COVID-19
ONLINE EDUCATIONAL PROGRAM

Pediatric COVID-19: Lessons Learned So Far

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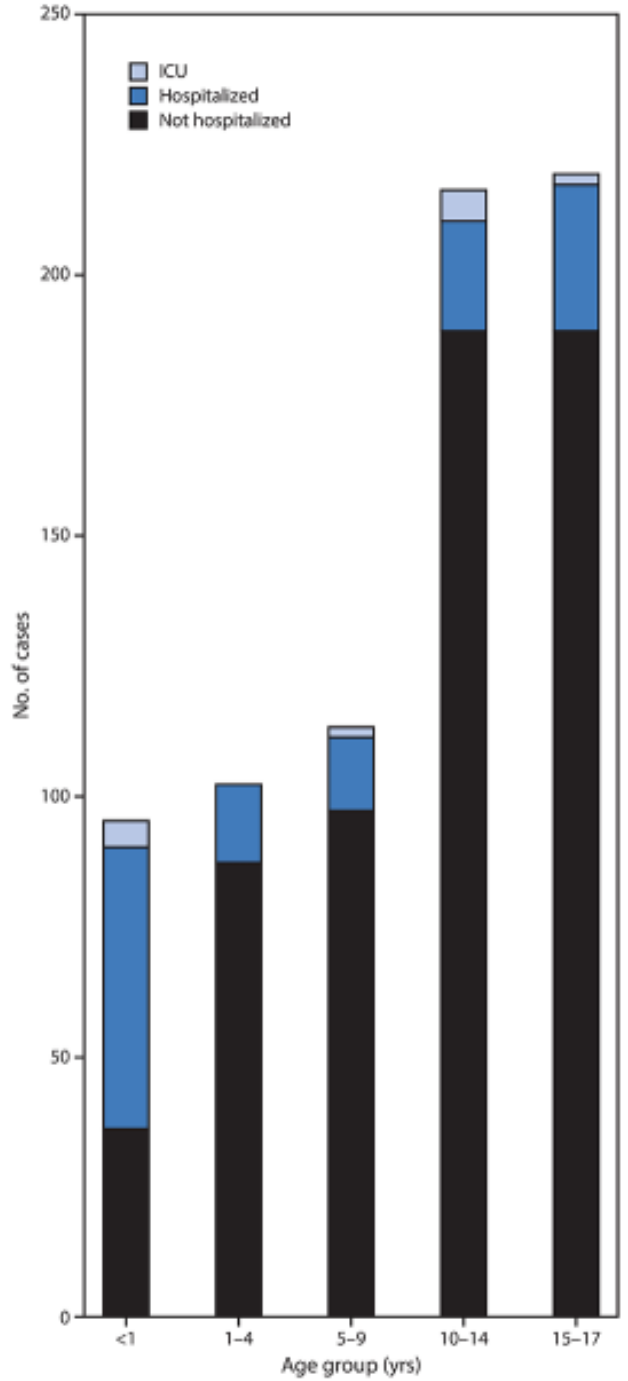
academic medical education

#1. Kids are GENERALLY less likely to get ill acutely from COVID-19



Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 69
April 6, 2020

Coronavirus Disease 2019 in Children — United States, February 12–April 2, 2020

CDC COVID-19 Response Team

- Children represent 22% of the US population
- Among 149,082 cases in the US, 1.7% are in children
- 0.58-2.0% are in the ICU
- Three deaths among ~2,500 cases

#2. Over Half of Children Have Milder Symptoms

1. Asymptomatic infection: **4%**

2. Mild: **51%** symptoms of acute URI or abdominal symptoms, normal lung exam.

3. Moderate: **39%** with pneumonia, frequent fever and cough, wheezing, but no obvious hypoxemia. **Some cases had no clinical signs and symptoms,** but chest CT showed lung lesions.

