ALASKA NATIVE MEDICAL CENTER

COVID-19 AND CRITICAL ILLNESS IN CHILDREN

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Objectives

- Review Pediatric Covid-19 (Covid) statistics
- Identify common presenting symptoms by age
- Discuss pathophysiology of Covid in Children
- Differentiating MIS-C from Kawasaki
- Review of current diagnostic and therapeutic algorithms for:
  - Covid respiratory disease
  - MIS-C

Covid Statistics in Children

- Approximately 1,040,000 pediatric Covid cases to date
- 11.5% of all diagnosed cases
- 1381/100,000 children in the population
- Cases rising as with population

Covid Statistics in Children

- 1.2% - 3.3% of all Covid related hospitalizations are in children
- Of all Pediatric diagnosed cases, about 2% result in hospitalization

Covid Statistics in Children

- **Age distribution** — Children of all ages can get COVID-19. In a multicenter cohort of 582 European children <18 years of age with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during April 2020 (the early peak of the European pandemic), the age distribution was as follows

- <1 month – 7 percent
- 1 month to 1 year – 22 percent
- 1 to 2 years – 10 percent
- 2 to 5 years – 11 percent
- 5 to 10 years – 16 percent
- >10 years through 18 years – 34 percent

Covid Statistics in Children

- Hospitalization is increasing and is currently at a cumulative rate of 8/100,000 population

- Cumulative rate of hospitalization is highest among children < 2 years of age (24.8/100,000)

Covid Statistics in Children

- ICU rates
  - Among children who were hospitalized with COVID-19 from 14 states by late July 2020, approximately 33 percent required intensive care and
  - 6 percent required invasive mechanical ventilation

Covid Statistics in Children - Mortality

- 0.1% - 0.2 % of all Covid deaths are in children
- 1% - 1.5% of all Pediatric hospitalizations for Covid result in death
- 16 states have reported zero Covid deaths in children (including AK)

Covid Statistics in Children - Mortality

- February – August 2020
  - 121 deaths in children
  - 15 of those from MIS-C

- 70% ages 10 – 18 years old
- 20% ages 1 – 9 years old
- 10% infants

- 75% at least 1 underlying medical condition
- 45% 2 or more underlying medical conditions
- 74% Hispanic or Black

Underlying conditions

- Obesity 38%
- Chronic pulmonary disease 18%
- Prematurity 15%

Common presenting symptoms by age 0 – 9 years

- Fever, cough, or shortness of breath – 63 percent
  - Fever – 46 percent
  - Cough – 37 percent
  - Shortness of breath – 7 percent
- Myalgia – 10 percent
- Rhinorrhea – 7 percent
- Sore throat – 13 percent
- Headache – 15 percent
- Nausea/vomiting – 10 percent
- Abdominal pain – 7 percent
- Diarrhea – 14 percent
- Loss of smell or taste – 1 percent

Common presenting symptoms by age
10 – 19 years

- Fever, cough, or shortness of breath – 60 percent
  - Fever – 35 percent
  - Cough – 41 percent
  - Shortness of breath – 16 percent
- Myalgia – 30 percent
- Rhinorrhea – 8 percent
- Sore throat – 29 percent
- Headache – 42 percent
- Nausea/vomiting – 10 percent
- Abdominal pain – 8 percent
- Diarrhea – 14 percent
- Loss of smell or taste – 10 percent

Potential markers of severe disease in children

- Elevated inflammatory markers (eg, CRP, procalcitonin, interleukin 6, ferritin, D-dimer) at admission or during hospitalization
- Gastrointestinal symptoms at admission
- NOT lymphocytopenia as seen in adults

The Critical Coronavirus and Kids Epidemiology Study

- Designed to study severe cases
- 60 centers in nearly 20 countries from the Americas and Europe
- Expected to run through December 2020

