

MMed and DCH Lectures

Weekly by Zoom

Prof Trevor Duke

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Dengue in children

May 18, 2020

Prof Trevor Duke

Aims of today's session

- Learn about Dengue
- Understand the immunopathology, including “antibody-dependent enhancement”
- Understand why there is vascular permeability

Classification

- Dengue fever
- Dengue with warning signs
- Severe dengue – dengue haemorrhagic fever, shock syndrome

Dengue fever

- Incubation period 4-10 days
- 2-7 days of high fever, muscle aches and pains, nausea, vomiting, rash
- Rash – erythematous, looks like any other viral rash, conjunctival injection
- To distinguish from influenza – dengue has no respiratory symptoms

Dengue haemorrhagic fever

- Warning signs 3-7 days after onset of symptoms:
 - Sudden weakness, severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness, blood in vomit
- Capillary leak, oedema (lung, pleural effusions, ascites), respiratory distress, mucosal bleeding, organ failure
- Hct ↑, Platelets ↓, AST and ALT ↑, albumin ↓
- Narrow pulse pressure, e.g. 90/70, then sudden hypotension
- Gastrointestinal haemorrhage – ischaemia, usually only in shock

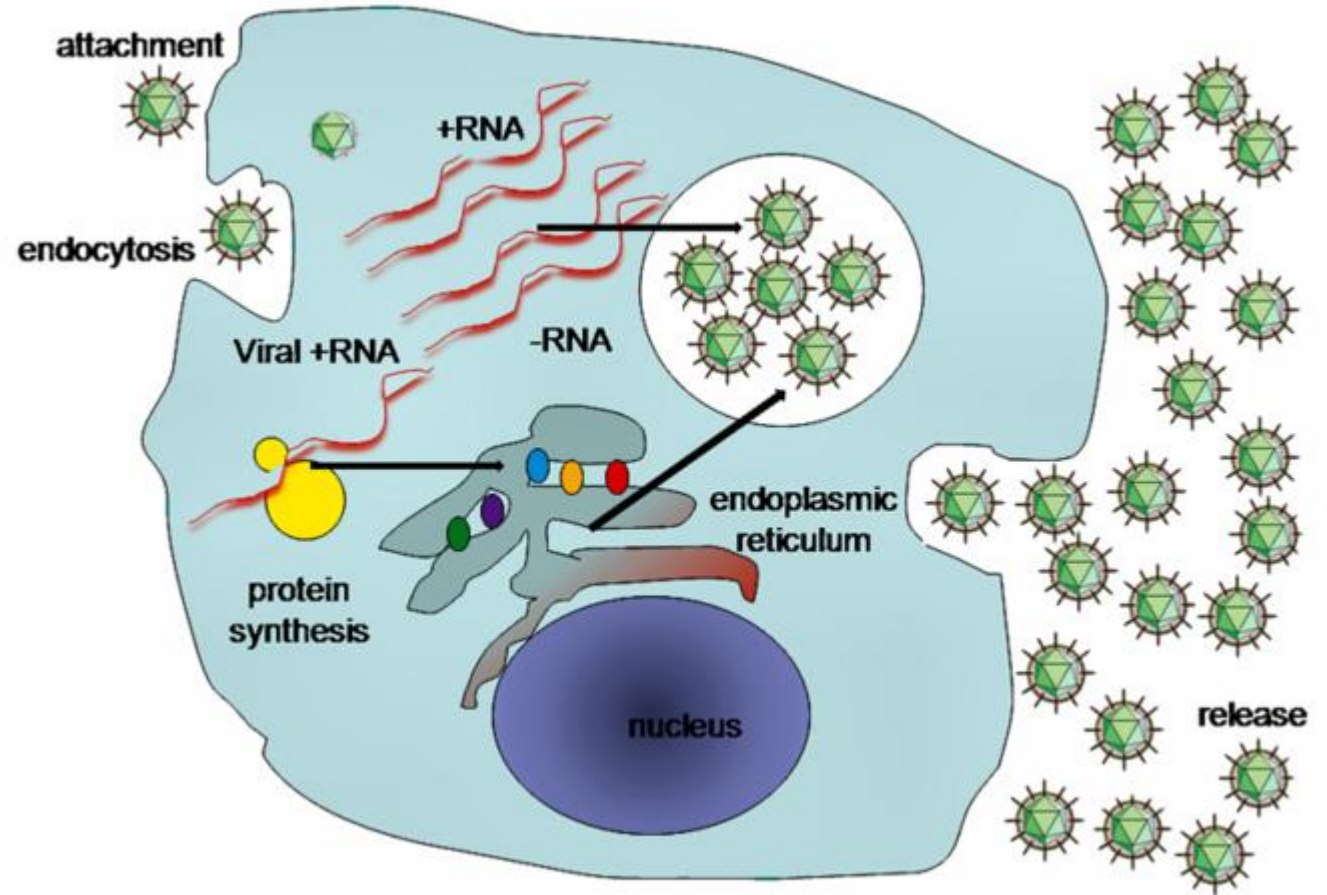
Dengue haemorrhagic fever

- Tourniquet test – inflate BP cuff between systolic and diastolic, leave for 5 minutes: >20 petechial spots = capillary fragility (+/= thrombocytopenia)
- *Non-specific*



Virus infections: the basics

- Viruses only replicate if they are intracellular
- They use host machinery (organelles)
- The ease with which a virus can enter a cell influences the amount of virus replication.

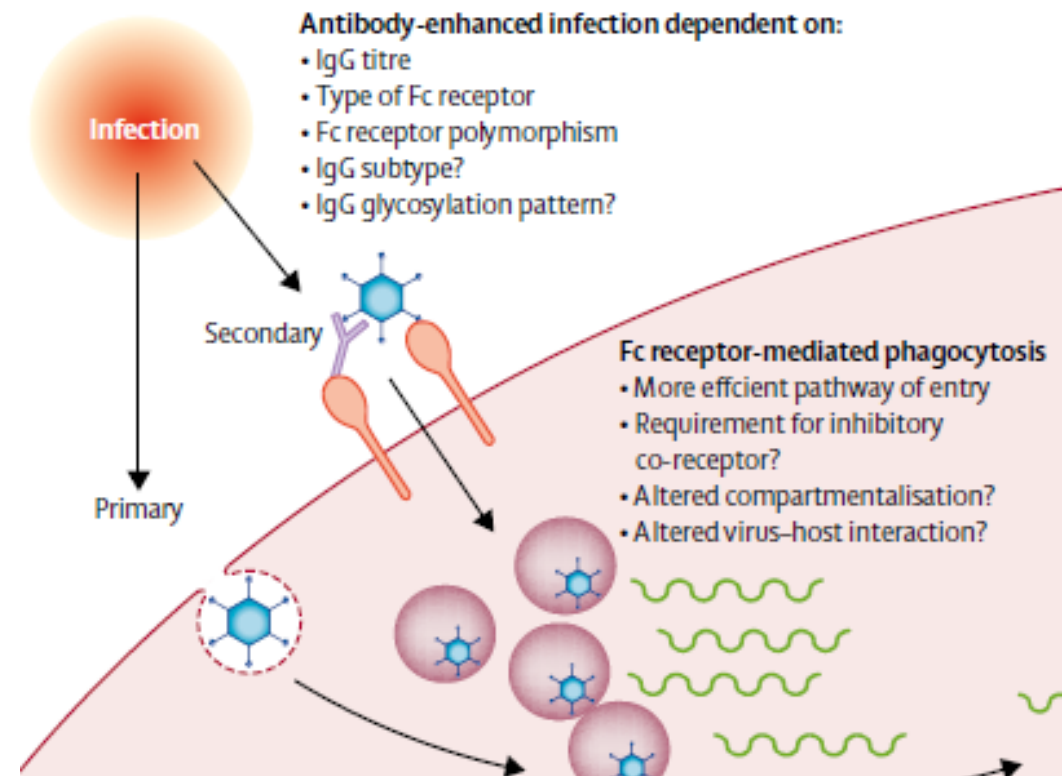


Antibodies produced in dengue

- Dengue type-specific neutralizing antibodies – protective (usually)
- Dengue cross-reactive *non-neutralizing* antibodies - enhancing

1. Antibody-dependent enhancement

- Primary infection: normal virus replication
- Secondary infection (when development of antibodies).
- Virus-IgG complex binds to Fc receptor on macrophages, monocytes
- 100-fold increase in virus production
- Enhanced disease severity



