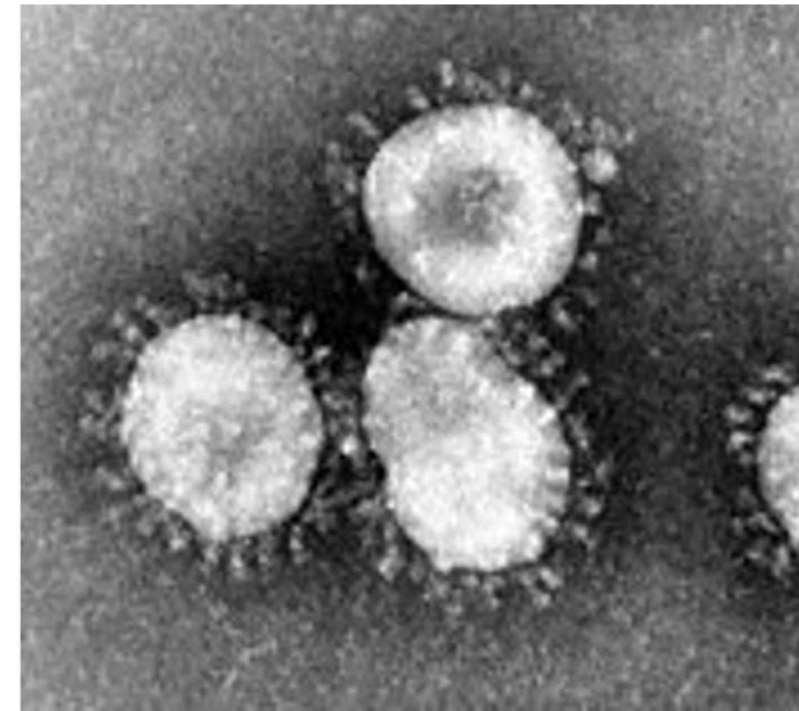
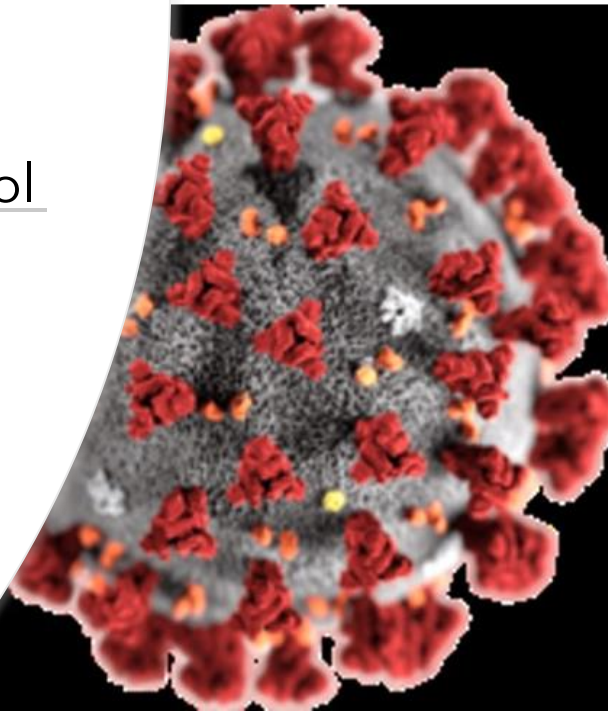


# COVID-19 in Children VS Kawasaki Disease and MIS-C: What Should We Aware?

By  
Kulkanya Chokephaibulkit, MD  
Faculty of Medicine Siriraj Hospital, Mahidol  
University

Webinar RCP, 4 June 2020



# Global Situation of COVID-19 27 May 2020

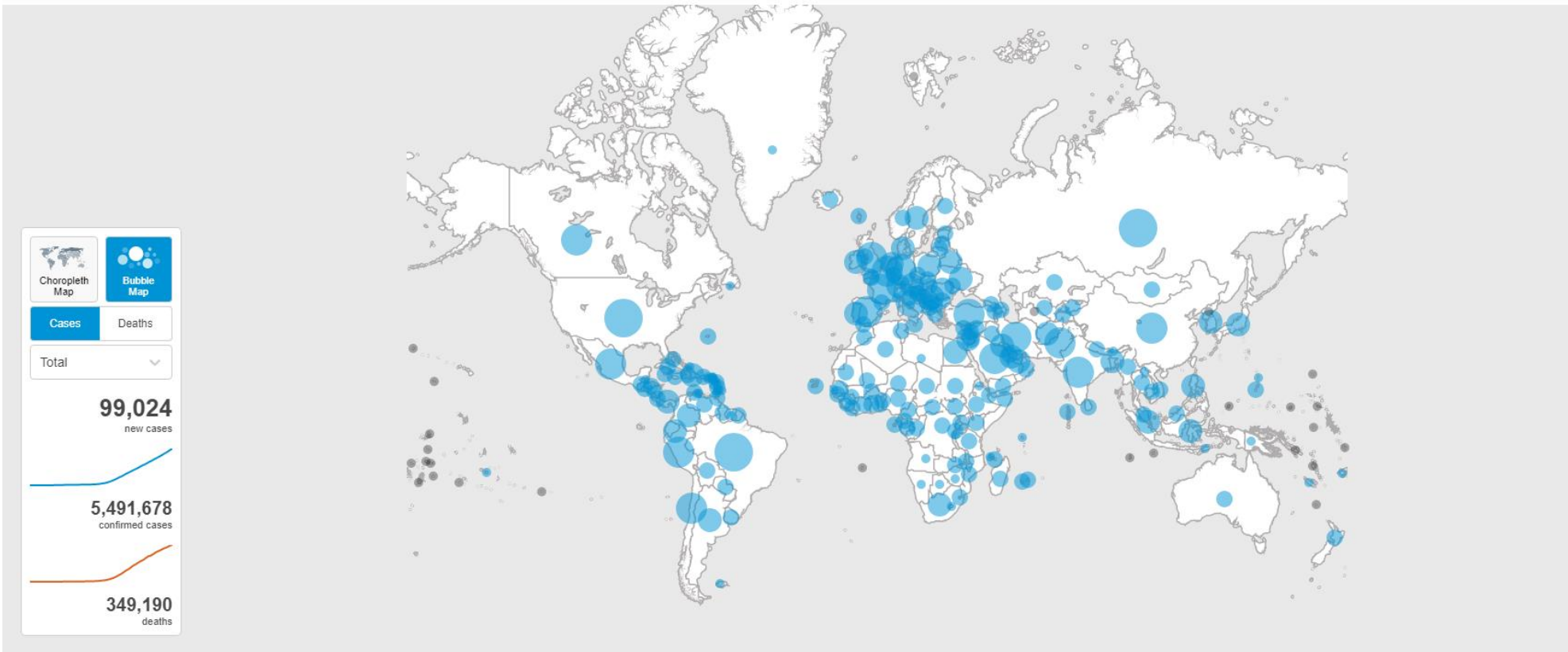


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WHO Coronavirus Disease (COVID-19) Dashboard  
Data last updated: 2020/5/27, 7:12pm CEST

[Overview](#) [Explorer](#)



Globally, as of 7:12pm CEST, 27 May 2020, there have been **5,491,678 confirmed cases** of COVID-19, including **349,190 deaths**, reported to WHO.

# Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China Summary of a Report of 72 314 Cases From the Chinese CDC

## Spectrum of disease (N = 44 415)

- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

## Case-fatality rate

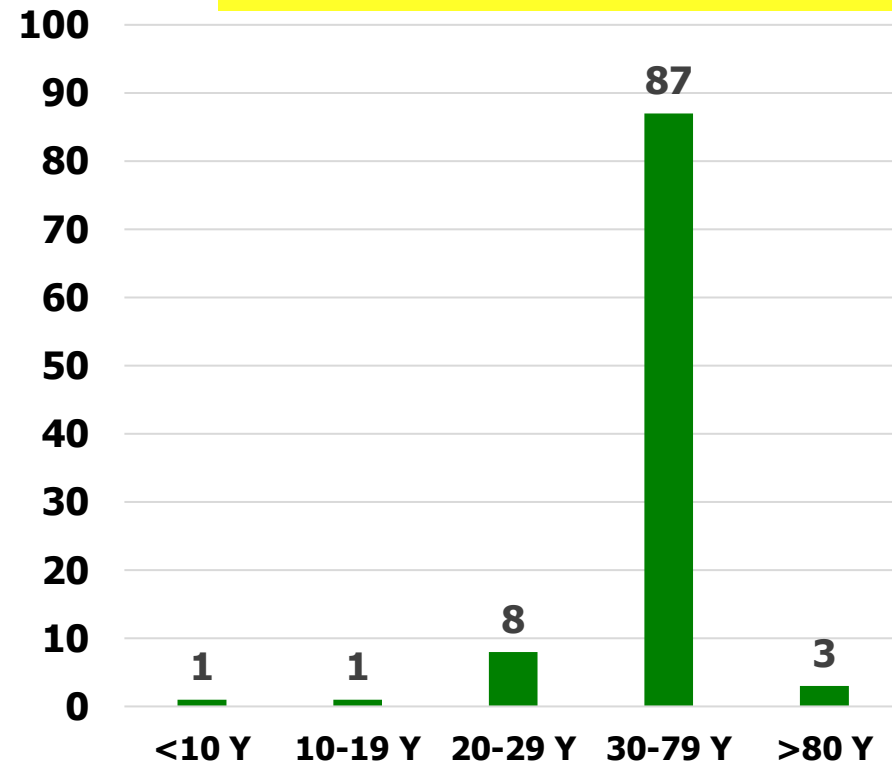
- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged  $\geq 80$  years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

## Health care personnel infected

- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

**อาการรุนแรง 14%,  
อายุ >80 ปี ตาม 15%  
บุคลากรทางการแพทย์ 3.8%  
หนัก 15%**

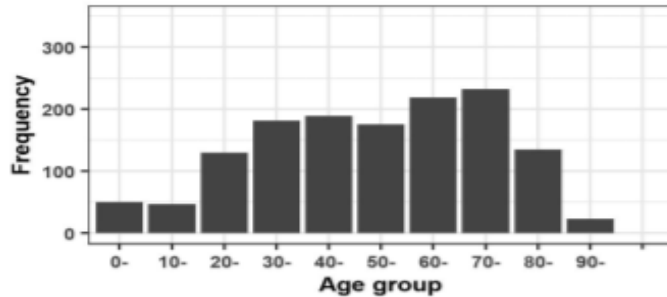
## Percent



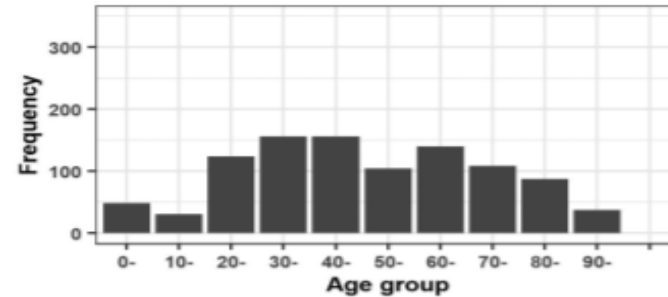
# Age specificity of cases and attack rate of novel coronavirus disease (COVID-19)

*313 domestically acquired confirmed cases among from 2496 close contact cases*

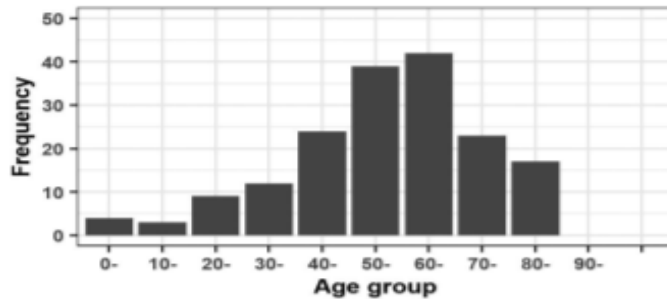
**A** Age distribution, Male Suspected close contacts



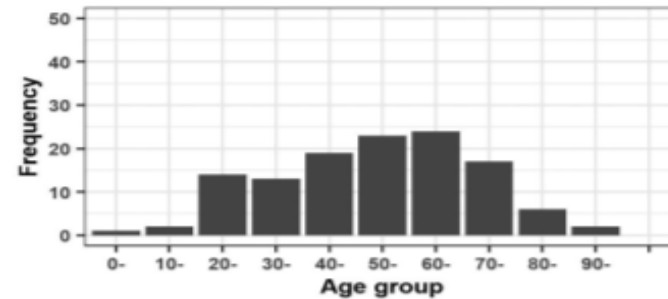
**B** Age distribution, Female Suspected close contacts



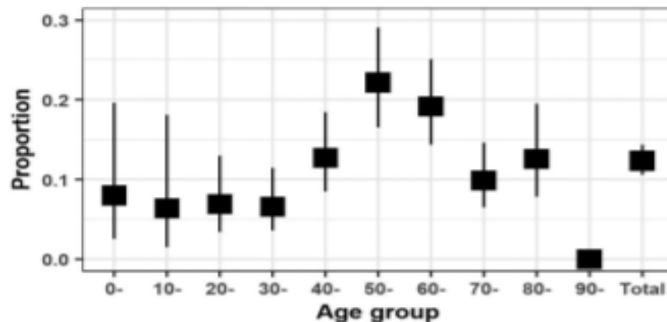
**C** Age distribution, Male Confirmed case



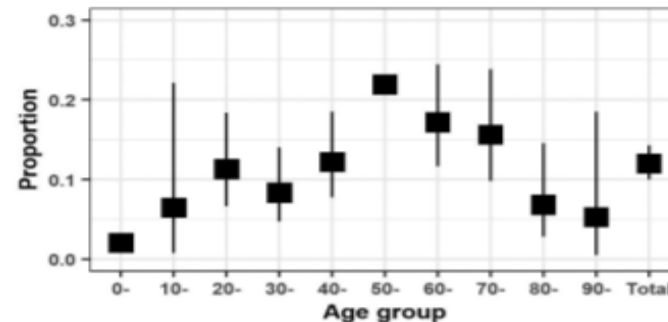
**D** Age distribution, Female Confirmed case



**E** Attack rate, Male



**F** Attack rate, Female



เด็ก ๆ ไม่ค่อย  
ติดโรคทั้ง ๆ ที่  
สัมผัส  
เหมือนกัน

Mizumoto K. medRxiv  
preprint doi:  
<https://doi.org/10.1101/2020.03.09.20033142>

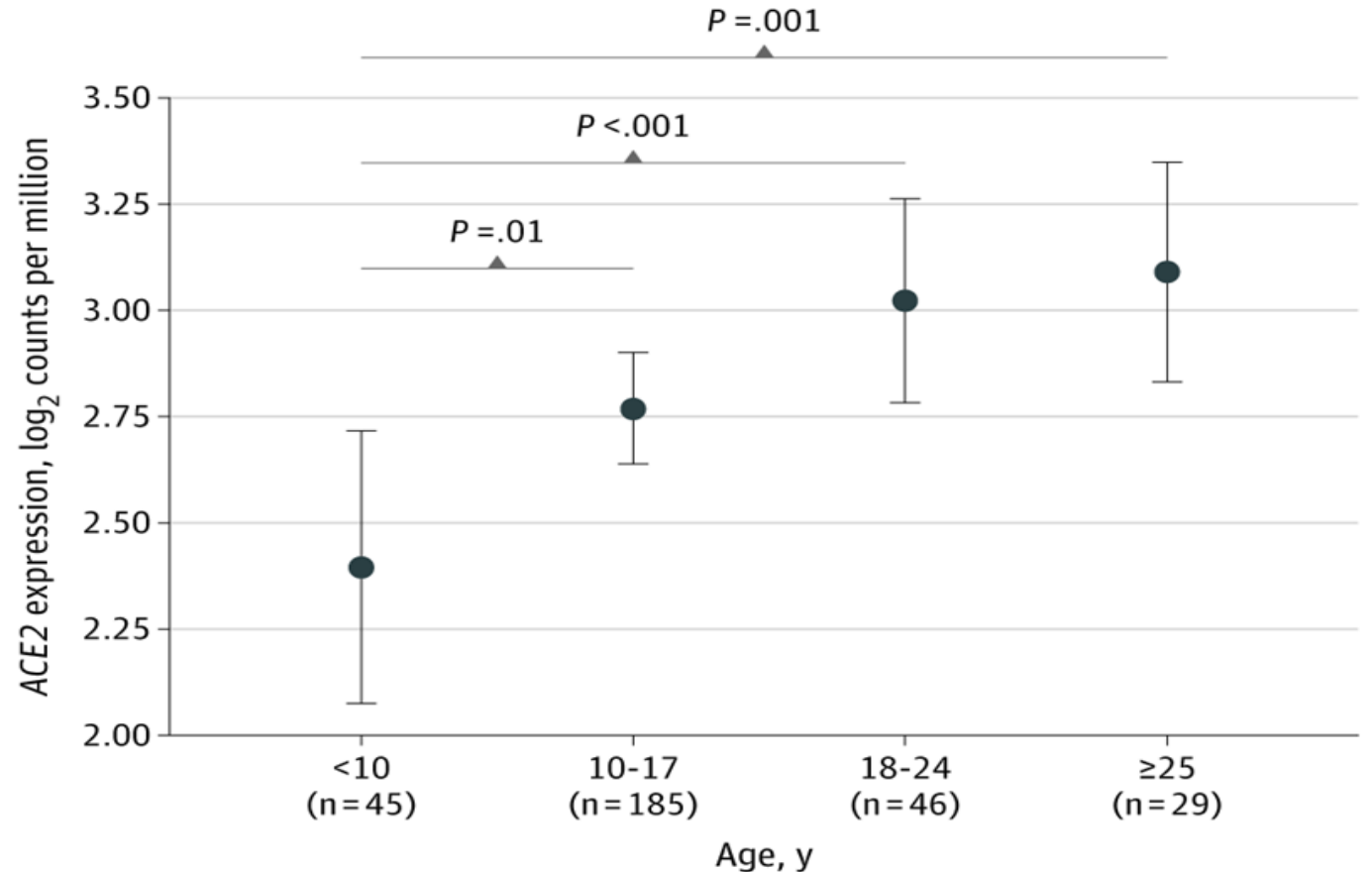
# Nasal Gene Expression of Angiotensin-Converting Enzyme 2 in Children is less than in Adults

While ACE2 binds to the receptor binding domain of SARS-CoV-2,....

...ACE2 can cleave angiotensin II to angiotensin 1-7, which can suppress inflammation and fibrosis and generate vasodilation by binding to the Mas receptor. Previous studies have found ACE2 to play a protective role in severe lung injury in ACE2 knockout mice.

....If ACE2 can mitigate lung injury but serves as a receptor for viral entry, then is more ACE2 or less ACE2 expression protective for children?

