

# Case discussion

## acute liver failure and Illness Scripts

### Acute liver failure Causes and management

Cheng-Yi WANG  
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- Q1, 急性肝衰竭有很多不同的原因你認為哪一個原因是最容易控制的就是能夠達到預防的目的.

# Ans: Acetaminophen

- 根據目前的臨床與公共衛生資料，藥物性肝損傷，尤其是由「乙醯胺酚」（acetaminophen，也就是普拿疼）過量引起的急性肝衰竭，是最容易透過行為改變與教育來預防的原因之一。

## 為什麼藥物性肝損傷最容易控制？

- 機制明確：乙醯胺酚在肝臟代謝時會產生毒性中間產物，過量時肝臟無法解毒，導致細胞壞死。
- 風險可預測：劑量超過每日建議（成人約4克）就有危險，尤其是多種藥物同時含有此成分時。
- 預防策略清晰：
  - 教育民眾不要自行混用退燒止痛藥。
  - 清楚標示藥品成分與劑量。
  - 建立藥師與醫師的用藥衛教機制。
  - 對高風險族群（如肝病患者）加強用藥監控。

## 相較之下，其他原因的預防難度

原因類型	預防難度	說明
B型肝炎病毒感染	中等	可透過疫苗與抗病毒藥物控制，但需長期追蹤與高覆蓋率。
草藥與偏方毒性	中等	須改變文化習慣與信任來源，教育挑戰較大。
酒精性肝損傷	中等偏高	涉及成癮行為與社會支持系統，需多層介入。
自體免疫或代謝疾病	高	難以預測與預防，多依賴早期診斷與專科治療。

## 總結

若以「可控性高、教育與制度可介入」為標準，藥物性肝損傷是最容易預防的急性肝衰竭原因。這也意味著，透過病人教育、醫療監管與社會宣導，可以大幅降低這類肝衰竭的發生率。

# 藥物過量導致急性肝衰竭

## 學生角色

- 急診住院醫師
- 護理師
- 家屬溝通者（可由學生扮演或由教師引導）

### 病人設定

- 姓名：林小姐，32歲
- 主訴：持續噁心、嘔吐、倦怠、右上腹悶痛
- 病史：三天前因感冒自行服用多種成藥（含乙醯胺酚），未注意劑量
- 現況：意識清楚但疲憊，皮膚略黃，肝功能指數急升，凝血功能異常

- A. History taking---Doctor/nurse/family
- B. 衛教重點：
- C. 如何說明及溝通事項特別注意情緒的支持



## ✓ 用藥安全衛教

- 「很多感冒藥都含有乙醯胺酚，重複服用容易超量。」
- 「成人每日最多攝取量是4克，但有肝病或營養不良者要更少。」
- 「請務必閱讀藥品成分標示，或詢問藥師。」

D. 設計一張簡明的「成藥安全衛教單張



## 1. 建立「成分導向」的衛教語言

- 不再只說「不要吃太多普拿疼」，而是說：
  - 請注意是否重複服用了含『乙醯胺酚』的藥物，不論品牌名稱為何。」
- 教導病人辨識：
  - 英文：Acetaminophen、Paracetamol
  - 中文：乙醯胺酚、撲熱息痛

## 2. 設計「成藥成分辨識卡」或「藥品成分速查表」

- 可列出常見含乙醯胺酚的商品名與外觀
- 搭配圖像與劑量標示，協助病人快速辨識

## 3. 推動藥局與診所的「成分標示優化」

- 鼓勵藥師在藥袋上加註「本藥含乙醯胺酚」

建議藥廠在包裝正面以紅字標示「含乙醯胺酚」

## 4. 教學模擬：讓學生練習「成分辨識與衛教對話」

- 例如：「病人拿出三種感冒藥，請學生判斷是否重複攝取乙醯胺酚」

## Acetaminophen Toxicity

[Rachel Whittaker](#) \*✉, [Navneet Cheema](#) \*

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University of Chicago, Department of Emergency Medicine, Chicago, IL

