, rapid strep

Right Coronary Artery (RCA) ≥2.5

Pathway)

- Obtain ECHO and Cardiology consult

dose). *Can start IVIG without obtaining ECHO first.*

- Medium dose **Aspirin PO** 30-50 mg/kg/day div q6hr until afebrile x48hr
- If any high risk conditions present[4], consider adding:
  - **Methylprednisolone IV** 1 mg/kg BID (max 60 mg/day) while febrile
  - When afebrile, change to **Prednisone/ Prednisolone PO** 1 mg/kg BID (max 60 mg/day)
  - When CRP normalizes, begin steroid taper with **Prednisone/ Prednisolone PO**:
    - 1 mg/kg once daily x5 days
    - then 0.5 mg/kg once daily x5 days
    - then stop

CRP >3 mg/dL and ESR >40 mm/hr, or meets additional Kawasaki disease criteria?

Yes → Obtain ECHO and Cardiology consult. If positive[2], treat[3] (Refer to Kawasaki Pathway)

No → Kawasaki unlikely. No treatment needed.

ECHO positive?[2]

No → Fever resolved?

Yes → Kawasaki unlikely. No treatment needed.

No → Consult Rheumatology; Consult ID if not already involved

Yes → Treat[3] (Refer to Kawasaki Pathway)

Discharge Criteria

- Afebrile x36 hours, well hydrated without need for IVFs

Discharge Instructions:

- **Aspirin PO** 3-5 mg/kg daily for about 6-8 weeks (as directed by Cardiology)
- Continue steroid taper, if indicated
- Avoid ibuprofen use while on ASA
- Delay live vaccines for 11 months post IVIG administration. Any live vaccines given within 2 weeks prior to IVIG administration should be repeated 11 months after IVIG dose
- Follow up outpatient with Cardiology in 2 weeks from onset of symptoms, then 6 weeks after disease onset (if ECHO positive[2], sooner follow up to be determined by Cardiology)
- Follow up with Rheumatology in 1-2 weeks if CRP remains elevated, or if child is sent home on steroids
- Follow up with Infectious Disease if needed
- PCP follow up within 2-3 days

[4] High Risk Conditions:

- <6 months age
- Positive echocardiogram[2]
- Kawasaki Shock syndrome
- Prior history of Kawasaki Disease

CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

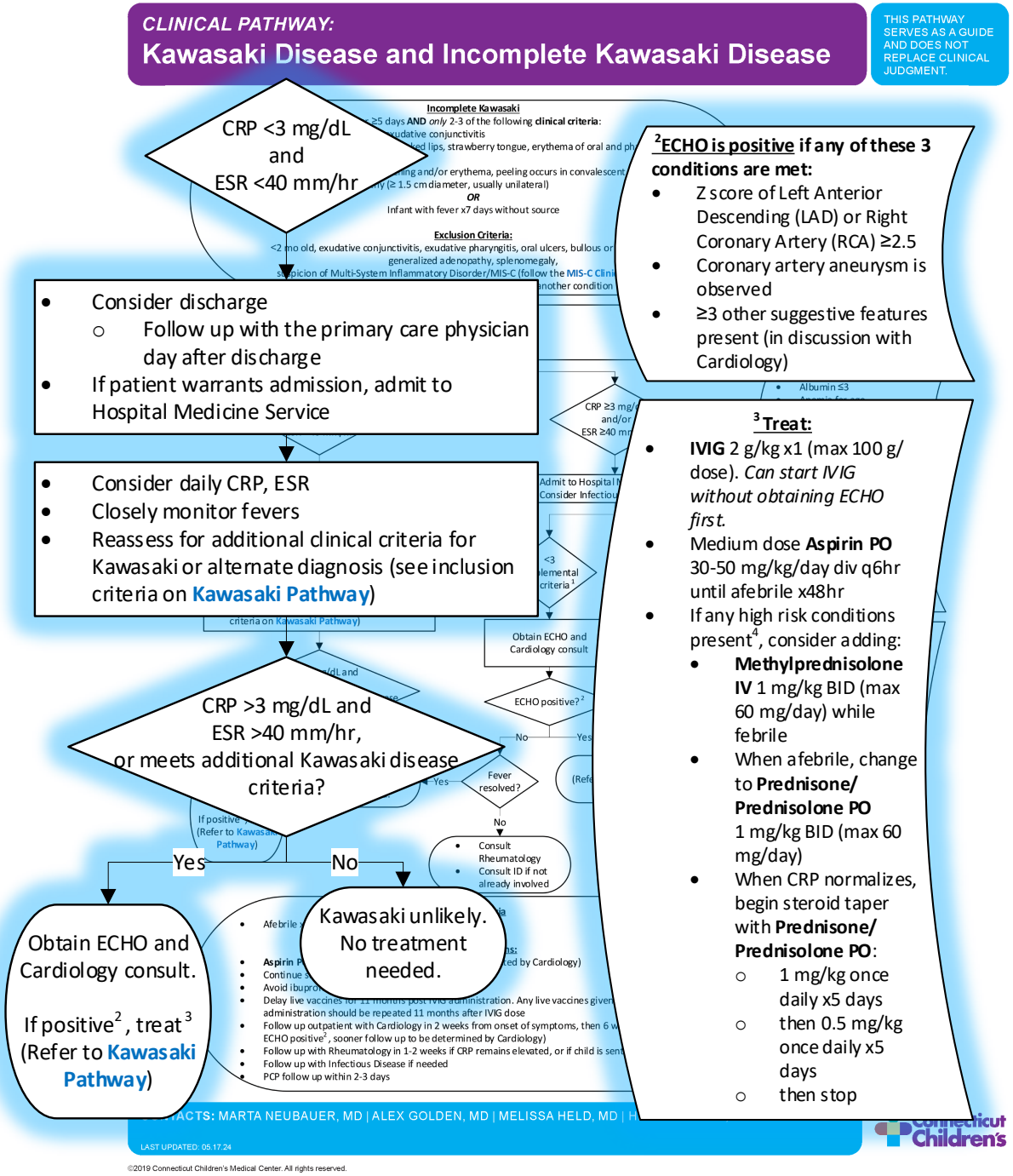
Connecticut Children's

Incomplete Kawasaki Disease

If inflammatory markers are NOT significantly elevated on presentation:

- Patient may be able to be discharged with close follow up with their PCP
- If the patient is admitted, monitoring for symptom progression and fevers should be done.
- If the patient meets Kawasaki criteria, or has elevated inflammatory markers, an ECHO and cardiology consult should be obtained.

If ECHO is positive – treatment is indicated.



Incomplete Kawasaki Disease

If inflammatory markers ARE significantly elevated at the time of initial evaluation:

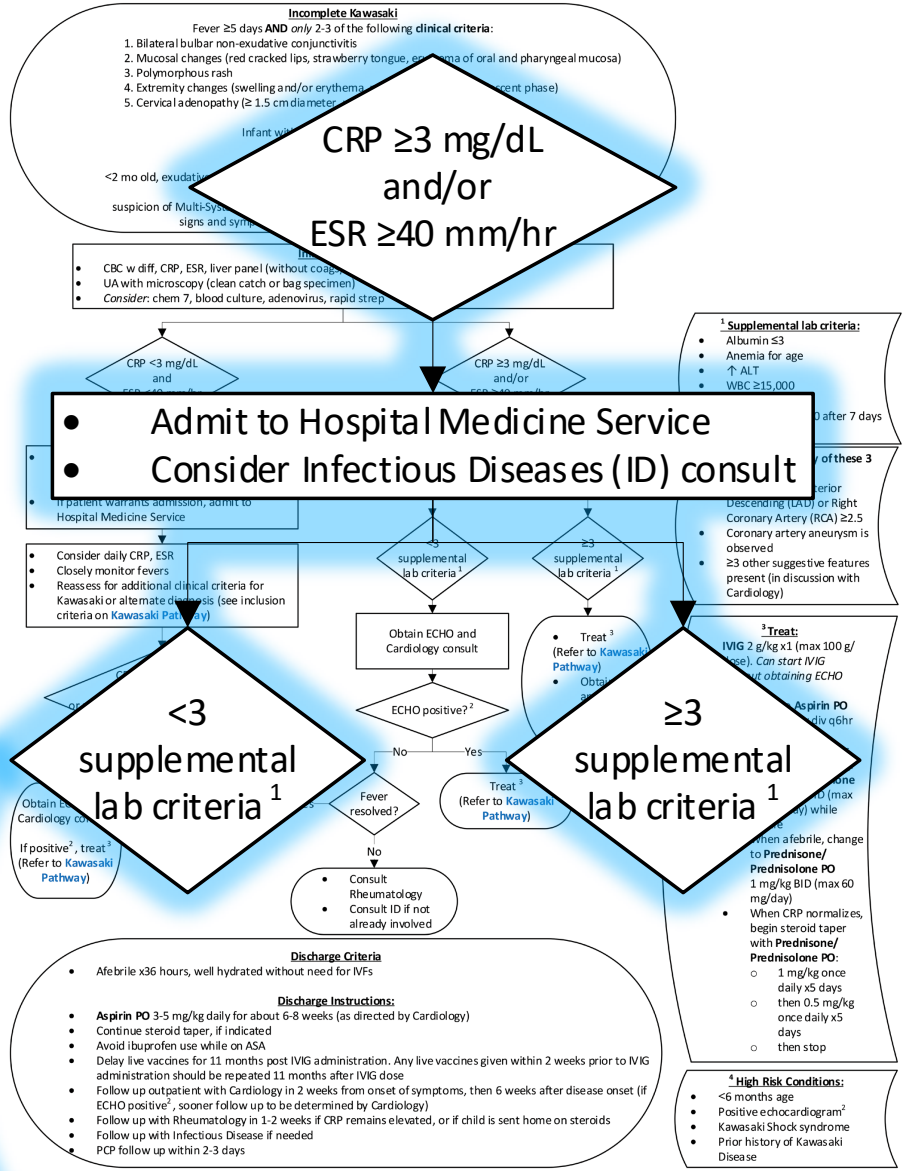
- Patient should be admitted to PHM
- The patient's supplemental labs will determine the next steps.

