

MMed and DCH Lectures

Covid-19 update: Delta variant, vaccine and MIS-C

August 16th 2021

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Update on COVID

- “Variants of concern”: Delta variant
 - Severity, transmissibility in children
 - Vaccine protection
- Multisystem Inflammatory Syndrome in Children (MIS-C)
 - Definition
 - Treatment
- COVID and children in Pacific

New SARS-CoV-2 genetic variants

- All variants affect the spike protein
- Mutations arise from viral replication normally
- Arise in heavily infected populations – in people with chronic COVID-19 infections, which allows time for virus to adapt and mutate
- Genetic variants only survive *if* they confer a competitive advantage
 - Replicate faster / easier
 - More transmissible
 - Escape immunity
- Many genetic variants don't survive because they are “inferior”
- Sometimes chance – if the first virus in a community, they will survive even if inferior (and may be less pathogenic) – “Founder effect”
- First spike protein genetic variant identified in March 2020 (but as early as Jan in China)

1st: Alpha

- Alpha variant (arose in UK):
 - B.1.1.7 – more transmissible, require more strict public health measures (masks, social distancing, limitation on gatherings)
 - Mortality ratio 1.36 (1.18-1.56): means it is 36% more likely to cause death

“Variants of concern”

Variant	Country of origin	Differences in characteristics	Other
Alpha	UK, Sept 2020	Increased transmission and virulence	
Beta	South Africa, May 2020	Increased transmission and virulence	
Gamma	Brazil, Nov 2020	Increased transmission and virulence, decreased neutralization *	
Delta	India, Oct 2020	Increased transmission and virulence, Decreased neutralization *	3-fold increase in mortality High viral load High transmission rates Reinfection Younger age groups
Kappa	India, Dec 2020	Increased transmission Decreased virulence	

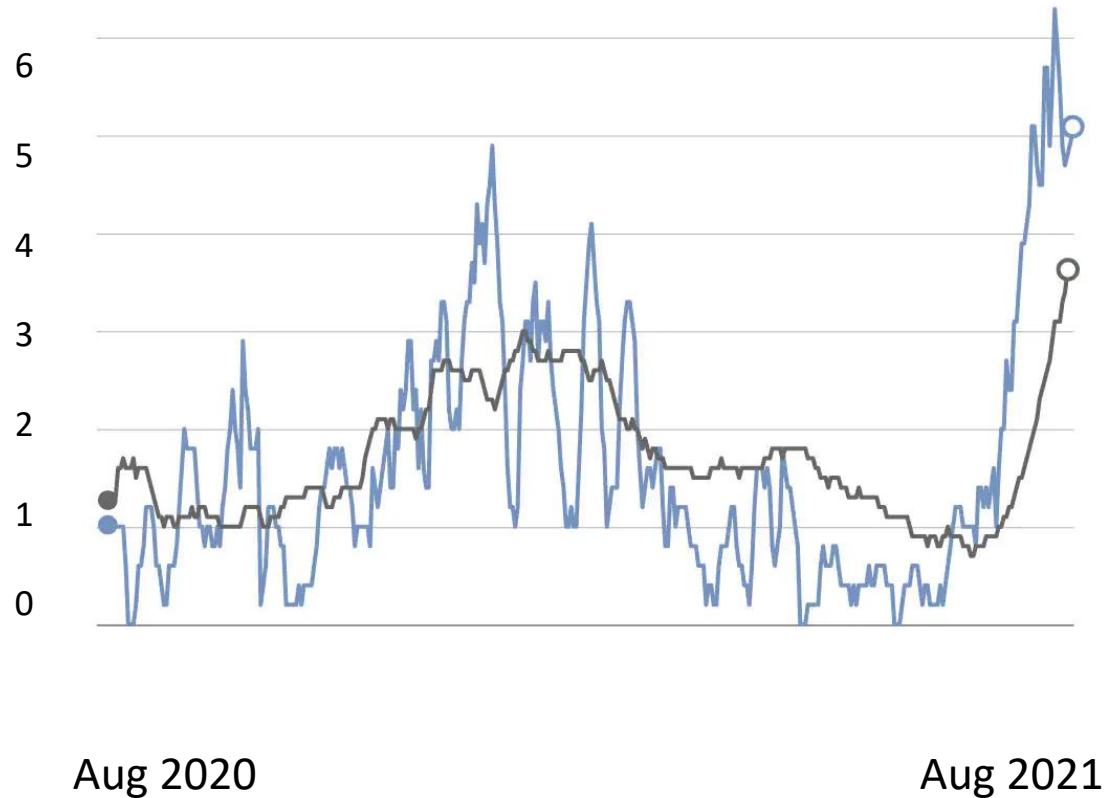
* using serum from vaccinated individuals