Bunyavanich S. JAMA. Published online May 20, 2020.  
doi:10.1001/jama.2020.8707



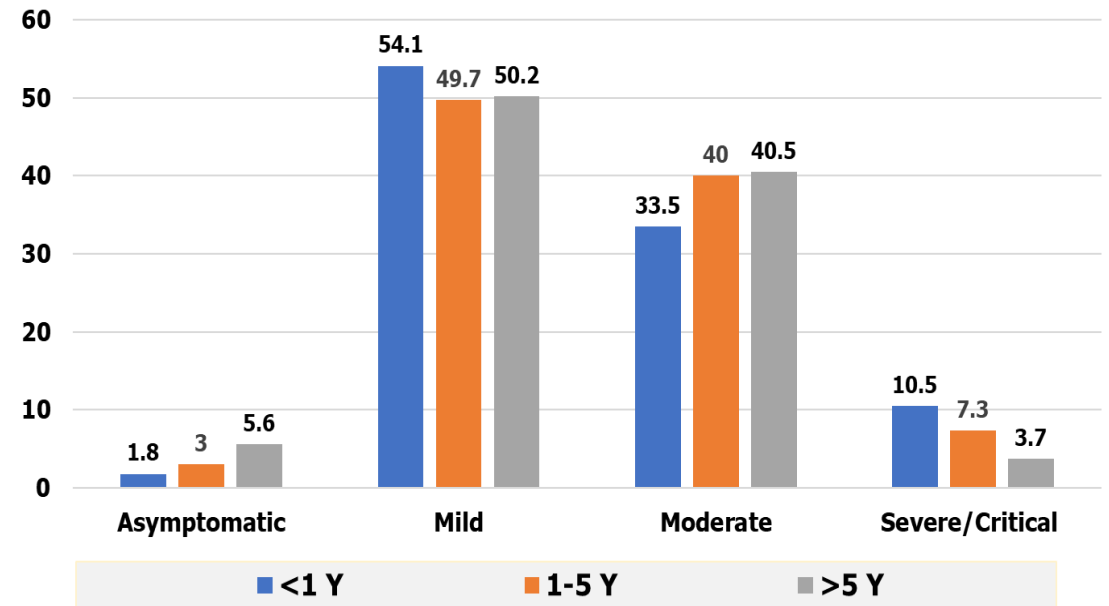
# Characteristics of Children' COVID-19 Cases in China (N=2143): เด็กส่วนใหญ่มีอาการน้อย ทารกมีโอกาสน้ำหนักมากกว่า

Characteristics All cases

Characteristics	All cases
Severity of illness	
Asymptomatic	94(4.4)
Mild	1091(50.9)
Moderate	831(38.8)
Severe	112(5.2)
Critical	13(0.6)
Missing	2(0.1)
Days from symptom onset to diagnosis	
Median days (Interquartile range)	2(4.0)
Range	0-42

Severe and critical 5.8% in children  
vs 20% in adults

Different Severity of Illness by Age Group

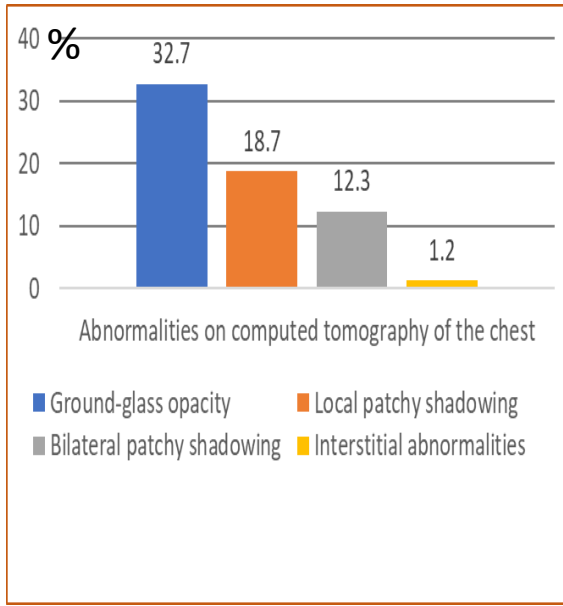
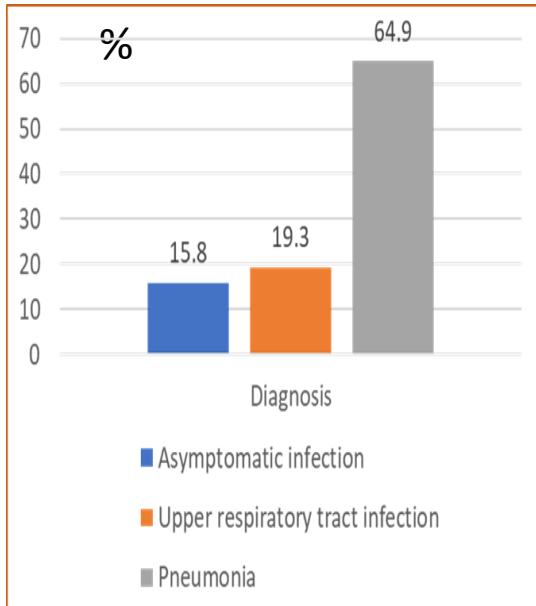
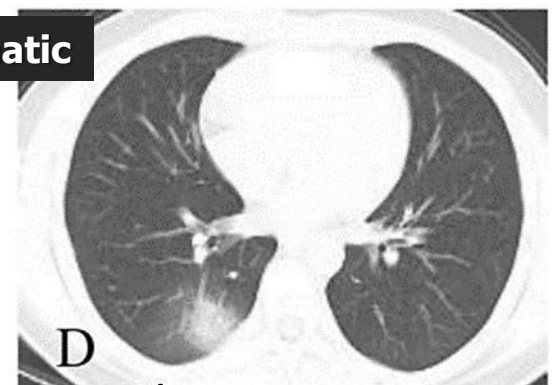
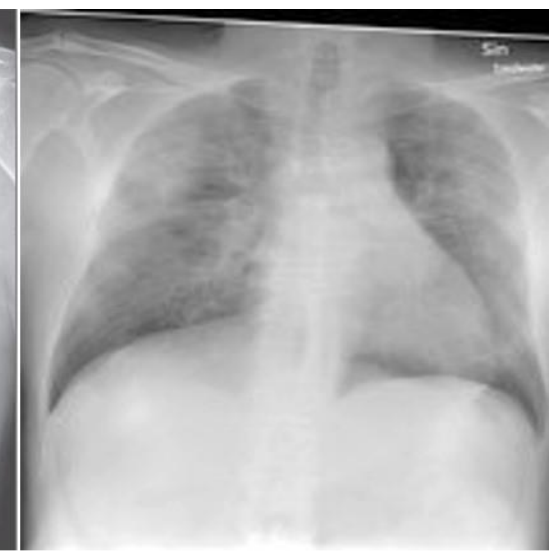
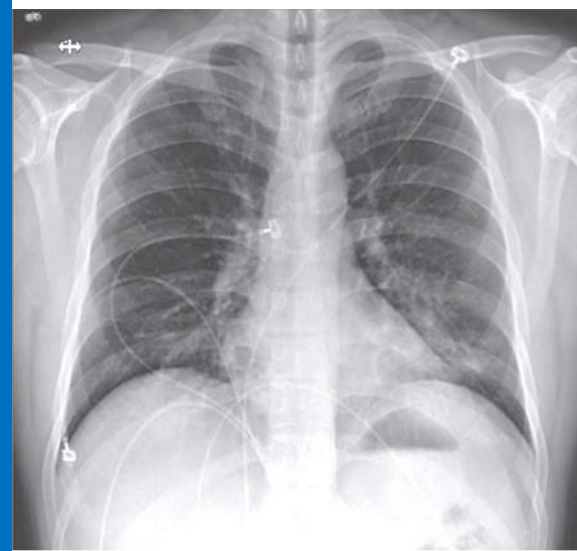


<1 y had higher rate of severe/critical  
(10% vs 3-7%)

# ลักษณะของ CXR/CT ในเด็กจะ

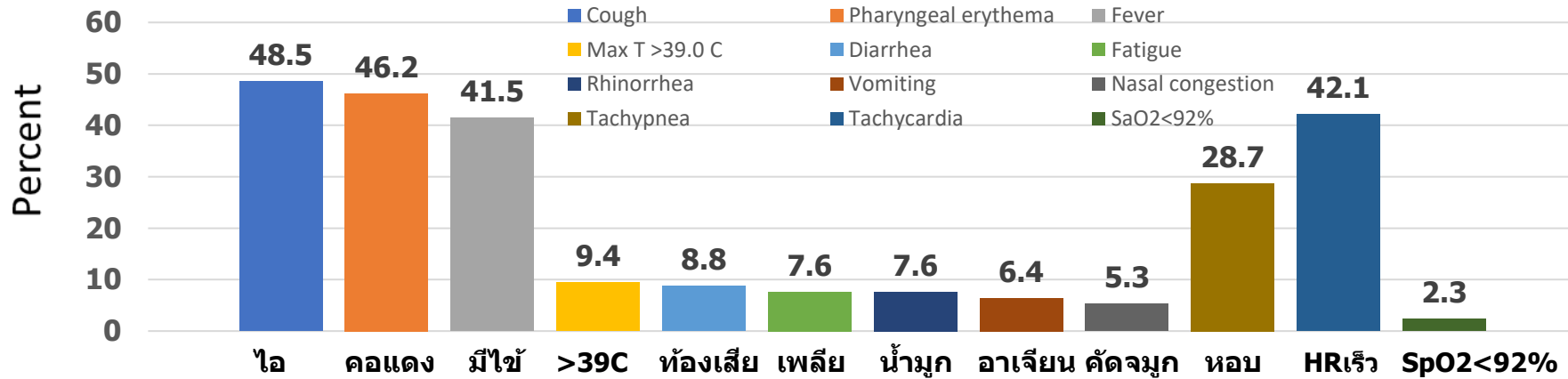
## เหมือนผู้ใหญ่ แต่เป็นน้อยกว่า

*The ground-glass and/or consolidative opacities are usually bilateral, peripheral, and basal in distribution. 54% of asymptomatic patients had pneumonic changes on CT*



# SARS-CoV-2 Infection in Children

## Epidemiologic Characteristics, Clinical Features, and Radiologic Findings of 171 Children with SARS-CoV-2 Infection



อาการในผู้ใหญ่	Patients (n=99)
<b>Signs and symptoms at admission</b>	
Fever	82 (83%)
Cough	81 (82%)
Shortness of breath	31 (31%)
Muscle ache	11 (11%)
Confusion	9 (9%)
Headache	8 (8%)
Sore throat	5 (5%)
Rhinorrhoea	4 (4%)
Chest pain	2 (2%)
Diarrhoea	2 (2%)
Nausea and vomiting	1 (1%)
More than one sign or symptom	89 (90%)
Fever, cough, and shortness of breath	15 (15%)

- เด็กมีไข่น้อยกว่าผู้ใหญ่
- ไอน้อยกว่าผู้ใหญ่
- อาการ URI, ท้องเสียน้อย เหมือนผู้ใหญ่



# Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China

- 36 children (mean age 8.3 years)
- The route of transmission: contact with family members (32 [89%]) or exposure to the epidemic area (12 [33%])
- 19 (53%) had pneumonia
- 10 [28%] asymptomatic (ten [28%])
- 7 [19%] had URI
- Common symptoms on admission were fever (13 [36%]) and dry cough (7 [19%]).
- Typical abnormal laboratory: elevated CK MB [31%], decreased lymphocytes [31%], leucopenia [19%], and elevated PCT [17%].
- 6 (17%) needed oxygen inhalation.
- Mean time in hospital was 14 (SD 3) days.

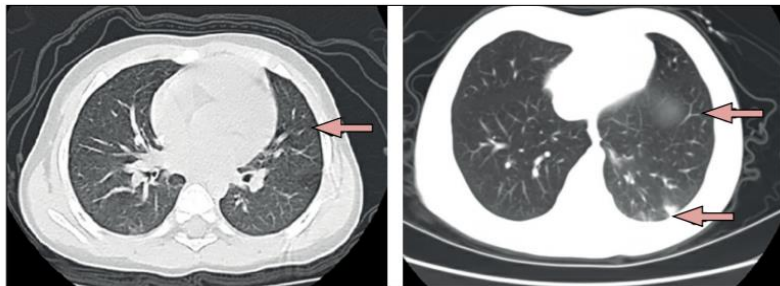


Figure 1: Chest CT scans from two paediatric patients with coronavirus disease 2019 (Left) CT of 10-year-old boy showing multiple opacities in lower lobes of both lungs (arrow). (Right) CT of 1.5-year-old girl showing multiple ground-glass opacities with a big patchy opacity in the right lung (arrows).

	Children with COVID-19 (n=36)	Adults with COVID-19 (n=175) <sup>17</sup>	Children with SARS (n=44) <sup>10</sup>	Children with H1N1 influenza (n=167) <sup>19</sup>
Age, years	8.3 (3.5)	45 (14)	12.2 (4.1)	4.1 (3.5)
Fever	13 (36%)	150 (86%)	44 (100%)	153 (92%)
Cough	7 (19%)	109 (62%)	28 (64%)	138 (83%)
Pharyngeal congestion or sore throat	1 (3%)	8 (5%)	6 (14%)	159 (95%)
Dyspnoea	1 (3%)	8 (5%)	6 (14%)	12 (7%)
Asymptomatic*	10 (28%)	1 (1%)	0 (0%)	<5%
Pneumonia	19 (53%)	109 (62%)	28 (64%)	138 (83%)
Comorbidities or complications (except pneumonia and bronchitis)				
Mild and moderate cases	27 (75%)	166 (95%)	44 (100%)	153 (92%)
Severe cases	9 (25%)	9 (5%)	0 (0%)	12 (7%)
Leucopenia	7 (19%)	61 (35%)	34 (77%)	65 (39%)
Lymphopenia	11 (31%)	61 (35%)	34 (77%)	NA
Myocardial enzymes elevated	11 (31%)	39 (22%)	3 (7%)	18 (11%)
Liver enzymes elevated	2 (6%)	32 (18%)	21 (48%)	12 (7%)
Elevated C-reactive protein	1 (3%)	86 (49%)	NA	42 (25%)
Antiviral therapy	14 (39%)	170 (97%)	42 (96%)	167 (100%)

เด็กโควิด19 มีไข้ ไอ น้อยกว่าผู้ใหญ่ และน้อยกว่าเด็กที่เป็นไข้หวัดใหญ่ และเจ็บคือน้อยกว่า

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เด็กโควิด19 ไม่ค่อยมีอาการ แต่พบเป็นปอดอักเสบถึง 53% (ผู้ใหญ่มีปอดอักเสบถึง 95%) ในขณะที่ใช้หวัดใหญ่ H1N1 เป็นปอดอักเสบน้อยกว่า มีอาการรุนแรงมากกว่า

- 6 (17%) children were asymptomatic
- Mean time in hospital was 14 (SD 3) days.

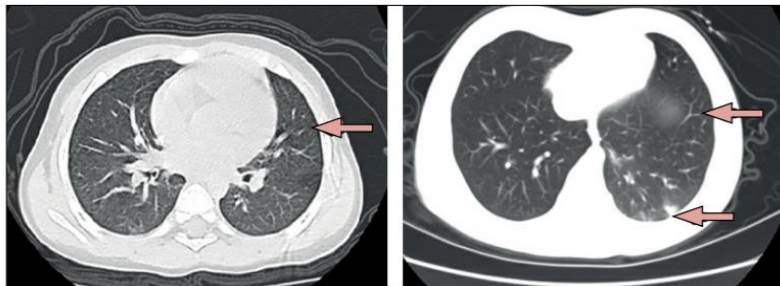
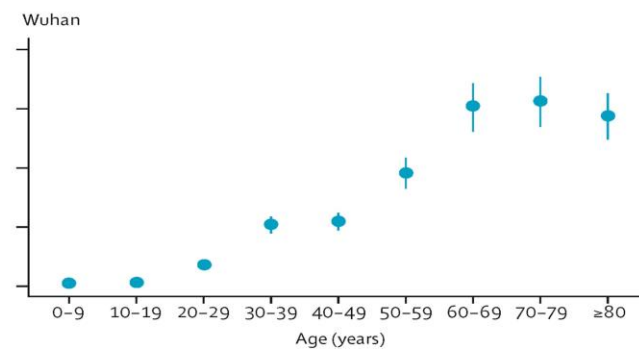
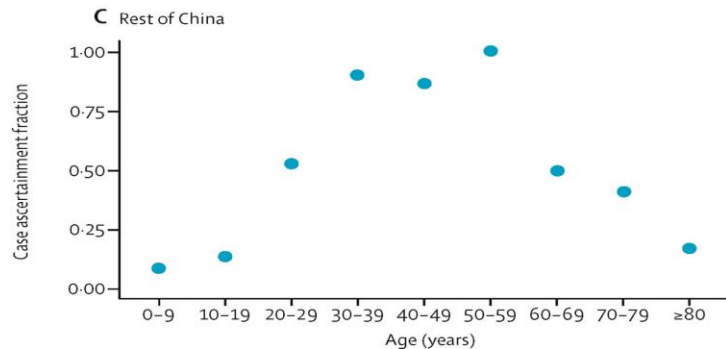
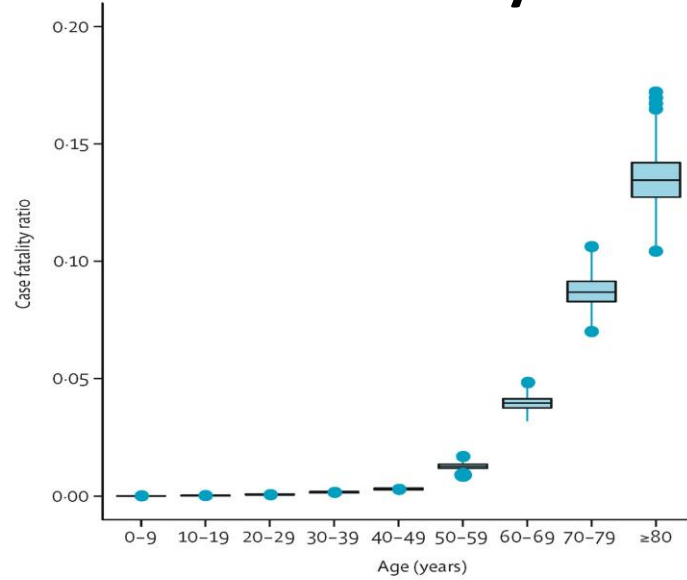
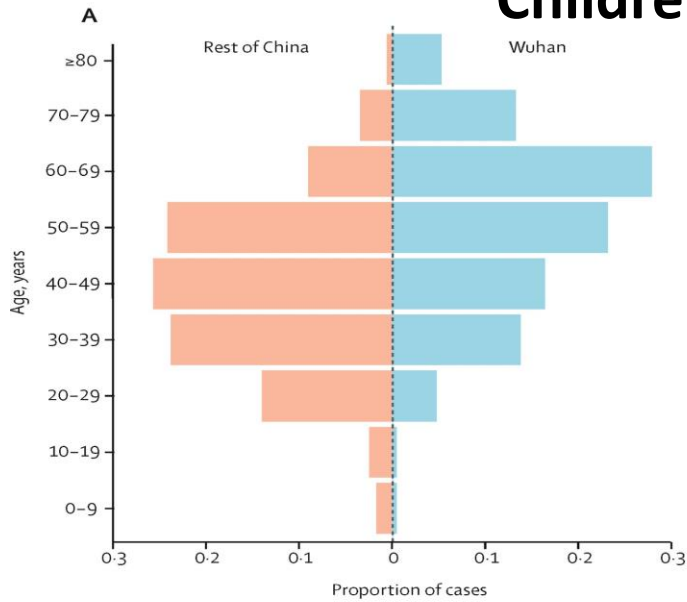


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Dyspnoea	1 (3%)	23 (13%)	4 (9%)	12 (7%)
Asymptomatic*	10 (28%)	<5%	0	<5%
Pneumonia	19 (53%)	166 (95%)	40/62 (65%)†	18 (11%)
Comorbidities or complications (except pneumonia and bronchitis)	0	10 (6%)	5 (11%)	7 (4%)
Mild and moderate cases	36 (100%)	136 (77%)	35 (79%)	135 (81%)
Severe cases	0	39 (23%)	9 (21%)	32 (19%)
Leucopenia	7 (19%)	44 (25%)	15 (34%)	65 (39%)
Lymphopenia	11 (31%)	61 (35%)	34 (77%)	NA
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Elevated C-reactive protein	1 (3%)	86 (49%)	NA	42 (25%)
Antiviral therapy	14 (39%)	170 (97%)	42 (96%)	167 (100%)

# Estimates of the severity of coronavirus disease 2019: a model-based analysis: Children has a lower fatality rates เด็กไม่ค่อยเสียชีวิต

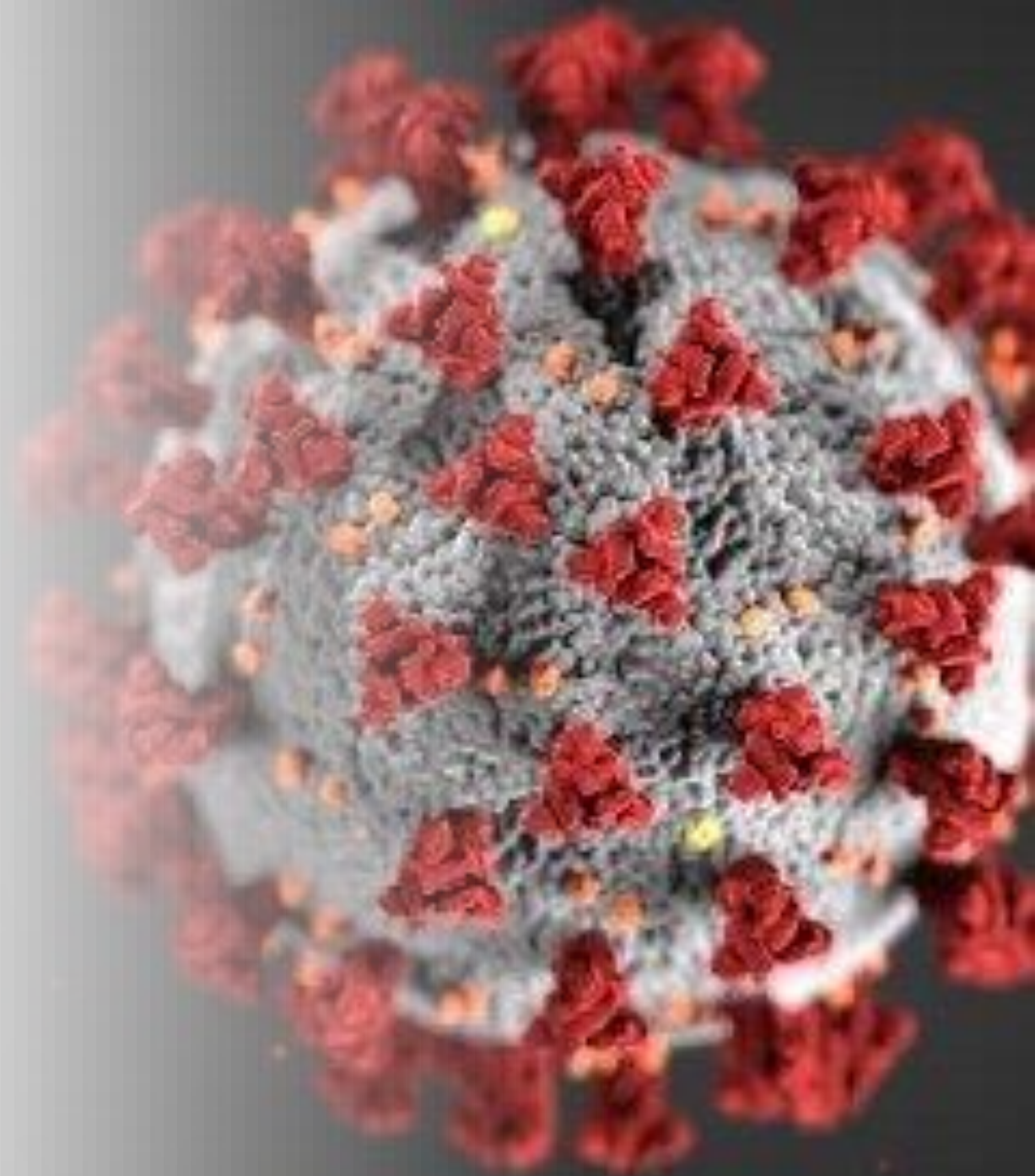


	Death	Fatality ratio
Overall	1023	0.657% (0.389-1.33)
Age group, years		
0-9	0	0.00161% (0.000185-0.0249)
10-19	1	0.00695% (0.00149-0.0502)
20-29	7	0.0309% (0.0138-0.0923)
30-39	18	0.0844% (0.0408-0.185)
40-49	38	0.161% (0.0764-0.323)
50-59	130	0.595% (0.344-1.28)
60-69	309	1.93% (1.11-3.89)
70-79	312	4.28% (2.45-8.44)
≥80	208	7.80% (3.80-13.3)
Age category (binary), :		
<60	194	0.145% (0.0883-0.317)
≥60	829	3.28% (1.82-6.18)