對乙醯氨基酚 (APAP) 是一種常用於成人和兒童的非處方藥。

雖然對乙醯氨基酚已被證實在治療劑量下相當安全且耐受性良好，但過量服用會導致嚴重的肝毒性

。對乙醯氨基酚毒性是美國急性肝衰竭最常見的原因，約佔所有報告病例的 50% 和肝臟移植的 20%。

2021年，中毒控制中心收到超過 80,000 起涉及含對乙醯氨基酚產品的病例

**病例摘要：**27歲女性，無重要既往病史，自昨日起因右上腹痛乘坐私家車前往急診就診。患者近期患有偏頭痛，並服用非處方藥（對乙醯氨基酚）止痛。她已連續多日服用數把對乙醯氨基酚，現表現為慢性對乙醯氨基酚中毒，並伴隨非血性、非膽汁性嘔吐。

**既往病史 (PMH)：**無已知疾病

She took an over-the-counter medicine (acetaminophen) for her pain.

**既往手術史 (PSH)：**無

**藥物：**無處方藥。近期服用過對乙醯氨基酚。

**過敏：**沒有已知的藥物過敏。

**家族及社會史：**不飲酒。無違禁物質。無重大家族史。

### Synopsis of Physical Exam:

T 98.6° F Oral, BP 115/75, HR 114, RR 18, Pulse Ox: 100% on RA.

Patient appears uncomfortable secondary to pain with scleral icterus, jaundiced skin, dry mucous membranes, and tenderness to palpation (TTP) in right upper quadrant of abdomen.

醫生您好，這是結構化訪談案例，不設角色扮演。為了回答我將要提出的問題，請提供一份您需要收集的資訊清單，以便最終做出診斷。有時，我可能會打斷您，讓您回顧整個案例；但這並非對您表現的反映。您將有15分鐘的時間來完成案例。在我們開始之前，您還有什麼問題嗎？

“患者是一名 27 歲的女性，出現嘔吐和右上腹痛症狀。”

年齡：	二十七
性別：	女性
到達方式：	私家車
主要投訴：	右上腹痛
提供病史的人：	病人

# 確認現在病史及嚴重性

整體表現/現病史： 患者自昨天起出現右上腹疼痛。今天還出現嘔吐。患者表示近期偏頭痛嚴重，需服用大量非處方藥。

確認嘔吐的狀況及量

- 1. 這是關於該患者的初步資訊。您閱讀完後，請給我一份您希望獲得的額外病史資訊的清單。
- 1). 例如：哪種非處方藥？用藥數量/劑量/頻率/療程？相關症狀（發燒、腹瀉、黃疸等）？
- 2). 社會史（飲酒和藥物濫用）？

1. 患者很少飲酒。沒有靜脈注射毒品。
2. 近期無旅遊史
3. 她沒有膽囊疾病病史。
4. 沒有出現黑便或嘔血。
5. 她已經服用對乙醯氨基酚治療偏頭痛好幾天了。她不確定特定的劑量，但每次頭痛加劇時，她都會服用一大把，因為她只想緩解疼痛。過去五天裡，她每天都服用好幾大把。

**Physical findings:** “根據您現在所了解的情況，請給我列出您想要尋找的具體體檢結果。”

例如：評估腹部檢查時壓痛的位置、脫水的徵兆、腹膜的徵兆、黃疸的存在

**Vital Signs:**

**Temp:** 96.6° F

**BP:** 115/75

**P:** 114

**RR:** 18

**Pulse Ox:** 100% on room air

### 評分準則：

基本原理：學習者應專注於檢查患者的腹部（壓痛部位、有無反跳痛或肌衛），並根據患者的對乙醯氨基酚攝入史評估是否有肝損傷的跡象（是否有皮膚黃疸、鞏膜黃疸）。他們還應根據患者的心動過速和嘔吐史（皮膚緊張度、毛細血管再充盈、黏膜乾燥）評估是否有脫水的跡象。

# Physical findings:

“您的體檢結果如下：”