Delta

Delta (B.1.617.2, AY.1, AY.2) – arose in India

- Increased transmissibility (40-60%, CDC)
- Increased severity of disease (Scotland, Canada)
- 98 countries around the world: the dominant variant > 12 countries, including India, UK, Israel, US, Fiji, Indonesia, Philippines, Thailand.
- Viral loads x 1000 (China)
- Children, school outbreaks, teachers often affected
- Symptoms
 - Fever, headache, sore throat, cough and nasal discharge common: “more like a cold”
 - Loss of smell rare (but does occur)
 - Abdominal symptoms less common?
 - Hearing impairment

US and Delta



US 3.6 per million people

hospitalized paediatric COVID-19 cases by August 2021

Children 15% of all new infections
Much lower % of all hospitalizations

Delta

- In children mostly mild, URTI only
- 1-3% of COVID infected children hospitalized
- Often another disease will cause hospitalization, with Delta a comorbidity

Table 2. Vaccine Effectiveness against the Alpha Variant or S Target–Negative Status and the Delta Variant or S Target–Positive Status, According to Dose and Vaccine Type.*

Vaccination Status	Test-Negative Status		Alpha Variant or S Target–Negative Status		Delta Variant or S Target–Positive Status		
	Controls	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)	Cases	Case:Control Ratio	Adjusted Vaccine Effectiveness (95% CI)
	<i>no.</i>	<i>no.</i>		%	<i>no.</i>		%
Unvaccinated	96,371	7313	0.076	Reference	4043	0.042	Reference
Any vaccine							
Dose 1	51,470	2226	0.043	48.7 (45.5–51.7)	1493	0.029	30.7 (25.2–35.7)
Dose 2	23,993	143	0.006	87.5 (85.1–89.5)	340	0.014	79.6 (76.7–82.1)
BNT162b2 vaccine							
Dose 1	8,641	450	0.052	47.5 (41.6–52.8)	137	0.016	35.6 (22.7–46.4)
Dose 2	15,749	49	0.003	93.7 (91.6–95.3)	122	0.008	88.0 (85.3–90.1)
ChAdOx1 nCoV-19 vaccine							
Dose 1	42,829	1776	0.041	48.7 (45.2–51.9)	1356	0.032	30.0 (24.3–35.3)
Dose 2	8,244	94	0.011	74.5 (68.4–79.4)	218	0.026	67.0 (61.3–71.8)

J Lopez Bernal *et al.* N Eng J Med 2021;385:585-594

- **Astra-Zeneca vaccine 2 doses 67% effective against Delta variant**
- **Even more protective** against severe disease and death
- Waning immunity over time (Israel, mRNA vaccine), booster may be needed
- However, most severe disease / death occurs in *unvaccinated*
- Fully vaccinated people with Delta breakthrough infections can spread the virus to others. However, vaccinated people are infectious for a shorter period.

- Sinopham vaccine (BIBP vaccine)
 - Inactivated whole-cell vaccine, contains a killed coronavirus that cannot replicate
 - Efficacious against Delta in Sri Lanka: 79% protective against both symptomatic disease and hospitalisation after 2 doses (WHO)
 - 2 doses 80%+, similar to natural infection
 - Higher rates in younger populations, less effective >80 years (Hungary)
 - Duration of antibodies...