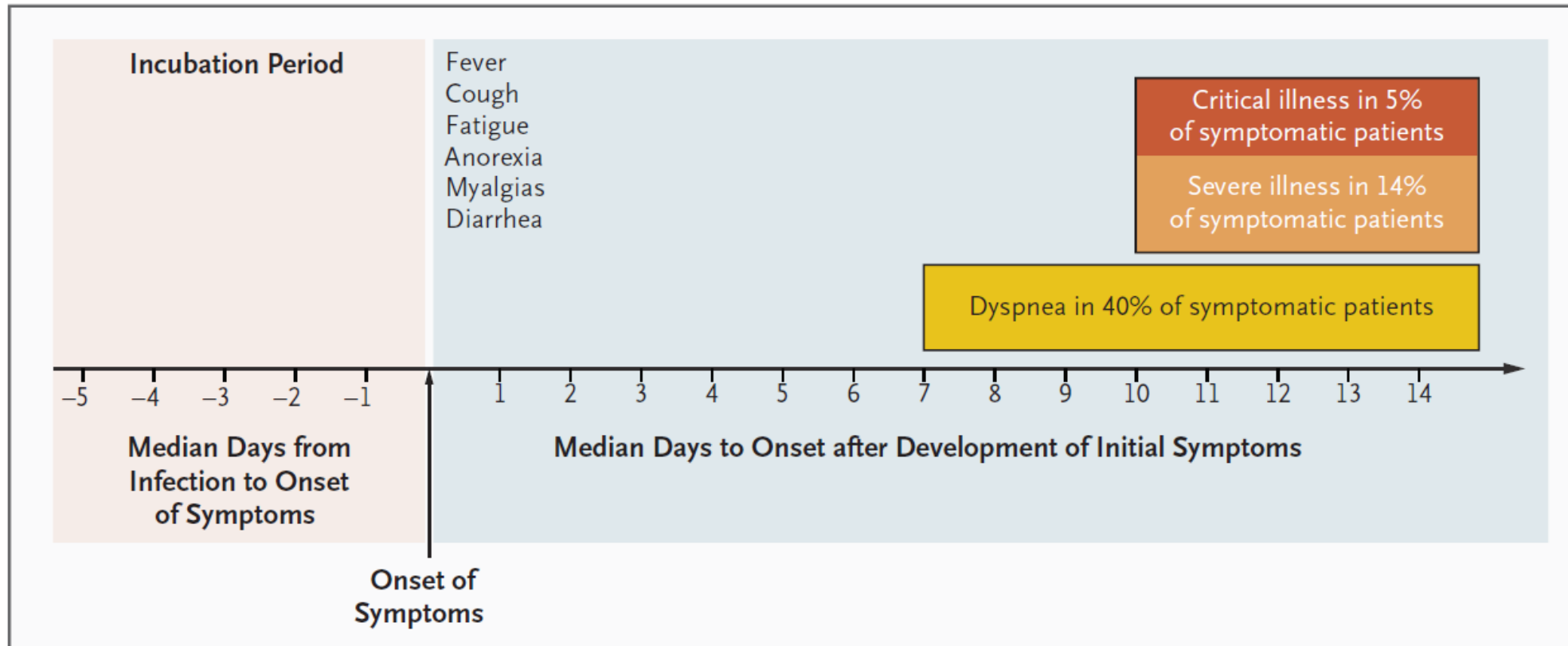
Estimated overall infection fatality ratio for China was 0.66% (0.39–1.33), with an increasing profile with age. Similarly, estimates of the proportion of infected individuals likely to be hospitalised increased with age up to a maximum of 18.4% (11.0–37.6) in those aged 80 years or older.

COVID-19 and  
Immune  
Mediated Events:  
We are learning  
more about this  
infection

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# Severe Covid-19: ผู้ป่วยจะเริ่มหนัก เกิดARDS ในสัปดาห์ที่สองซึ่งเป็นช่วงที่ไวรัสเริ่มลดลง แต่เกิดจาก cytokine storm

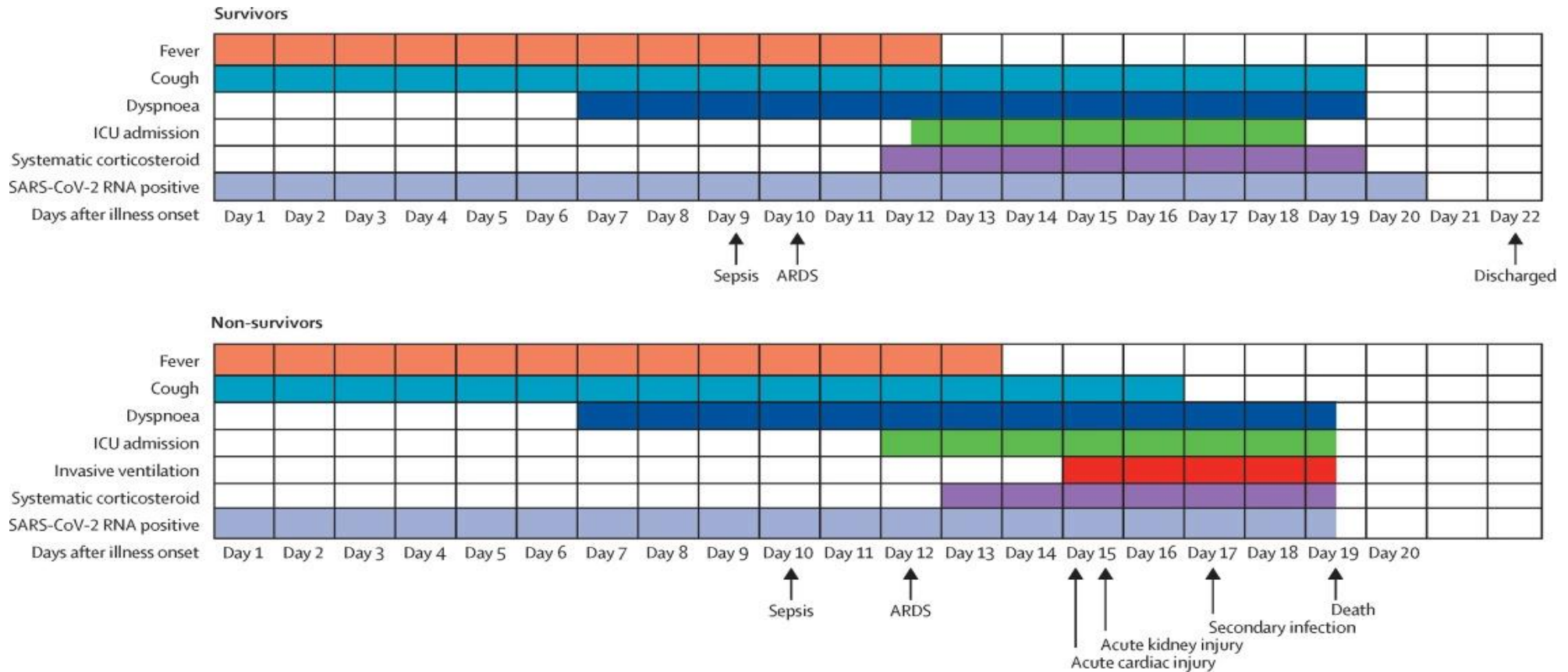


**Figure 1.** Timeline of Symptoms of Severe Coronavirus Disease 2019 (Covid-19).

The left border of the colored boxes shows the median time to onset of symptoms and complications. There is wide variation in the duration of symptoms and complications. Adapted from Zhou et al.<sup>2</sup> and the Centers for Disease Control and Prevention.<sup>1</sup>

# Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study

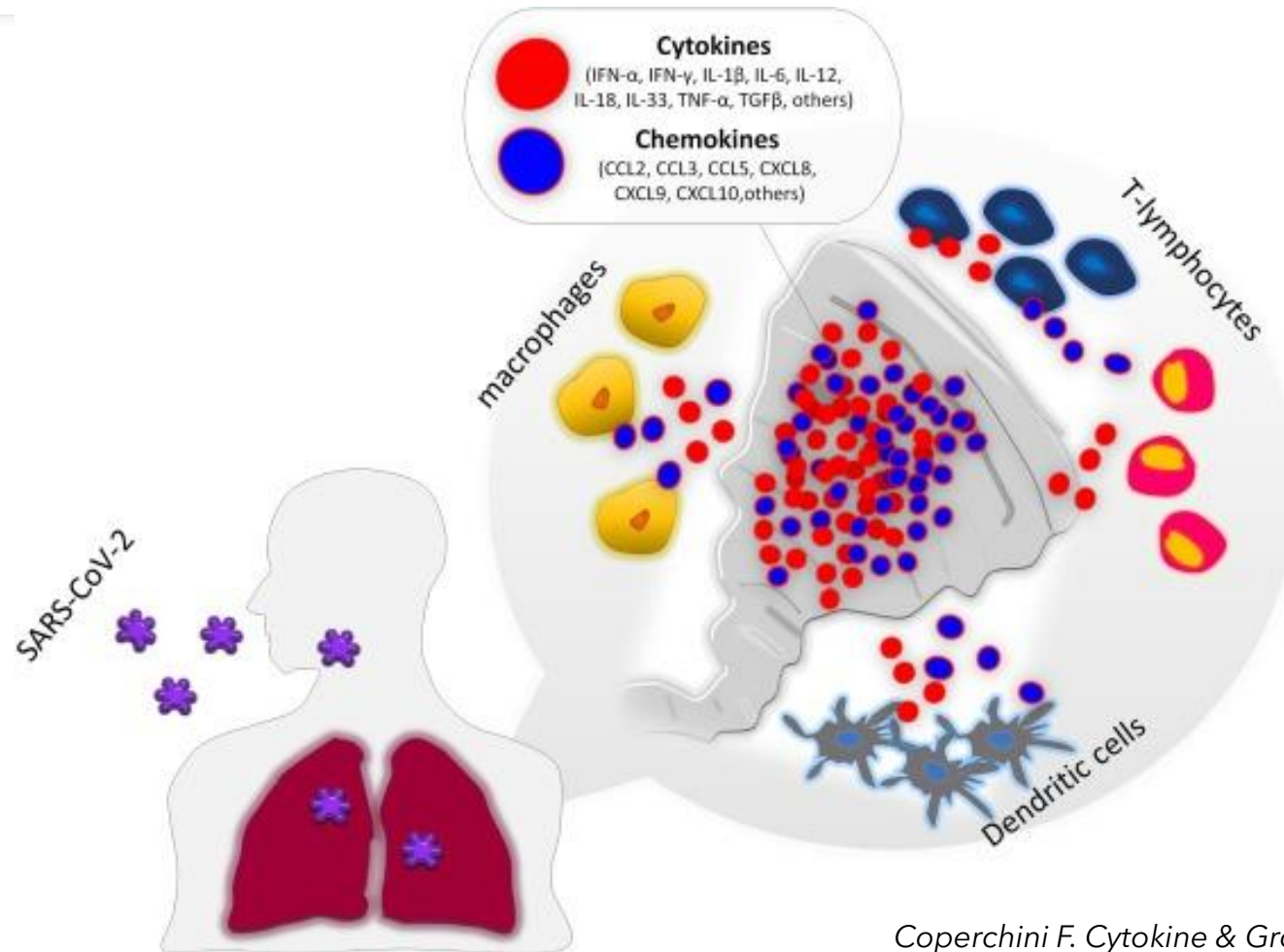
ผู้ป่วยจะเริ่มหนัก ARDS cytokine storm หลังจากสัปดาห์แรก



Clinical courses of major symptoms and outcomes and duration of viral shedding from illness onset in patients hospitalised with COVID-19

Zhou F. Lancet MARCH 28, 2020

# The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system: *The “cytokine storm” and the subsequent ARDS result from the effects of the combination of several immune-active molecules.*



The presence of SARS-CoV-2 in the lung induces an uncontrolled generalized immune response. Several immune cells (like T-lymphocytes, macrophages and dendritic cells) sustain the impressive secretion of cytokines and chemokines ultimately leading to acute respiratory distress syndrome.

# Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19: Autopsy in 7 Covid-19 vs 7 Influenza

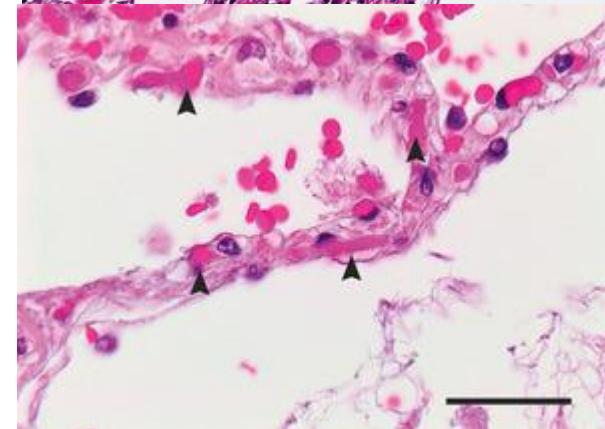
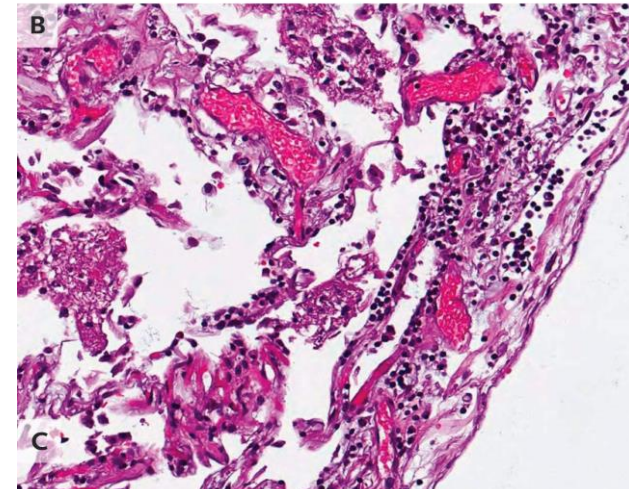
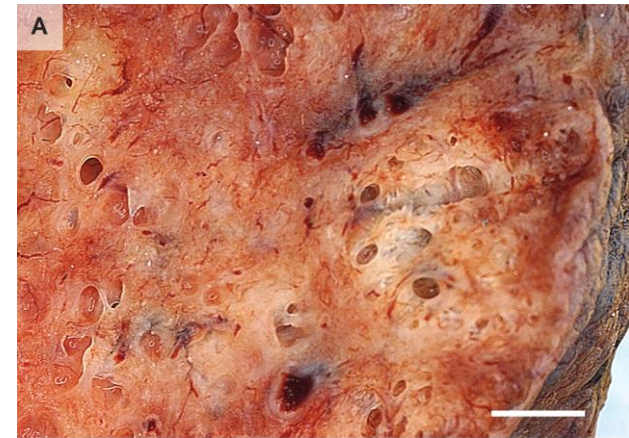
... severe endothelial injury associated with intracellular SARS-CoV-2 virus and disrupted endothelial cell membranes.....

- Alveolar capillary microthrombi were 9 times more than in patients with influenza ( $P < 0.001$ ).
- The amount of new vessel growth — predominantly through a mechanism of intussusceptive angiogenesis — was 2.7 times higher than those with influenza ( $P < 0.001$ ).

Ackermann M, et al. NEJM May 21, 2020  
DOI: 10.1056/NEJMoa2015432

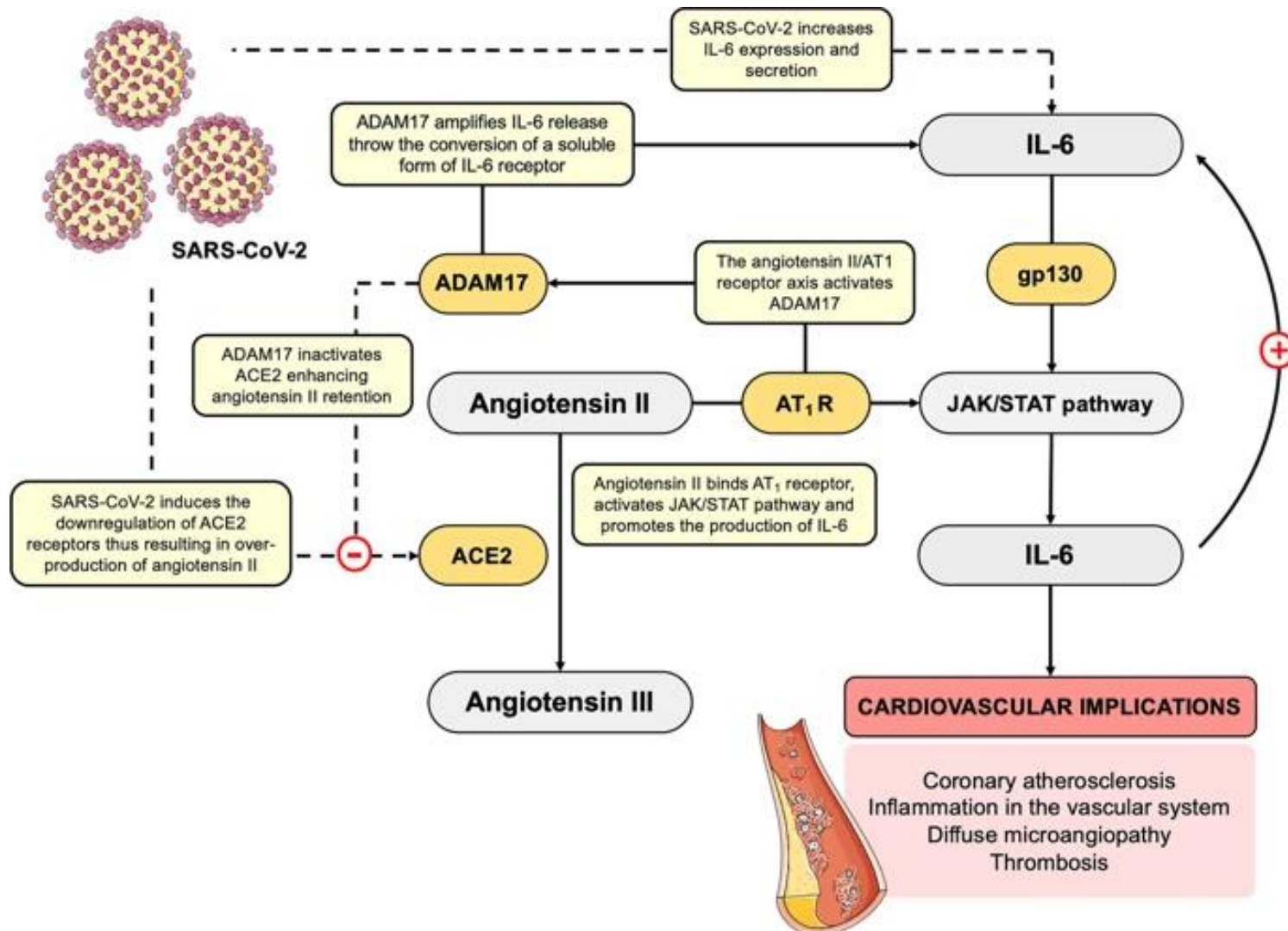
The histopathological examination, shown in Panel B, revealed interstitial and perivascular predominantly lymphocytic pneumonia with multifocal endothelialitis

Microthrombi in the Inter-alveolar Septa of a Lung from a Patient Who Died from Covid-19.