- **整體外觀**：清醒、警覺，檢查時顯得不舒服。
- **生命徵象**：口腔溫度 98.6°F，血壓 115/75，心跳 114，呼吸頻率 18，脈搏血氧飽和度：RA 為 100%。
- **頭部**：頭型正常，無創傷。
- **眼睛**：鞏膜黃染，瞳孔大小相等，呈圓形，對光和調節有反應 (PERRLA) (4 毫米至 3 毫米)。
- **耳朵**：外部檢查正常，耳道和鼓膜 (TM) 正常。
- **口腔/喉嚨**：黏膜乾燥。
- **頸部**：柔軟，活動範圍充分，無頸部淋巴結腫大。
- **皮膚**：皮膚黃疸，無皮疹。
- **肺部**：雙側聽診清晰，氣體流通良好。
- **心臟**：心跳過速，無雜音、摩擦音或奔馬律。
- **腹部**：右上腹TTP，無反跳痛或肌衛，墨菲徵陰性，大便潛血陰性。
- **四肢**：脈搏良好，無杵狀指、紫紺或水腫。
- **神經系統**：警覺，對人、地點、時間有定向力 (AOX3)，腦神經 II-XII 正常，四肢肌力 5/5，感覺正常，小腦檢查正常，反射正常。
- **心理**：情緒和情緒正常，沒有自殺意念。

# Laboratory EXAMINATION

WBC	$5.4 \times 10^3/\mu\text{L}$
Hgb	12.0 g/dL
Hct	36%
Platelets	$173 \times 10^3/\mu\text{L}$

PTT:	33.8 seconds
PT:	15.1 seconds
INR:	1.2

Na	142 mEq/L
K	3.4 mEq/L
Cl	92 mEq/L
CO2	22 mEq/L
BUN	16 mg/dL
Cr	0.9 mg/dL
Glucose	86 mg/dL
ALT	194 Units/L
AST	137 Units/L
Alk phos	104 Units/L
Serum bilirubin	3.4 mg/dL (total) 0.3mg/dL (direct)

您如何解釋這些結果？

「根據您現在所知道的，根據最可能的病症，您的鑑別診斷中最重要的三項是什麼？」（如果提到了三種以上的病症，請說：「好的，謝謝。請告訴我您最可能的三種診斷，而且只有三種。」）

適當的鑑別診斷範例包括：

- 對乙醯氨基酚毒性
- 病毒性肝炎
- 肝膽疾病
- 酒精性肝炎
- 胰臟炎
- 自體免疫性肝炎
- 布德-加利氏症候群
- 化膿性肝膿腫
- 盲腸後闌尾炎
- 菲茨-休·柯蒂斯綜合徵
- Acetaminophen toxicity
- Viral hepatitis
- Hepatobiliary disease
- Alcohol hepatitis
- Pancreatitis
- Autoimmune hepatitis
- Budd-Chiari syndrome
- Pyogenic liver abscess
- Retrocecal appendicitis
- Fitz-Hugh Curtis syndrome

# 挑出2種檢查最能夠幫助你的診斷

## DIAGNOSTIC STUDIES

Prompt 6:

“Based on what you know and your working differential diagnosis, what, if any, diagnostic studies would you order?”

Prompt 7:

“Doctor, you ordered X. Why X?”

***ASK THIS PROMPT TWICE ABOUT TWO SEPARATE TOPICS***

**Urine Drug Screen:**

Ethanol Screen:	None Detected
Amphetamines:	None Detected
Barbiturates:	None Detected
Benzodiazepines:	None Detected
Cocaine:	None Detected
Opiates:	None Detected
Phencyclidine (PCP):	None Detected
Methadone:	None Detected
Oxycodone Screen:	None Detected
Fentanyl, Urine	None Detected

**Serum Alcohol:**

<25 mg/dL

Stimulus #6

APAP, Salicylate level

Acetaminophen:

327  $\mu$ g/mL

Salicylates:

<1 mg/dL

#### Right Upper Quadrant US

No evidence of gallstones. No gallbladder wall thickening. No pericholecystic fluid.

## **TREATMENT AND OTHER ACTIONS**

Prompt 8:

“Based on what you now know, what treatments, if any, would you order and/or what actions, if any, would you perform?”

Prompt 9:

“Doctor, you ordered X. Why X?”

## ***ASK THIS PROMPT TWICE ABOUT TWO SEPARATE TOPICS***

*Examples: “Doctor, you ordered intravenous fluids (IVFs), why IVFs? Doctor, you ordered N-Acetylcysteine (NAC), why NAC?”*

Scoring Guidelines:

Rationale: NAC for elevated acetaminophen level and abnormal liver function tests (LFTs)  
(chronic ingestions so unable to use Rumack-Matthews nomogram)

Intravenous fluids (IVFs) for tachycardia and dry mucous membranes on exam

## FINAL DIAGNOSIS

Prompt 10:

“Based on everything you know about this case, what is your final diagnosis?”