Summary

- No vaccines are 100% effective (but close to 100% against mortality)
- Immune response to vaccines take a few weeks to fully develop. Some people may have been infected soon after their dose (which is *not* vaccine failure).
- Cases in vaccinated people are milder than in unvaccinated people
- A mild case of COVID despite vaccine is not a “vaccine failure” as the patient is much less likely to die.
- Breakthrough outbreaks have been more noticeable in countries using the Sinopharm vaccine, because of its lower efficacy.

Multisystem inflammatory syndrome in children

- 1-2 weeks after COVID infection
- First reported in UK, US, Europe in 2020
- >2000 cases reported in India in 2021
- 100 cases in South Africa
- Uncommon in a severe form:
 - South Africa 93,400 cases, 2910 paediatric, 100 cases of MIS-C
- Usually not life threatening (first 23 cases in South Africa all survived)

Multisystem inflammatory syndrome in children: WHO criteria

All

- Fever $>38.5^{\circ}\text{C}$ for 3-5 days

Any 2 multi-system abnormalities

Skin

- Rash – erythematous, generalised
- Red mucous membranes
- Conjunctivitis
- Swollen hands, feet, neck
- Lymphadenopathy

Respiratory

- Cough, respiratory distress, hypoxaemia, crepitations

Multi-system abnormalities

Cardiovascular

- Hypotension, cardiovascular signs

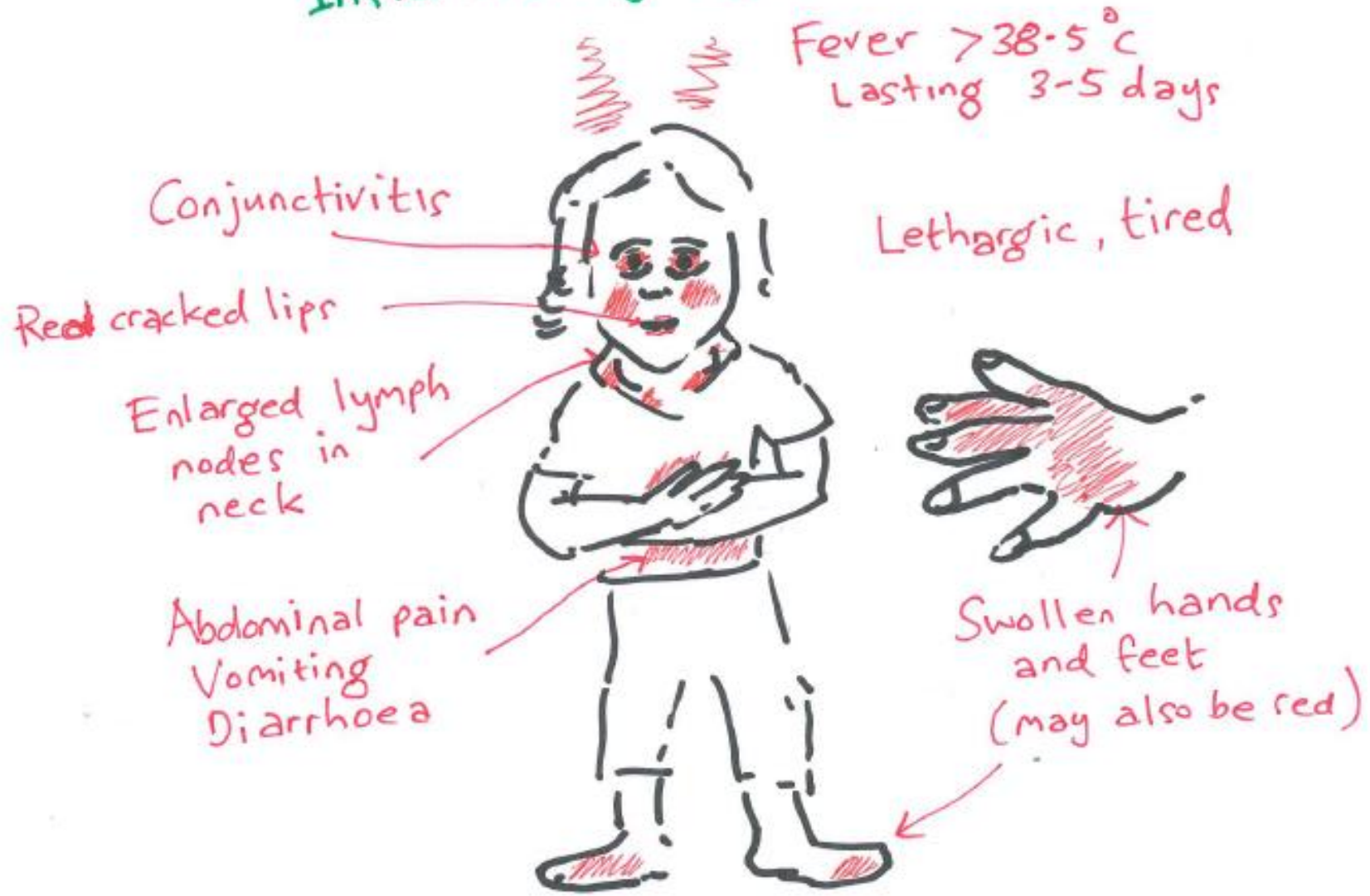
CNS

- Headache
- Myalgia
- Confusion, lethargy

Gastrointestinal