4. Severe: **5.2%** Oxygen saturation is less than 92%, with other hypoxia manifestations.

5. Critical: **0.6%** Respiratory failure, shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury.

14 year old boy died

Dong, Pediatrics, 2020

#3. There are risk factors for severe illness

- Underlying chronic illness (39%)
- Asthma, neurologic, diabetics, cardiac, hematologic/oncologic
- Obesity-2%

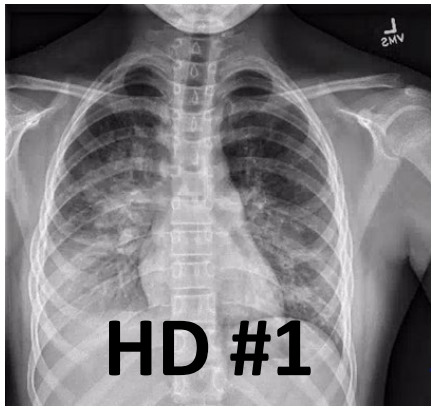
Debiasi, Journal of Pediatrics, 2020

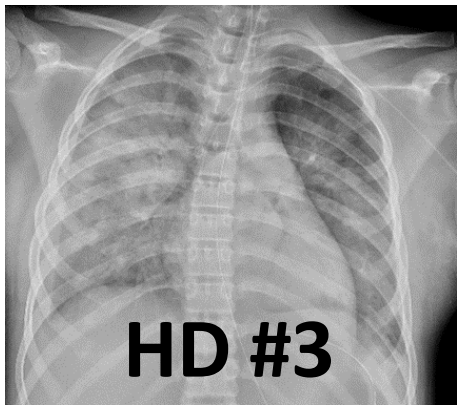
Table 1. Presentation and Demographic Characteristics of 48 Children Treated in Pediatric Intensive Care Units for Coronavirus Disease 2019 (COVID-19)

Characteristic	No. (%)
Age, median (IQR), y	13 (4.2-16.6)
Age group, y	
<1	8 (17)
1-5	6 (13)
6-10	7 (15)
11-21	27 (56)
Male	25 (52)
Presentation	
Asymptomatic	1 (2)
Respiratory	35 (73)
Gastrointestinal	1 (2)
Neurological	2 (4)
Circulatory	2 (4)
Other	7 (15)
Comorbidities	
None	8 (17)
Medically complex[a]	19 (40)
Immune suppression/malignancy	11 (23)
Obesity	7 (15)
Diabetes	4 (8)
Seizures	3 (6)
Congenital heart disease	3 (6)
Sickle cell disease	2 (4)
Chronic lung disease	2 (4)
Other congenital malformations	2 (4)

Shekerdemian et al. JAMA Peds. 2020

- 12 y/o: day 2 of illness: Came to ED with fevers, vomiting
- Day 3 of illness: Returned to ED with persistent fevers, new cough,
- Day 5 of illness: Returned to ED with fevers, SOB
  - 39.6°C HR 129 BP 108/63 RR 26-40 89% O2 saturation
  - Due to increased distress on HFNC 15L 100%, transferred to PICU for BiPAP





#4 Children Can Transmit the Disease…but MAYBE not that often

Transmission

- From March 10 – April 10, 2020,
- 40 children <16 years of age: contact tracing to identify infected household contacts (HHC).
  - In 3, there was suspected child to adult transmission
- 9 students/9 staff in Australia with SARS-CoV-2 had close contact with a total of 735 students and 128 staff.
  - 2 secondary infections noted