2. T-cell activation and memory T-cells

- Secondary infection
 - Enhanced pro-inflammatory response (↑ interleukin-6)
 - Diminished antiviral immune response (↓interferon)
 - Increased complement activation

3. Dengue vascular permeability syndrome

- Late in the febrile period of dengue – sudden vascular permeability syndrome, massive capillary leak
 - → oedema, hypovolaemia, ↑ Hct, pleural effusions, ascites
- The cause – **a dengue virus protein toxin: NS1**
- NS1 (non-structural protein 1) produced when cells are infected by *any* of the 4 dengue viruses.
- NS1 interacts with receptors on monocytes, macrophages and endothelial cells → cytokines (e.g. IL-6)
- NS1 stimulates enzymes which directly break down endothelial barriers.

Who is at risk?

- Children (and adults) who become infected with a second dengue serotype after an initial 'primary' dengue infection with a different serotype (peak 3-5 years)
- Infants with primary dengue infections whose mothers have some DV immunity
 - Peak 7 months (2 months after neutralising antibodies have degraded below a protective level, but *non-neutralising* antibodies may still lead to enhanced virus replication)
- Secondary infections: 40 x risk of DHF than primary infections

Care of any seriously ill child

- Triage
- Emergency treatment
- History and examination
- Laboratory investigations, if required
- Main diagnosis and other diagnoses
- Treatment
- Supportive care
- Monitoring
- Discharge planning
- Follow-up

Triage

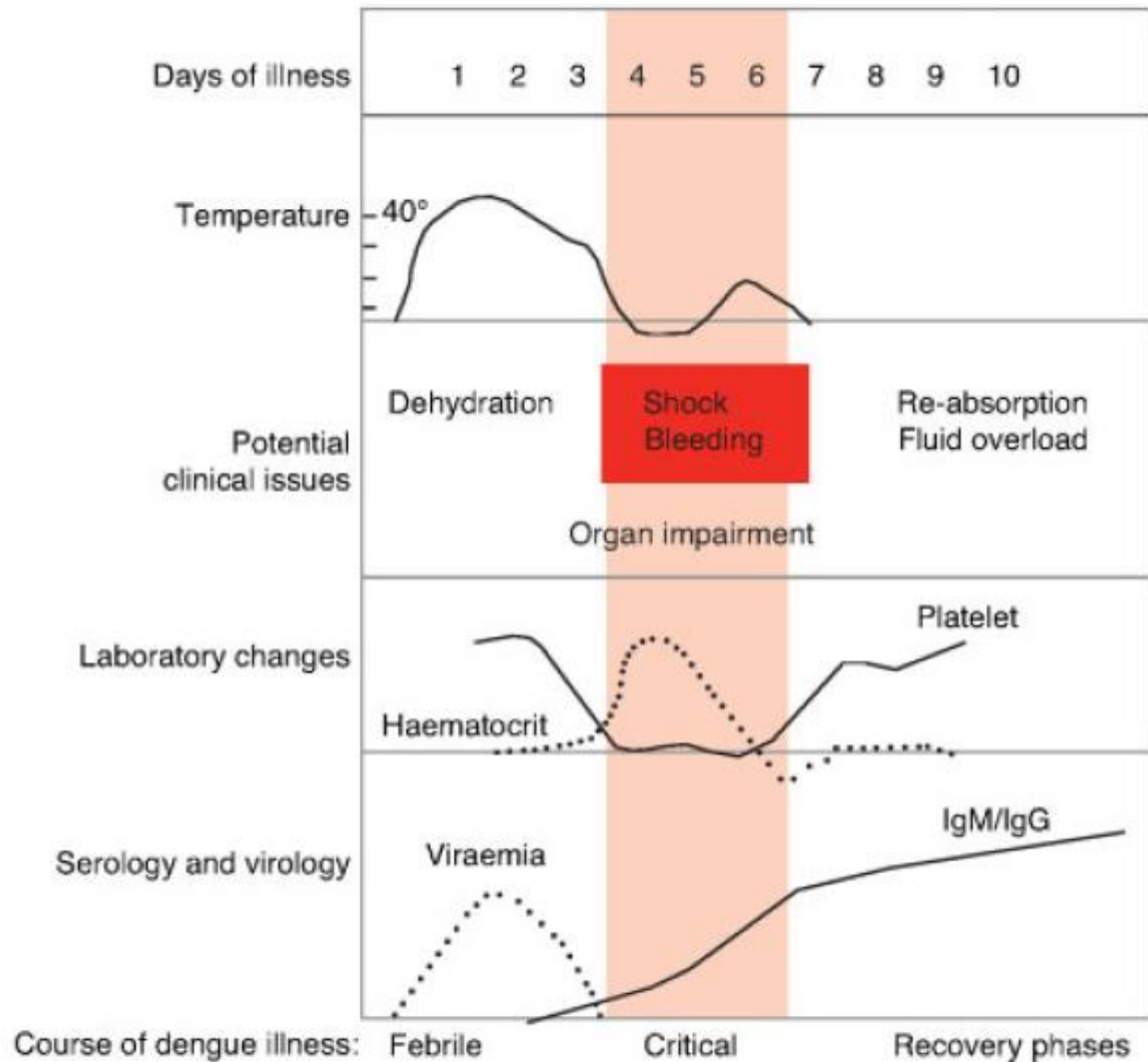
- Brief history of the presenting problem
- Take temperature and weight
 - A. Listen for stridor or obstructed breathing
 - B. Look for cyanosis and for signs of respiratory distress (chest indrawing, tracheal tug), check SpO₂
 - C. Feel the skin temperature of the hands and feet, feel the pulse for volume (narrow pulse pressure), check capillary refill time
 - D. Assess for lethargy and level of interaction.