1. Acetaminophen toxicity

### Scoring Guidelines:

Rationale: Verbalizing acetaminophen toxicity or acetaminophen overdose meets the critical action. If the candidate mentions something vague such as abdominal pain or liver dysfunction, examiner asks “Can you be more specific about the diagnosis?”

# 處置

Prompt 11:

“Based on what you know, what should be the disposition of this patient?”

Prompt 12:

“Why would you [admit/discharge] this patient?”

# 必須住院，並觀察肝功能的變化， 必要給解毒劑

## 評分準則：

理由：口頭說明因對乙醯氨基酚中毒而需要重症監護病房 (ICU) 級別的入院治療，並解釋密切監測肝功能、併發症和解毒劑管理 (NAC) 的必要性。

## TRANSITION OF CARE

Prompt 13:

“What specific actions would you take at the time of [admission/discharge]?

評分準則：

理由：口頭表達最後的行動，例如向患者解釋診斷、向重症監護團隊簽署護理協議以及聯繫中毒中心或肝臟服務部門以獲取進一步的建議。

## Acute Liver Failure: Is Acetaminophen the Only Culprit?

Scott D McLaughlin <sup>1,✉</sup>, Jason Z Amaral <sup>2</sup>, Joshua Thomas <sup>3</sup>, Keith Z Amaral <sup>4</sup>, Anthony Scalzo <sup>5</sup>

Editors: Alexander Muacevic, John R Adler

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<sup>1</sup> Department of Internal Medicine, Advocate Lutheran General Hospital, Park Ridge, USA

<sup>2</sup> Department of Orthopedic Surgery, Texas Children's Hospital, Baylor College of Medicine, Houston, USA

- (EBV) 是一種常見的皰疹病毒，與傳染性單核細胞增多症和肝炎等罕見併發症有關。急性感染期間的 EBV 相關性肝炎可能會改變肝臟代謝，增加藥物毒性的風險。
- 一例 16 歲急性 EBV 感染女性病例，該女性在服用用於緩解偏頭痛的對乙醯氨基酚後出現嚴重的毒性反應。N-乙醯半胱氨酸(**N-acetylcysteine**)對她的病情無反應，但加用甲吡唑(**fomepizole**)後病情有所改善。甲吡唑可能透過抑制 CYP2E1 並抑制發炎來減少 N-乙醯對苯醌亞胺 (NAPQI) 的產生，從而減輕肝損傷。  
(reducing N-acetyl-p-benzoquinone imine (NAPQI) production via CYP2E1 inhibition and suppressing inflammation.