Posfay-Barbe K , Pediatrics 2020

National Centre for Immunization, Australia, 2020

Case	Age (years)	# total child household members	# adult household members	Potential Exposures (household member exposed)	Household contact with symptoms PRIOR to case	Household contact with symptoms AFTER to case	Days PRIOR or AFTER patient's first symptoms	# secondary cases/total susceptible household members
1	0.17	6	2	School (adult)	0	0	N/A	0 of 7 (0%)
2	0.58	2	2	Daycare (child)	0	1 (parent)	+18	1 of 3 (33%)
3	0.26	1	2	Hospital-acquired (child)	0	0	N/A	N/A
4	3	1	2	Unknown	0	0	N/A	0 of 3 (0%)
5	5	1	3	Cleaning houses (adult)	1	0	-1	1 of 3 (33%)
6	8	1	3	Unknown	1	0	-14	1 of 3 (33%)
7	9	1	2	Positive co-worker (adult)	1	0	-5	1 of 2 (50%)
8	11	1	2	Co-worker travel to NYC (adult)	2	0	-8	2 of 2 (100%)
9	12	2	2	School (child)	0	1 (parent)	Unknown	1 of 3 (33%)
10	12	1	2	Cereal factory (adult)	2	0	-8	2 of 2 (100%)
11	13	3	5	Unknown	3 (sibs)	1 (parent)	Before: unknown, After: +3	4 of 7 (57%)
12*	13	1	3	Cleaning houses (adult), *	1	0	-2	1 of 3 (33%)
13	14	3	2	Construction (adult)	0	0	N/A	0 of 4 (0%)
14	14	2	4	Unknown	0	0	N/A	0 of 5 (0%)
15	15	2	2	Positive co-worker (adult)	1	0	-14	1 of 3 (33%)
16	15	2	2	Cook (adult)	1 (parent)	2 (parent + sib)	Before: unknown, After: +12	3 of 3 (100%)
17	15	6	2	Unknown	0	0	N/A	0 of 7 (0%)
18**	16	1	2	Grocery store clerk (child)	0	1	+28	1 of 2 (50%)
19	16	2	2	Unknown	0	0	N/A	0 of 3 (0%)
20***	16	2	1	***	0	0	0	0 of 3 (0%)
21	16	5	6	Mattress factory (adult)	3	3	Before: -3, 0, After: +2, +15	6 of 10 (60%)
22	17	3	3	School	0	1 (parent)	6	1 of 5 (20%)

Unpublished data

Lesson #5..Children may have an immune response that is worse than the original illness…

Multisystem Inflammatory Syndrome in Children
MIS-c

HPI

7y old male with no significant PMH p/w fever, vomiting, and abdominal pain x 5 days

- Increasing irritability
- Decreased PO intake
- ROS negative for URI symptoms (cough, congestion, sore throat), chest pain, SOB, diarrhea, dysuria, confusion

D#1

- Fevers ranged from 102-104F
- Abd pain is constant
- NBNB emesis 1-2 episodes per day
- Rash: "red dots like mosquito bites" on b/l palms

D#2

- Went to PCP
- Rx Zofran for presumed AGE
- Rash progressed → red and splotchy on shoulders, arms, back

D#5

- Redness of his b/l eyes (no discharge)
- Dry, cracked lips
- Tenderness of his neck b/l (but denies stiffness)

OSH COURSE

- Admitted to OSH on 5/4 due to persistent fever, rash, SIRS
- Initial work up:
  - WBC 12.5 (N-79, B-6, L-8), Hb 11.8, Plt 204
  - CMP unremarkable (albumin 4.1, Cr 0.53, LFTs normal)
  - U/A with <1 WBC
  - ESR 67 mm/hr, CRP >8 mg/dL
- Clinical decompensation by 5/5 with hypotension (80s/50s) refractory to IVFs
- Transferred to EG PICU; started on norepi gtt en route

PHYSICAL EXAM

Vitals: BP **87/45**, HR **157**, T **38.8 °C**, RR **44**, SpO2 93 % room air

GENERAL: Awake, alert, Irritable, nontoxic appearing

HEENT: NCAT, mild periorbital edema, injected conjunctiva, PERRL, EOMI. No nasal congestion. EACs clear, TMs intact. Mucous membranes moist. Swollen red lips that are mildly dry/cracked, tongue mildly swollen

Neck: supple, tender lymphadenopathy cervical chains (none >1.5cm) b/l difficult to palpate due to pain on exam

CV: tachycardic, +S1, S2 with ?gallop, no murmur. Cap refill < 2 secs, 2+ peripheral pulses b/l

CHEST: Clear to auscultation bilaterally. No retractions.