- Diarrhoea and abdominal pain, vomiting

Symptoms of Multisystem Inflammatory Syndrome in Children







MIS-C – Assessment and treatment

Supportive

- A
- B – oxygen
- C – assess the circulation: feel the hands and feet, feel radial pulse, carefully check capillary refill
 - Shock = cold hands and feet, low volume pulses, prolonged cap refill
 - Good circulation = warm hands and feet, easily palpable radial pulse, dorsalis pedis and posterior tibial
 - Fluid, avoid fluid overload, adrenaline
- Prednisolone 2mg/kg for 7 days, or Dexamethasone 0.15mg/kg QID
- Aspirin 5mg/kg/day for 10 days
- Antibiotics – ceftriaxone, flucloxacillin

Assessment of the circulation

Healthy circulation

- Warm hands and feet
- Easily palpable radial pulse, dorsalis pedis and posterior tibial
- Normal BP with good pulse pressure
- Urine output (>1ml/kg/hour)

Shock

- Cold hands and feet
- Low volume pulses
- Prolonged capillary refill
- Hypotension, narrow pulse pressure
- Oliguria (<0.5ml/kg/hour)
- Other: mottled skin, lethargic, acidosis

Age	Systolic blood pressure	Diastolic blood pressure	Pulse pressure
Birth and neonate	60-85	45-55	25-35
Infant (1-12 mo)	80-100	55-65	35-45
Pre-school (1-5 y)	95-107	60-71	35-45
School-age (6-9 y)	95-110	60-73	35-50
Preadolescent (10-11 y)	100-119	65-76	35-50
Adolescent (12-15 y)	110-124	70-79	40-50

Adrenaline infusion

- 1mg (1ml of 1:1000) in 1000ml and run at 5ml/kg/hour (0.1 mcg/kg/min)

