

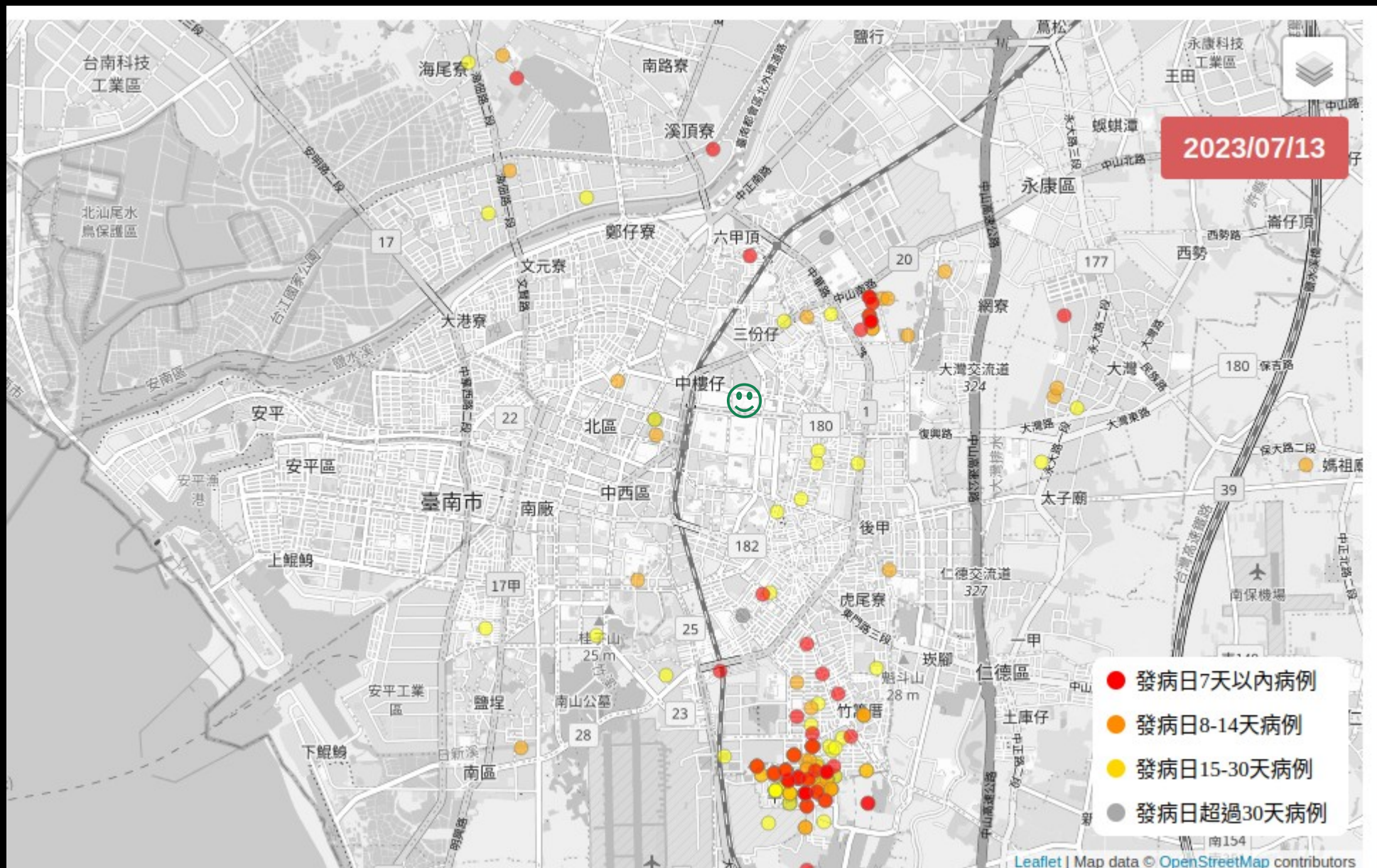
# 登革熱重症 個案處理原則

謝宗達

成大醫院重症加護科 / 感染管制中心

2023/07/13

# 台南疫情 2023



至 2023/07/11 累計本土個案 286

<https://cdcdengue.azurewebsites.net/>

<https://health.tainan.gov.tw/dengue/>

# 台南疫情 2015/05 - 2016/01

通報確診感染

登革熱相關死亡

22780

112

[http:// www.cdc.gov.tw/](http://www.cdc.gov.tw/)

參考數字 (Taiwan 2003 – 2013)

通報確診 11691

死亡 24

本院成人加護病房  
登革熱病人死亡率

41.3%

# 台灣加護病房的登革熱病人 世界最老

國家	年齡中位數
斯里蘭卡	20
新加坡	44
印度	39
巴西	43
台灣	<b>72</b>

# Underlying diseases of adult critically ill dengue patients, NCKUH

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Hypertension	72.0%
Diabetes mellitus	42.7%
Chronic kidney disease	22.7%
Dyslipidemia	21.3%
Coronary artery disease	18.7%
Malignancy	14.7%
Stroke	13.3%
Chronic lung disease	9.3%
Heart failure	9.3%
Liver disease	6.7%

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# 2015 登革熱高峰期 台南醫療系統的負擔

某應變醫院同時有

130

人住院

本院同時有

15

人住在加護病房

在重症病人診斷登革熱



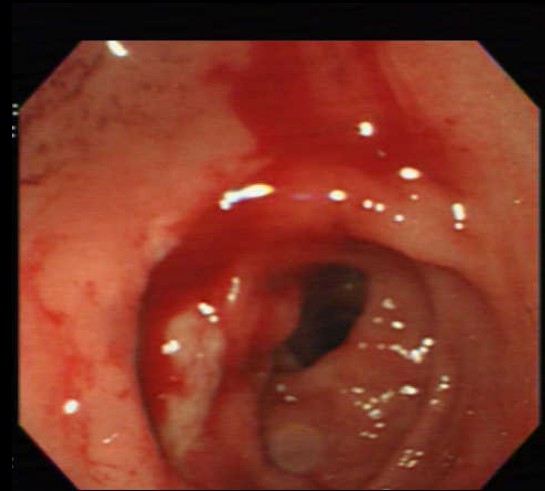
[Case 01]

65-year-old man with HTN and HIVD

Presenting symptoms: bloody stool,  
dizziness, fainting

WBC	Hb	Plt	PT-INR	aPTT
4.1	10.5	15	1.28	29.90

EGD: GU with major SRH, DU  
Admitted to the GI ward



# [01] Soon transferred to ICU

- Massive bleeding, hypotension at night
- Tracheal intubation and transfer to ICU.
- Hb 10.0 → 7.0 → 4.6 g/dL
- Vasopressor was administered
- 2nd EGD on the next day: GU with bleeding vessel
  
- Positive dengue tests (ordered by the intensivist)
  - NS1 Ag+, IgM+, IgG+, PCR+
- The patient did have dengue symptoms
  - fever, myalgia, arthralgia

# [Case 02]

56-year-old woman

Multiple sclerosis at bed-ridden status.