[1] Supplemental lab criteria:

- Albumin ≤3
- Anemia for age
- ↑ ALT
- WBC ≥15,000
- UA ≥10 WBC
- Platelets ≥450,000 after 7 days of fever

CLINICAL PATHWAY:
Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

CLINICAL PATHWAY:

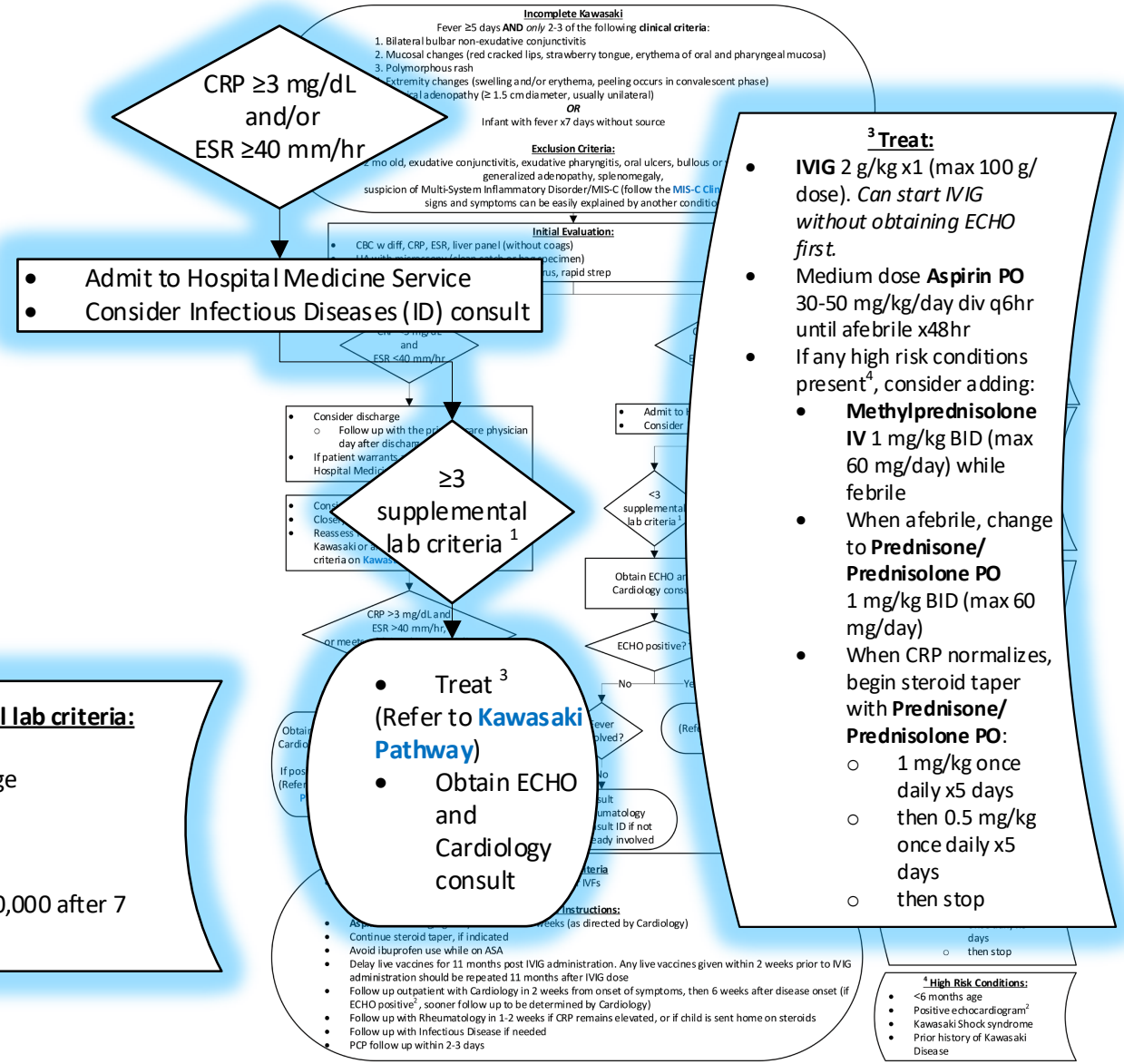
Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Incomplete Kawasaki Disease