PICU Therapies and Medications

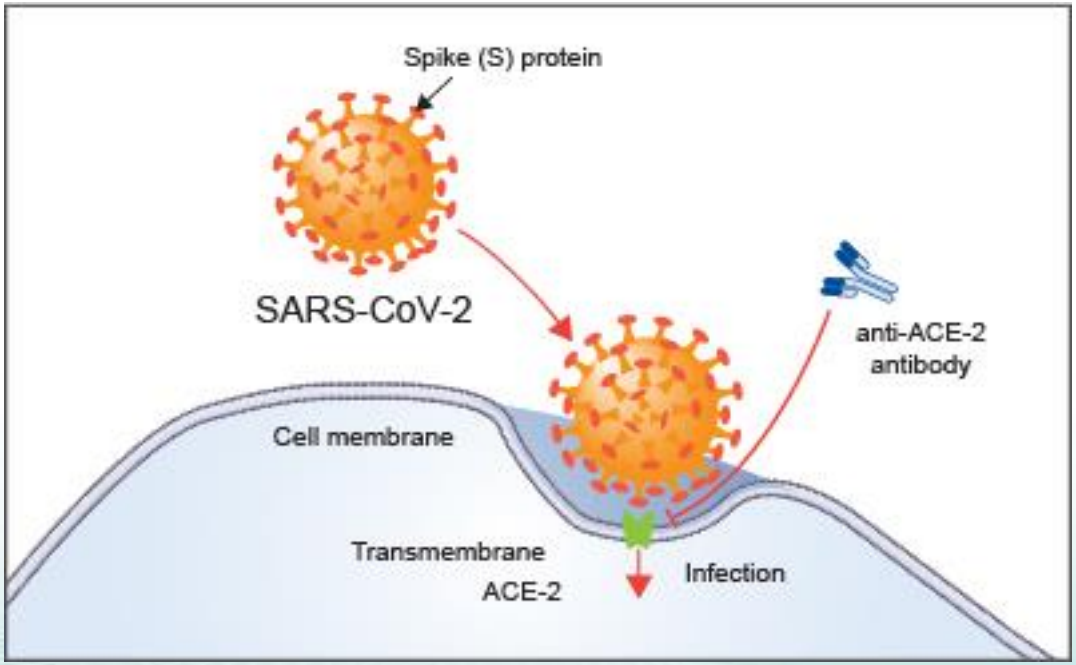
- **Respiratory support**
  - None 3 (18)
  - HFNC 7 (41)
  - NIV 4 (24)
  - IMV 8 (47)
- Respiratory adjuncts 1 (6)

- **Medications**
  - Vasoactive infusion 9 (53)
  - Antibiotics 15 (88)
  - Remdesivir 4 (24)
  - Lopinavir and/or ritonavir 1 (6)
  - Corticosteroids 9 (53)
  - Tocilizumab 7 (41)
  - Hydroxychloroquine 8 (47)

PICU diagnosis and/or complications

- Pneumonia 13 (76)
- ARDS 8 (47)
  - 2 mild,
  - 1 moderate,
  - 3 severe
- Myocarditis 4 (24)
- Cardiac arrest 3 (18)
- AKI 3 (18)

Pathophysiology – why children less susceptible?



Pathophysiology – why children less susceptible?

- Less expression of the ACE-2 receptor in the upper airway
- ACE-2 expression increases with age
- Children have less maladaptive immune response – possible less severe infection