DM. Breast Ca.

Home MV. PEG. Foley catheter.

Frequent hospitalization for recurrent UTI.

Fever, chills, respiratory distress.

Cough, sputum, turbid urine.

WBC	Hb	Plt	PT-INR	aPTT	
9.7	10.4	378	1.20	32.60	
U-WBC	U-Bac	U-Nitrate	Dengue NS1	Dengue IgM	Dengue IgG
6	Trace	Negative	Negative	Negative	Negative

## [02] Admission to ICU after 6-day ED stay

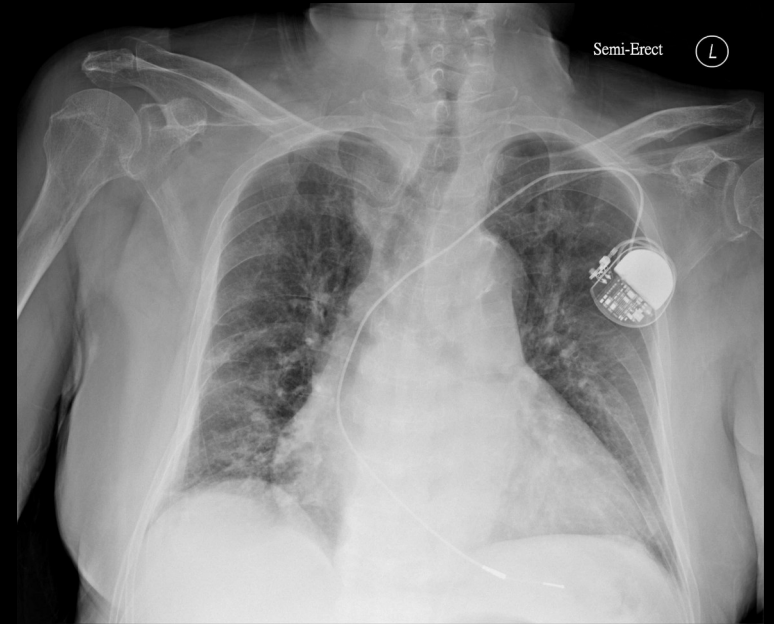
- Hypotension requiring vasopressors after admission. Hemogram looked WNL.
- 2 days later...
  - Thrombocytopenia
  - Massive GI bleeding
  - Skin rashes at trunk and face
- Dengue viral load:  $2.85E8$  copies/mL

[Case 03]  
80-year-old man.  
HTN. DM. SSS s/p pacemaker.

Productive cough for one day  
Mild fever, weakness

Pyuria.

CXR: Cardiomegaly. New RLL patches.



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WBC	Hb	Plt	PT-INR	aPTT
11.4	11.1	235	1.14	32.70

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Dengue NS1	Dengue IgM	Dengue IgG
Negative	Negative	Negative

---

# [03] In-hospital cardiac arrest at ED

- ROSC after CPR for 5 minutes
  - ABG: PaCO<sub>2</sub> 73.1 mmHg, pH 6.939
- Admitted to the medical ICU
  - PEA s/p CPR
  - Massive GI bleeding
  - Expired within 24 hours

4 days later...

Dengue viral load:  $1.43E4$  copies/mL

# [Case 04]

89-year-old woman

DM. CKD. HTN. Gout. Dementia  
Dependent ADL.



Altered mental status at home for one day.

Fever 39.5°C at ED.

Tracheal intubation at ED for hypoxemia.

UGI bleeding and shock after intubation

WBC	Hb	Plt	PT-INR	aPTT	⇒	Hb	Plt	
16.8	14.2	152	1.1	33.0		11.4	61	
BUN	Cr	Na	K	AST	ALT	PCT	lactate	Dengue NS1
92	4.30	147	5.8	334	79	1.79	6.1	Negative



[Case 04]

Admission to ICU on D+1

CT: pelvic soft tissue swelling

Skin: localized erythema

Gluteal SSTI?

Hypotension improved.

LGI bleeding

Repeat dengue study on D+2

Dengue PCR	Dengue IgM	Dengue IgG
Negative	Positive	Negative

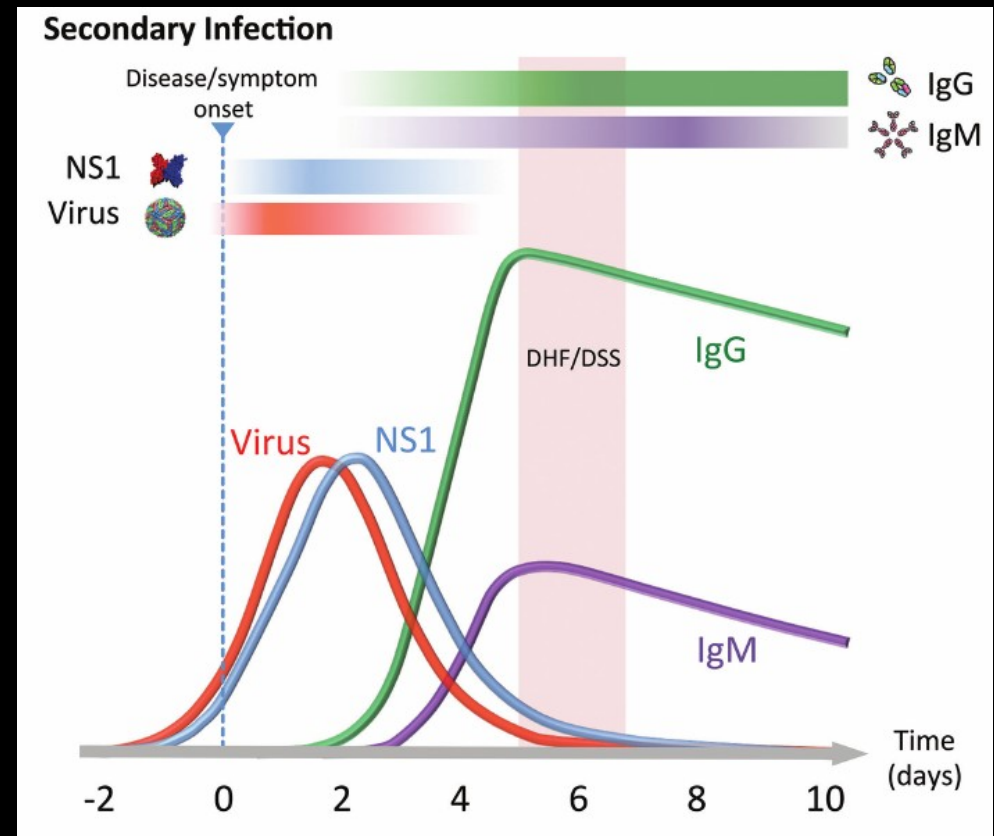
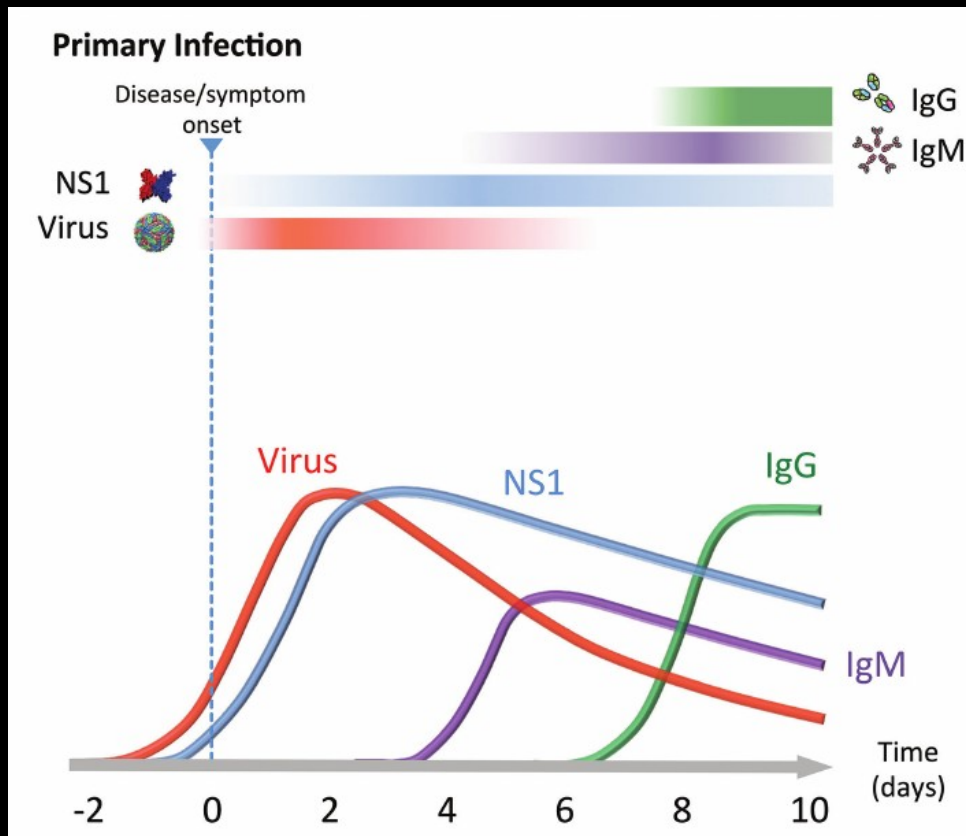