ABD: full but soft, diffusely tender to palpation especially right side. No rebound or guarding. No CVA tenderness

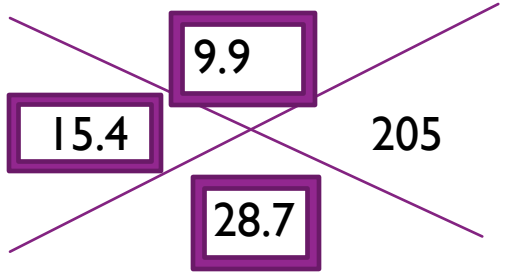
EXT: No cyanosis. Mild edema of b/l hands

MSK: MAES, normal tone. No joint swelling.

NEURO: grossly normal without focal deficits

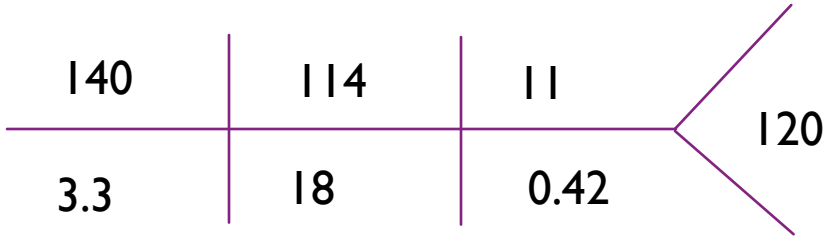
SKIN: Good turgor, blanching erythematous macular rash on shoulders, b/l UEs, back, and on groin. No diffuse erythroderma. No peeling. No vesicular lesions. No rash on palms or soles.

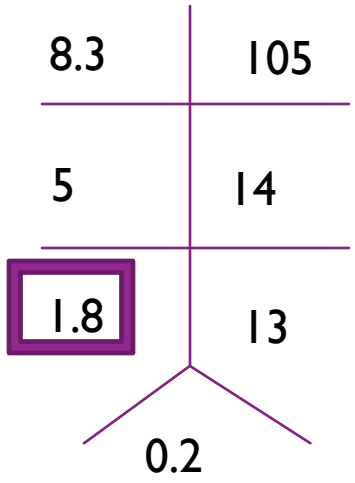
INITIAL LABS



- MCV: 82.7

Differential:
- N: 77%
- B: 4%
- L: 12%





- Ferritin 298.37
- Procalcitonin: 8.52
- CRP: 15.1

- U/A: unremarkable (WBC 3)

- PT 16.5/INR 1.3
- PTT 47.4
- Ddimer 689
- Fibrinogen 601

DIFFERENTIAL DIAGNOSIS

- Kawasaki Disease Shock Syndrome
- Pediatric Inflammatory Multisystem Syndrome (post-COVID hyperinflammatory shock syndrome)
- SARS-CoV-2 infection
- TSS (Staph aureus? GAS?)
- Enterovirus
- Less likely adenovirus, leptospirosis, RMSF, Ehrlichiosis

COVID-19 IgG, Qualitative by CIA

ARUP test code 3002776

COVID-19 IgG, Qualitative	**Positive** *	(Ref Interval: Negative)

A positive result suggests exposure to SARS-CoV-2 (COVID-19) but does not necessarily indicate immunity. Results from antibody testing should not be used as the sole basis to diagnose or exclude SARS-CoV-2 infection or to inform infection status. False positive results can occur due to past or present infection with non-SARS-CoV-2 coronavirus strains, such as coronavirus HKU1, NL63, OC43, or 229E.

INTERPRETIVE INFORMATION: COVID-19 IgG, Qualitative by CIA

The COVID-19 IgG, Qualitative by CIA test is for in vitro diagnostic use under an FDA Emergency Use Authorization (EUA). In compliance with this authorization, please visit https://www.aruplab.com/infectious-disease/coronavirus/testing for more information and to access the applicable information sheets. This test should not be used for screening of donated blood.