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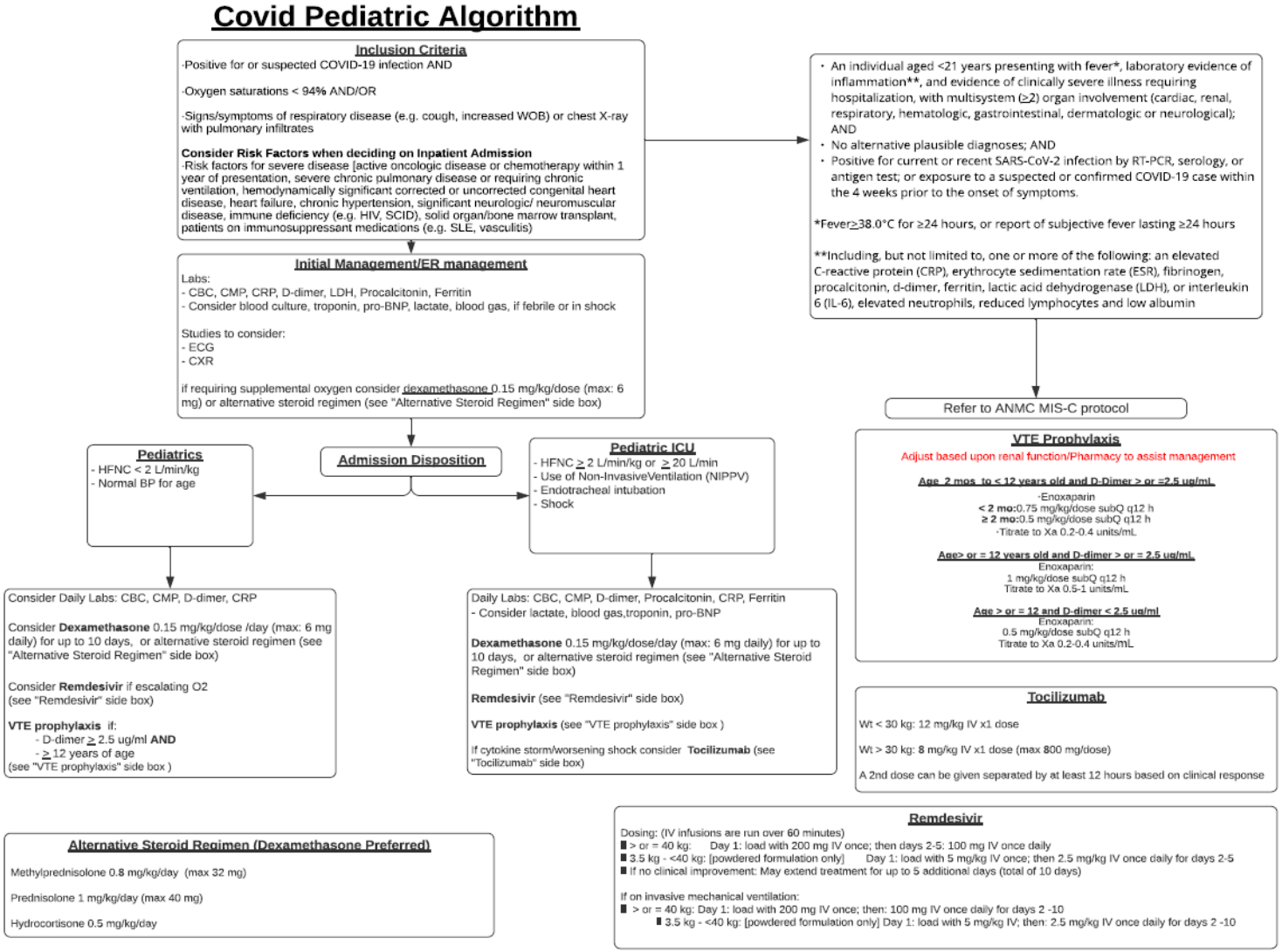
Guidelines

Covid (non MIS-C)



Inclusion and Initial Management

Inclusion Criteria

·Positive for or suspected COVID-19 infection AND

·Oxygen saturations < 94% AND/OR

·Signs/symptoms of respiratory disease (e.g. cough, increased WOB) or chest X-ray with pulmonary infiltrates

Consider Risk Factors when deciding on Inpatient Admission

·Risk factors for severe disease [active oncologic disease or chemotherapy within 1 year of presentation, severe chronic pulmonary disease or requiring chronic ventilation, hemodynamically significant corrected or uncorrected congenital heart disease, heart failure, chronic hypertension, significant neurologic/ neuromuscular disease, immune deficiency (e.g. HIV, SCID), solid organ/bone marrow transplant, patients on immunosuppressant medications (e.g. SLE, vasculitis)