If inflammatory markers ARE significantly elevated **and** 3 or more supplemental laboratory criteria are met:

Treatment is indicated



[1] Supplemental lab criteria:

- Albumin ≤3
- Anemia for age
- ↑ ALT
- WBC ≥15,000
- UA ≥10 WBC
- Platelets ≥450,000 after 7 days of fever

CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

CLINICAL PATHWAY:

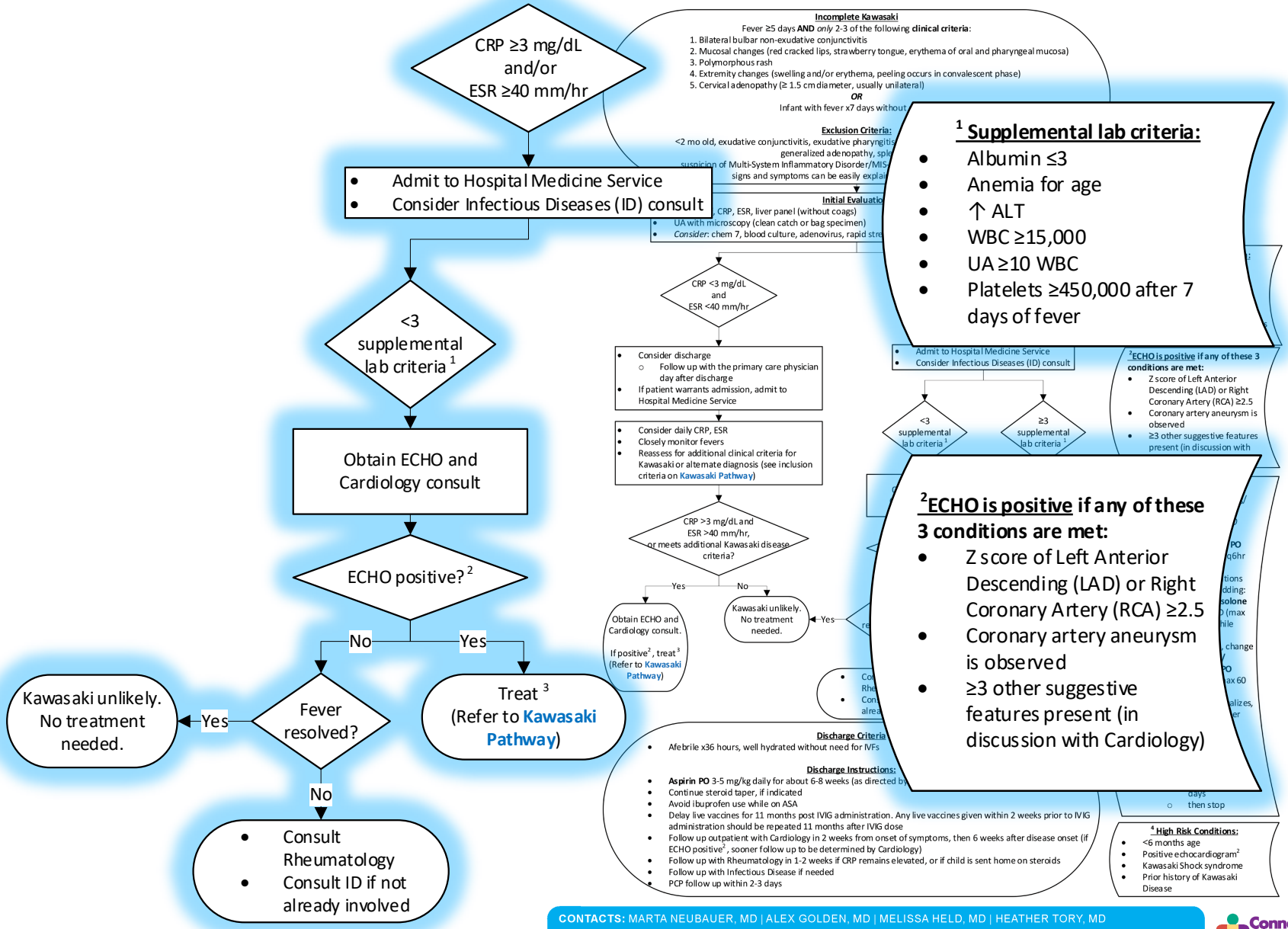
Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Incomplete Kawasaki Disease