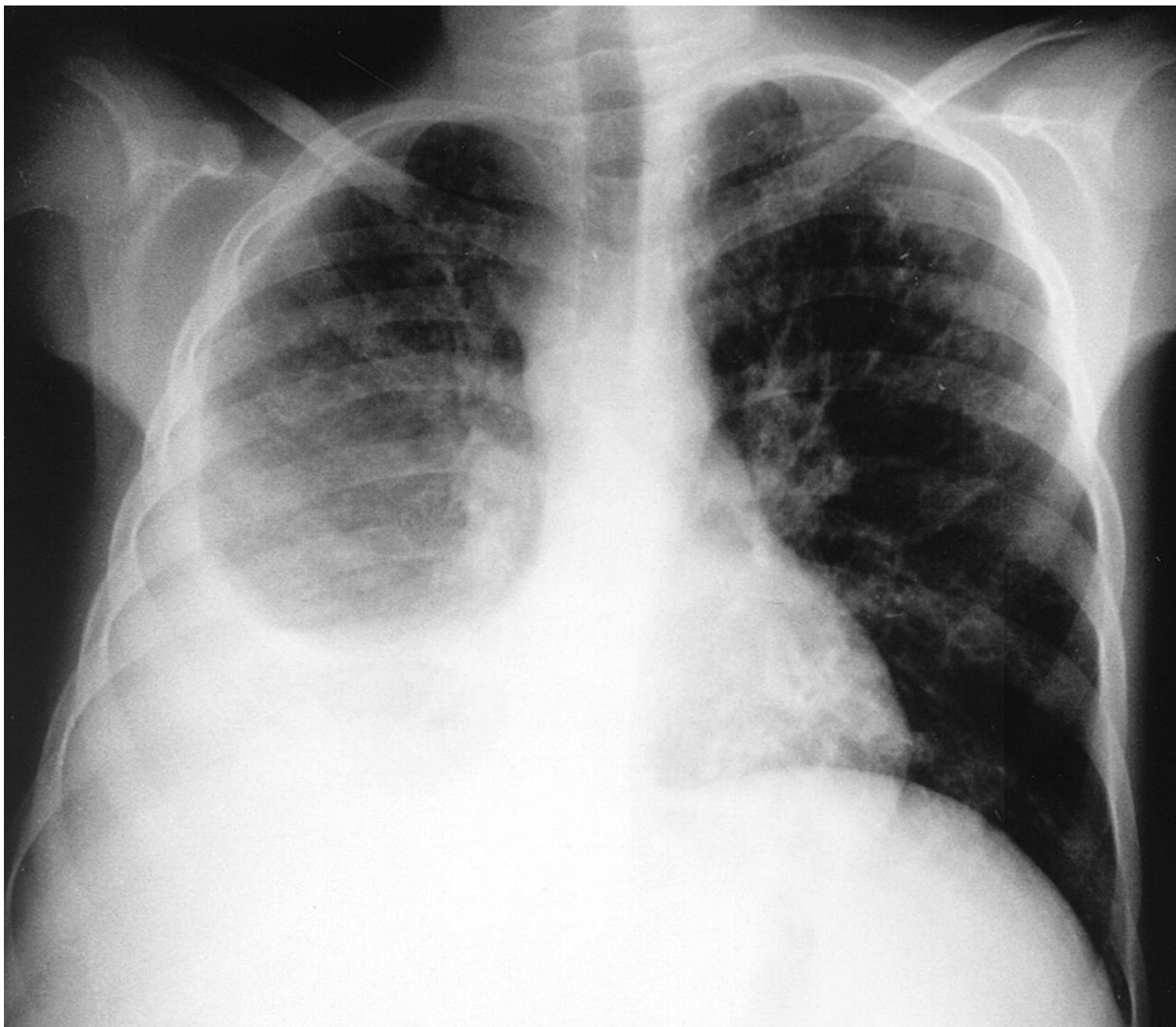
Check for dengue warning signs

- Abdominal pain (hepatomegaly)
- Persistent vomiting
- Oedema
- Respiratory distress
- Bleeding
- Lethargy
- Oliguria
- Hct ↑, platelets ↓

Investigations

- Dengue virus PCR
- Viral antigen NSI
- Dengue IgM – non specific, and late
- Leukopenia
- Hypoalbuminaemia
- Metabolic acidosis
- Pleural effusion





Fluid management: 3 phases of management

- Fever phase
 - Assess hydration, oral rehydration, watch for warning signs
- Severe dengue
 - Plasma leak into extravascular compartment
 - Intravascular volume depletion
 - Cold limbs, pulse pressure <20 , rapid weak pulse
 - Coagulopathy
 - Replace fluid deficit IV
- Convalescent phase
 - Excess extravascular fluid is reabsorbed into the intravascular space
 - Patient is fluid overloaded, reduce fluid to avoid pulmonary oedema

- Isotonic crystalloid
- Give whole blood first if severe bleeding and shock
- Platelet transfusion if $<50,000$ and severe bleeding, or <5000 with any bleeding

Name: Ratu Age: 11 months
Frequency of observations: 1-2 Hourly

Weight: 8.2 kg UR number: 267198



Frequency of observations: 1 2 Hourly												
Date												
Time												
Temp °C	≥ 39	15/4									>39	
	38-38.9	37.9									38-38.9	
Respiratory Rate (bpm)	36-37.9										36-37.9	
	<36										<36	
	≥ 80										≥ 80	
	70	X									70	
	60		X								60	
	50			X							50	