Initial Management/ER management

Labs:
- CBC, CMP, CRP, D-dimer, LDH, Procalcitonin, Ferritin
- Consider blood culture, troponin, pro-BNP, lactate, blood gas, if febrile or in shock

Studies to consider:
- ECG
- CXR

if requiring supplemental oxygen consider dexamethasone 0.15 mg/kg/dose (max: 6 mg) or alternative steroid regimen (see "Alternative Steroid Regimen" side box)

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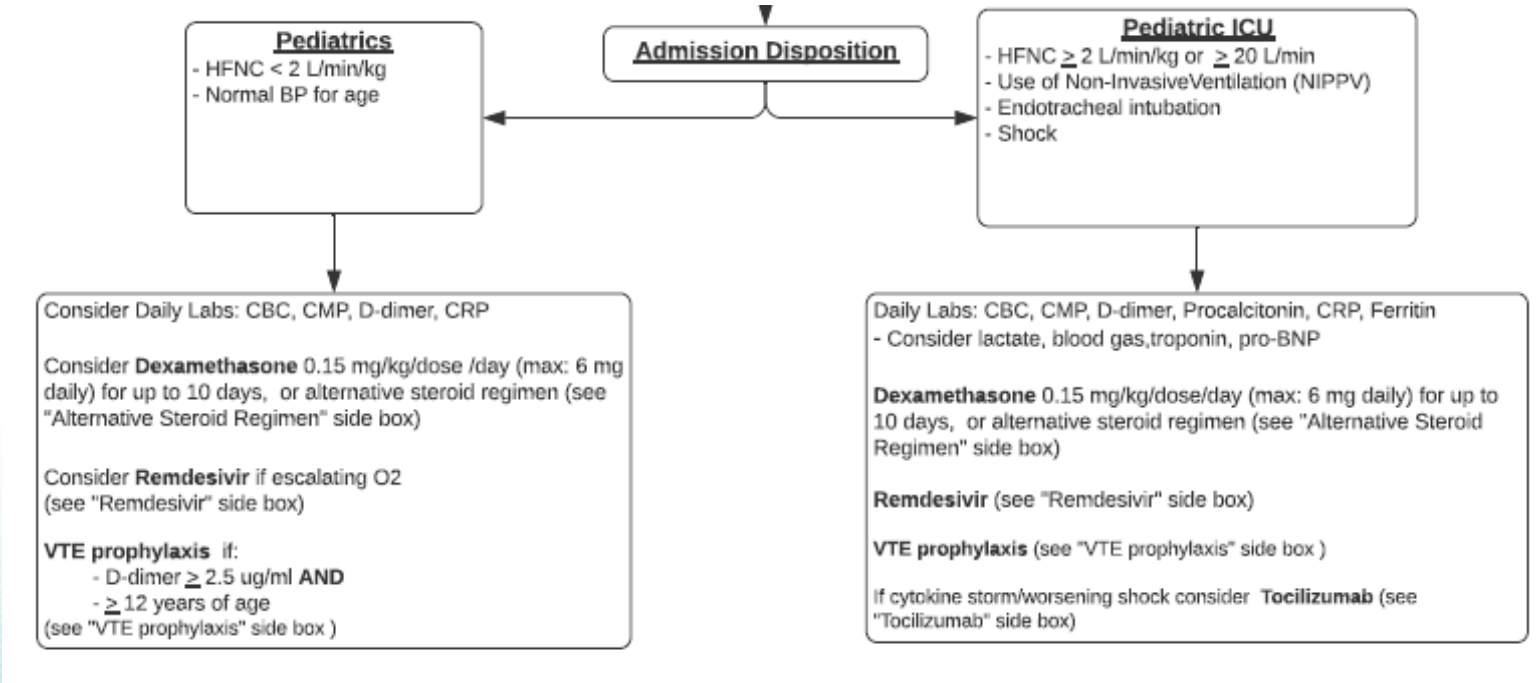
Alternative Steroid Regimen