# Immune Response to COVID-19: SARS-CoV-2 in establishing an inflammatory feedback loop between IL-6 and angiotensin II.



Cytokine IL-6 has been found increased in COVID-19 patients, thus suggesting a direct role of SARS-CoV-2 in a massive cytokine release. IL-6 is able to activate a soluble form of IL-6 receptor interacting with gp130, thereby promoting the downstream activation of JAK/STAT signaling, and thereby production of IL-6. Moreover, SARS-CoV-2 has been directly related with the occurrence of cardiovascular implications, such as coronary atherosclerosis, inflammation in the vascular system and diffuse microangiopathy with thrombosis. Synthesis and secretion of IL-6 are directly implicated in cardiovascular damages. Indeed, IL-6 production is also induced by angiotensin II in AT<sub>1</sub>/JAK/STAT-dependent manner. As observed in SARS-CoV, also SARS-CoV-2 may be hypothesized to downregulate ACE2 expression, thus resulting in over-production of angiotensin II by the related enzyme ACE. In turn, increased angiotensin II enhances IL-6 production via JAK/STAT pathway, thus establishing a positive inflammatory feedback loop, ultimately resulting in the exacerbation of vascular and lung injuries. Moreover, the angiotensin II/AT<sub>1</sub> receptor axis activates ADAM17 that cleaves and inactivates ACE2, enhancing angiotensin II retention. In addition, ADAM17 induction has been found to process the membrane form of IL-6R $\alpha$  to the soluble form (sIL-6R $\alpha$ ), followed by the gp130-mediated activation of STAT3 via the sIL-6R $\alpha$ -IL-6 complex in a variety of IL-6R $\alpha$ -negative non-immune cells. The IL-6 amplifier promotes the production and secretion of several pro-inflammatory cytokines and chemokines, such as IL-6, sustaining the IL-6 amplifier-driven positive feedback. 17

# Skin manifestation of COVID-19

## A report of 375 cases from Spain

C. Galván Casas.  
BJD, 29 Apr 2020

- Erythema with vesicles or pustules in acral areas (Pseudo-chilblain) (19%), appears late (59% after other symptoms)
- vesicular eruptions (9%), appear early (15% before other symptoms).
- urticarial lesions (19%),
- maculopapular eruptions (47%)
- Livedo or necrosis (6%).



Courtesy of Dr. Randy Jacobs

## COVID RASHES · EMERGING SKIN MANIFESTATIONS OF COVID-19



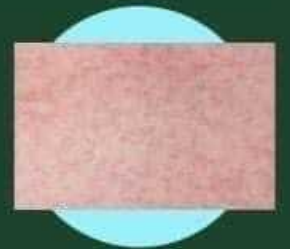
### URTICARIA

Urticarial wheals were reported in COVID-19 patients in Italy and have been observed in confirmed as well as suspected cases in France, Finland and US.



### ACRAL ISCHEMIA

Micro-thrombi caused by COVID-19 cause acral ischemic lesions, resembling perniosis, that are often painful or itchy. Seen in many healthcare workers in US.



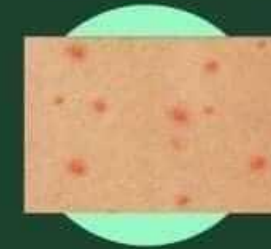
### MORBILLIFORM

Diffuse maculopapular eruption seen in COVID-19 patients in Italy, France and Finland as seen in many viral exanthems including Dengue



### LIVEDO RETICULARIS

Transient blanching or mottling of skin from ischemia of cutaneous blood vessels



### VESICULAR

Chicken pox-like vesicles on erythematous base seen in COVID patients in Italy



### PETECHIAL

Italian study reported petechial eruption in COVID-19 confirmed patients from bleeding under the skin

COVID-19 associated rashes were reported in 20% of patients in a northern Italian hospital. Dermatologists across the nations and borders are reporting many manifestations of this rash, in confirmed, suspected, and asymptomatic cases. The latter represents a potentially infectious, and possibly even a plasma-donor population. Submit your suspicious cases to national registry at [AAD.org](http://AAD.org). References and updates available. If you are a health care worker you can get free evaluation by texting your history and clinical photos to a dermatologist near you.

# Hyperinflammatory shock in children during COVID-19 pandemic: South Thames Retrieval Service, London, UK รายงานแรกที่พบ KD-like

- **In mid-April 2020, an unprecedented cluster of 8 children with hyperinflammatory shock, similar to atypical Kawasaki disease, Kawasaki disease shock syndrome, or TSS**
- **All children were previously fit and well. 6/8 were Afro-Caribbean descent, and 5/8 were boys**
- **All progressed to warm, vasoplegic shock, refractory to volume resuscitation and eventually requiring noradrenaline and milrinone for haemodynamic support.**
- **Most had no significant respiratory involvement**
- **Other notable features (besides persistent fever and rash) included development of small pleural, pericardial, and ascitic effusions, suggestive of a diffuse inflammatory process.**
- **Echo found bright coronary vessels, which progressed to giant coronary aneurysm in one patient within a week, one died**
- **SARS-COV-2 PCR positive in 2 patients**

27 April 2020

## Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19

### Case definition:

1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features (see listed in [Appendix 1](#)). This may include children fulfilling full or partial criteria for Kawasaki disease.
2. 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).
3. SARS-CoV-2 PCR testing may be positive or negative

มีการออก **Case Definition** เพื่อรวบรวม  
ผู้ป่วยที่สงสัยโดยเร็ว พบ **38** ราย

**38 cases identified between  
25 March - 1 May 2020**

#### Demographic features

<b>Age</b>	1 – 16 years (Median 11 years)
<b>Sex</b>	62% male (23 /37)
<b>Co-morbidities</b>	1 asthma, 1 epilepsy

*Michael Levin, MBE, PhD, FRCPCH, FMedSci.  
Imperial College  
London, United Kingdom  
Presented for COCA Webinar, May 19, 2020*

# Clinical Experience in UK

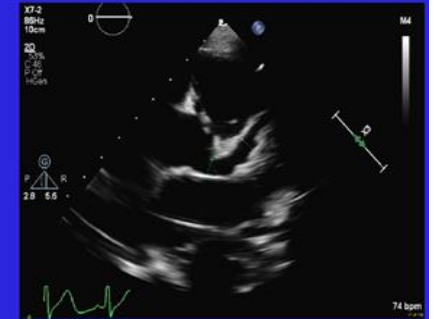
## Clinical presentations

- 75% shock, 51% Myocardial involvement
- 54% rash
  - 30% conjunctivitis, 20% mucus membrane
- 57% abdominal involvement
- 38% acute kidney injury, only 1 required renal replacement therapy
- Unlike adults - only 32% respiratory symptoms

Symptom	Number	Percentage
Shock	28	75.7
Rash	20	54.1
Conjunctivitis	12	32.4
Mucus membrane Involvement	7	18.9
Swollen hands/feet	3	8.1
Abdominal pain	21	56.8
Syncope	1	2.7
Lymphadenopathy	4	10.8
Sore Throat	5	13.5
Neck Swelling	3	8.1
Diarrhoea	22	59.5
Vomiting	16	43.2
Respiratory symptoms	12	32.4
Cough	7	18.9
Oxygen requirement	19	51.4
Neurological symptoms	7	18.9
Headache	12	32.4
Meningism	2	5.4
Confusion	5	13.5
Myocardial Involvement	19	51.4
Coronary Artery Involvement	6	16.2
Proven Vasculitis	1	2.7
Thrombosis	1	2.7
Acute Kidney Injury	14	37.8
Renal replacement therapy	1	2.7
Peripheral Oedema	4	10.8
Ascites	9	24.3

## Echocardiography

- 19/25 at least 1 echo performed
- 08/19 significantly impaired ventricular function (SF% <28 or equivalent)
- 05/19 dilated coronaries or aneurysms



Echo – LCA giant aneurysm (z+15) - Early echo had normal coronaries

LMCA mm (z)	LAD mm (z)	RCA mm (z)	comment
4.6 (+4.6)	8.0 (+15)	4.0 (+3.7)	Early echo had normal coronaries
	5.0 (+4.9)		uniformly dilated LMS to LAD coronary arteries
<2.0	<2.0	<2.0	dilated left circumflex
3.5 (+0.7)	3.7 (+4.2)	3.7 (+1.8)	diffuse coronary ectasia:
4.4 (+1.8)	6.8 (+12.5)	5.4 (+4.5)	Severe coronary ectasia involving both right & left coronary artery

## Management

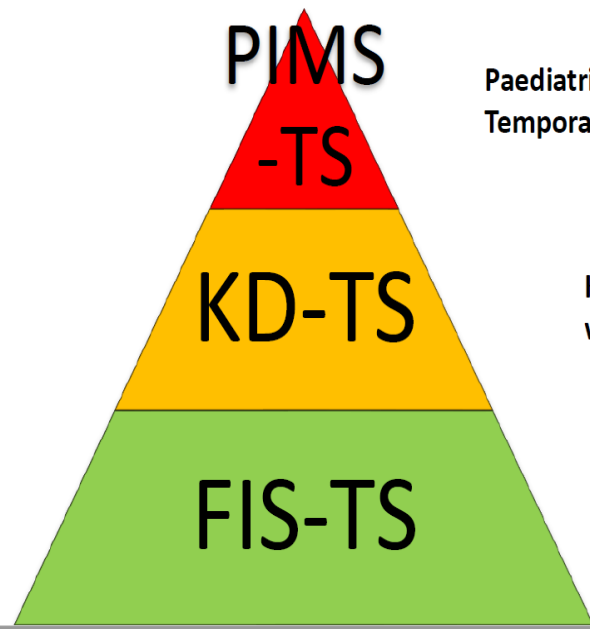
- All admitted to HDU/PICU for supportive care
- All required fluid resuscitation
- Inotropes required for 26 (70%)
- 38% of children did not received IVIG, just supportive care

TREATMENT	n=	%
Intravenous immunoglobulin (IVIG)	23	62.2
Corticosteroid	19	51.4
Anakinra	3	8.1
Tocilizimab	0	0.0
Infliximab	2	5.4

**SARS-CoV-2: PCR Positive 12, Ab positive 23**

# An emerging new spectrum of SARSCov2 in children- not just COVID

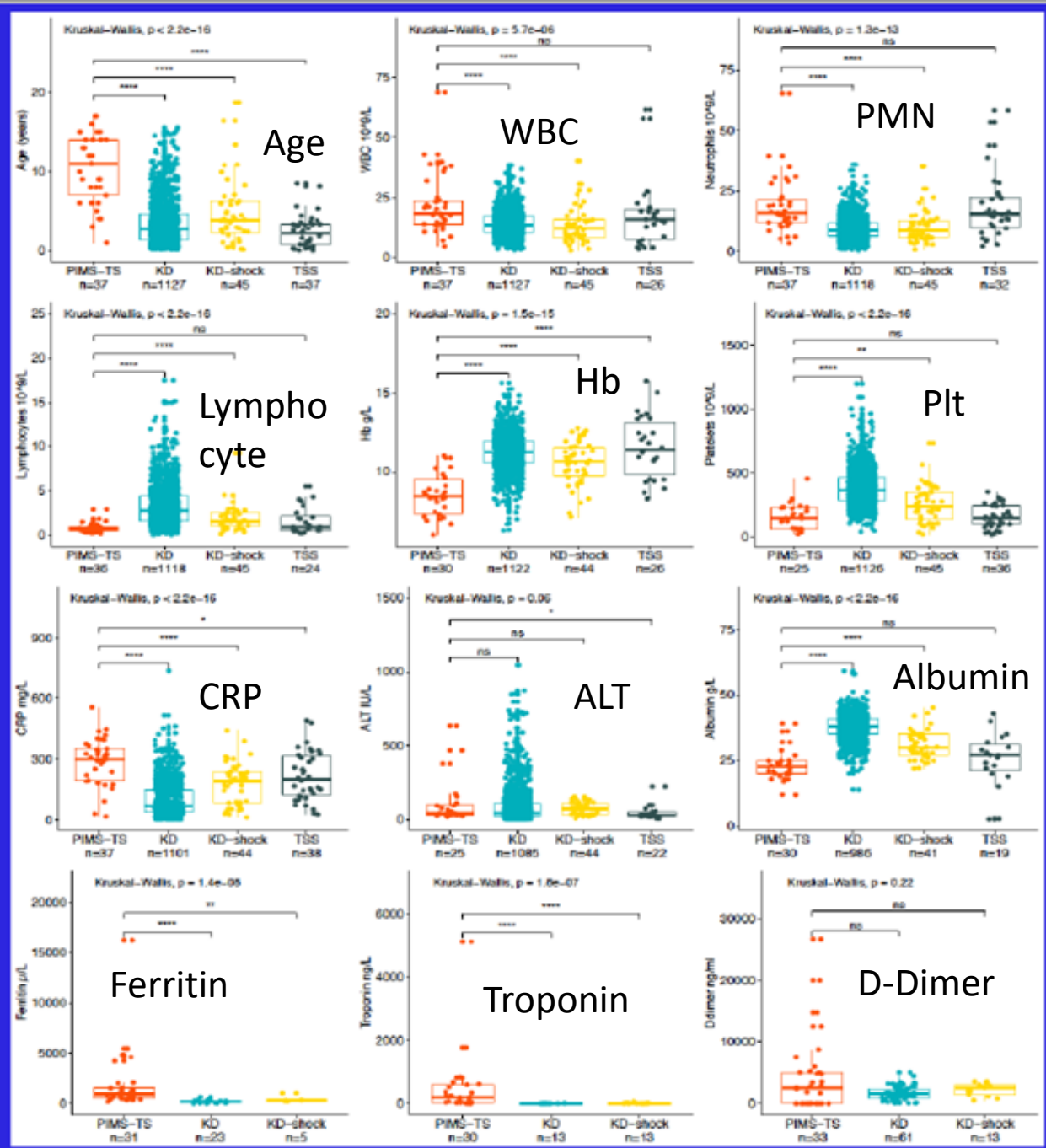
COVID 19 in children:  
generally mild or asymptomatic



**PIMS-TS**  
Paediatric Inflammatory Multisystem Syndrome-Temporally associated with SARS-CoV-2

**KD-TS**  
Kawasaki Disease-Temporally associated with SARS-CoV2-

**FIS-TS**  
Febrile Children with Inflammation-Temporally associated with SARS-CoV-2



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Presented for COCA Webinar, May 19, 2020

# Multisystem Inflammatory Syndrome in Children Associated with COVID-19

James Schneider, MD, FAAP, FCCP  
Chief, Division of Pediatric Critical Care Medicine  
Associate Professor of Pediatrics

- Patients included: April 17- May 13, 2020
- Patients Included: 33 (43 currently reported to NYS DOH)
- Age: 8.6 yr (Range: 2.2-17 yr)
- Gender: 61% male
- Race: Black 24%, Asian 9%, White 9%
- Ethnicity: Hispanic 27%

- No underlying medical conditions (excluding obesity): 79%
- Normal weight: 45%; Obese: 39%
- Reactive airway disease: 15%

IgG+, PCR+ 18%  
IgG+, PCR- 73%

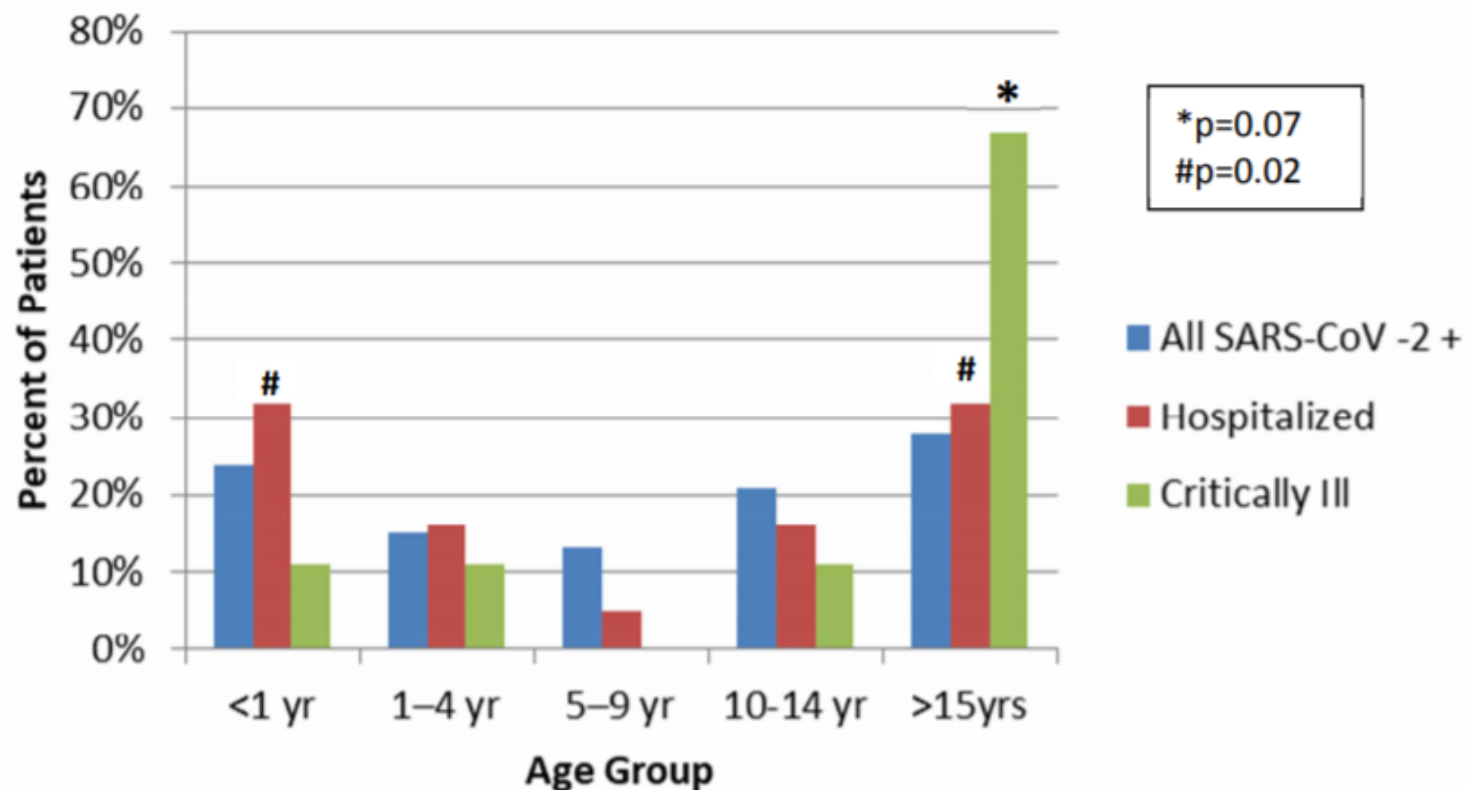
- Fever duration prior to presentation: 4 dy (IQR: 3, 5)
- Neurocognitive sx's: 58%
- GI sx's: 97%
- Respiratory sx's: 52%
- Shock: 76%
- Complete Kawasaki disease criteria: 64%
  - With shock: 76%

- Any coronary artery abnormalities: 48%
- LAD/RCA findings: Z-score 2-2.49: 9%; Z-score >2.5: 15%; lack of tapering (Z-score <2): 24%
- Any myocardial dysfunction: 58%
  - Mild: 33%
  - Moderate: 24%
  - Severe: 0%

Acute liver injury: 21%  
AKI: 70%  
O2 or Positive Pressure: 52%  
Mechanical ventilation: 18%  
IVIg 100%, Tocilizumab 70%

# Severe COVID-19 in Children and Young Adults in the Washington, DC Metropolitan Region

พบ 1 ราย สูงวัย



Underlying conditions present in 39% overall but hospitalized and critically ill patients were more likely to have underlying conditions.