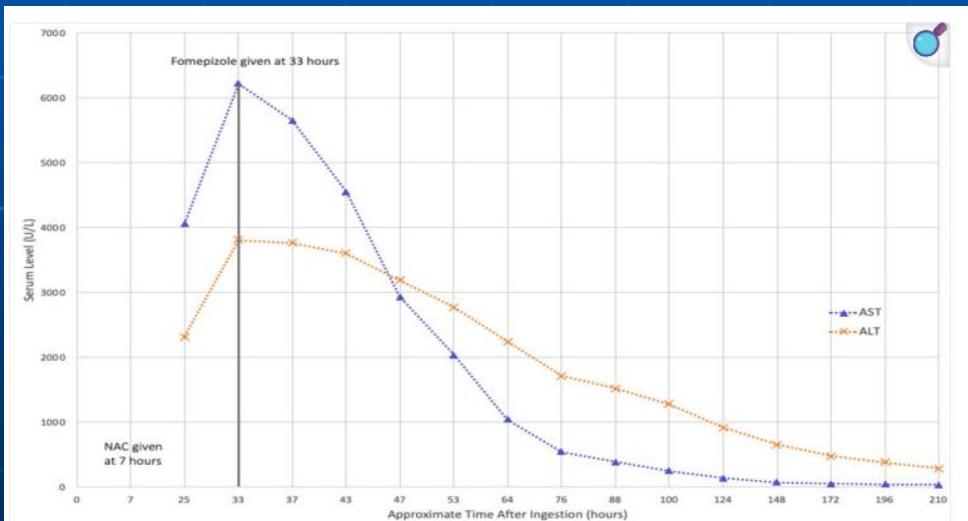
# 急性肝衰竭：對乙醯氨基酚是唯一的罪魁禍首嗎？

# Laboratory findings

- Laboratory values were significant for K 5.5 mmol/L, HCO<sub>3</sub> 18 mmol/L, aspartate transaminase (AST) 3,812 IU/L, alanine aminotransferase (ALT) 6,222 IU/L, international normalized ratio (INR) 2.5, prothrombin time (PT) 26.8 sec, and ammonia 119 µmol/L. Comprehensive urine drug screening (UDS) was positive for tetrahydrocannabinol (THC). The patient had undetectable ethanol and salicylate levels. An acetaminophen level was found to be 24 mcg/mL at ~24 h post-ingestion . NAC infusion at 12.5 mg/kg/hour was initiated at this time.
- EBV PCR was positive, EBV Capsid Ag IgM was elevated (96.4), and EBV Capsid Ag IgG was negative.

Ammonia	119 µmol/L	9-26 µmol/L
AST	3,812 IU/L	5-40 U/L
ALT	6,222 IU/L	7-56 U/L
PT	26.8 seconds	10.0-14.0 seconds
INR	2.5	0.8-1.2
Ethanol Levels	Undetectable	Undetectable
Salicylate Levels	Undetectable	Undetectable
Acetaminophen Level (24 Hours Post-ingestion)	24 mcg/mL	0 mcg/mL

- Addition of a fomepizole IV loading dose of 15 mg/kg to prevent additional hepatic injury in the setting of refractory LFT elevations. AST and ALT levels slowly decreased and she was eventually cleared for discharge with instructions for strict outpatient follow-up



Approximate Time Post-ingestion (hours)	AST (U/L)	ALT (U/L)
25	4,062	2,314
33	6,222	3,812
37	5,657	3,764
43	4,552	3,601
47	2,931	3,192
53	2,033	2,770
64	1,045	2,244
76	543	1,709
88	387	1,519
100	251	1,281
124	139	915
148	74	654
172	47	478
196	41	377
210	37	284

4-甲基吡唑 (INN: fomepizole) 是一種用於治療甲醇或乙二醇中毒的藥物。  
 [1]可單獨使用，也可與血液透析同時使用。[1]通常利用靜脈注射的方式給藥。[1]

# EBV 會加重acetaminophen引發的肝臟毒性

- acetaminophen引發的肝臟毒性是不可否認的事實.所以臨床上應該注意不要長期使用,用量也要減少.

哈佛醫學院與Oxford Academic的報告：

- 劑量接近4000mg時，部分人仍可能出現肝毒性，尤其是：
- 體型較小者
- 有肝病、酗酒、營養不良、禁食者
- 長期服用acetaminophen者

哈佛健康建議：每日劑量應盡量控制在3000mg以下，尤其是高風險族群。

臨床實務建議：

- 單次劑量不超過 500 mg
- 每日總劑量不超過 3000mg

# Case history

- A 26-year-old nonalcoholic female presented to the emergency department with a history of 4 days fever which was intermittent; the maximum temperature recorded was 102°F, associated with headache, retroorbital pain, and myalgia but without chills and rigor.

一個年輕的女性發高燒(hight fever) 4天在病史上  
你還想知道一些什麼來解決發燒的原因

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1. There was no history of mucocutaneous bleeding or bruises.
- 2. There was a history of multiple episodes of nausea and vomiting along with diffuse abdominal pain and distension, loss of appetite, and the generalized weakness associated with acute shortness of breath.
- 3. There was no history of chest pain, palpitation, orthopnea, dizziness, loss of consciousness, abnormal body movements, or altered sensorium. There was no similar history in the past.
- 4. Gyn-Obs history---病人否認有任何性關係,LMP: 3天前OK
- 5. 有沒有被蟲咬或被蚊子咬的病史.

Physical examination 要特別注意哪一些變化?

# Physical examination 要特別注意哪一些變化？

- On examination, her blood pressure was 100/60 without a significant postural drop, pulse was 106 beats/min, oxygen saturation at room temperature was 98%, respiratory rate was 20/min, and the temperature was 101.4°F. **She was well-oriented to time, place, and person.** On abdominal examination, it was grossly distended with dull percussion with decreased bowel sound. There was the presence of crackles over the lower surface of both lung fields. Her heart sound was normal.