Management for possible severe dengue.  
Dengue IgG became positive one week later.

# 在重症病人診斷登革熱

- 好好問病史
- 登革熱有潛伏期，在急診 / 住院中也可以發病
- 流行期的時候，有一點症狀 / 徵象就要懷疑，特別是重症病患
- 每個檢驗都有其限制，不要太依賴單一檢驗

# One negative test result may be misleading



# 登革熱重症處置

No specific treatment.

真正考驗各位  
supportive care 的功力

## [Case 05]

74-year-old woman

HTN; CKD baseline Cr 2.9; Anemia Hb 8.6

Fever for 3 days. Abdominal pain, mild diarrhea, gum bleeding.

Tachycardia 120/min

BP 111/79 (baseline 118/58)

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WBC	Hb	Plt	Cr	AST	ALT	Lipase	Vein pH	Vein BE	Dengue NS1
7.9	13.8	9	5.54	1482	883	2264	7.084	-20.6	Positive

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# 登革熱病人患從穩定到休克的表徵

臨床徵象	循環穩定	代償性休克	低血壓休克
意識狀態	清楚	清楚	變差
微血管回填時間	小於兩秒	超過兩秒	極度延長、出現大理石斑
肢體	溫暖有血色	肢端冰冷	冰冷無血色
週邊脈搏強度	正常	減弱縮小	微弱甚至摸不到
心搏速率	正常	過速	明顯太快 晚期變為心搏過緩
血壓	正常	收縮壓正常、舒張壓上升 脈壓下降 姿勢性低血壓	脈壓下降至 < 20 mmHg 低血壓 (MAP < 70 mmHg, SBP < 90 mmHg 或下降超過 40 mmHg)
呼吸速率	正常	呼吸速率急促	代謝性酸中毒引起呼吸急促 及 Kussmaul breathing



# Compensated shock

- Capillary refill time  $> 2$  secs
- Pulse pressure  $< 20$  mmHg
- Cool peripheries
- Tachycardia
- Tachypnea

# [05] IVF during the first 12 hours

- First 6 hours

- NS 80 mL/hr ivd x 20 min
- NaHCO<sub>3</sub> 16.67mEq x 6 amp ivd stat
- NS 40 mL/hr ivd x 1.2 hr
- NaHCO<sub>3</sub> 16.67mEq x 6 amp ivd stat
- NS 80 mL/hr ivd x 4 hours

- Second 6 hours

- NS 80 mL/hr ivd
- NS 500 mL ivd stat
- Pantoprazole;  
tranexamic acid

I/O: 1615 mL / 20 mL

# [05] No improvement at all

- Third 6 hours: NS 80 mL/hr
- At the 21th hour of ED stay...

The patient tried voiding, then AMS with cyanotic lips.

- Tracheal intubation was done

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	baseline	H+1hr	H+13hr	H+19hr
Hct	25.3	41.9	32.2	33.7

---

# [05] In-hospital cardiac arrest

- Frank shock developed after intubation
- Then PEA / asystole occurred within one hour after intubation
- The patient was soon admitted to the medical ICU but expired within 3 hours
  - GI bleeding, hematuria, pulmonary hemorrhage
    - Hct 33.7 → 21.5
  - Multiple organ failure

# 典型登革熱病人惡化進程

有登革熱症狀  
但尚稱穩定

數小時  
數日

警示徵象出現

數小時

代償性休克  
(血壓仍正常)