- **Dexamethasone** 0.15 mg/kg orally, intravenously (IV), or nasogastrically (NG) once daily (maximum dose 6 mg)
- **Prednisolone** 1 mg/kg orally or NG once daily (maximum dose 40 mg)
- **Methylprednisolone** 0.8 mg/kg IV once daily (maximum dose 32 mg)
- **Hydrocortisone**
  - For neonates (<1 month of age): 0.5 mg/kg IV every 12 hours for 7 days followed by 0.5 mg/kg IV once daily for 3 days
  - For children ≥1 month: 1.3 mg/kg IV every 8 hours (maximum dose 50 mg; maximum total daily dose 150 mg)

Admission Disposition and Management



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Remdesivir

Remdesivir

Dosing: (IV infusions are run over 60 minutes)

- > or = 40 kg: Day 1: load with 200 mg IV once; then days 2-5: 100 mg IV once daily
- 3.5 kg - <40 kg: [powdered formulation only] Day 1: load with 5 mg/kg IV once; then 2.5 mg/kg IV once daily for days 2-5
- If no clinical improvement: May extend treatment for up to 5 additional days (total of 10 days)

If on invasive mechanical ventilation:

- > or = 40 kg: Day 1: load with 200 mg IV once; then: 100 mg IV once daily for days 2 -10
- 3.5 kg - <40 kg: [powdered formulation only] Day 1: load with 5 mg/kg IV; then: 2.5 mg/kg IV once daily for days 2 -10

- WHO no longer recommends?

Venous Thromboembolism Prophylaxis

- VTE prophylaxis only considered if requiring hospitalization
- No VTE prophylaxis needed for under age 12 unless critically ill
- If not critically ill but hospitalized, VTE prophylaxis used only for 12 years and older AND elevated D-dimer
- If critically ill, VTE prophylaxis recommended for all ages

Venous Thromboembolism Prophylaxis

VTE Prophylaxis

Adjust based upon renal function/Pharmacy to assist management

Age 2 mos to < 12 years old and D-Dimer > or =2.5 ug/mL

·Enoxaparin
< 2 mo:0.75 mg/kg/dose subQ q12 h
≥ 2 mo:0.5 mg/kg/dose subQ q12 h
·Titrate to Xa 0.2-0.4 units/mL

Age> or = 12 years old and D-dimer > or = 2.5 ug/mL
Enoxaparin:
1 mg/kg/dose subQ q12 h
Titrate to Xa 0.5-1 units/mL

Age > or = 12 and D-dimer < 2.5 ug/ml
Enoxaparin:
0.5 mg/kg/dose subQ q12 h
Titrate to Xa 0.2-0.4 units/mL

Multi-Inflammatory Syndrome in Children (MIS-C)

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MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C) According to the CDC:

- **An individual aged <21 years presenting with:**
  - **Fever** ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours if shock (3 days if not in shock)
  - Laboratory evidence of **inflammation**
    - Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin
  - Evidence of **clinically severe illness** requiring hospitalization with multisystem (≥2) organ involvement (rash, GI symptoms, extremity changes, oral mucosal changes, conjunctivitis, lymphadenopathy, neurologic symptoms).
    - Rash: polymorphic, maculopapular, petechial, NOT vesicular
    - GI symptoms: diarrhea, abdominal pain, vomiting
    - Extremity Changes: Erythema and edema of hands and feet
    - Oral Mucosal Changes: Erythema and cracking of lips, strawberry tongue, erythema of oral and pharyngeal mucosa
    - Conjunctivitis: Bilateral bulbar conjunctival injection without exudate
    - Lymphadenopathy: Cervical > 1.5 cm unilateral
    - Neurologic: Headache, irritability, lethargy, AMS
- **AND No alternative plausible diagnoses**
- **AND Positive** for current or recent **SARS-CoV-2** infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms
  - Clinicians may consider diagnosis while awaiting serology or if all SARS-CoV-2 testing is negative but clinical suspicion for MIS-C still remains high