MAY 6, 2020

Hyperinflammatory shock in children during COVID-19 pandemic

South Thames Retrieval Service in London, UK, provides paediatric intensive care support and retrieval to 2 million children in South East England. During a period of 10 days in mid-April, 2020, we noted an unprecedented cluster of eight children with hyperinflammatory shock, showing features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome,[1] or toxic shock syndrome (typical number is one or two children per week). This case cluster formed the basis of a national alert.

All children were previously fit and well. Six of the children were of Afro-Caribbean descent, and five of the children were boys. All children except one were well above the 75th centile

Published Online
May 6, 2020
https://doi.org/10.1016/
S0140-6736(20)31094-1

- Lancet online

Riphagen et al. Hyperinflammatory shock in children during COVID-19 pandemic. *The Lancet*. 5/6/2020.

CLINICAL CHARACTERISTICS

- > 5yoa
- Abdominal symptoms
  - May look like appendicitis
- Otherwise healthy kids
- Some with conjunctivitis and/or rash
- All required inotropic support

Riphagen et al. Hyperinflammatory shock in children during COVID-19 pandemic. *The Lancet*. 5/6/2020.

MAY 13, 2020

An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study

Lucio Verdoni, Angelo Mazza, Annalisa Gervasoni, Laura Martelli, Maurizio Ruggeri, Matteo Ciuffreda, Ezio Bonanomi, Lorenzo D'Antiga

CASE DEFINITION FOR MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C)

- An individual aged <21 years presenting with fever[i], laboratory evidence of inflammation[ii], and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); **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

[i]Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours

[ii]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

Additional comments:

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should 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

CDC, 5/14/2020

World Health Organization[8]	Royal College of Paediatrics and Child Health (United Kingdom)[7]	Centers for Disease Control and Prevention (United States)[9]
Children and adolescents 0-19 y of age with fever >3 d AND 2 of the following: 1. Rash or bilateral nonpurulent conjunctivitis or mucocutaneous inflammation signs (oral, hands, or feet) 2. Hypotension or shock 3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP) 4. Evidence of coagulopathy (by PT, APTT, elevated D-dimers) 5. Acute gastrointestinal problems (diarrhea, vomiting, or abdominal pain) AND Elevated markers of inflammation such as ESR, CRP, or procalcitonin. AND No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. AND Evidence of COVID-19 (RT-PCR, antigen test, or serology positive), or likely contact with patients with COVID-19 Consider this syndrome in children with features of typical or atypical Kawasaki disease or toxic shock syndrome	A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP, and lymphopenia) and evidence of single or multiorgan dysfunction (shock, cardiac, respiratory, kidney, gastrointestinal, or neurological disorder) with additional features (see listed in eAppendix in Supplement 2). This may include children fulfilling full or partial criteria for Kawasaki disease[a] Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus (waiting for results of these investigations should not delay seeking expert advice) SARS-CoV-2 PCR test results may be positive or negative	An individual aged <21 y presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, kidney, respiratory, hematologic, gastrointestinal, dermatologic, or neurological) Fever >38.0 °C for ≥24 h or report of subjective fever lasting ≥24 h Laboratory evidence including, but not limited to, ≥1 of the following: an elevated CRP level, ESR, fibrinogen, procalcitonin, D-dimer, ferritin, lactic acid dehydrogenase, or IL-6; elevated neutrophils; reduced lymphocytes; and low albumin 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 wk prior to the onset of symptoms Additional comments Some individuals may fulfill full or partial criteria for Kawasaki disease but should 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

JUNE 8, 2020

JAMA | Original Investigation

Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2

Elizabeth Whittaker, MD; Alasdair Bamford, MD; Julia Kenny, MD; Myrsini Kaforou, PhD; Christine E. Jones, MD; Priyen Shah, MD; Padmanabhan Ramnarayan, MD; Alain Fraisse, MD; Owen Miller, MD; Patrick Davies, MD; Filip Kucera, MD; Joe Brierley, MD; Marilyn McDougall, MD; Michael Carter, MD; Adriana Tremoulet, MD; Chisato Shimizu, MD; Jethro Herberg, MD; Jane C. Burns, MD; Hermione Lyall, MD; Michael Levin, MD; for the PIMS-TS Study Group and EUCLIDS and PERFORM Consortia