One previously well child had hyper-inflammatory phenotype of SARS-CoV-2- associated KD-like shock syndrome



# Hospitalized and Critically Ill Children and Adolescents with COVID-19 at a Tertiary Care Medical Center in New York City

*Severe cases are not uncommon*

Clinical outcomes and therapies administered to patients with COVID-19

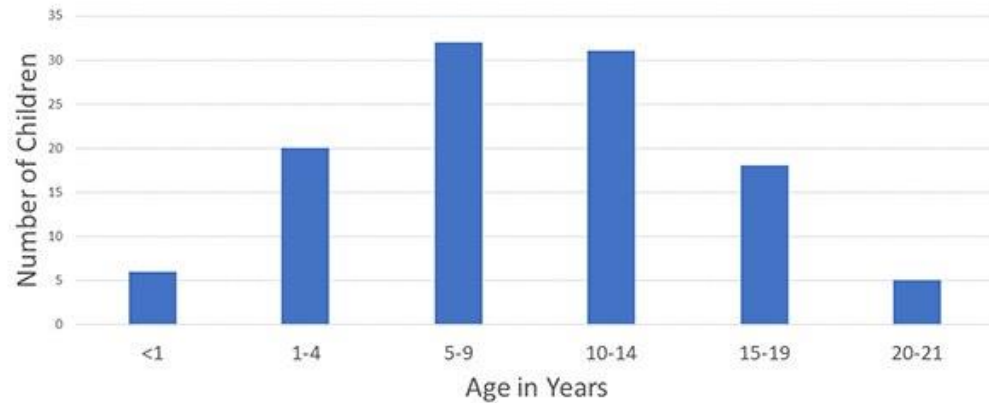
<b>Parameters no. (%) or median (IQR)</b>	<b>Admitted to floor (n= 33)</b>	<b>Admitted to PICU (n = 13)</b>
<b>ARDS</b>	0 (0)	10 (76.9)
<b>Mild ARDS</b>	0 (0)	4 (30.8)
<b>Moderate ARDS</b>	0 (0)	5 (38.5)
<b>Severe ARDS</b>	0 (0)	1 (7.7)
<b>Severe Sepsis</b>	0 (0)	4 (30.8)
<b>Septic Shock</b>	0 (0)	3 (23.1)

- Of 67 children, 31.3% were outpatients, 13 (28%) were admitted to PICU. Obesity and asthma were highly prevalent.
- Admission to the PICU associated with higher C-reactive protein, procalcitonin, and pro-B type natriuretic peptide levels and platelet counts ( $p < 0.05$  all)

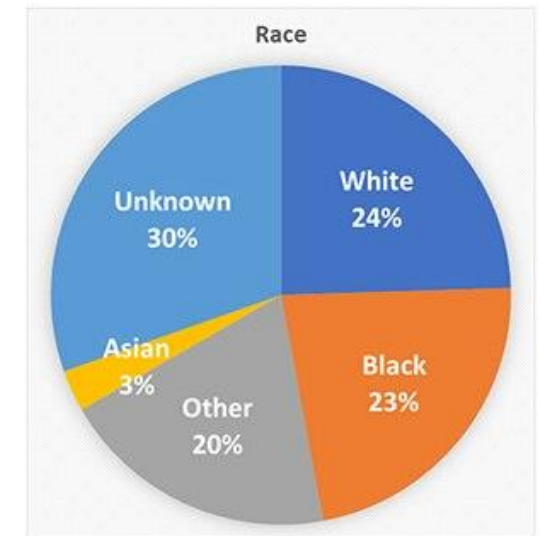
# More Early Data of 110 suspected MIS from NYC

In New York, 1% of those hospitalized are under the age of 20; around 750 children, of which 110 had MIS and 3 death.

Age Distribution of 110 MIS Cases, NYC



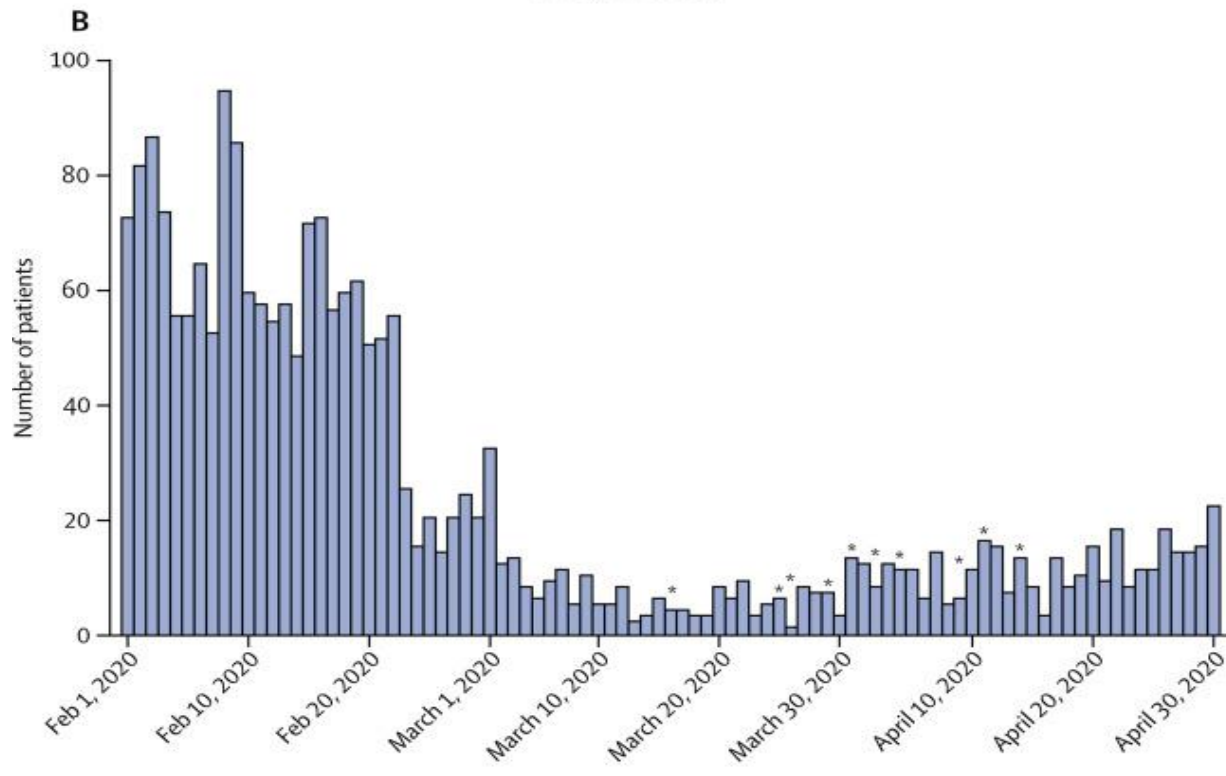
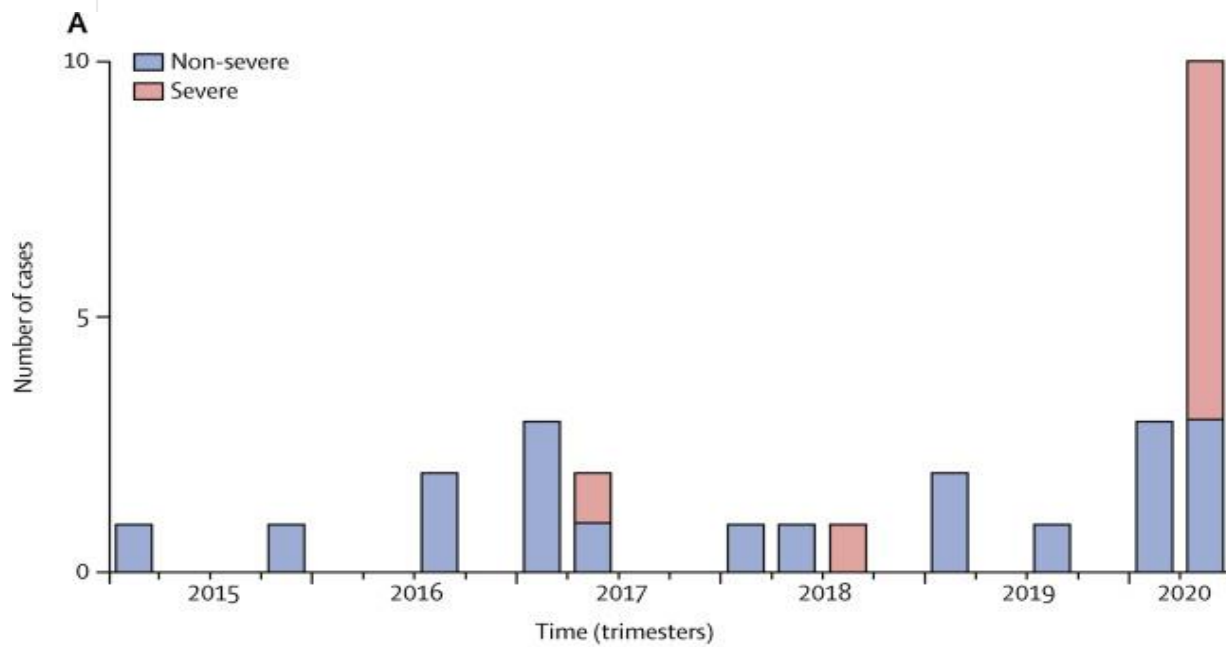
Racial Breakdown of MIS, NYC



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

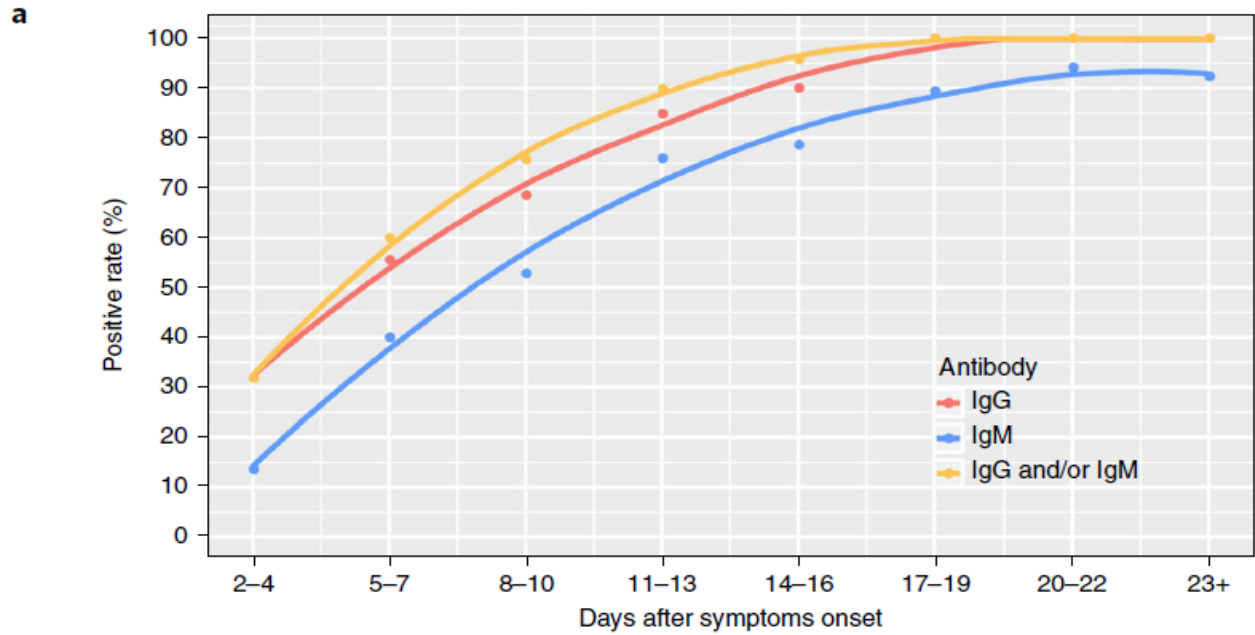
- 30-fold increased incidence of Kawasaki-like disease after COVID-19 outbreak
- 8/10 cases after the outbreak had evidence of COVID-19 infection (**swab PCR+2/10, IgG+8/10, IgM+3/10, Contact Hx 5/10**)

Verdoni L. Lancet May 13, 2020



# Antibody responses to SARS-CoV-2 in patients with COVID-19 appeared in the second week when viable virus fading

การเกิด MIS-C พบในผู้ป่วยที่มี Antibody แล้ว แสดงว่าเกิดหลังจากการติดเชื้อแล้วอย่างน้อย 2 สัปดาห์

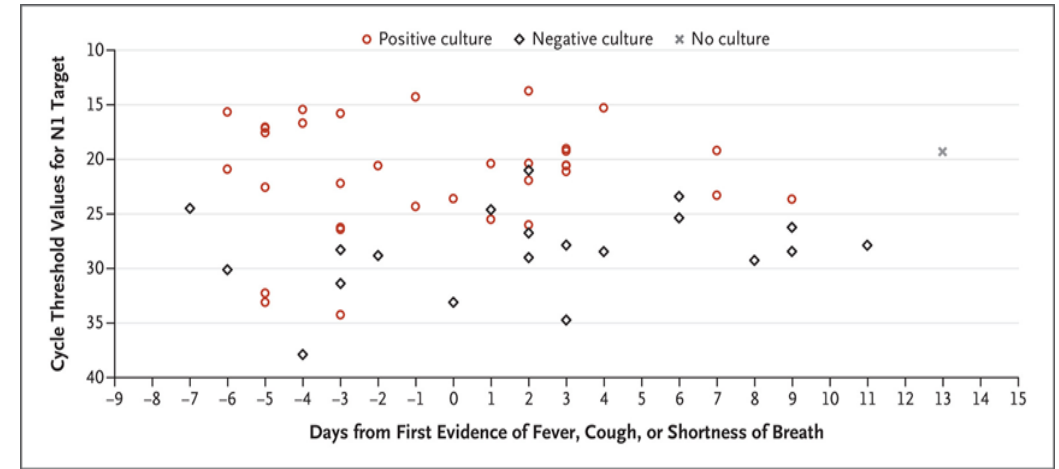


* / Days	2-4 (N = 22)	5-7 (N = 45)	8-10 (N = 70)	11-13 (N = 79)	14-16 (N = 70)	17-19 (N = 47)	20-22 (N = 17)	23+ (N = 13)
IgG	7	25	48	67	63	47	17	13
IgM	3	18	37	60	55	42	16	12
IgG and/or IgM	7	27	53	71	67	47	17	13

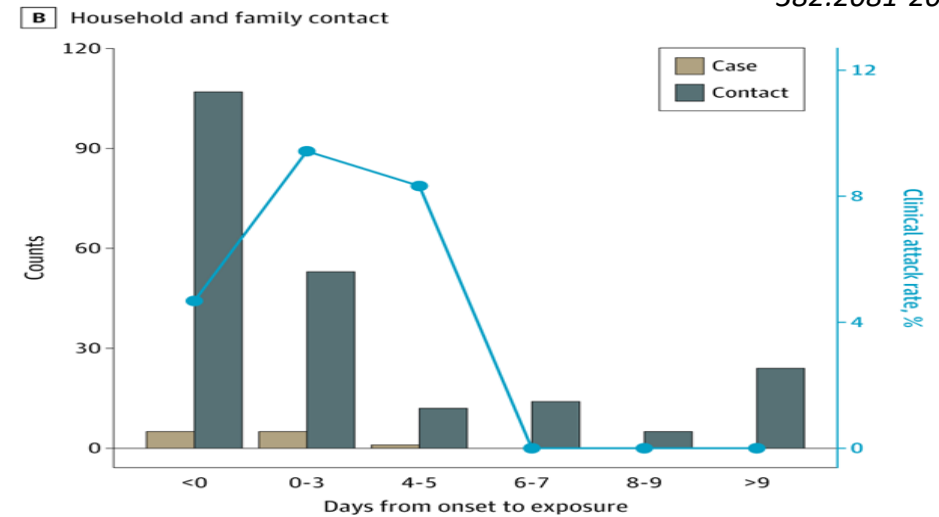
\* Number of serum samples with positive results

Antibody responses against SARS-CoV-2. a, Graph of positive rates of virus-specific IgG and IgM versus days after symptom onset in 363 serum samples from 262 patients.

Long QX. *Nature Medicine* <https://doi.org/10.1038/s41591-020-0897-1>



Arons MM. *N Engl J Med* 2020; 382:2081-2090



Cheng H-Y et al. *JAMA Intern Med* 2020 May 1

# An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic:

*More severe in KD associated with COVID-19*


Characteristics	KD before outbreak (N=19)	KD after outbreak (N=10)	P value
Age	3.0 (2.5)	7.5 (3.5)	0.00035
Incidence	0.3/month	10/month (<1:1000 COVID-19)	<0.00001
Incomplete Kawasaki disease	6/19 (31%)	5/10 (50%)	0.43
CRP, mg/dL	16.3 (8.0)	25 (15.3)	0.05
Lymphocytes, × 10 <sup>9</sup> /L	3.0 (1.8)	0.86 (0.4)	0.0012
Platelets, × 10 <sup>9</sup> /L	457 (96)	130 (32)	<0.00001
Ferritin, ng/mL	187 (89)	1176 (1032)	0.011
Troponin I, ng/L	..	1004 (1862)	..
proBNP, ng/L	..	1255 (929)	..

**Older, more RS and GI involvement, meningeal signs, cardiovascular involvement, marked lymphopenia, thrombocytopenia, increased ferritin, markers of myocarditis**

# An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: *KD associated with COVID-19 was more severe*

Characteristics	KD before outbreak (N=19)	KD after outbreak (N=10)	P value
Kobayashi score $\geq 5$	2/19 (10%)	7/10 (70%)	0.0021
MAS <sup>18</sup>	0/10 (0%)	5/10 (50%)	0.021
KDSS <sup>14</sup>	0/10 (0%)	5/10 (50%)	0.021
Abnormal echocardiography	2/19 (10%)	6/10 (60%)	0.0089
Adjunctive steroid treatment	4/19 (16%)	8/10 (80%)	0.0045
Inotropes treatment	0/19 (0%)	2/10 (20%)	0.11
Response to treatment	19/19 (100%)	10/10 (100%)	1

**More cardiac involvement KDSS, MAS, and need for adjunctive steroid treatment p<0.01).**



Naïve T cells enable the defenses against new and previously unrecognized infection by a massive and tightly coordinated release of cytokines, whereas memory T cells mediate antigen-specific immune response. A dysregulation in their balance, favoring naïve T cells activity compared with regulatory T cells, could highly contribute to hyperinflammation.

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In a retrospective, single-center study enrolling a cohort of 452 patients with COVID-19 in Wuhan, patients with severe COVID-19 displayed a significantly lower number of total T cells, both helper T cells and suppressor T cells. In particular, among helper T cells, a decrease in regulatory T cells, with a more pronounced reduction according to the severity of the cases, and in memory T cells has been observed, whereas the percentage of naïve T cells was found increased.

# Kawasaki Disease

Dr. Tomisaku Kawasaki first reported his 50 cases in Japan in 1961.