OR

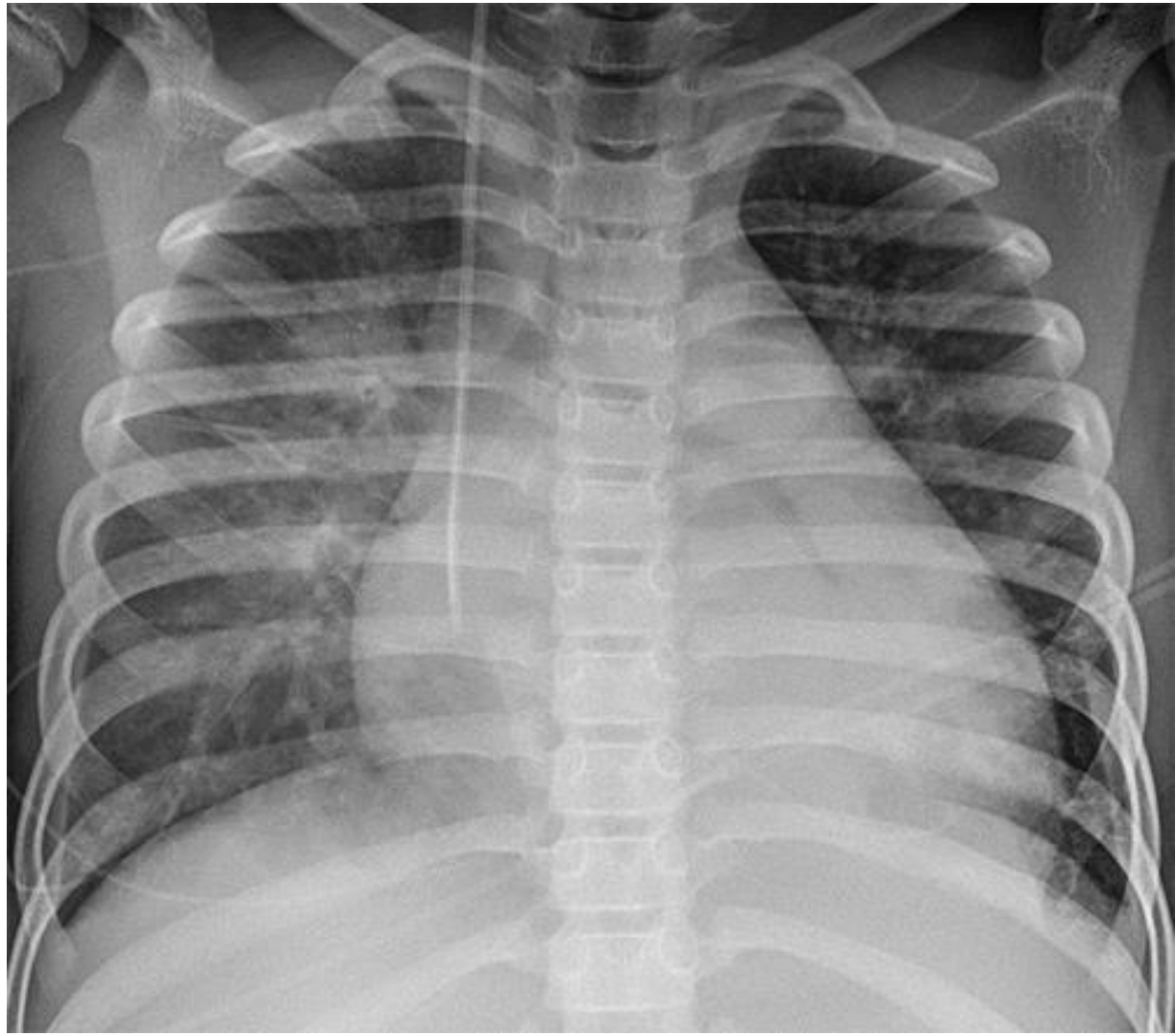
- 6mg adrenaline (6ml of 1:1000) in 1000ml and run at 0.5ml/kg/hour = 0.05mcg/kg/min

OR

- 0.01 ml/kg of adrenaline 1:1000 (=10mcg/kg) by deep intramuscular injection

Laboratory investigations

- Laboratory investigations
 - Lymphocytes ↓, platelets ↓, albumin ↓, ferritin ↑ and D-dimers ↑
 - Echo shows myocardial dysfunction
- Can look like toxic shock syndrome from Staph or Streptococcal infection, or Kawasaki disease or macrophage activation syndrome
- Most children are not very unwell, just have fever, vomiting and diarrhoea



Covid-19 in Fiji

- High community prevalence
- Many hospitalized children are COVID-19 positive
- COVID (like other viruses) may predispose to bacterial infection
- COVID a common bystander / contributor
- Rare cases of MIS-C

