Kawasaki Disease Reconsidered

New AHA Guidelines

John Darby, MD
Nisha Tamaskar, MD
Stanford Shulman, MD
Marietta DeGuzman, MD
Kristin Sexson, MD, PhD

Pediatrics

Introductions

- John Darby, MD
  - Texas Children's Hospital, Baylor College of Medicine

- Nisha Tamaskar, MD
  - Texas Children's Hospital, Baylor College of Medicine
  - Children's National Health System

- Marietta DeGuzman, MD
  - Texas Children's Hospital, Baylor College of Medicine
- Kristen Sexson, MD, PhD
  - Texas Children's Hospital, Baylor College of Medicine
- Stanford Shulman, MD
  - Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern McGaw School of Medicine

Disclosures

- None of the presenters have any relevant financial relations to disclose
- We do not intend to discuss an unapproved or investigative use of a commercial product or device in our presentation

Pediatrics

Objectives

- At the conclusion of this activity, participants will be able to:
  - Compare Kawasaki Disease practice patterns and evaluate recently published clinical guidelines
  - Recognize features of typical and atypical presentations of Kawasaki Disease
  - Identify potential complications of Kawasaki Disease and of its treatment and prepare management plans

Presentation Outline

- Introduction to new guidelines (10 minutes)
- Etiology and pathogenesis (10 minutes)
- Diagnosis (20 minutes)
- Management (30 minutes)
- Wrap up (5 minutes)

Survey

- Survey questions via audience response using the PHM App

  1) Search for the session title in the mobile app using the search bar or in the agenda layout

  2) Select the session to open the session page and select “Live Polls”

  3) Select your desired answer and then select “Finish” to submit

Survey

- Survey is part of a research project approved by Baylor College of Medicine IRB
- Aim: Evaluate hospitalist knowledge, practice patterns, and comfort level in caring for children with Kawasaki Disease
- Survey questions are completely optional and anonymous
- Participation in the survey implies consent to participate
- May opt out at any time

Audience Response Question 1

- Which of the following best describes you?
  - a) Hospitalist with 0 – 4 years of practice
  - b) Hospitalist with 5 – 10 years of practice
  - c) Hospitalist with > 10 years of practice
  - d) Hospitalist fellow
  - e) Other trainee (medical student, resident)
  - f) Other (including outpatient pediatrics, subspecialty, advanced practice providers, etc.)

Audience Response Question 2

- Which of the following best describes your primary practice location?
  - a) Outside the USA
  - b) Northeast
  - c) Mid-Atlantic / Southeast
  - d) Midwest
  - e) South / Southwest
  - f) West / Pacific Northwest

Audience Response Question 3

- Which of the following best describes your primary practice setting?
  - a) Urgent Care
  - b) Community hospital
  - c) Community hospital with academic affiliation
  - d) Tertiary care children's hospital
  - e) Outpatient clinic
  - f) Other

Introduction to New Guidelines

Introduction to New Guidelines

- Dajani, et al. published first AHA Guideline in 1993
- 5 Pages

Introduction to New Guidelines

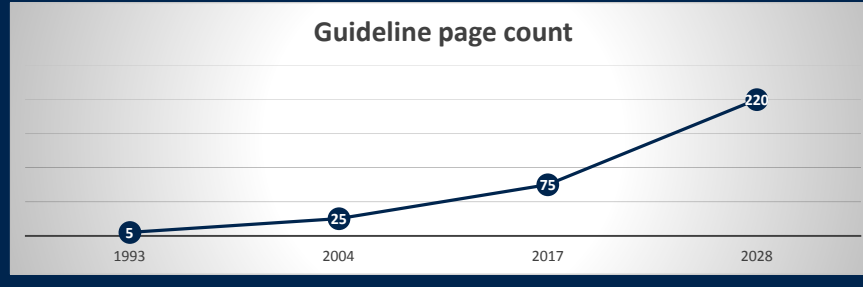
- Newburger et al. published revision to AHA guideline in 2004
- 25 Pages

Pediatrics

Introduction to New Guidelines

- McCrindle et al. published revision to AHA guideline in 2017
- 75 Pages

Introduction to New Guidelines



Pediatrics

Guideline Process

- Diverse group of content experts
- Representatives from North America, Taiwan, and Japan
- Careful review of the 2004 guidelines
- Background sections drafted to provide content for guidelines
- All recommendation statements reviewed by writing group and then submitted for peer review

2017 Stated Updates

- New evidence regarding underlying pathology
- An algorithm to ensure capture of incomplete KD during effective window of therapy
- Improved management of the acute illness that includes the use of additional therapies for IVIG refractory patients

2017 Stated Updates

- Greater use of Z-scores for classifying coronary artery involvement
- Greater specification of long-term management based on both initial and current coronary artery involvement
- Acknowledgement of care needs of growing population of adults with a previous history of KD and coronary artery aneurysms