- Some individuals may fulfill full or partial criteria for Kawasaki Disease but should still be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection

***MIS-C is a reportable disease

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MIS-C vs. Kawasaki

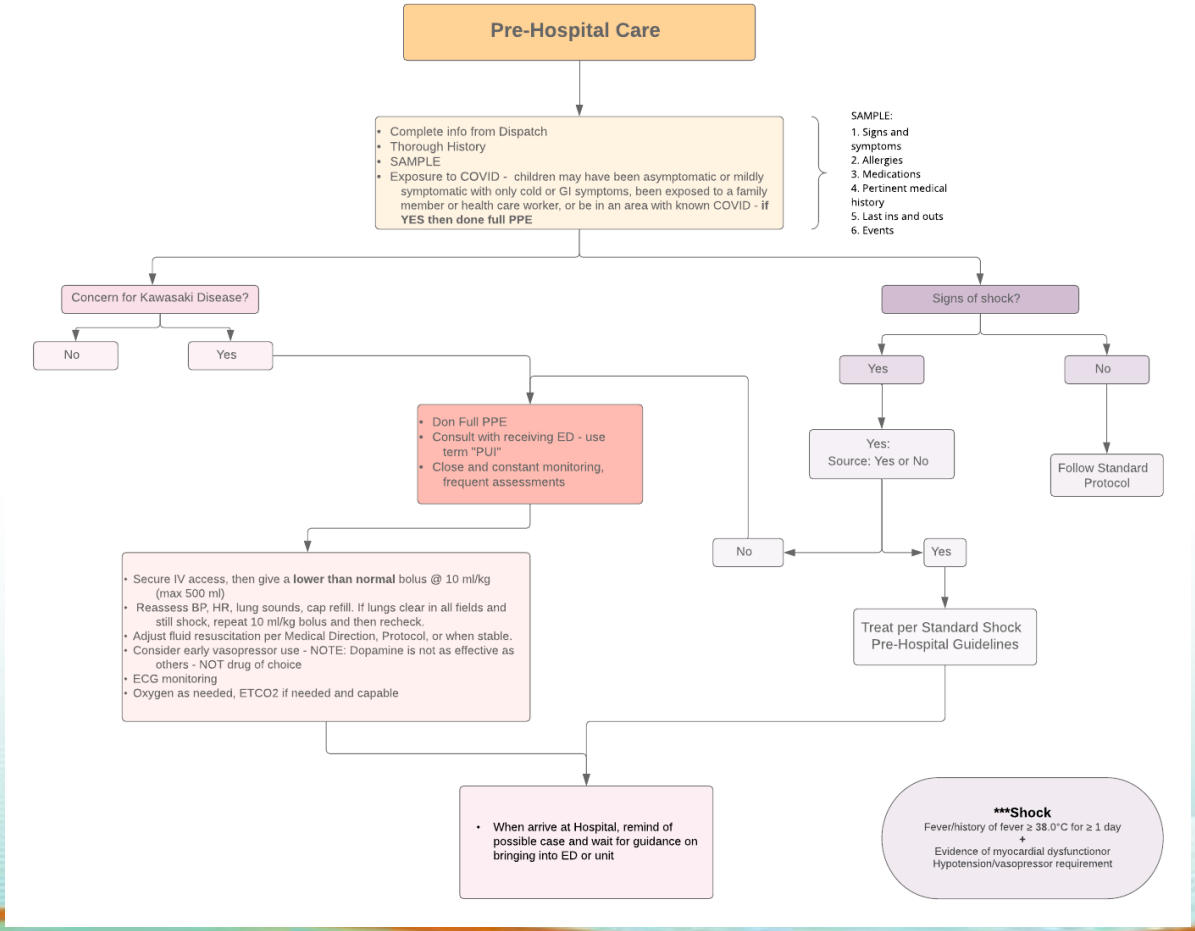
- MIS-C typically older children
- MIS-C high Ferritin
- MIS-C high D-Dimer
- MIS-C increased Troponin - myocarditis

Kawasaki Diagnostic Criteria

Table 1: Criteria to Diagnose KD

Classical/ Traditional	> Fever of at least five days' duration. > Presence of four of the following five principal features: 1. Changes in extremities; 2. Polymorphous exanthema; 3. Bilateral conjunctival injection; 4. Changes of the lips and oral cavity; and 5. Cervical lymphadenopathy. > Exclusion of other diseases causing similar findings.
Modified[1]	Classical criteria with the modification: > Fever and fewer than four principal features along with coronary artery disease as detected by two-dimensional echocardiography or coronary angiography. > Inclusion of select lab studies.