If inflammatory markers ARE significantly elevated **but** patient has less than 3 supplemental lab criteria present:

- Obtain an ECHO to determine next steps.
- If ECHO is positive, treatment is indicated.
- If ECHO is negative, proceed with work up based on clinical picture.



CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

Connecticut Children's

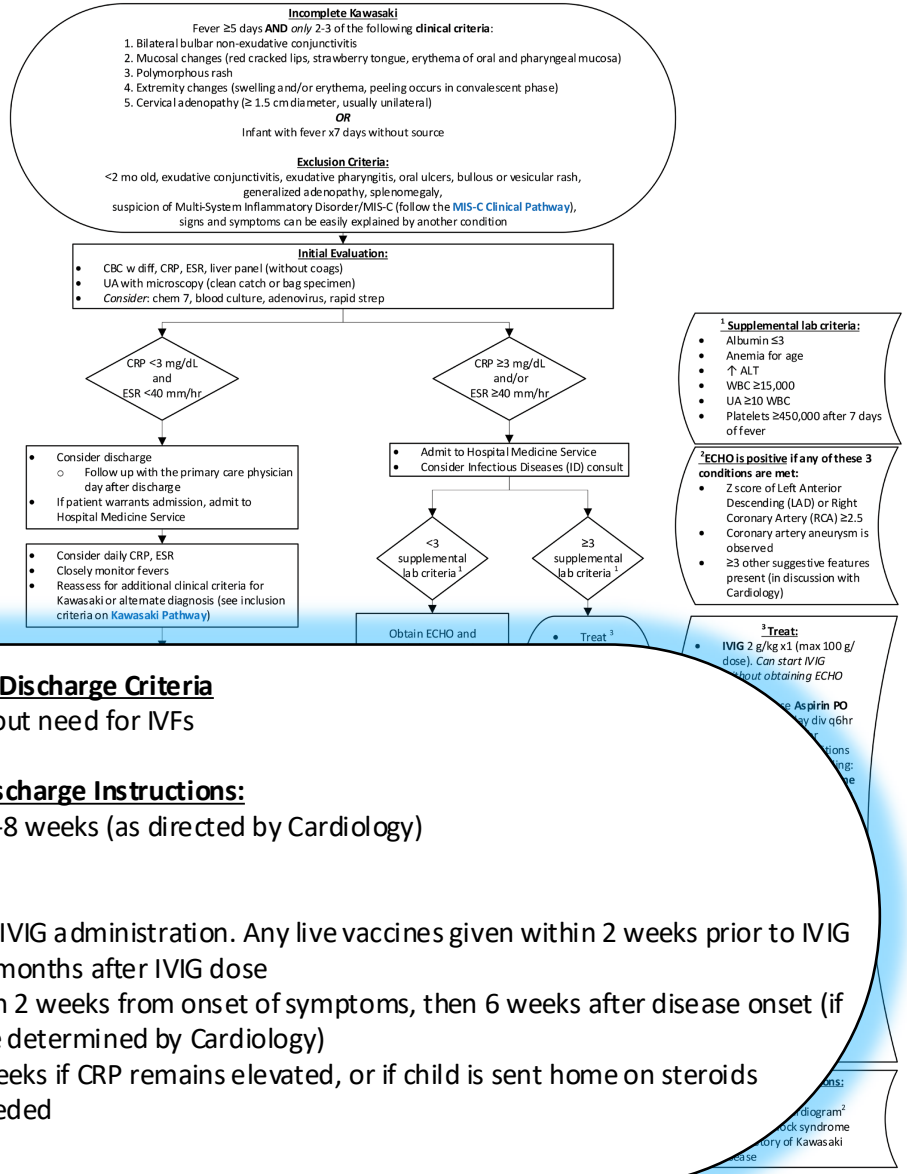
CLINICAL PATHWAY:

Kawasaki Disease and Incomplete Kawasaki Disease

THIS PATHWAY SERVES AS A GUIDE AND DOES NOT REPLACE CLINICAL JUDGMENT.