- 58 children from 8 hospitals in England from 3/23-5/16
  - 26% SARS-CoV-2 PCR +
  - 87% SARS-CoV-2 IgG +
  - Fever + ~50% with nonspecific GI syx; rash; conjunctival injection
  - Labs with marked inflammation (CRP, ferritin)
  - 29 developed shock with myocardial dysfunction
  - 14% developed CA dilatation or aneurysm
- Compared to children with KD, KDSS, and TSS who had been admitted in Europe/US from 2002-2019
  - Older age
  - Greater elevation of inflammatory markers

JUNE 8, 2020

June 8, 2020

Multisystem Inflammatory Syndrome Related to COVID-19 in Previously Healthy Children and Adolescents in New York City

Eva W. Cheung, MD[1]; Philip Zachariah, MD, MS[1]; Mark Gorelik, MD[1]; et al

» Author Affiliations | Article Information

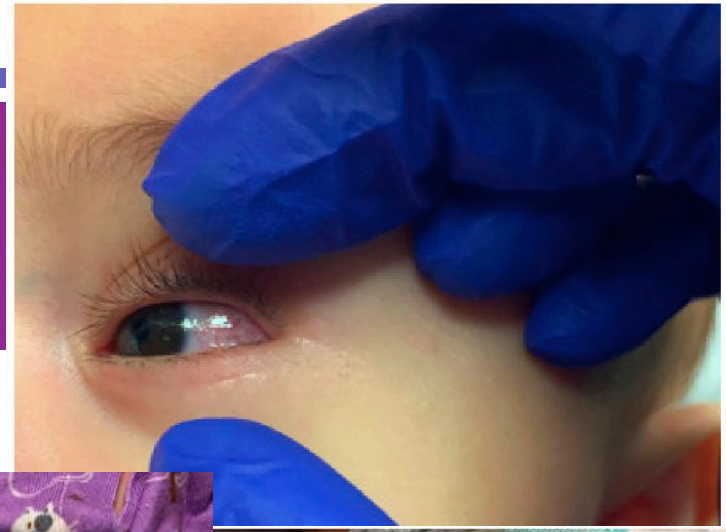
JAMA. Published online June 8, 2020. doi:10.1001/jama.2020.10374

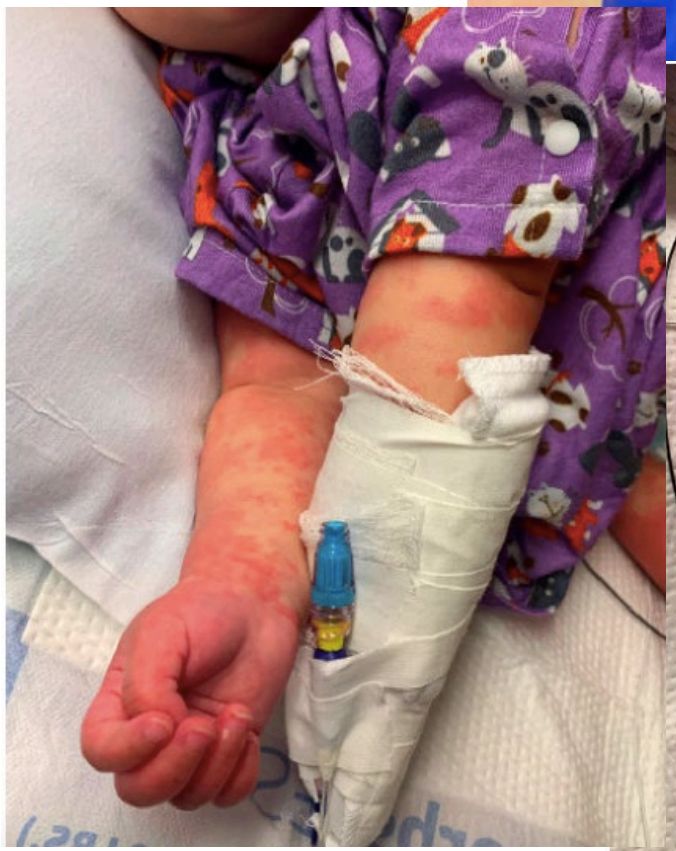
- Columbia Children's Hospital in NYC between 4/18 – 5/5
- 17 patients
  - Fever (100%)
  - GI syx (82%)
  - Mucocutaneous findings common
  - Shock (13)
- SARS-CoV-2 PCR + (47%)
- SARS-CoV IgG + (53%)