Pre-hospital care



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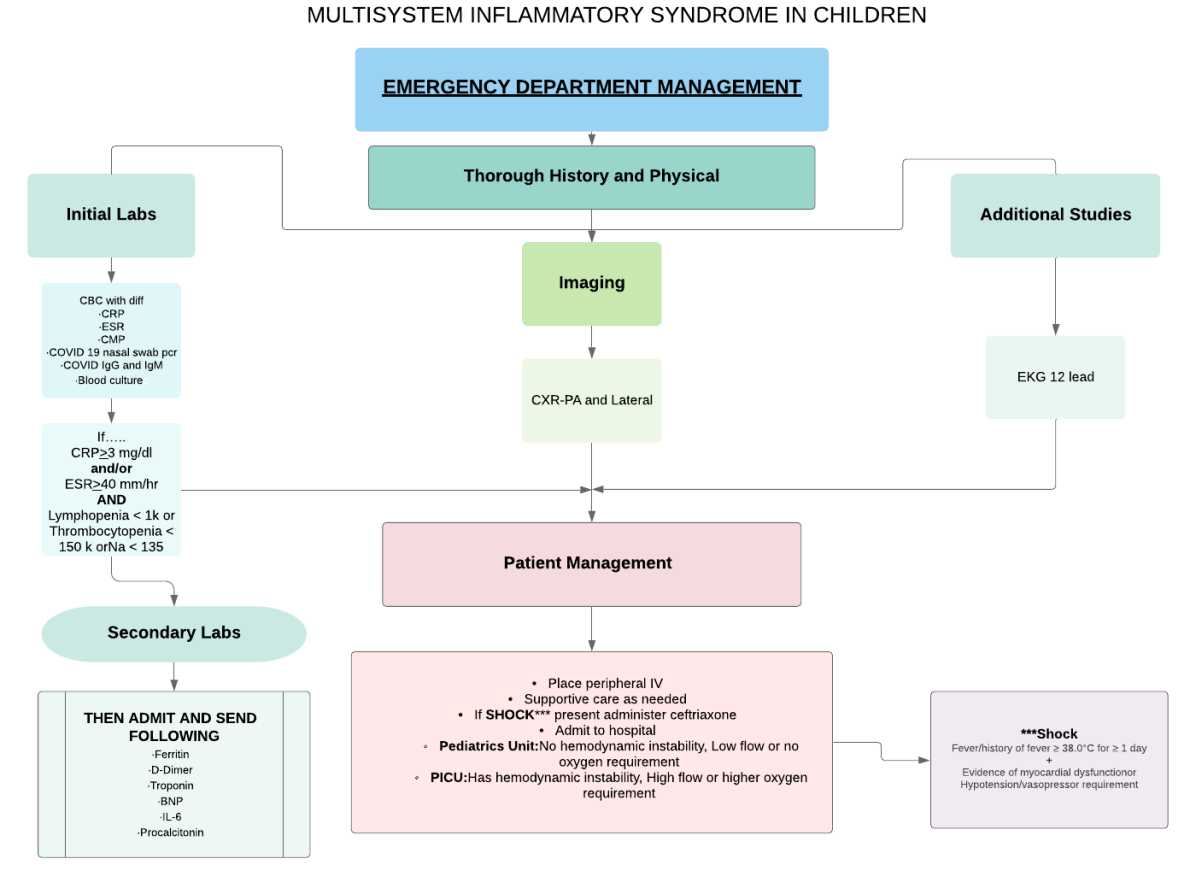
ED Management