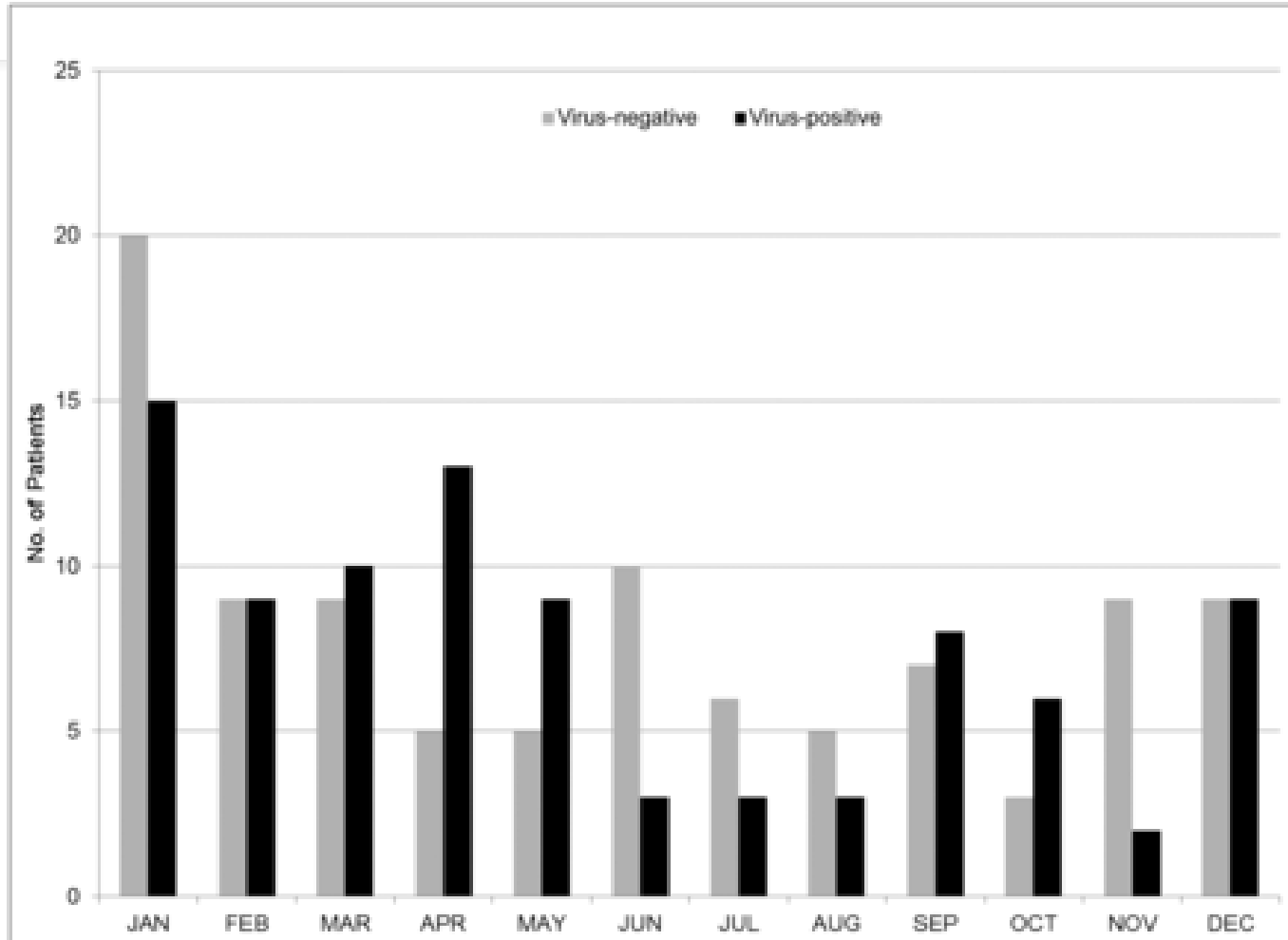
- Always think and search for criteria Kawasaki (*need fever for at least 5 days and 4/5 criteria*)
  - Bilateral bulbar conjunctival injection (Not exudative)
  - Erythematous mouth, cracked lips, and strawberry tongue(Not discrete lesions or exudative)
  - Rash (Not vesicle or bullous)
  - Changes of extremities
  - Lymphadenitis >1.5 cm (usually unilateral)
- Incomplete KD may present with 2-3 criteria, esp. in infants with fever > 7 days without source need to w/u for incompleated KD
  - >> Need to work up for supplementary lab criteria
    - Albumin <3.0, anemia, elevated transaminase, Platelet at > D7 of >=450,000,*
    - WBC >=15,000, U/A WBC >= 10, CRP>=3*
  - >> Echocardiogram

**Pathogenesis of KD: an aberrant immune response to unidentified pathogens in genetically predisposed patients**



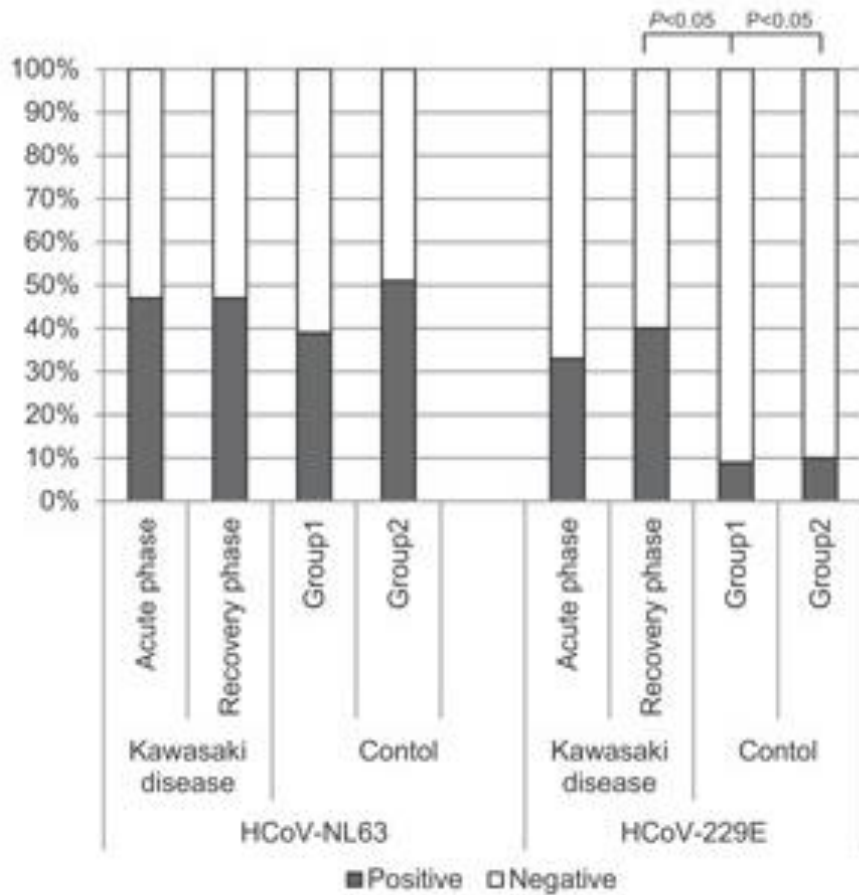


# Concurrent Respiratory Viruses and Kawasaki Disease: ประมาณครึ่งหนึ่งของ KD พบมีการติดเชื้อไวรัส



41.9% of the 192 patients with KD had a positive respiratory viral PCR, and the majority were positive for rhinovirus/enterovirus. No statistically significant differences were found in the clinical characteristics and laboratory values between the groups with and without positive respiratory viral PCR findings. Both groups had the same frequency of upper respiratory and gastrointestinal symptoms and had the same incidence of admission to the PICU, intravenous immunoglobulin-resistant disease, and coronary artery lesions.

**b**



Possible involvement of infection with human coronavirus 229E, but not NL63, in Kawasaki disease

The breakdown of the results

**HCoV-NL63**

Kawasaki disease	Positive (%)	Negative (%)	Total
Acute phase	7 (47)	8 (53)	15
Recovery phase	7 (47)	8 (53)	15
Control			
Group1	9 (39)	14 (61)	23
Group2	15 (51)	14 (49)	29

**HCoV-229E**

Kawasaki disease	Positive (%)	Negative (%)	Total
Acute phase	5 (33)	10 (67)	15
Recovery phase	6 (40)	9 (60)	15
Control			
Group1	2 (9)	21 (91)	23
Group2	3 (10)	26 (90)	29

Paired serum samples were obtained from patients with Kawasaki disease who had not been treated with  $\gamma$ -globulin.

# Kawasaki and Kawasaki Disease Shock Syndrome

## KDSS จะเป็นในเด็กที่โตกว่า ใช้นานกว่า

Outcome	KDSS (n = 27)	KD (n = 43)	P value
CAAs, no(%)	15(55.56)	4(9.30)	< 0.001 <sup>c</sup>
Aseptic meningitis, no. (%)	13(48.15)	2(4.65)	< 0.001 <sup>c</sup>
ECG abnormality,no.(%)	18 (66.67)	2(4.65)	0.001 <sup>c</sup>
IVIg-resistance,no.(%)	19 (70.37)	1(2.30)	0.001 <sup>c</sup>
Second dose of IVIG,no(%)	10 (37.04)	2(4.65)	0.002 <sup>c</sup>
ICU, no.(%)	13 (48.15)	0(0.00)	< 0.001 <sup>c</sup>
vasopressor,no.(%)	8 (29.63)	0(0.00)	< 0.001 <sup>c</sup>
Other organ damage,no. (%)	23 (85.19)	6(14.00)	0.001 <sup>c</sup>
KD recurrence,no. (%)	2(7.41)	1 (2.3)	0.555 <sup>c</sup>
Incomplete KD,no. (%)	8(29.62)	2(4.65)	0.010 <sup>c</sup>

**KDSS were older age (43.41 vs 28.81 M), longer duration of fever (10.63 vs 6.98 d), higher IL-6, IL-10,TNF- $\alpha$  and IFN- $\gamma$  (all P < 0.05).**

Li, Y. *Pediatr Rheumatol* 17, 1 (2019).  
<https://doi.org/10.1186/s12969-018-0303-4>

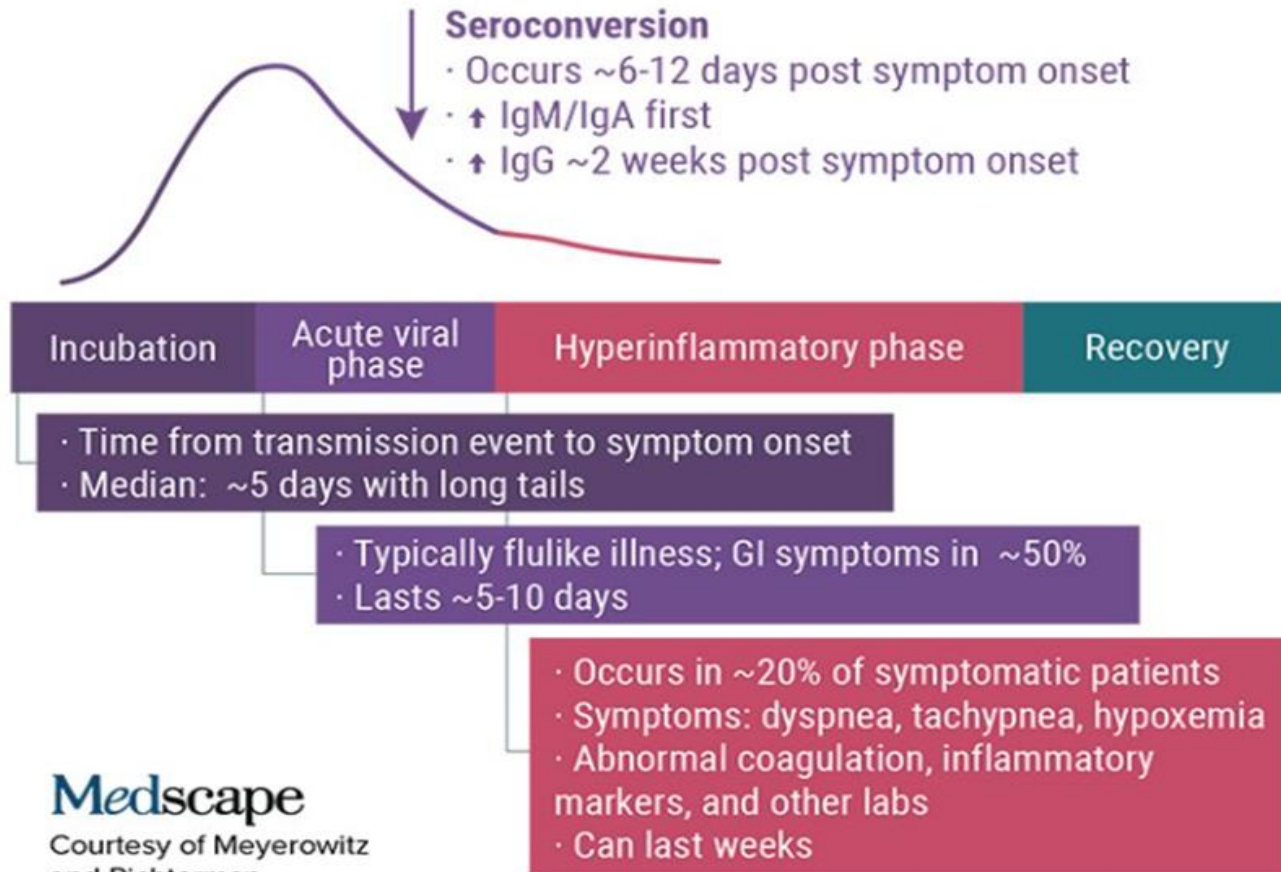


The Figure below illustrates what we know about the clinical course of the disease

## COVID-19 Illness Course Schematic

### Viral load

- Peaks in respiratory tract ~1 day pre symptom onset (peak infectiousness)
- ↑viral load → more severe disease
- Some patients develop viremia (can persist for days)



**Medscape**

Courtesy of Meyerowitz  
and Richterman

# A Quick Summary of the COVID-19 Literature So Far

MIS-C or KD-like is another FACE  
of COVID-19 in children caused by  
host immune excessive response

*Eric A. Meyerowitz, MD; Aaron G. Richterman, MD, MPH  
DISCLOSURES May 18, 2020.*

*[https://www.medscape.com/viewarticle/930588?src=wnl\\_newsalert\\_200519\\_MSCPEDIT&uac=67754AJ&implID=2386374&faf=1#vp\\_2](https://www.medscape.com/viewarticle/930588?src=wnl_newsalert_200519_MSCPEDIT&uac=67754AJ&implID=2386374&faf=1#vp_2)*

# Multisystem Inflammatory Syndrome in Children (MIS)

Persistent fever

Hypotension

Elevated inflammatory markers

Multiorgan dysfunction

No other identifiable cause

Evidence of SARS-CoV-2 Infection (mostly Ab)

- Though MIS shares features of Kawasaki disease, the classic bilateral conjunctival injection, rash, and strawberry tongue aren't always present.

# Multisystem inflammatory syndrome in children and adolescents with COVID-19:

*WHO calls for standardized data describing clinical presentations, severity, outcomes, and epidemiology*

## **Preliminary case definition**

- Children and adolescents 0–19 years of age with fever  $\geq 3$  days

**AND** two of the following:

1. Rash or bilateral non-purulent conjunctivitis or muco-cutaneous 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, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

**AND**

- Elevated markers of inflammation such as ESR, C-reactive protein, 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.

# Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C), US-CDC

- **An individual aged <21 years presenting with fever<sup>i</sup>, laboratory evidence of inflammation<sup>ii</sup>, and evidence of clinically severe illness requiring hospitalization, with multisystem ( $\geq 2$ ) 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**

*<sup>i</sup>Fever  $\geq 38.0^{\circ}\text{C}$  for  $\geq 24$  hours, or report of subjective fever lasting  $\geq 24$  hours*

*<sup>ii</sup>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

## Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19

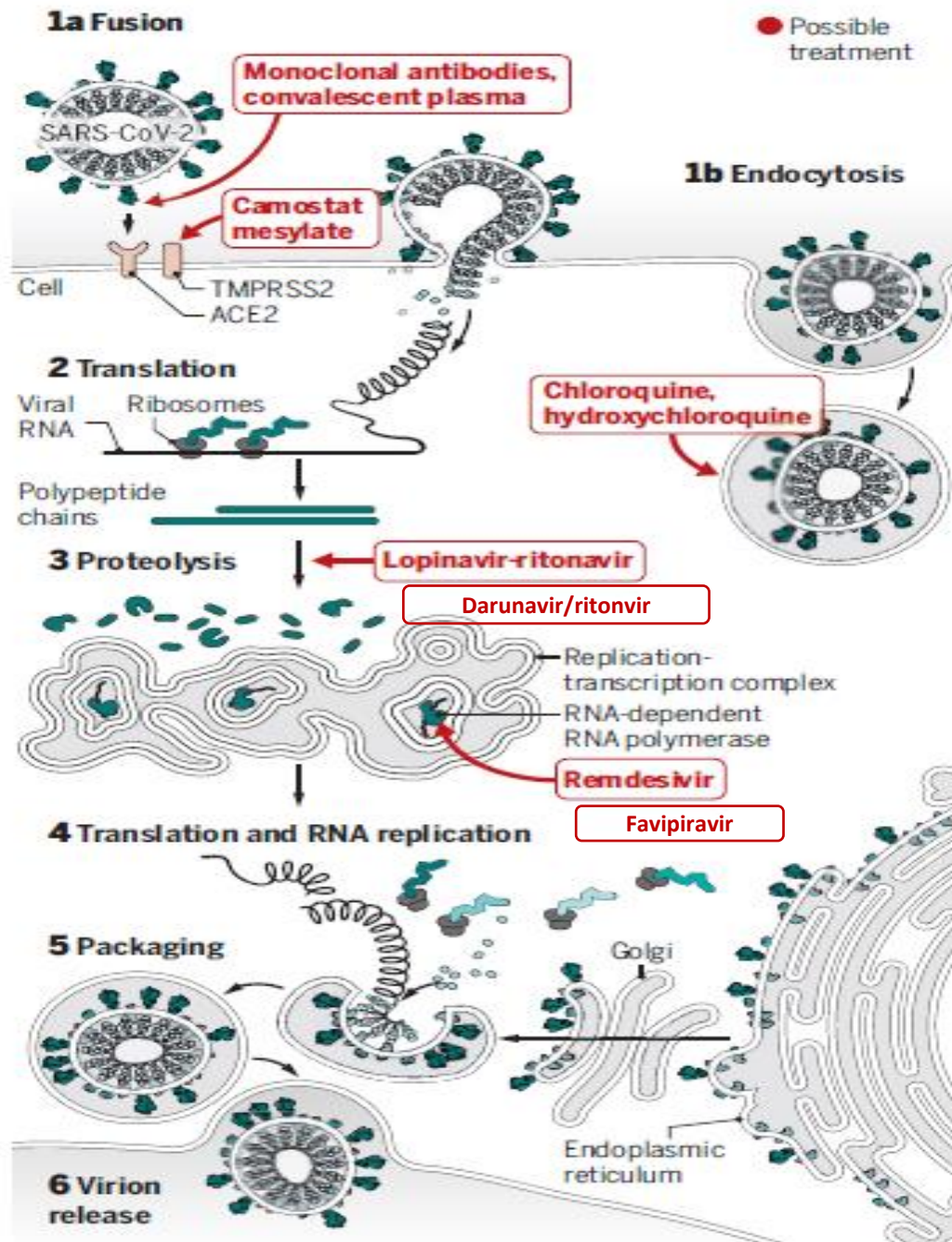
### Case definition:

- **1. A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP and lymphopaenia) and evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki disease.**
- **2. 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).**
- **3. SARS-CoV-2 PCR testing may be positive or negative**

*All stable children should be discussed as soon as possible with specialist services to ensure prompt treatment (paediatric infectious disease / cardiology / rheumatology\*).*



# ยาต้านไวรัส เพื่อรักษา ผู้ป่วย COVID-19



## Mechanism of action:

- Convalescent plasma: neutralize virus
- Camostat: inhibit transmembrane protease, serine 2 (TMPRSS2)
- CQ, HCQ: reduce pH, inhibit endosome-mediated fusion

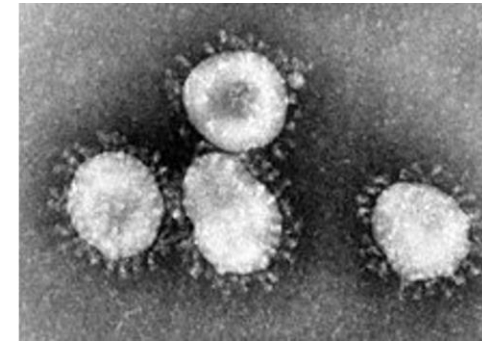
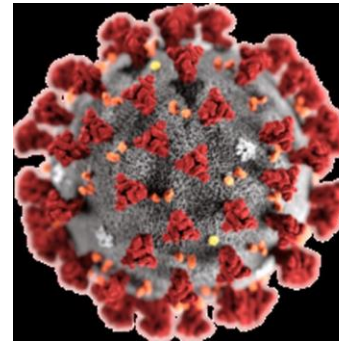
Suppress TNF, IL-6 release

- bPI (LPV/r, DRV/r): inhibit protease
- Remdesivir, favipiravir: inhibit RdRp
- Interferon: Enhance host immunity
- Ivermectin: Protecting host antiviral response

# แนวทางเวชปฏิบัติ กรมการแพทย์ 1

## พฤษภาคม 2563

### กรณีโรคติดเชื้อโคโรนา 2019 ผู้ป่วยเด็ก



#### การรักษา COVID-19 ในผู้ป่วยเด็ก

1. Confirmed case with mild symptoms and no risk factors ที่ไม่มีปัจจัยเสี่ยง/โรคร่วมสำคัญ และภาพถ่ายรังสีปอดปกติ  
แนะนำให้ดูแลรักษาตามอาการ และพิจารณาให้ยา 2 ชนิดร่วมกัน คือ chloroquine หรือ hydroxychloroquine ร่วมกับ darunavir + ritonavir หรือ lopinavir/ritonavir หรือ azithromycin นาน 5 วัน
2. Confirmed case with mild symptoms and risk factors ที่มีปัจจัยเสี่ยง/โรคร่วมสำคัญ (อายุน้อยกว่า 5 ปี และภาวะโรคเรื้อรังอื่นๆ) แนะนำให้ยาอย่างน้อย 2 ชนิด นาน 5 วัน ได้แก่
  - Chloroquine หรือ hydroxychloroquine ร่วมกับ
  - Darunavir + ritonavir (ถ้าอายุมากกว่า 3 ปี) หรือ lopinavir/ritonavir (ถ้าอายุน้อยกว่า 3 ปี)อาจพิจารณาให้ยาชนิดที่ 3 ร่วมด้วยคือ azithromycin
3. Confirmed case with pneumonia หรือ ผู้ป่วยมีอาการ หรือ อาการแสดง เข้าได้กับปอดบวมโดยไม่พบรอยโรคแต่มี SpO2 ที่ room air น้อยกว่า 95% แนะนำให้ยาอย่างน้อย 3 ชนิดคือ favipiravir เป็นเวลา 5-10 วัน และยาอีก 2 ชนิดตามข้อ 2 เป็นเวลา 5-10 วัน อาจพิจารณาให้ยาชนิดที่ 4 ร่วมด้วยคือ azithromycin เป็นเวลา 5 วัน