- 1.體溫與脈搏的變化有沒有相對性的脈搏緩慢(relative bradycardia)
- 2.有無皮膚出血的徵象破文整叮咬的傷口或紅腫
- 3.有無肺炎注意兩邊肺的呼吸聲.
- 4.血氧濃度:室溫氧飽和度為 98%，呼吸頻率為 20/分，
- 4.腹部檢查有無腹膜炎的徵象,特別注意疼痛的位置在何處確定是否需要找 婦科做內診

抽血檢查要特別注意哪一些事項?

# 請問血液檢查 有什麼異常？

**Table 1****Investigations done on the day of admission**

Investigations	Results	Reference range
Total leukocyte count (cells/mm <sup>3</sup> )	11 950	4000–11 000
Differential count (%)	Neutrophils: 60.90, lymphocytes: 34.30	Neutrophils: 40–70, lymphocytes: 20–45
Hemoglobin (g%)	12.4	11.9–14.6
Packed cell volume (%)	35.20	40–50
Platelets (cells/mm <sup>3</sup> )	78 000	150 000–450 000
Alanine transaminase (U/l)	2202	9.0–52
Aspartate transaminase (U/l)	74 160	14–36
Total bilirubin (mg/dl)	4.70	0.2–1.3
Conjugated bilirubin (mg/dl)	1.40	0–0.3
Unconjugated bilirubin (mg/dl)	1.20	0.01
Alkaline phosphatase (U/l)	311	30–126
Prothrombin time (s)	19.50	11.0–16
Control (s)	14	
Random blood glucose (mg/dl)	60	80–140
C-reactive protein (mg/l)	87	0–10
Creatinine (mg/dl)	0.60	0.52–1.04
Urea (mg/dl)	19	15–45
Total protein, serum (g/dl)	5.30	6.3–8.2
Albumin, serum (g/dl)	2.20	3.5–5.0
Serum lactate (mmol/l)	5.1	0.7–2.0

- 1.白血球增加
- 2.中性球增加
- 3.血小板明顯減少
- 4.AST很高
- 5.ALT很高
6. AST>>ALT
- 7.ALK-P-tase不正常
- 8.血膽色素不正常
- 9.非結合性膽色素很高
10. Prothrombin time 延長
- 11.血糖稍低
12. CRP明顯增高
13. Cr:正常
14. Serum Albumin很低
15. Serum lactate增高

這些結果代表什麼意義.

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這些結果代表什麼意義.

- 1.感染發炎,
- 2.極嚴重肝細胞壞死
- 3.血清白蛋白偏低可能是肝功能萎縮造成
4. Metabolic acidosis.



Acute liver failure

# Blood examination

- 1.瘧疾、肝炎病毒、恙蟲病和鉤端螺旋體的血液檢查結果為陰性。malaria, hepatitis viruses, scrub typhus, and leptospira were negative.
- 2.但在她的血液中檢測到登革熱病毒抗原非結構蛋白1 dengue viral antigen nonstructural protein 1 was detected in her blood.

dengue viral antigen nonstructural protein 1,這是什麼？

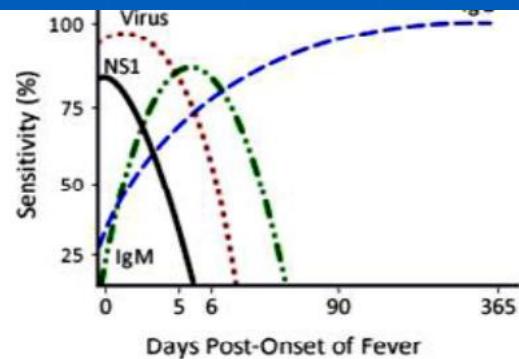
Hong-Ru Chen, Yen-Chung Lai & Trai-Ming Yeh

Dengue virus non-structural protein 1: a pathogenic factor, therapeutic target, and vaccine candidate *Journal of Biomedical Science J Biomed Sci* 25, 58 (2018).