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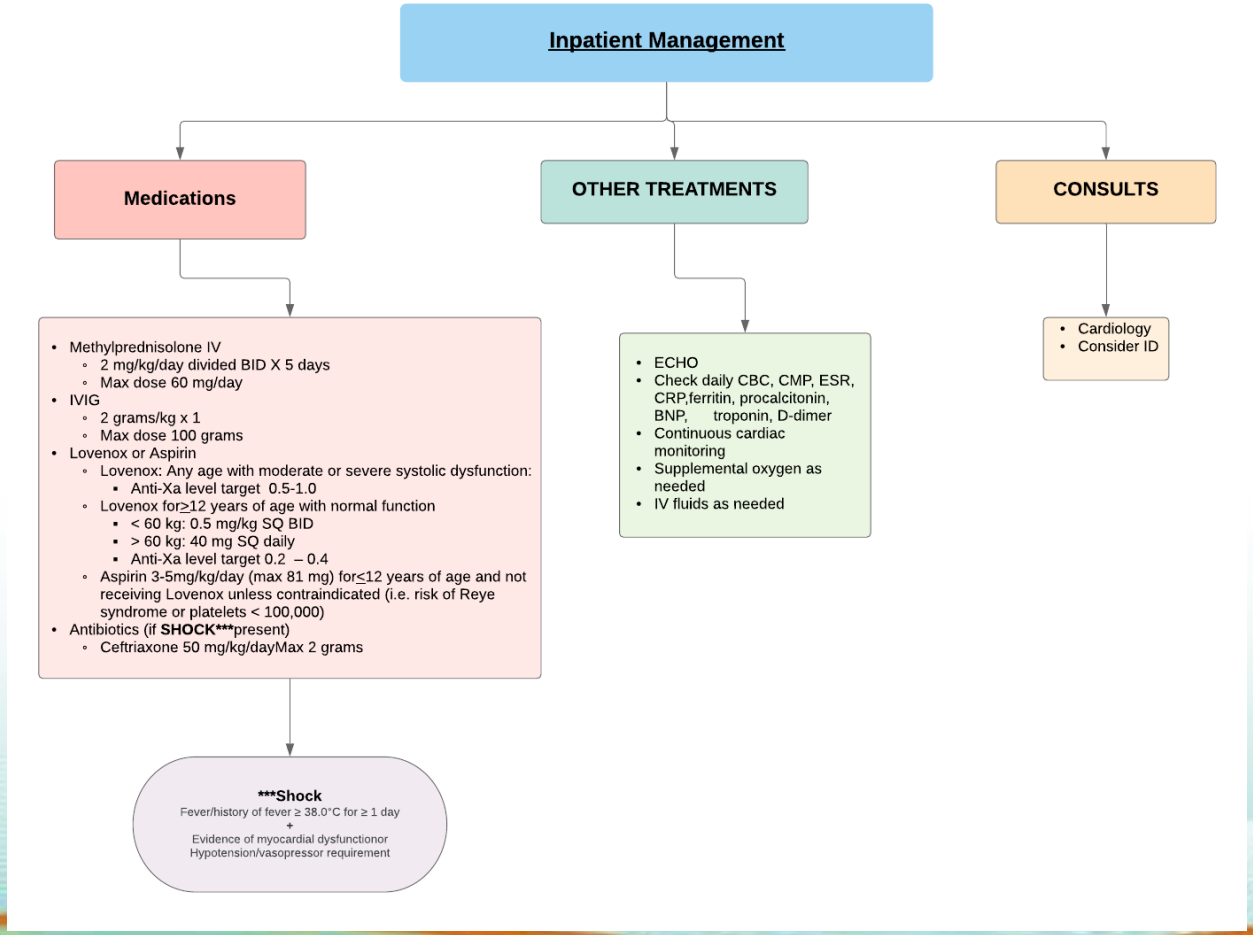
Inpatient Management



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