Summary

- Still do not know the cause of KD
- KD in infants can be very challenging
- Steroids likely have a role in the treatment of patients at high risk for IVIG resistance if given early
- Aspirin is likely safe to give at moderate dose and maybe even low dose

Pediatrics
Ann & Robert H. Lurie Children's Hospital of Chicago
Children's National
Texas Children's Hospital
Baylor College of Medicine

Summary

- A second dose of IVIG is our recommended therapy for refractory KD
- For patients with coronary artery abnormalities (CAA) we recommend early cardiology involvement

Section 1: Pathophysiology

Pediatrics

Ann & Robert H. Lurie Children's Hospital of Chicago · Children's National · Texas Children's Hospital · Baylor College of Medicine

Section 1: Pathophysiology

- Moderator and audience questions (10 minutes)

Section 1: Pathophysiology

- Moderator and audience questions (10 minutes)

Pediatrics

Section 2: Diagnosis

Audience Response Question 4

- What is your comfort level in independently (without a consulting service) diagnosing incomplete Kawasaki Disease?
  - a) Very comfortable
  - b) Somewhat comfortable
  - c) Somewhat uncomfortable
  - d) Very uncomfortable

Audience Response Question 5

- What is your comfort level in independently managing classic Kawasaki Disease?
  - a) Very comfortable
  - b) Somewhat comfortable
  - c) Somewhat uncomfortable
  - d) Very uncomfortable

Audience Response Question 6

- What is your comfort level in independently managing KD complicated by mild coronary artery dilation (no aneurysms) diagnosed prior to day 10 of fever?
  - a) Very comfortable
  - b) Somewhat comfortable
  - c) Somewhat uncomfortable
  - d) Very uncomfortable

Audience Response Question 7

- Is any subspecialty/department typically consulted when a patient is diagnosed with classic KD without complications?
  - a) No
  - b) Yes, ID
  - c) Yes, Cardiology
  - d) Yes, Rheumatology
  - e) Yes, Cardiology and ID
  - f) Yes, Cardiology and Rheumatology
  - g) Yes, other

Audience Response Question 8

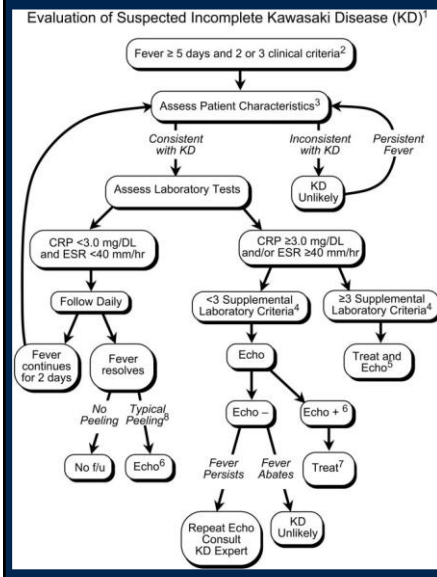
- In addition to the PCP, who follows patients with classic KD without complications after discharge?
  - a) None (PCP only)
  - b) Cardiology
  - c) ID
  - d) Rheumatology
  - e) ID and Cardiology
  - f) Cardiology and Rheumatology
  - g) Other

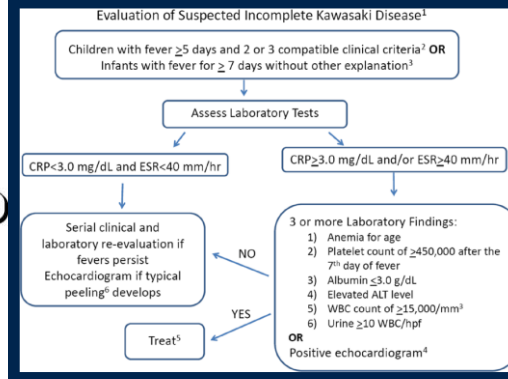
Diagnosis

- Moderator and audience questions (20 minutes)

Diagnosis

Pediatrics





Evaluation of Suspected Incomplete Kawasaki Disease[1]
Children with fever ≥5 days and 2 or 3 compatible clinical criteria[2] OR Infants with fever for ≥ 7 days without other explanation[3]
Assess Laboratory Tests
CRP<3.0 mg/dL and ESR<40 mm/hr
CRP≥3.0 mg/dL and/or ESR≥40 mm/hr
Serial clinical and laboratory re-evaluation if fevers persist Echocardiogram if typical peeling[6] develops
NO
YES
Treat[5]
3 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[4]

Pediatrics

- Is 2.5 the magic number?