Dengue virus (DENV) infection is the most common mosquito-transmitted viral infection. DENV infection can cause mild dengue fever or severe dengue hemorrhagic fever (DHF)/**dengue shock syndrome (DSS)**. Hemorrhage and vascular leakage are two characteristic symptoms of DHF/DSS. However, due to the limited understanding of dengue pathogenesis, no satisfactory therapies to treat nor vaccine to prevent dengue infection are available, and the mortality of DHF/DSS is still high. **DENV nonstructural protein 1 (NS1)**, which can be secreted in patients' sera, has been used as an early diagnostic marker for **dengue infection** for many years. However, the roles of NS1 in dengue-induced vascular leakage were described only recently. In this article, the pathogenic roles of DENV NS1 in hemorrhage and vascular leakage are reviewed, and the possibility of using NS1 as a therapeutic target and vaccine candidate is discussed.

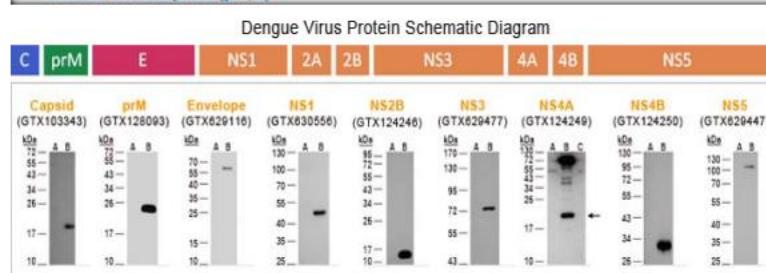
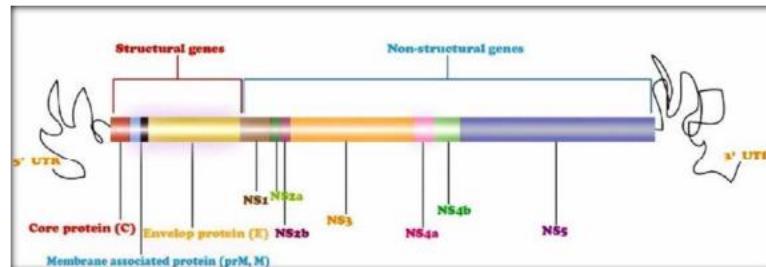
# 登革熱確定診斷的依據

- (一) 臨床檢體(血液)分離並鑑定出登革病毒。
- (二) 臨床檢體分子生物學核酸檢測陽性。
- (三) 血清學抗原(登革病毒的非結構蛋白**non-structural protein 1**，簡稱**NS1**)檢測陽性。
- (四) 急性期(或初次採檢)血清中，登革病毒特異性**IgM**或**IgG**抗體為陽性者。
- (五) 成對血清(恢復期及急性期)中，登革病毒特異性**IgM**或**IgG**抗體(二者任一)有陽轉或 $\geq 4$ 倍上升。



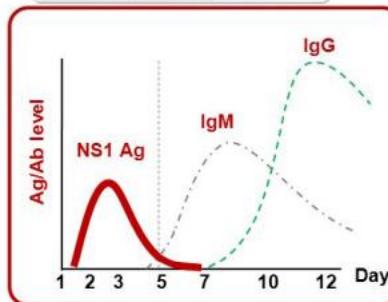
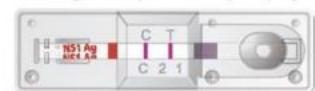
# 登革熱確定診斷之依據

~登革病毒的結構包括3種結構蛋白(**structural protein**)和7種非結構蛋白(**nonstructural protein**)，其中非結構蛋白**NS1 antigen**在感染初期可於感染者血清中偵測到，所以用來研發登革熱快速診斷試劑。目前市售的快速診斷試劑可用人體血清、血漿或全血來進行定性檢測，操作方法簡便，約20–30分鐘可知道檢驗結果。目前市售登革熱**NS1**抗原快速診斷試劑有些可檢驗**NS1**抗原；有些並可合併**IgM**、**IgG**抗體檢測。



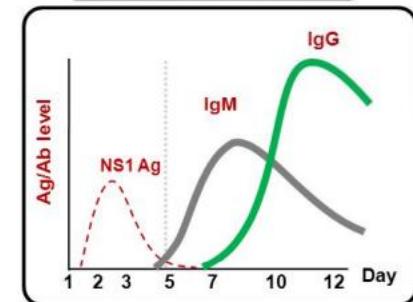
## NS1 Ag

3 drops (110  $\mu$ l) of plasma or serum for early acute phase samples (day 1 ~5)