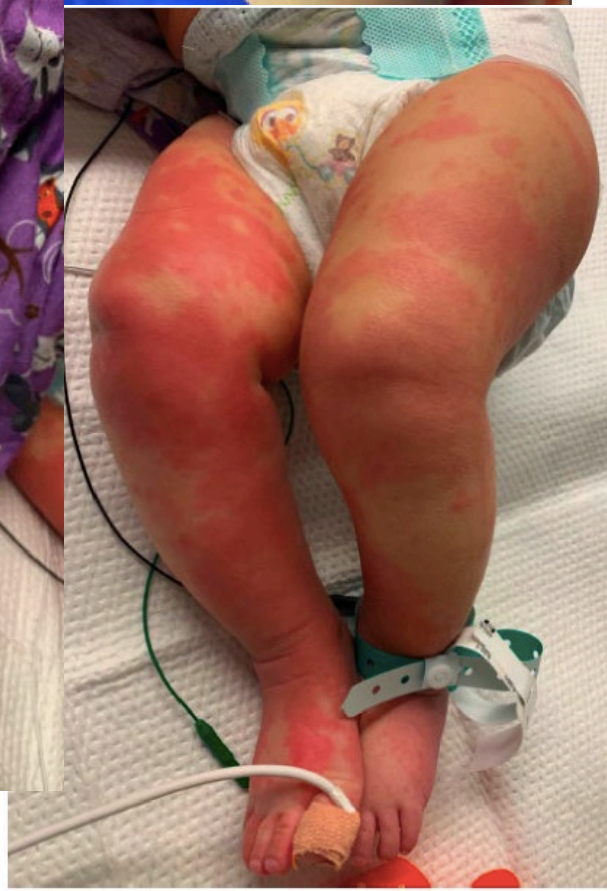
	Verdoni n=10	Belhadjer N=35	Whittaker N=58	Cheung N=17
Treatments	IVIG in all MP in 8 for Kobayashi score>5	25 with IVIG, one with two doses, 12 steroids, 3 anakinra	41 with IVIG, 37 with MP, 3 with anakinra, 8 with infliximab	13 received IVIG, 14 with steroids, 1 received toci
Outcome, death	0	No death, but several on EcMO	1 death, 3 required ECMO	0
Cardiac	2 dilated, no aneurysm	6 dilated, no aneurysm	8 with CAA	1developed medium sized CAA

COVID-19 AND KAWASAKI DISEASE: NOVEL VIRUS AND NOVEL CASE

- 6 mo with fever, fussiness, decreased PO
- Rash on day 2
- Irritability, limbic-sparing conjunctivitis, and dry lips on day 4
- Swelling of hands on day 5
- Left shift, anemia, elevated CRP and ESR, low albumin
- Treated with IVIG and high dose ASA
- Echo normal
- SARS-CoV-2 RT-PCR positive from admission







Jones, VG, Hospital Pediatrics 2020

#1: Children Less Likely to Become Ill than Adults

#2: Most Children Have Mild Symptoms

#3: Risk Factors for Severe Illness: obesity, underlying respiratory conditions

#4: Children Can Transmit the Disease but Perhaps less common

#5: Multi-system Inflammation can Occur (we think!) after SARS CoV-2 infection


What You Know
What You Need To Learn