數小時

低血壓休克

數分鐘 / 數小時

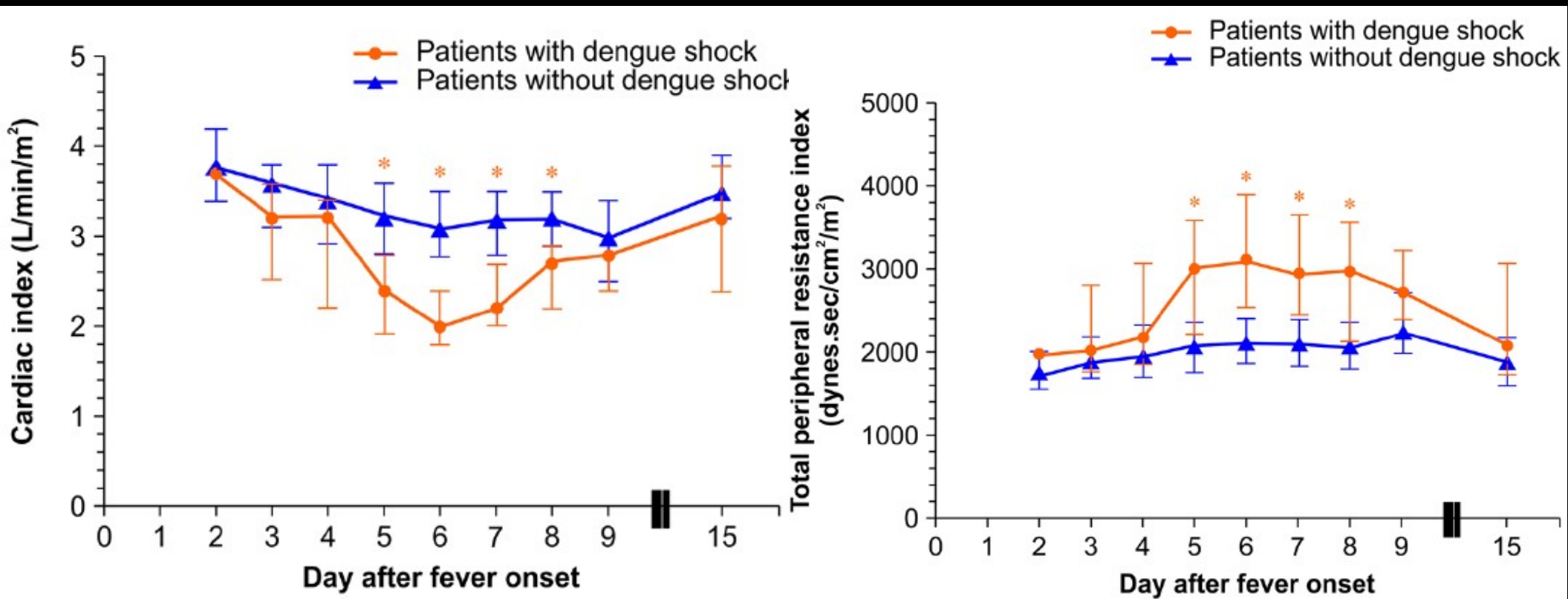


Among 13 patients experiencing cardiac arrest event (OHCA 5, IHCA 8), only one survived to discharge.

# Dengue shock

- The main haemodynamic elements of septic shock are maldistribution of blood volume resulting from an increased vascular capacitance and myocardial suppression, while dengue shock is hypovolaemia with decreased vascular capacitance resulting from plasma leakage.
- IV fluid is life-saving in dengue shock.

# Dengue shock: either hypovolemic or cardiogenic **not septic shock**



Cardiac index ↓

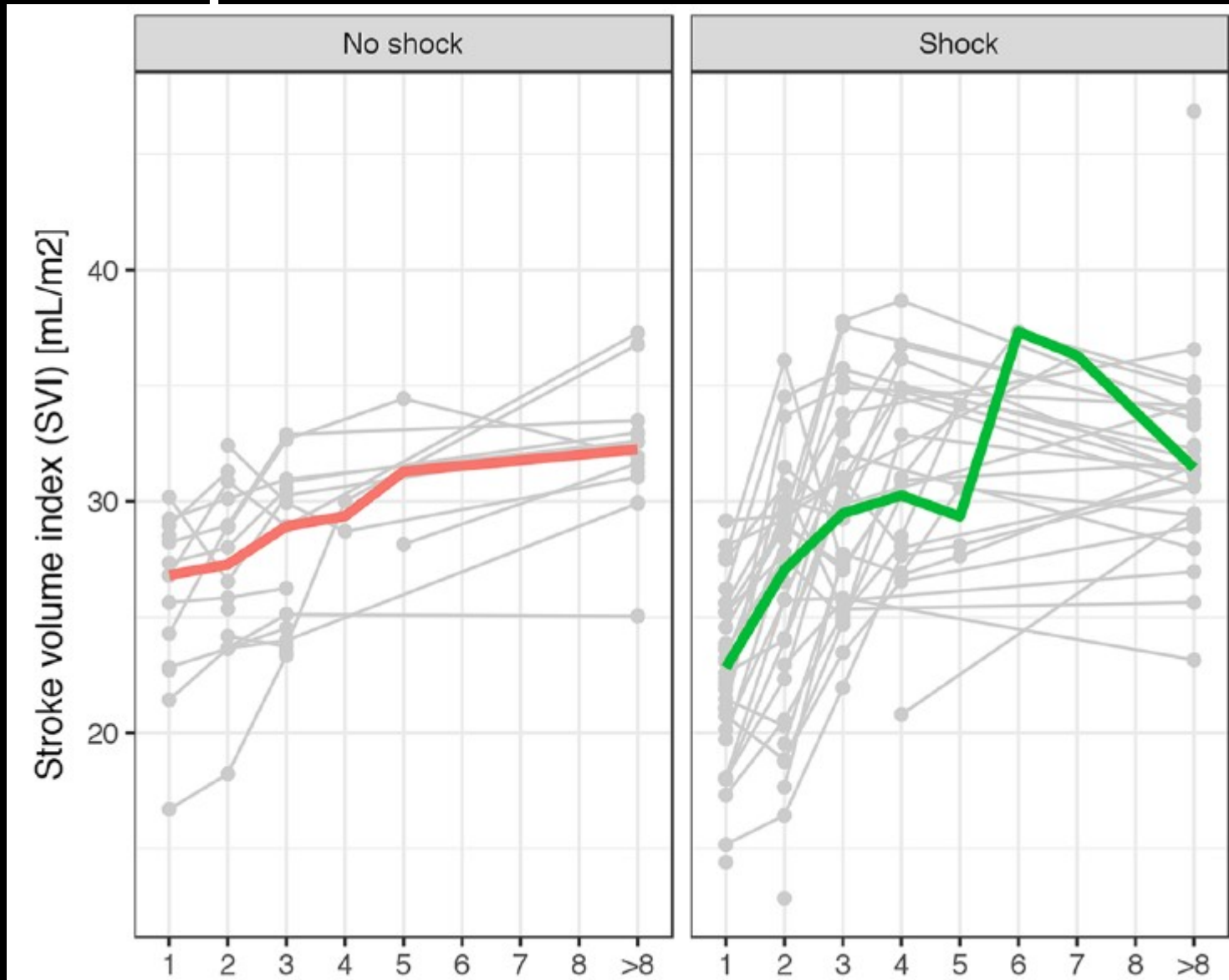
Peripheral resistance ↑



# Dengue shock: hypovolemic or cardiogenic

- 17 dengue patients with shock in this study
- 9 hypovolemic shock (CVP↓, CI↓, PVR↑)
- 8 cardiogenic shock (CVP↑, CI↓, PVR↑)
- No septic shock at all

# Lower cardiac output in dengue patients with shock



# Predictors for dengue shock and/or organ failure

	Odds ratio (95% CI)
Procalcitonin $\geq$ 0.7 ng/mL	4.80 (1.60-14.45)
Lactate $\geq$ 2.5 mmol/L	27.99 (8.47-92.53)
Combined procalcitonin & lactate	
0	1.00 (reference)
1	22.23 (7.85-63.00)
2	30.00 (5.76-156.31)