Incomplete Kawasaki Disease

Discharge criteria and instructions are the same as for Kawasaki Disease.



Discharge Criteria

- Afebrile x36 hours, well hydrated without need for IVFs

Discharge Instructions:

- **Aspirin PO** 3-5 mg/kg daily for about 6-8 weeks (as directed by Cardiology)
- Continue steroid taper, if indicated
- Avoid ibuprofen use while on ASA
- Delay live vaccines for 11 months post IVIG administration. Any live vaccines given within 2 weeks prior to IVIG administration should be repeated 11 months after IVIG dose
- Follow up outpatient with Cardiology in 2 weeks from onset of symptoms, then 6 weeks after disease onset (if ECHO positive[2], sooner follow up to be determined by Cardiology)
- Follow up with Rheumatology in 1-2 weeks if CRP remains elevated, or if child is sent home on steroids
- Follow up with Infectious Disease if needed
- PCP follow up within 2-3 days

CONTACTS: MARTA NEUBAUER, MD | ALEX GOLDEN, MD | MELISSA HELD, MD | HEATHER TORY, MD

LAST UPDATED: 05.17.24

Review of Key Points

- Kawasaki Disease is defined as:
  - fever for ≥5 days **and** *at least* 2 out of 5 clinical features, **or**
  - fever for ≥4 days **and** *at least* 4 out of the 5 clinical features
- Incomplete Kawasaki Disease is when a patient presents with 5 days of fever, but may only have 2 or 3 clinical features (or when an infant has 7 days of fever without a source)
  - Inflammatory labs, supplemental labs, and ECHO may be used to help guide management.
- Initial treatment and work-up includes IVIG, medium dose Aspirin, ECHO, and Cardiology consult
  - IVIG and aspirin should not be delayed while awaiting ECHO and Cardiology consult

Quality Metrics

- Percentage of patients with pathway order set usage
- Average time from admission to time of IVIG administration
- Number of patients with coronary artery aneurysms or ectasia at diagnosis
- Percentage of patients receiving medium dose aspirin in the acute phase of treatment
- Percentage of patients scheduled at discharge for follow up with a cardiologist
- Average length of stay (days)
- Number of patients readmitted due to Kawasaki Disease within 30 days

Pathway Contacts

- Marta Neubauer, MD
  - Pediatric Hospital Medicine
- Melissa Held, MD
  - Pediatric Infectious Diseases
- Heather Tory, MD
  - Pediatric Rheumatology
- Alex Golden, MD
  - Pediatric Cardiology

References

- Abrams JY, Belay ED, Uehara R, Maddox RA, Schonberger LB, Makamura Y. Cardiac Complications, Earlier Treatment, and Initial Disease Severity in Kawasaki Disease. *J Pediatr.* 2017 Sept;188:64-69.
- Baker AL, Lu M, Minich LL, et al. Associated symptoms in the ten days before diagnosis of Kawasaki disease. *J Pediatr.* 2009 Apr; 154(4):592-595.
- Chen S, Dong Y, Kiuchi MG, et al. Coronary Artery Complication in Kawasaki Disease and the Importance of Early Intervention: A Systematic Review and Meta-analysis. *JAMA Pediatr.* 2016 Dec;170(12):1156-1163.
- 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 Apr;135(17):e927-e999.
- Shao, S., Luo, C., Zhou, K. *et al.* Predictive value of serum procalcitonin for both initial and repeated immunoglobulin resistance in Kawasaki disease: a prospective cohort study. *Pediatr Rheumatol Online J.* 2019 Nov 27;17(1):78. doi:10.1186/s12969-019-0379-5.

Thank You!

About Connecticut Children's Pathways Program

Clinical pathways guide the management of patients to optimize consistent use of evidence-based practice. Clinical pathways have been shown to improve guideline adherence and quality outcomes, while decreasing length of stay and cost. Here at Connecticut Children's, our Clinical Pathways Program aims to deliver evidence-based, high value care to the greatest number of children in a diversity of patient settings. These pathways serve as a guide for providers and do not replace clinical judgment.