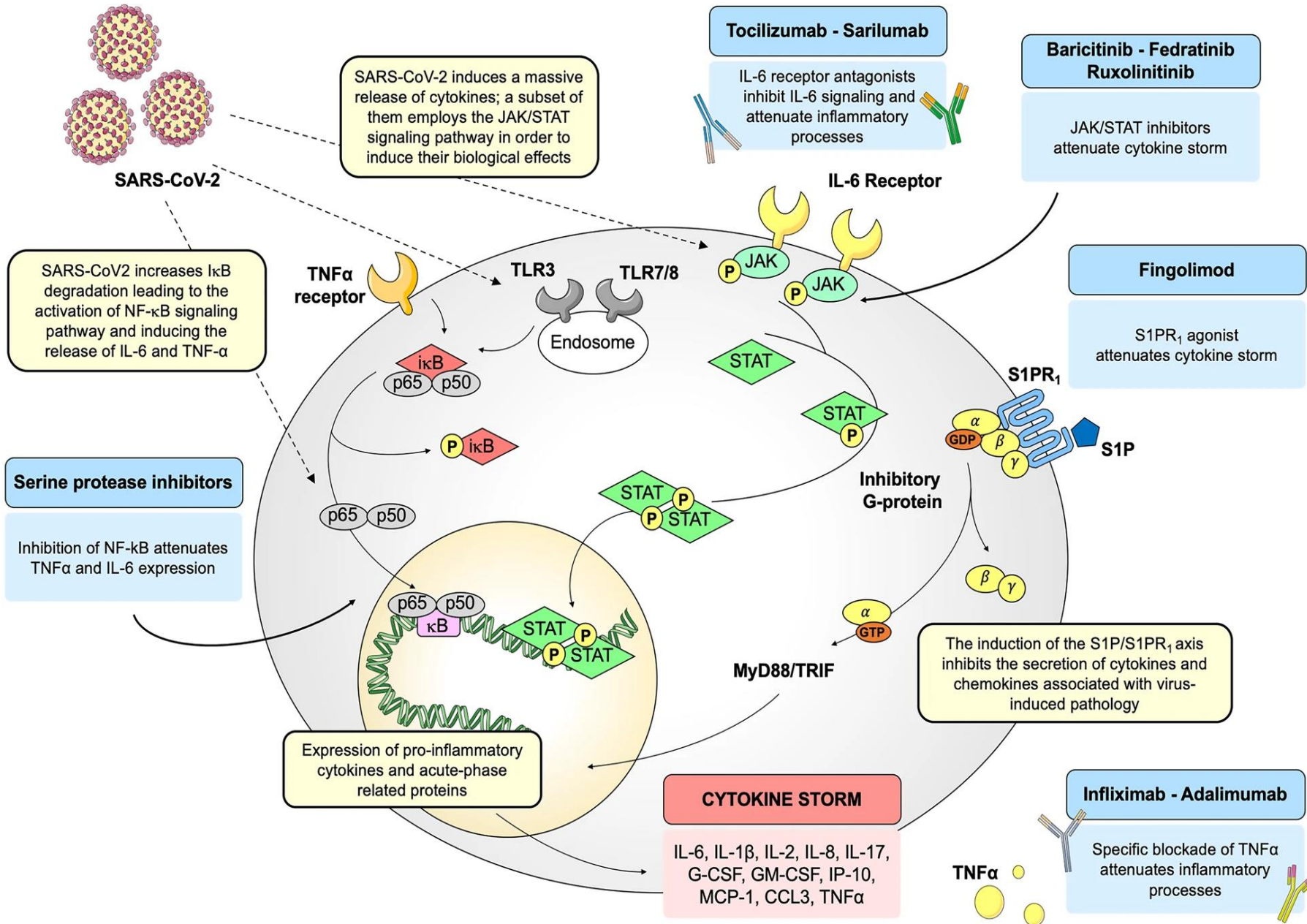
# แนวทางเวชปฏิบัติ การแพทย์ 1 พฤษภาคม 2563

## กรณีโรคติดเชื้อโคโรนา 2019 ผู้ป่วยเด็ก

	DRV/r if > 3 Yo LPV/r if < 3 Yo	CQ or HCQ	Favipiravir	Azithromy cin
Mild without risk factors	+/- 5 วัน	+/- 5 วัน	-	-
Mild with risk factors	+/-	5 วัน	-	+/- 5 วัน
Any Pneumonia	5-10 วัน	5-10 วัน	5-10 วัน	+/- 5 วัน

ปัจจัยเสี่ยง: อายุน้อยกว่า 5 ปี, โรคปอด หัวใจ เบาหวาน ความดัน ตับ อ้วน เส้นเลือดสมอง ภูมิคุ้มกันต่ำ มะเร็ง

- ใช้ DRV/r ก่อน LPV/r เพราะลด AE, และลด drug-drug interaction กับ CQ
- CQ หรือ HCQ ไม่แตกต่างกัน แต่ CQ ราคาถูกกว่า
- เป็น G6PD deficiency ก็ให้ CQ ได้ เพราะโอกาสเกิด hemolysis น้อยกว่า 1%
- การใช้ยา CQ ในหญิงตั้งครรภ์ ยังมีข้อมูลไม่มาก ให้ชั่งน้ำหนักประโยชน์และโทษ ยากผ่านรกได้ดี และไปสะสมที่ตาของทารก แต่ไม่มีหลักฐานเป็นอันตราย ระดับยาอาจไม่พอในน้ำนม **ไม่มีข้อห้ามการใช้ในทารกหรือหญิงตั้งครรภ์**
- FPV มีข้อมูลตั้งแต่อายุ 1 ปี แต่ไม่มีข้อห้ามในทารก แต่ไม่ควรใช้ในหญิงตั้งครรภ์



Immune response in COVID-19: addressing a pharmacological challenge by targeting pathways triggered by SARS-CoV-2

Schematic representation of host intracellular signaling pathways induced by SARS-CoV-2 infection. Selected drugs, acting on these pathways, are repurposed to manage the cytokine storm induced by the viral infection.

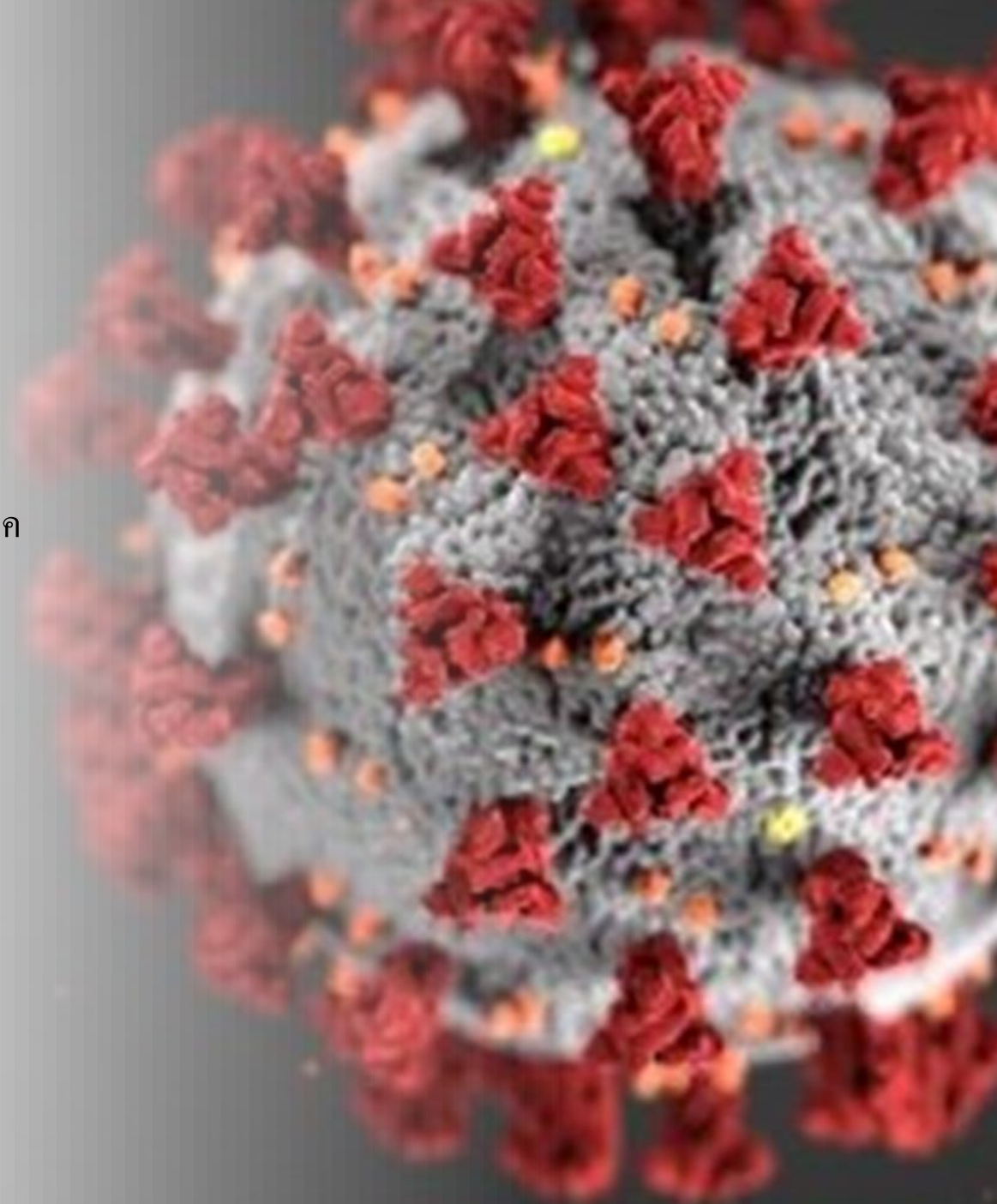
## **Guidance: Paediatric multisystem inflammatory syndrome temporally associated with COVID-19**

### **Early medical management:**

- **Wear appropriate PPE**
- **Standard APLS resuscitation and supportive management. Deterioration can be rapid**
- **Empiric antibiotics should be commenced as per local sepsis protocols with blood cultures taken.**
- **Close cardiorespiratory monitoring including continuous saturations and ECG, with BP monitoring. • Early 12-lead ECG / echocardiography are indicated if possible (timing determined by clinical picture)**
  - o **Look for multisystem involvement (liver, renal, neurological etc.)**
  - o **If not already done, additional research samples. Consent may be taken retrospectively.**
  - o **Consider IVIG and aspirin early if fulfils criteria for Kawasaki Disease. o Consider IVIG if fulfils criteria for toxic shock syndrome**
  - o **All cases with suspected myocardial involvement (elevated troponin I / ECG change and / or ECHO abnormalities) should be transferred to a cardiac centre with continuous infectious disease / immunology input.**

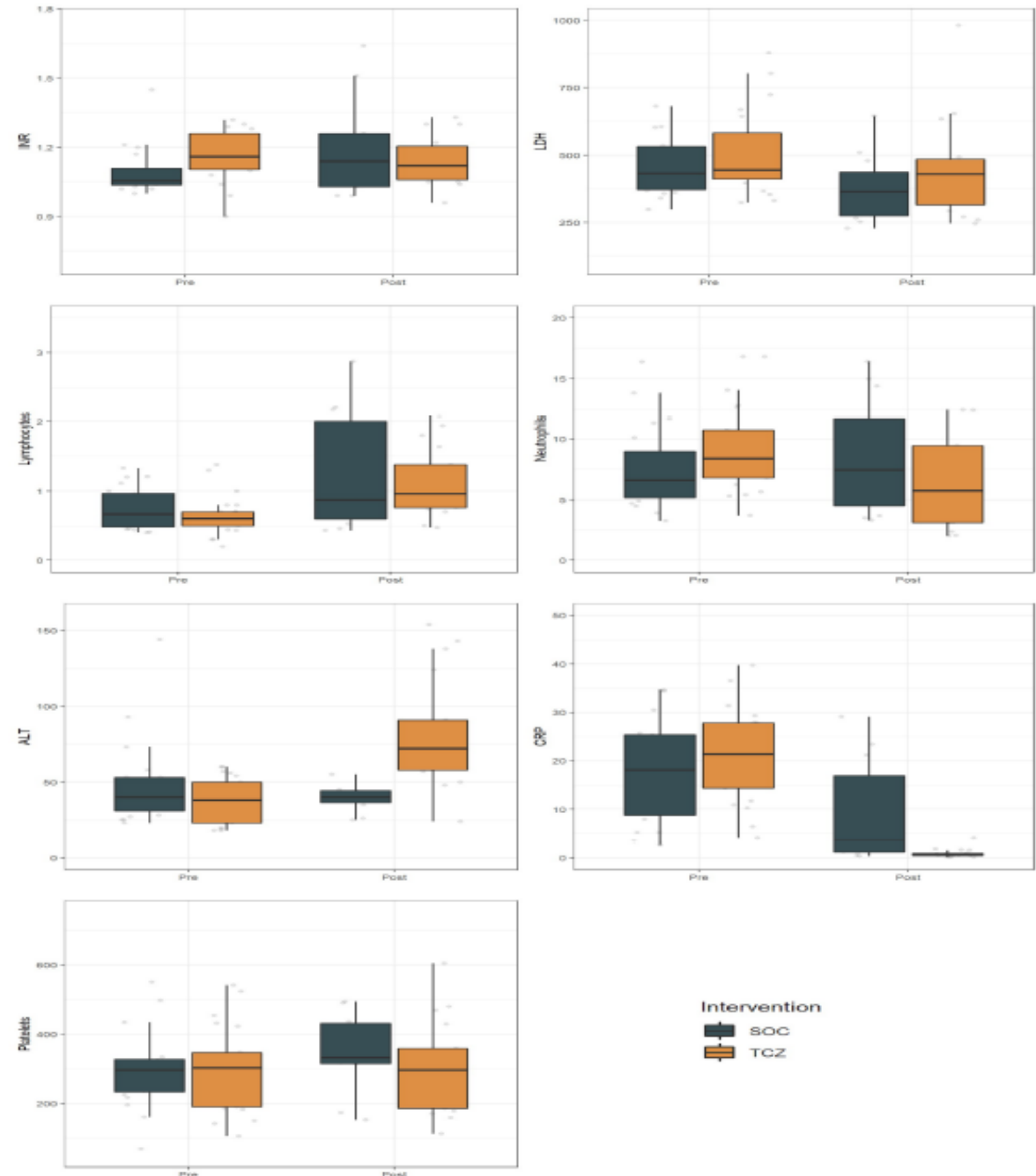
## Conclusion: บทสรุป MIS-C

- พบการระบาดของ KD-like ซึ่งรุนแรงแบบ KDSS ในเด็ก ที่สัมพันธ์กับโรค COVID-19 นิยามใหม่ว่า MIS-C คาดว่า น่าจะเกิดจากไวรัสกระตุ้น immune response in susceptible population มี inflammatory markers <sup>สูง</sup>ขึ้นสูง
- อาการรุนแรง shock 70%, Abnormal Echo 50-60% และเสียชีวิตได้
- รักษาด้วย IVIG และ adjunctive steroid/immunomodulating treatment (Tocilizumab, Infliximab, Anakinra, etc.)
- พบประมาณ <1:1,000 ราย



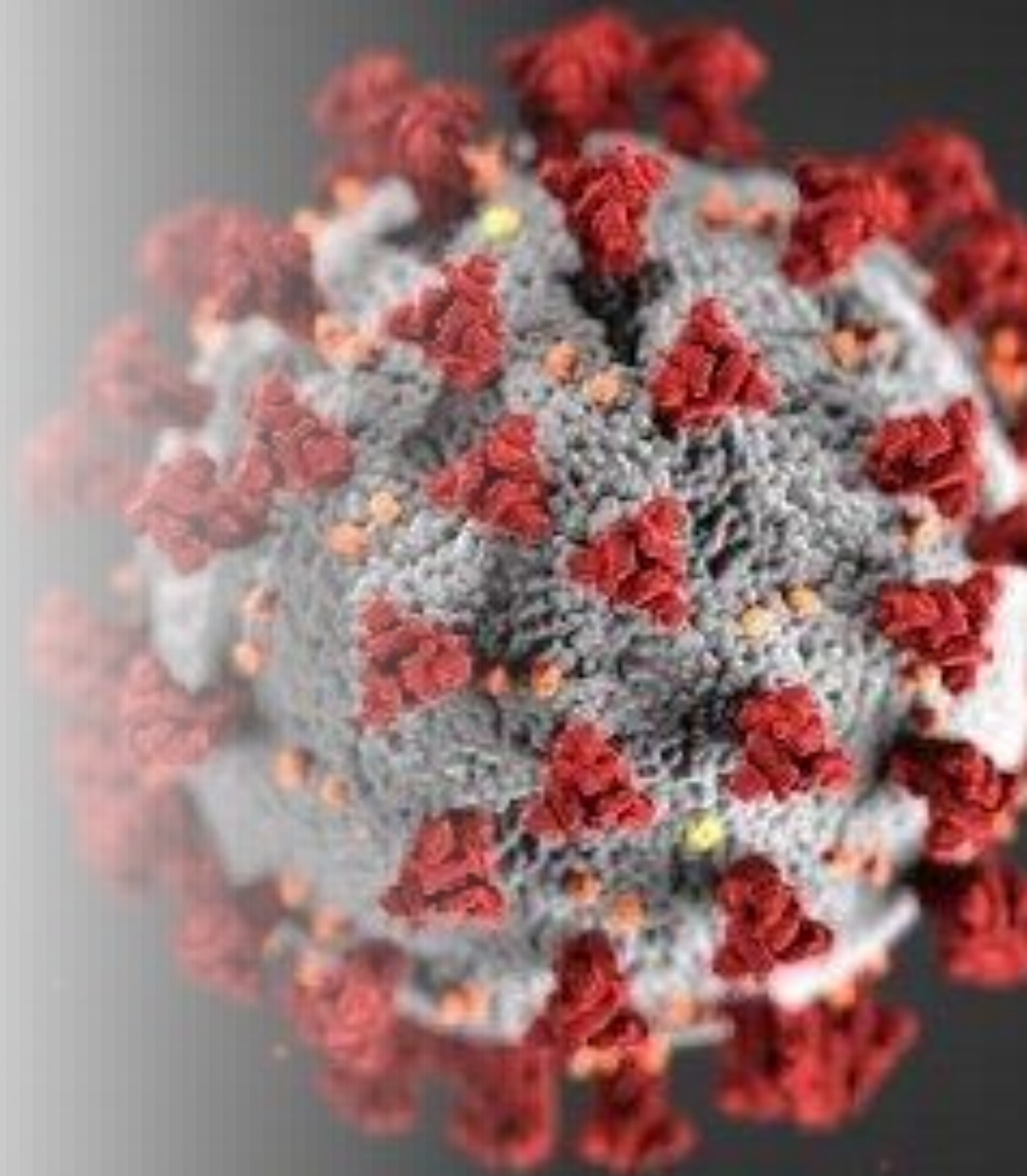
# Tocilizumab for Treatment of Severe COVID-19 Patients: Preliminary Results from SMAtteo COvid19 REgistry (SMACORE) N=21

TCZ did not significantly affect ICU admission (OR 0.11; 95% CI between 0.00 and 3.38;  $p = 0.22$ ) or 7-day mortality rate (OR 0.78; 95% CI between 0.06 and 9.34;  $p = 0.84$ ) when compared with SOC. Analysis of laboratory measures showed significant interactions between time and treatment regarding CRP, ALT, platelets, and INR levels.



ต้องติดตามต่อไป  
Thank you

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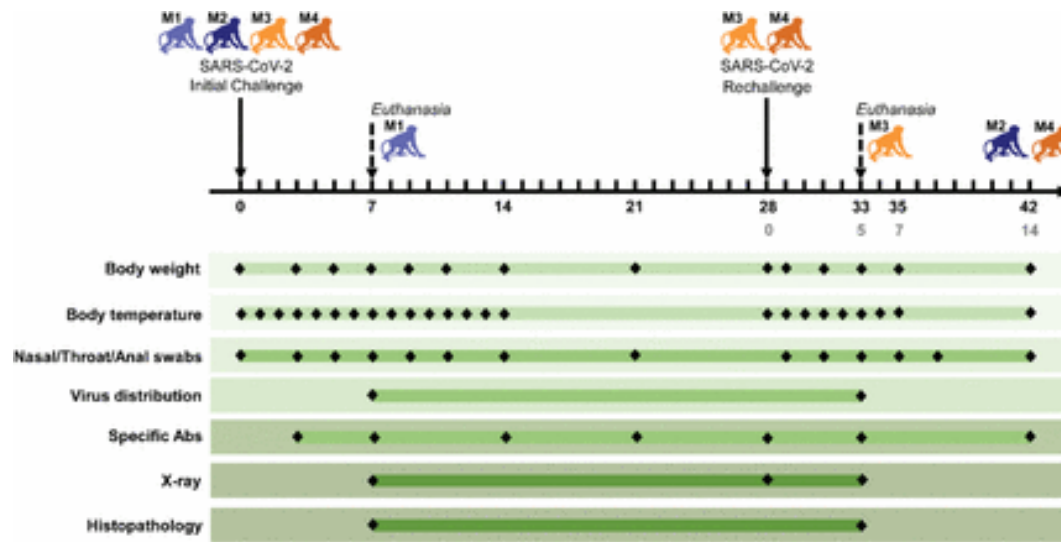
## FDA Approves Phase III Clinical Trial of Tocilizumab for COVID-19 Pneumonia

novel monoclonal antibody that competitively inhibits the binding of interleukin-6 (IL-6) to its receptor (IL-6R). Inhibiting the entire receptor complex prevents IL-6 signal transduction to inflammatory mediators that summon B and T cells.