- sensitivity 81.2%; specificity 84.4%; AUROC 0.83
- Better than WHO 2009 warning signs (WSs  $\geq$  4)

# IVF duration

- The critical phase lasts no longer than 48 hours.
- The total duration of intravenous fluid resuscitation **should not exceed 48 hours.**

# How much IVF to administer

## Consider the following factors

- Disease severity and phase
- Volume status
- Fluid tolerance
- Response to fluid therapy

## Resuscitation goal

- 平均動脈壓 (mean arterial pressure, MAP)  $\geq 65$  mmHg
- 肢體恢復溫暖；微血管回填時間  $< 2$  秒
- 尿量  $\geq 0.5$  mL/kg/hr
- 乳酸偏高的患者的乳酸值持續下降
- ScvO<sub>2</sub>  $> 70\%$  & PvaCO<sub>2</sub>  $< 6$  mmHg

# Fluid amount according to severity

- Patients with warning signs
  - 5-7 ml/kg x 1-2 hr, 3-5 ml/kg x 2-4 hr, then 2-3 ml/kg/hr
- Compensated shock
  - 5-10ml/kg in the first hour.
  - If unstable & Hct↑, repeat 10-20ml/kg within 1 hour
  - If stable, manage as group B (5-7 ml/kg x 1-2 hr, 3-5 ml/kg x 2-4 hr, then 2-3 ml/kg/hr)
- Hypotensive shock
  - 20mg/kg bolus within 15 minutes
  - If unstable & Hct↑, colloid 10-20ml/kg bolus
  - improved, 10mg/kg x1 hr, then 5-7, 3-5, ...

# Back to case 05, the IVF amount was insufficient

- The patient received 1615 mL during the first 12 hours after ED arrival
- According to the guideline, at least 2200 mL should be administered if the patient has compensated shock and soon became stable.

# Traditional tools to monitor IVF response in patients with dengue

- Clinical assessment + hematocrit
- If the patient becomes stable with acceptable perfusion, taper or discontinue the IVF
- If unstable,

Shock +  $\uparrow$ Hct

Hemoconcentration

Shock +  $\downarrow$ Hct

Bleeding



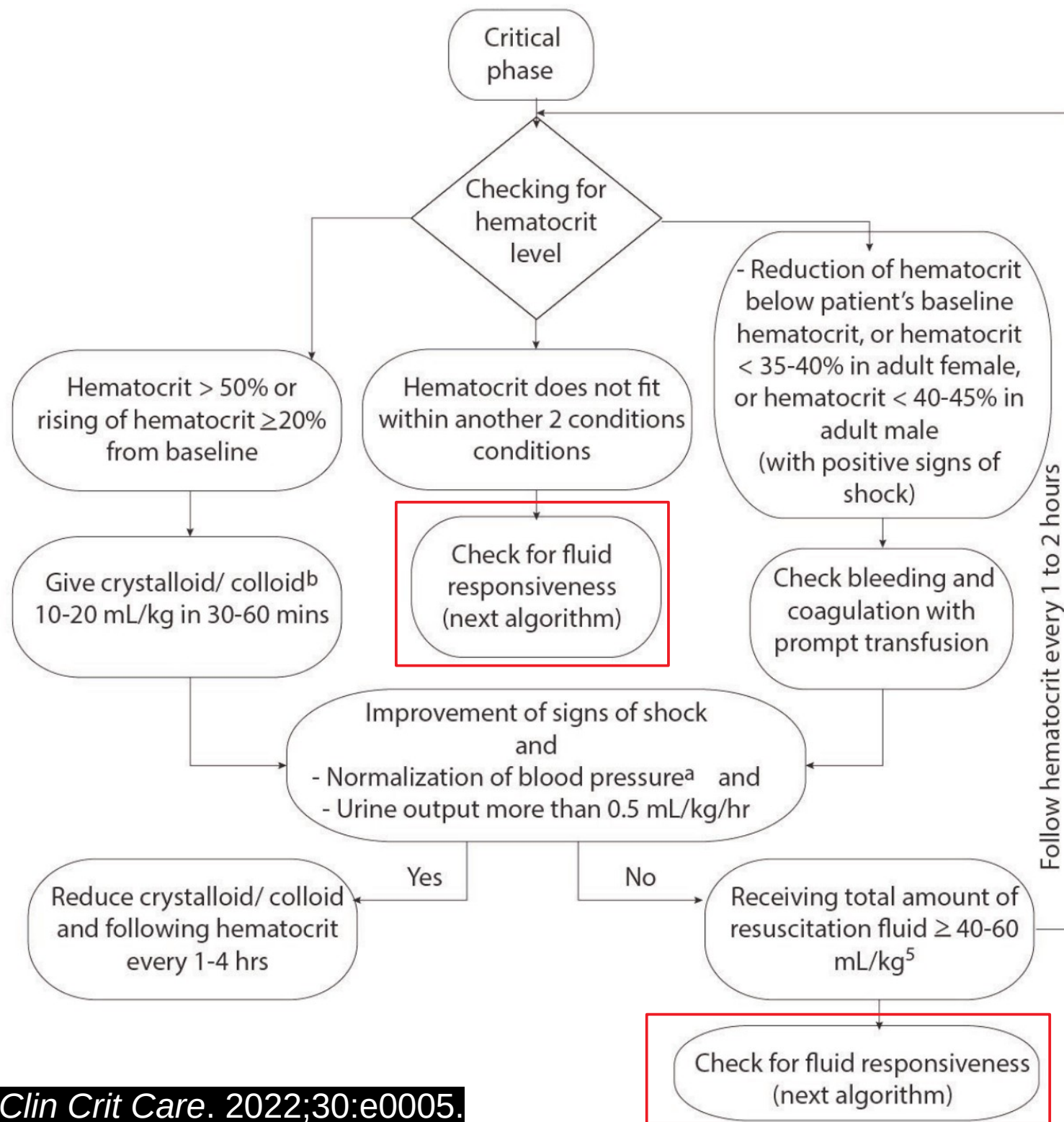
# Modern tools to monitor fluid response in ICUs