Bratincsak, et al. *Pediatr Infect Dis J.* 2012;31:924-926

Section 3: Management

Audience Response Question 9

- In a patient with classic KD and a normal initial echocardiogram, what is your initial treatment?
  - a) IVIG and high dose aspirin (80 – 100 mg/kg/day)
  - b) IVIG and medium dose aspirin (30 – 50 mg/kg/day)
  - c) IVIG and low dose aspirin (3 – 5 mg/kg/day)
  - d) IVIG alone
  - e) IVIG and corticosteroids (with or without aspirin)
  - f) Corticosteroids alone
  - g) Other

Audience Response Question 10

- In a patient with classic KD and no complications who receives IVIG, how long do you typically observe following completion of IVIG prior to discharge?
  - a) <24 hours
  - b) About 24 hours
  - c) About 36 hours
  - d) About 48 hours
  - e) >48 hours

Audience Response Question 11

- In a patient with classic KD and no complications who received IVIG, which of the following most closely approximates the number of hours after the completion of IVIG when you would consider fever (>100.4 F) to indicate non-response to IVIG?
  - a) 18 hours
  - b) 24 hours
  - c) 36 hours
  - d) 48 hours
  - e) Other

Audience Response Question 12

- You have a patient with classic KD who is found to have coronary artery dilation (but no aneurysm formation) on initial echocardiogram. Aside from giving aspirin, what is your most typical initial step?
  - a) IVIG alone
  - b) IVIG and corticosteroids
  - c) IVIG and TNFα inhibitor (infliximab or etanercept)
  - d) Corticosteroids alone
  - e) TNFα inhibitor alone
  - f) Other

Audience Response Question 13

- You are caring for a patient with classic KD and no coronary artery changes who has recurrence of fever. You consider this recurrence to indicate a failed to response to an initial dose of IVIG. Which of the following is your most typical next step?
  - a) Observe
  - b) Second dose of IVIG
  - c) IVIG and corticosteroids
  - d) Corticosteroids alone
  - e) TNFα inhibitor alone (infliximab or etanercept)
  - f) IVIG and TNFα inhibitor
  - e) Other

Section 3: Management

- Moderator and audience questions (30 minutes)

Pediatrics
Ann & Robert H. Lurie Children's Hospital of Chicago
Children's National
Texas Children's Hospital
Baylor College of Medicine

Steroids:

- RAISE study (2012)
  - Prospective, randomized, open-label, blinded endpoint trial
  - 74 hospitals in Japan
  - Patients selected for severe presentation
  - IVIG and aspirin OR
  - IVIG and aspirin and prednisolone 2 mg/kg over 15 days

Steroids

- RAISE study
  - Incidence of CAA significantly lower in steroid group
    - 3% in steroid group vs 23% in control group
  - Serious adverse events were similar

Steroids

- Chen et al. JAMA Pediatrics (2016)
  - Relative Risk Reduction of 58% in CAA
  - No benefit as rescue therapy
  - High risk patients received greatest risk reduction
  - No difference in adverse events

Steroids

- Cochrane Systematic Review
  - Wardle et al. January, 2017
  - 7 studies (6 out of 7 were in JAMA Peds meta-analysis)
  - "Moderate quality evidence shows that the use of steroids in the acute phase of KD can be associated with improved CAA, shorter duration of stay and decreased duration of symptoms."

Steroids

- Cochrane Systematic Review
  - Note that the most benefit may be in:
    - Japanese populations
    - Higher risk score patients
    - Those receiving a longer course of steroids
  - Acknowledge that there may be a confounding bias
  - **"Treatment with a long course of steroids should be considered in <u>all</u> children diagnosed with KD until further studies are performed."**

Aspirin

- "Aspirin does not appear to lower the frequency of development of coronary abnormalities."
- Japan and Europe use 30 – 50 mg/kg/day
- US uses 80 – 100 mg/kg/day
- "There are no data to suggest that either does of ASA is superior."

Aspirin

- Cochrane review (2006)
- "Until good quality RCTs are conducted, there is insufficient evidence to indicate whether children with KD should receive ASA."

Aspirin

- Pediatrics June 2017
  - Multicenter, retrospective, nonrandomized cohort study in Canada
  - 1213 children ages 0 to 10 with acute KD
  - Low dose ASA was not inferior to high dose for reducing CAA
  - Rate of fever recurrence and fever duration not significantly different

Other therapies

Section 3: Management

- Moderator and audience questions (30 minutes)

Summary

- Still do not know the cause of KD
- KD in infants can be very challenging
- Steroids likely have a role in the treatment of patients at high risk for IVIG resistance if given early.
- Aspirin is likely safe to give at moderate dose and maybe even low dose

Summary

- A second dose of IVIG is our recommended therapy for refractory KD
- For patients with coronary artery abnormalities (CAA) we recommend early cardiology involvement.