SpO ₂ (%)	40			X							40	
	30				X						30	
	20					X					20	
	10						X				10	
	0							X			0	
	100										100	
	90		X		X		X	X	X		90	
	80	X									80	
	70										70	
	<70										<70	
Oxygen	L/min										L/min	
Respirat distress	Severe	X	X								Severe	
	Mod.			X	X	X	X				Mod.	
	Mild							X			Mild	
	Normal										Normal	
Heart rate (bpm)	≥ 200										≥ 200	
	190										190	
	180										180	
	170	X									170	
	160		X								160	
	150			X							150	
	140				X	X					140	
	130						X				130	
	120										120	
	100										100	
	90										90	
	80										80	
	70										70	
	60										60	
	<60										<60	
	Cap refill	≥ 3 secs									≥ 3 secs	
	< 3 secs	X	X	X	X	X	X	X			< 3 secs	
	Blood Pressure (mmHg) > <	≥ 150										≥ 150
		140										140
		130										130
120											120	
110											110	
100											100	
90											90	
80											80	
70											70	
60											60	
50											50	
Alert		X	X	X	X	X	X	X			Alert	
Verbal											Verbal	
Pain											Pain	
None										None		
Pain score (/10)										Pain		
Blood sugar	1.8									BSL		
Feeds given: volume	4.5											

Oxygen

IV glucose

Antibiotics

Blood Transfusion

Feeds

Commenced (ML)



Covert COVID-19 and false-positive dengue serology in Singapore

- 2 patients
- Cross reactivity of dengue IgM and IgG, initially positive, but later COVID-19 PCR positive and dengue serology negative