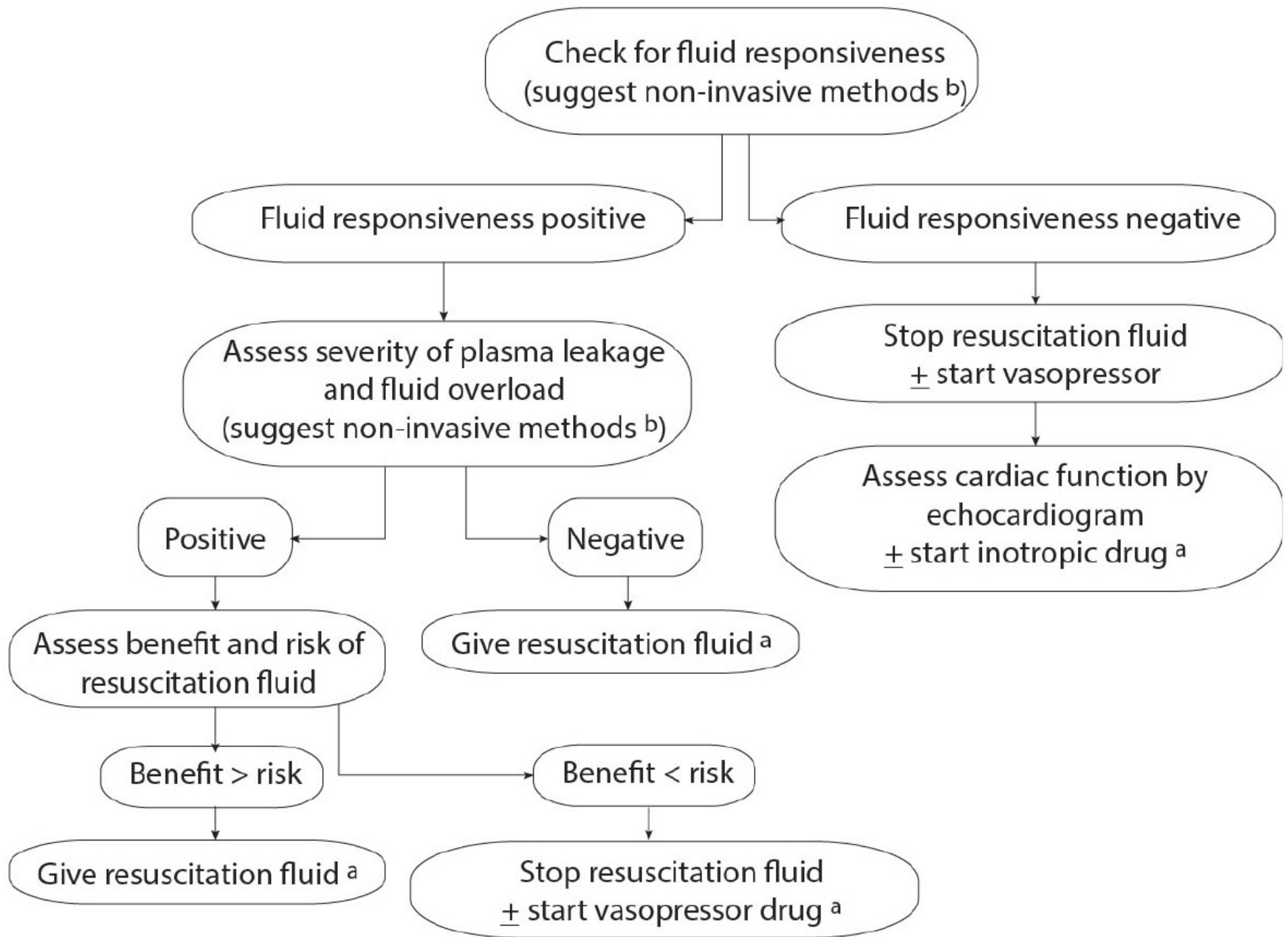
- Static variables

- Heart rate
- Serum lactate
- CVP, PCWP
- IVC diameter on US
- LV size, motion (TTE)
- B-lines on lung US
- Vascular pedicle width and lung infiltrates on CXR

- Dynamic variables

- Passive leg raising test
- Stroke volume variation (SVV)
- Pulse pressure variation (PPV)
- End-expiratory occlusion test
- Tidal volume changes
- Minimal fluid challenge





# Non-invasive cardiac output monitoring



No matter what parameter / tool you use  
Re-assessment every 1-2 hours

# Vasopressors & inotropes

- **As a temporary measure** to prevent life-threatening hypotension. Should be weaned off as intravascular volume is restored and end-organ perfusion re-established.
- Documented cardiogenic shock – dobutamine
- Concomitant septic shock owing to bacterial or fungal infection – norepinephrine

[Case 06]

86-year-old woman

DM, HTN, CKD

Fever. Dengue NS1 positive

Return to ED 2 days later because of AMS

AKI, respiratory failure s/p intubation

Admitted to ICU after ED stay for 2 days

Difficult to place a peripheral IV line

Left femoral CVC; Right IJV CVC

Femoral arterial line (failed)

[06] Hb 14.0 → 6.1 within one day

- NG aspirate: no bleeding
- No tarry or bloody stool
- Active oozing at the right IJV CVC insertion site with ecchymosis and hematoma in progression
- Femoral arterial puncture site: no hematoma
- Bleeding at the oral cavity as well



# Invasive procedures

- Arterial line is recommended for patients with shock
- Realtime ultrasound for deep vascular access
- DO NOT delay tracheal intubation
  - Beware of hypotension after that



WHO. *Handbook for Clinical Management of Dengue*. 2012.  
Frankel HL. *Crit Care Med*. 2015;43(11):2479-502.  
Schmidt GA. *Intensive Care Med*. 2019;45(4):434-446.

# Gastrointestinal bleeding

- May be **devastating in a hypovolemic patient**
- Conservative treatment for mild-to-moderate GI bleeding, consider proton pump inhibitor, tranexamic acid, and desmopressin administration
- EGD & TAE for severe bleeding not responding to medical therapies
- Do not rely on single hemoglobin / hematocrit level

[Case 07]

A 67-year-old man.

DM, HTN, Non-alcoholic steatotic hepatitis,  
renal angiomyolipoma

Tarry stool > 5 times

NG irrigation: fresh blood → coffee-ground

EGD: UGI bleeding, focus unknown

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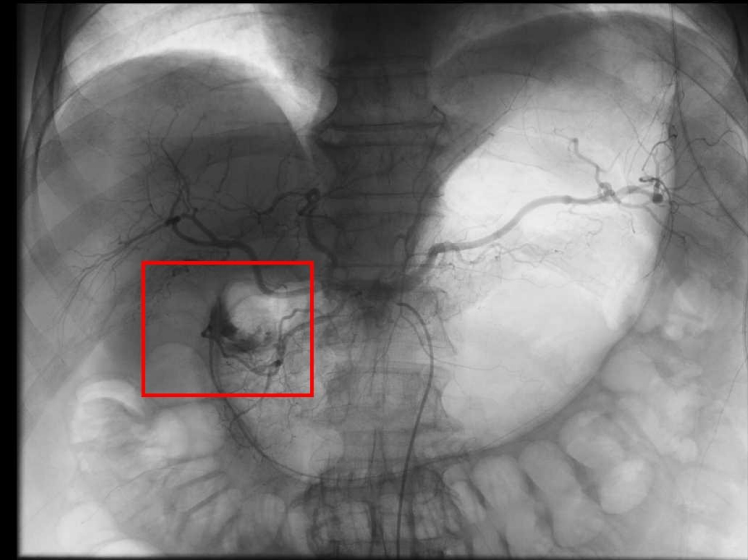
WBC	Hb	Plt	PT-INR	aPTT
7.3	10.4	163	1.28	33.9

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# [07] Massive GI bleeding

During the first 24 hours

- Tarry bloody stool > 3000 ml
- Hb 10.4 → 4.3 within 24 hr
- Norepinephrine up to 32 µg/min
- 18 U of RBC or whole blood
- Trans-arterial embolization (TAE) twice
- No vasopressor within 24 hr after the 2<sup>nd</sup> TAE



# Transfusion

- RBC or whole blood for **bleeding patients**

WHO. *Handbook for Clinical Management of Dengue*. 2012.