- Tocilizumab (Actemra<sup>™</sup>) is already approved by the FDA for the treatment of cytokine release syndrome (CRS) that is severe or life-threatening. The agent is used in adults and children aged 2 years and older who have CRS caused by CAR T-cell therapy.

# Reinfection could not occur in SARS-CoV-2 infected rhesus macaques

หลังจากการติดเชื้อ ป้องกันโรคได้ (ที่ 1 เดือน)



Four monkeys were initially challenged with  $1 \times 10^6$  TCID<sub>50</sub> SARS-CoV-2 with the intratracheal route. To investigate the influence of reinfection, M3 and M4 after recovery were intratracheally rechallenged with the same dose of SARS-CoV-2 at 28 days post-infection (dpi). Two animals (M1 and M3) were sacrificed at 7 dpi and 5 days post-rechallenge (dpr), respectively. M2 with single infection and M4 with primary infection followed by secondary challenge were longitudinally monitored during the entire observation.

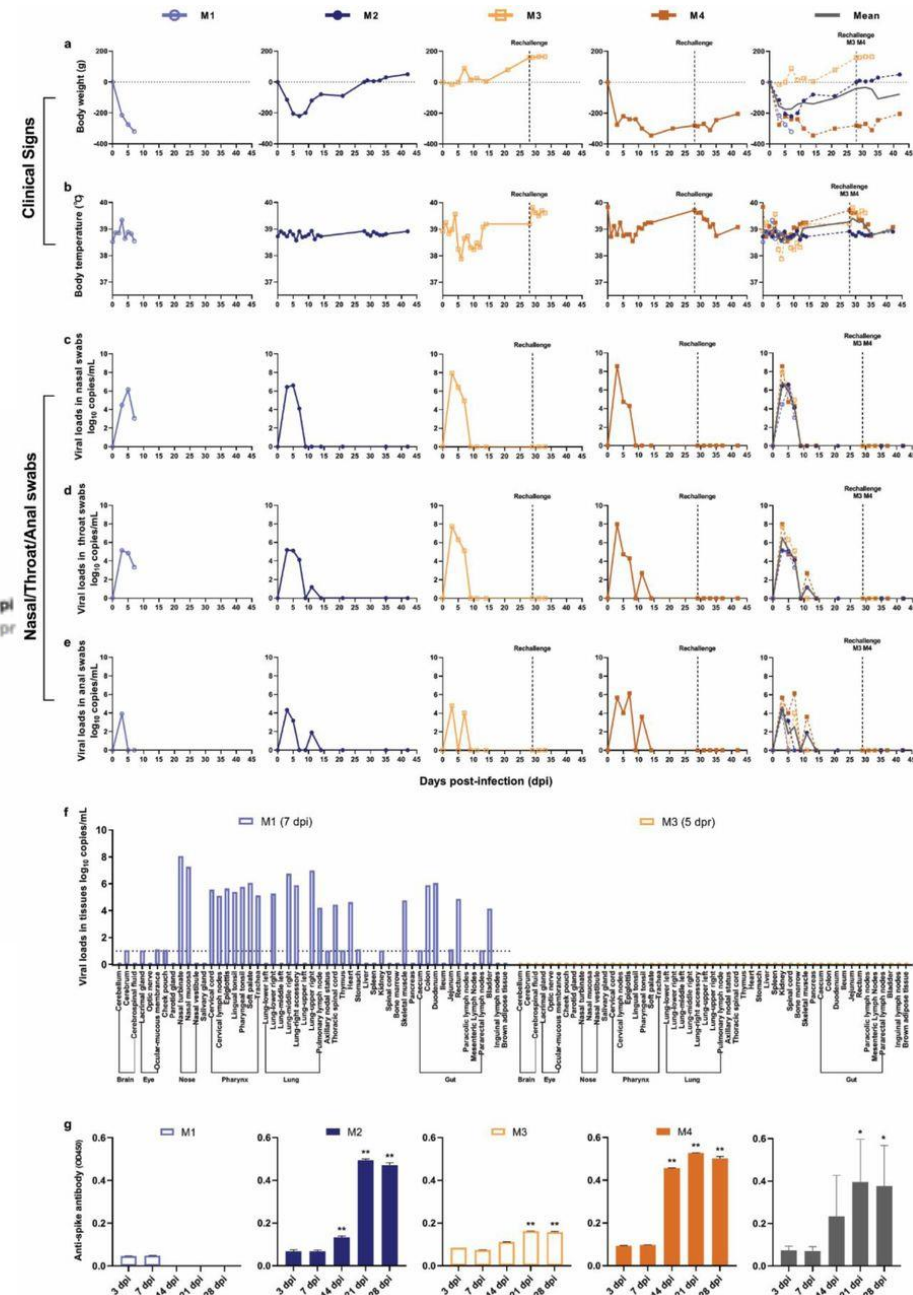
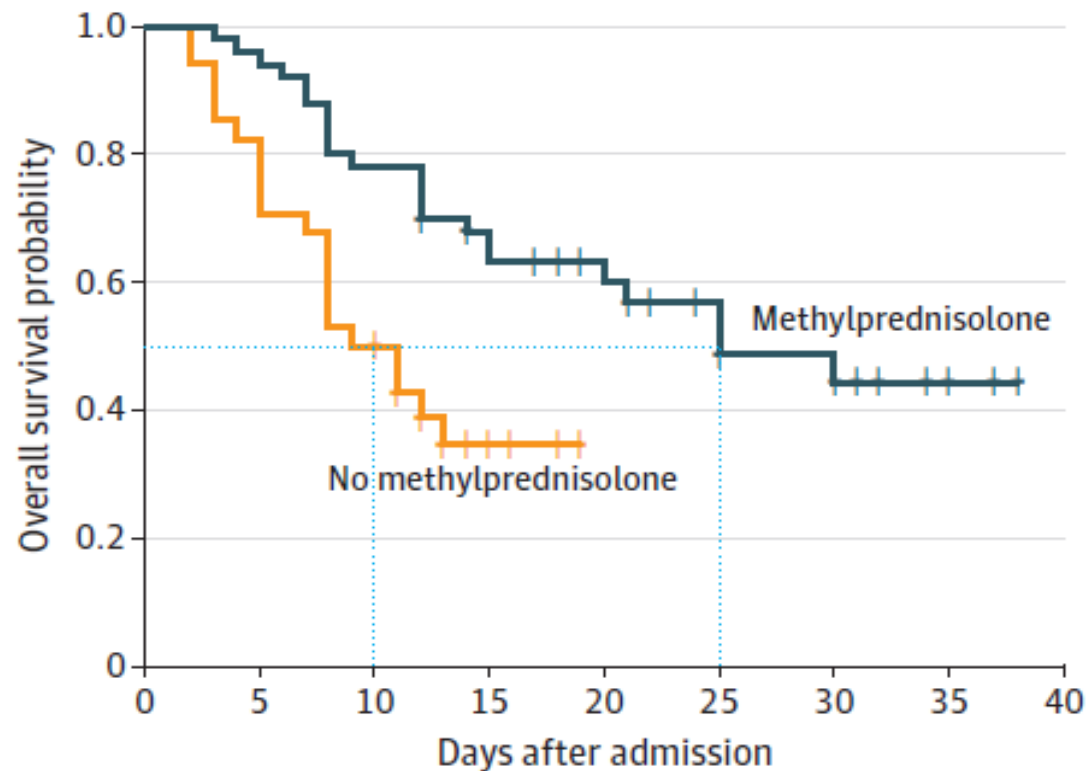


Figure. Survival Curve in Patients With Acute Respiratory Distress Syndrome Who Did and Did Not Receive Methylprednisolone Treatment

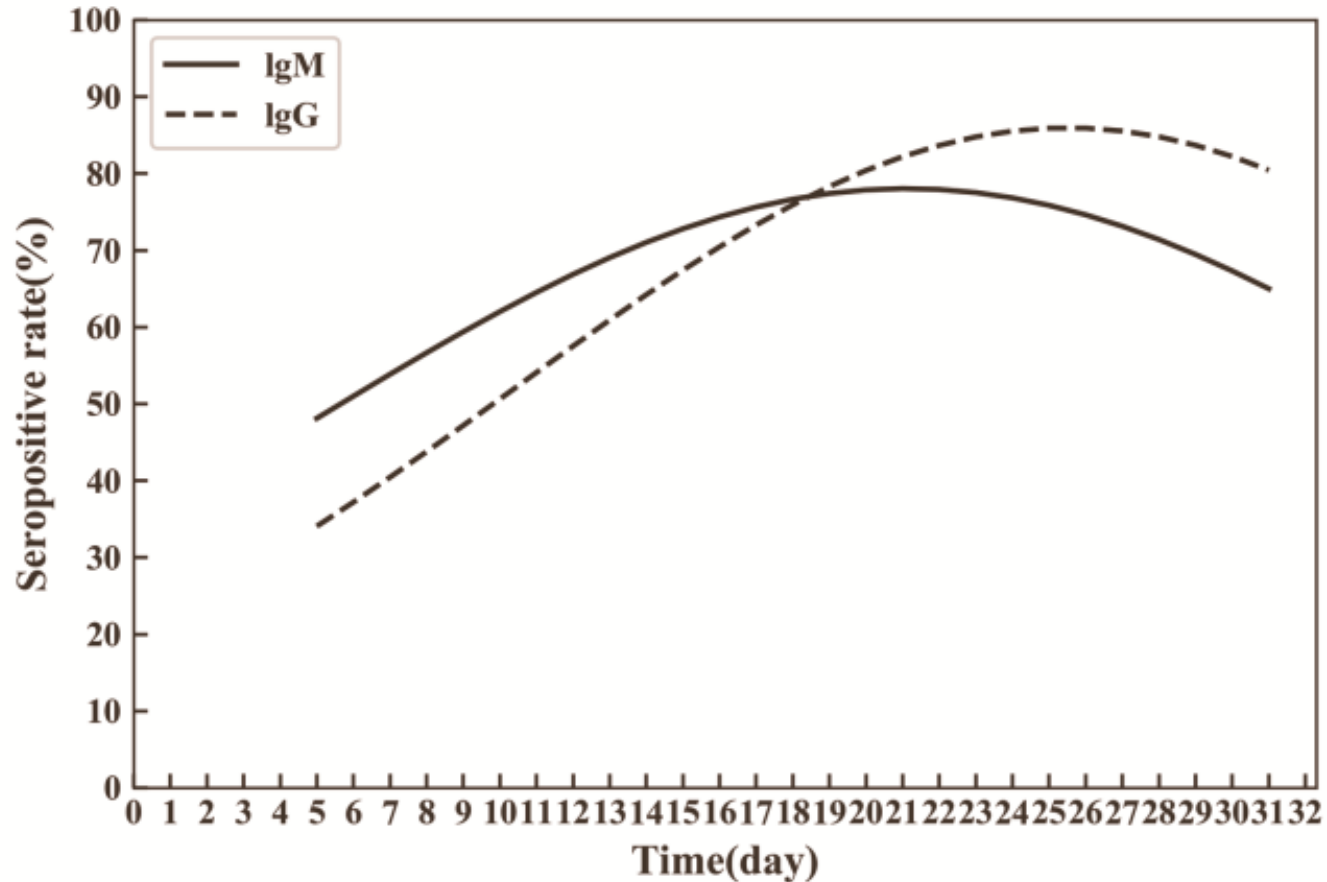


No. at risk	0	5	10	15	20	25	30	35	40
No methylprednisolone	34	28	17	4	0	0	0	0	0
Methylprednisolone	50	48	39	29	20	14	11	4	0

Administration of methylprednisolone reduced the risk of death (hazard ratio, 0.38; 95% CI, 0.20-0.72;  $P = .003$ ).

Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China

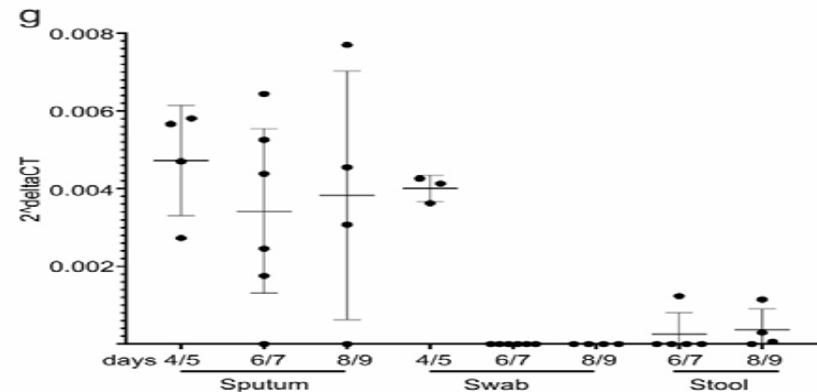
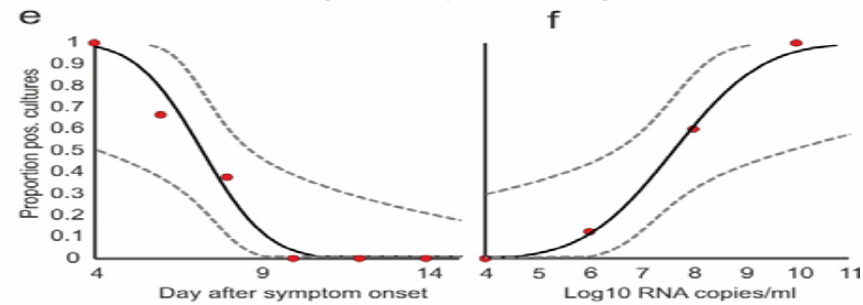
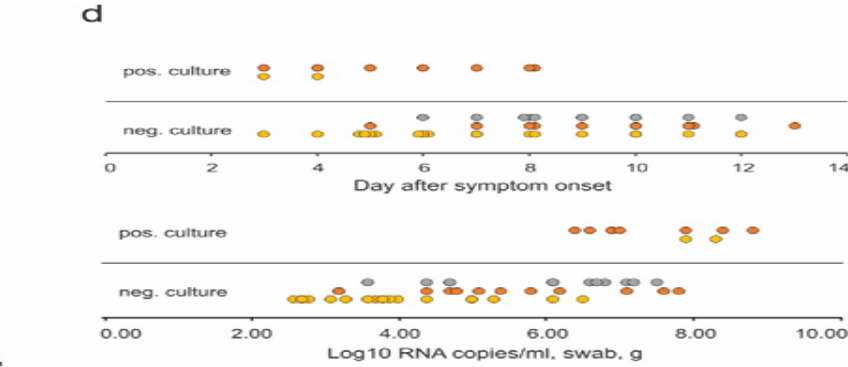
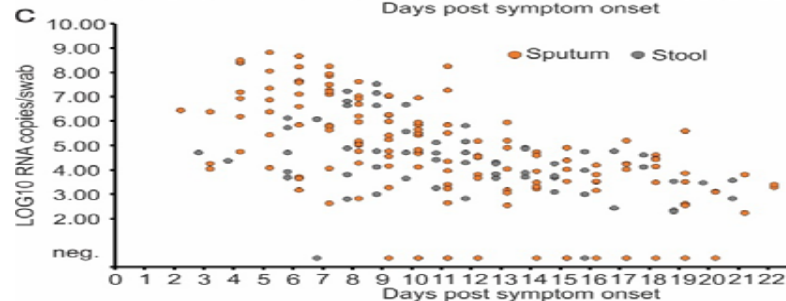
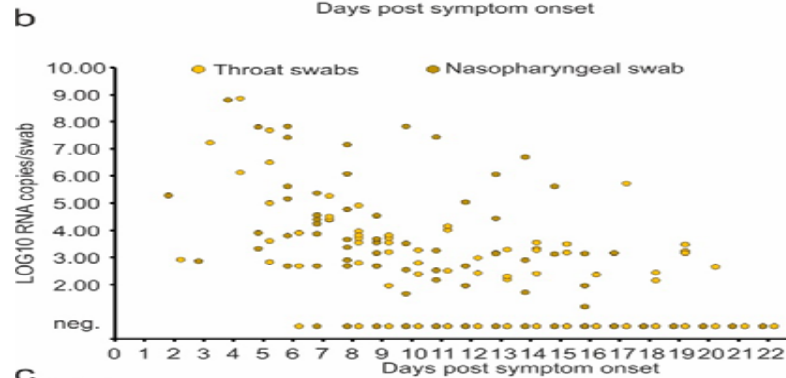
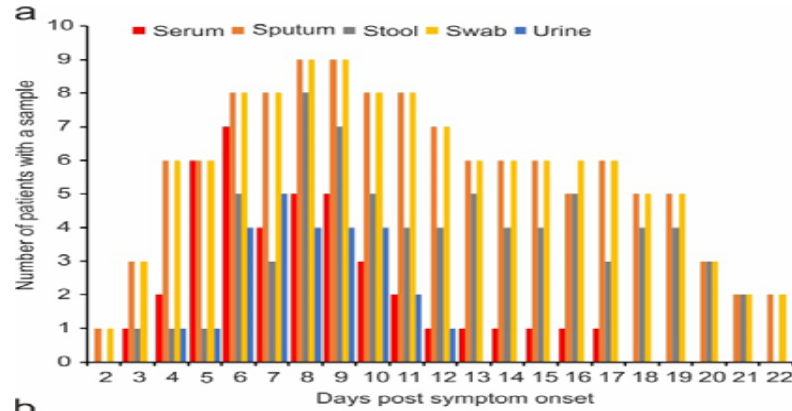
# Antibody Detection and Dynamic Characteristics in Patients with COVID-19



Detection of IgM and IgG antibodies in different periods. A log-distribution was used to describe the distribution time period of seropositive rate of the two types of antibodies. Serological IgM and IgG antibodies tested by ELISA in patients with confirmed diagnosis. The IgM and IgG antibodies were detected as positive as early as on the 4th day after onset, the seropositive rate of IgM increased gradually; however, IgG was increased sharply on the 12th day after onset.

# Virological assessment of hospitalized cases of COVID-19

ไวรัสเพาะเชื้อไม่ขึ้น ตั้งแต่วันที่ 8 ตั้งแต่เริ่มมีอาการ ในขณะที่ RNA ยังบวกถึงมากกว่า 3 สัปดาห์



## Clinical and laboratory features:

### Clinical

#### All:

- Persistent fever >38.5°C

#### Most:

- Oxygen requirement
- Hypotension

#### Some:

- Abdominal pain
- Confusion
- Conjunctivitis
- Cough
- Diarrhoea
- Headache
- Lymphadenopathy
- Mucus membrane changes
- Neck swelling
- Rash
- Resp symptoms
- Sore throat
- Swollen hands and feet
- Syncope
- Vomiting

### Imaging and ECG

- Echo and ECG – myocarditis, valvulitis, pericardial effusion, coronary artery dilatation
- CXR – patchy symmetrical infiltrates, pleural effusion
- Abdo USS – colitis, ileitis, lymphadenopathy, ascites, hepatosplenomegaly
- CT chest – as for CXR – may demonstrate coronary artery abnormalities if with contrast

### Laboratory

#### All:

- Abnormal Fibrinogen
- Absence of potential causative organisms (other than SARS-CoV-2)
- High CRP
- High D-Dimers
- High ferritin
- Hypoalbuminaemia
- Lymphopenia
- Neutrophilia in most – normal neutrophils in some

#### Some:

- Acute kidney injury
- Anaemia
- Coagulopathy
- High IL-10 (if available)\*
- High IL-6 (if available)\*
- Neutrophilia
- Proteinuria
- Raised CK
- Raised LDH
- Raised triglycerides
- Raised troponin
- Thrombocytopenia
- Transaminitis

\*These assays are not widely available. CRP can be used as a surrogate marker for IL-6.

## General principles

- Discuss early with PICU and paediatric infectious diseases / immunology / rheumatology\*

team

- All children should be treated as suspected COVID-19

- For mild to moderate disease supportive care only is recommended

- If clinically deteriorating or severe disease discuss transfer with PICU retrieval teams

- Candidate antiviral therapies should only be given in the context of a clinical trial if available

- Immunomodulatory therapy should be discussed with paediatric ID and/or clinicians with appropriate experience in their use (e.g. rheumatology, immunology, haematology) on a case by case basis and used in the context of a trial if eligible and available.

\* Each Region may have a different specialty delivering support for inflammatory conditions including immunology, infectious diseases and rheumatology.