- Prophylactic platelet transfusion is **not recommended**

- Except for invasive procedures

Lye DC. *Lancet*. 2017;389(10079):1611-1618.

Rajapakse S. *Trans R Soc Trop Med Hyg*. 2017;111(10):433-439.

- No restriction on transfusion for patient with moderate-to-severe bleeding

Concurrent and subsequent  
non-viral infections

# Concurrent infections at presentation dengue patients in ICU, 2015

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Concurrent bacterial infection	
No	45
Yes	30
Lower respiratory tract infection	18
Urinary tract infection	6
Intra-abdominal infection	2
Primary bacteremia	4
Total	75

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# Which antibiotics?

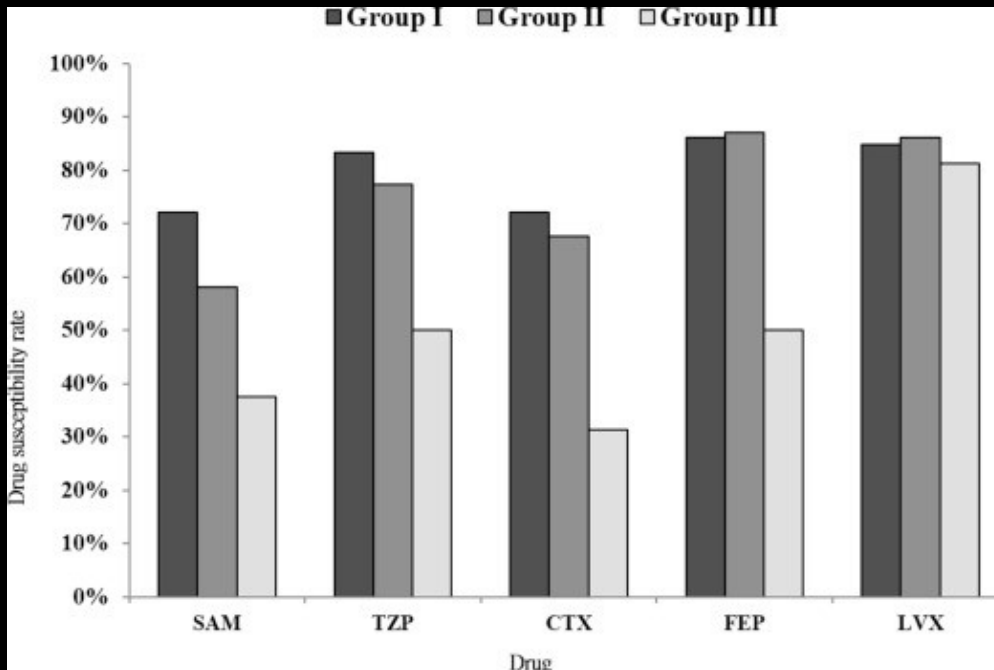
75 pts	HAI risk		No HAI risk		LRTI		No LRTI	
MDRO	6	4	8	2				
No MDRO	13	52	12	53				
MDRO (%)	31.58%	7.14%	p=0.058	40.00%	3.64%	p=0.002		

- For a patient without risk of HAI or LRTI, MDR pathogens rarely present. (0/41)
  - Ampicillin/sulbactam or a 1<sup>o</sup>-3<sup>o</sup> cephem is sufficient
- Empiric antipseudomonas coverage for patients with HAI risk or LRTI is acceptable.



# Bacteremia among patients with dengue hospitalized at NCKUH, 2015, n=80

- $\leq 48$  hr: streptococci, E. coli
- 48 hr – 1 wk: Enterobacterales
- $\geq 1$  wk: HAI GNBs



- SAM: ampicillin-sulbactam
- TZP: piperacillin-tazobactam
- CTX: cefotaxime
- FEP: cefepime
- LVX: levofloxacin

# Concurrent bacteremia in patients with dengue

- Risk factors
  - Acute kidney injury
  - Fever more than 5 days
  - Pitt bacteremia score  $\geq 4$
  - procalcitonin (PCT)  $> 1.14$  ng/mL
- Common pathogens of primary bacteremia
  - streptococci
  - Enterobacterales

[Case 08]

82-year-old man

DM. HTN. Cardiac disease.

Fever & myalgia 8/29 – 30

Weakness, AMS, lying on the ground for hours on 8/31

Hospitalized at a regional hospital 8/31

NS1 antigen test – positive

Diarrhea & abdominal tenderness

Transferred to NCKUH on 8/31 night

## [08] 1<sup>st</sup> – 3<sup>rd</sup> day

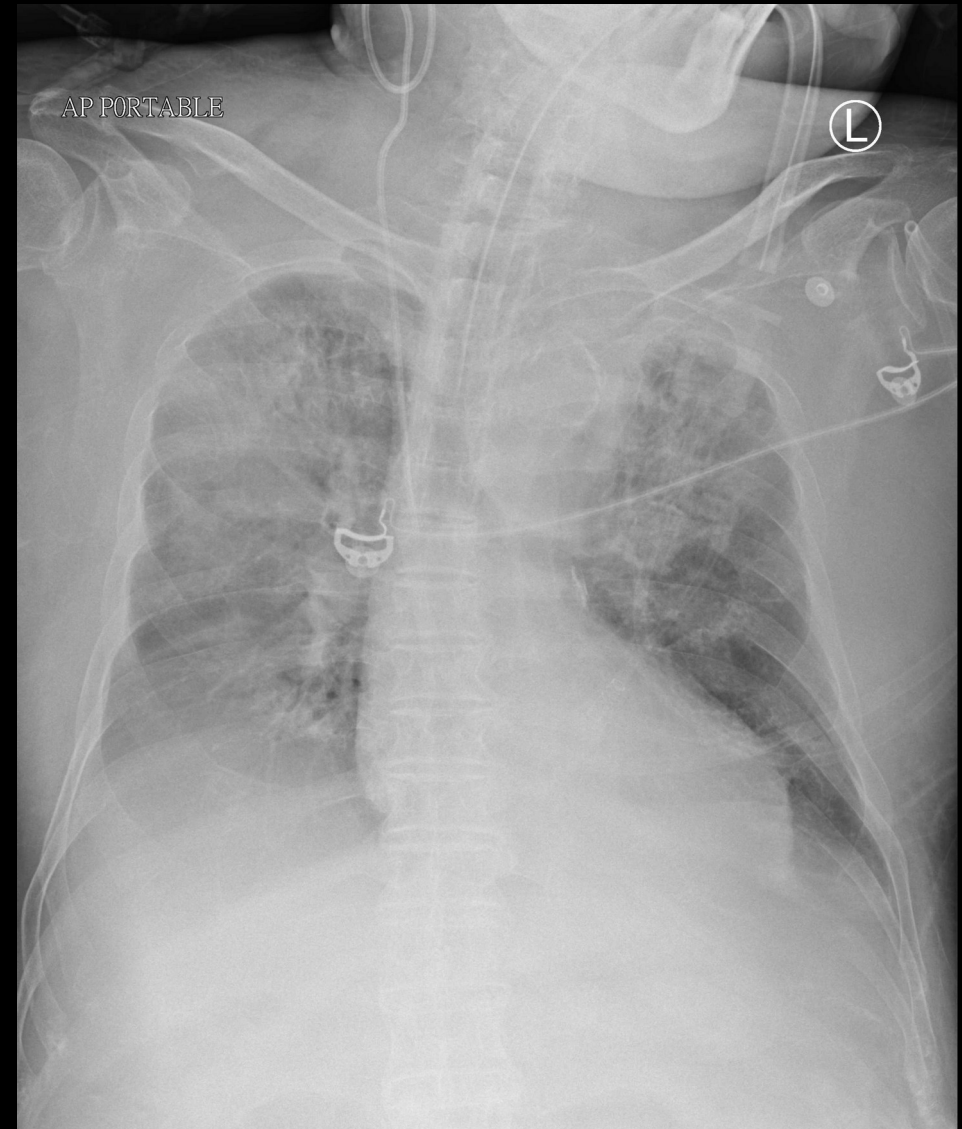
- Rhabdomyolysis and AKI
- Abdominal CT:
  - A-colon wall thickening
  - possible pneumonia
- Empiric cefotaxime + metronidazole
- Intubation for respiratory distress and much airway secretion
- GI bleeding; Oronasal bleeding

## [08] 3<sup>rd</sup> - 6<sup>th</sup> day

- Vasopressor was discontinued
- Urine amount increased to 1980mL/24hr
- FiO<sub>2</sub> 80 → 40%
- Bleeding improved

# [08] 7<sup>th</sup> day

- Hypotension. Anuria.
- Norepinephrine ↑↑
- FiO<sub>2</sub> 50 → 60 → 100%
- Abx switch to imipenem (10 hours after shock)
  
- Expired on 7<sup>th</sup> day



# [08] Killed by VAP with bacteremia

- Blood culture: MDR *Klebsiella pneumoniae* resistant to
  - all penicillins
  - cephalosporins
  - gentamicin

# Cause of death among patient with dengue at NCKUH, 2015

	Death $\leq$ 7 days n = 40	Death $>$ 7 days n = 20
Cause of death		
Severe dengue	24 (60%)	4 (20%)
Secondary infections	14 (35%)	10 (50%)
Pneumonia	6 (13.3%)	8 (40%)

Severe dengue: die of severe plasma leakage, major bleeding, or organ failure in the critical phase.



[Case 09, summer 2017]

85-year-old woman.

Atrial fibrillation history. ADL independent.

Fever, chills, cough, malaise, myalgia for 3 days.  
Hypoglycemia with altered consciousness.

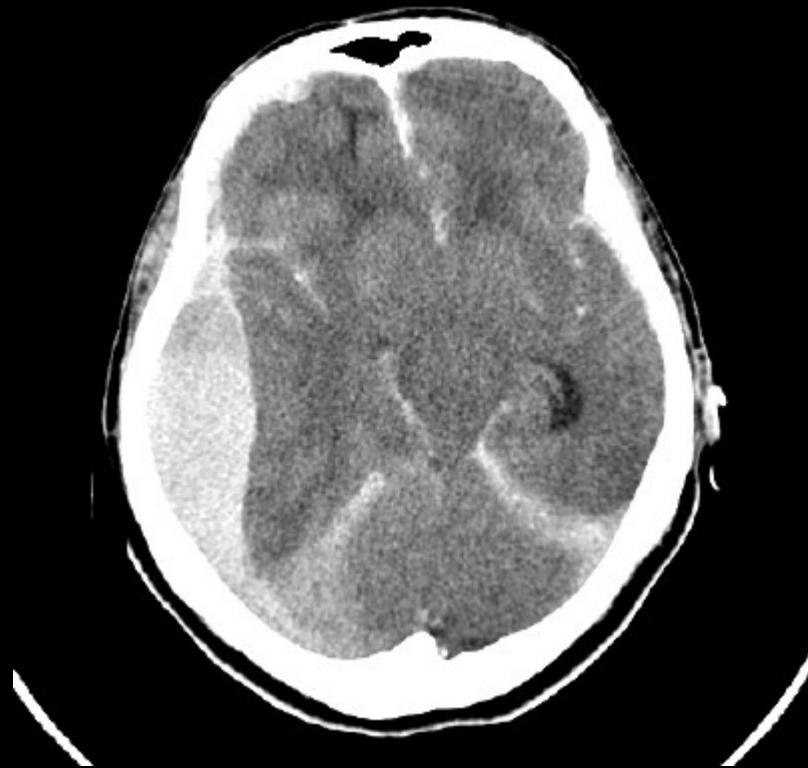
Consciousness improved but shock.

Chest X ray: bilateral patches

Intubation and mechanical ventilation at ED

WBC	Hb	Plt	PT-INR	aPTT	Cr	AST	ALT	Bil-T
5.4	14.9	27	2.44	47.50	2.25	14821	3439	1.2
CRP	pH	PCO2	HCO3	Dengue NS1 Ag	Dengue IgM	Dengue IgG		
40.5	7.27	52.0	21.0	Positive	Negative	Positive		

[09] Altered consciousness again  
within 12 hours after ICU admission



Brain CT: Acute SDH with mass effect; SAH

# [09] Not dengue, but influenza!

- Dengue PCR: negative
- Dengue IgM (ELISA): negative x2
- Dengue IgG (ELISA): negative x2
  
- Throat swab: influenza A/H3 (PCR & isolation)
- Sputum: influenza A/H3 (PCR)

# Not all patients with positive NS1 rapid test have dengue

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Age/Sex	Acute diseases with <b>false positive</b> dengue NS1 rapid test, 2016-2017
37y/M	Lemierre's syndrome with <i>Fusobacterium necrophorum</i> bacteremia and <b>septic shock</b>
58y/M	Spondylodiskitis and psoas muscle abscess with MRSA bacteremia and <b>septic shock</b>
10m/F	Roseolla infantum
19y/M	Acute suppurative tonsillitis
78y/F	Acute ischemic stroke
65y/M	Scrub typhus
85y/F	Influenza A(H3) with <b>septic shock</b>

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Conslusion



Assess your patient frequently  
during the critical phase

Fig from Wikipedia

# Take Home Messages

- High index of suspicion during epidemic periods
- Dengue shock is mainly hypovolemic shock caused by plasma leakage, not septic shock
- Adequate fluid resuscitation to restore organ perfusion at the right time
- The critical phase lasts for 48 hours
- Manage its complications and associated diseases cautiously
- Frequent re-assessment is invaluable

登革熱重症病人  
絕大部份日常生活都能自理  
是重症照護最能發揮效用的病人群