## IgG/IgM Ab

10  $\mu$ l of plasma or serum for early convalescence phase samples (after day 5 ~14)



Slide courtesy of Dr. Subhamoy Pal

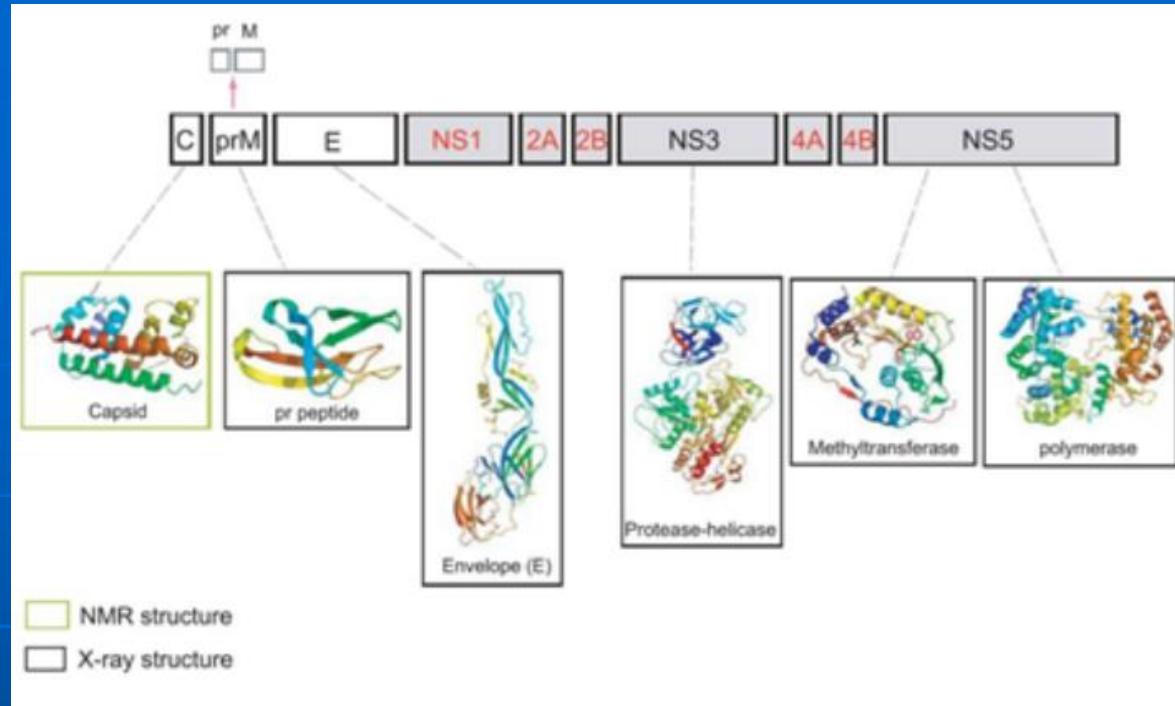
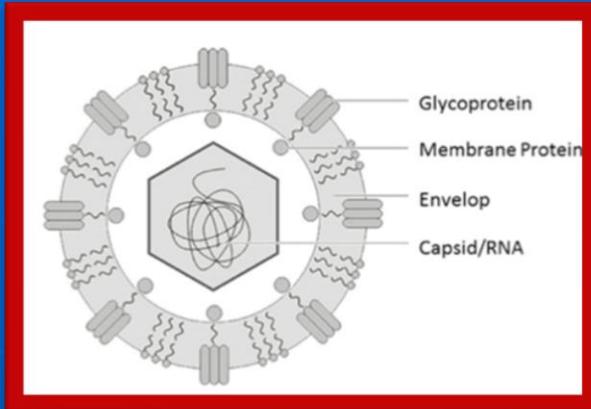


Fig. 2 Structural proteome of dengue virus

**Dengue Fever virus is a RNA virus and homogeneous to West Nile virus, Japanese encephalitis virus and yellow fever virus.** Genome of the dengue virus contains about 11,000 nucleotide bases, which code three different types of protein molecules (C, prM and E) that form the virus particle and seven other types of protein molecules that are found in infected host cells only and are required for life cycle of the virus.

1. **Capsid protein (C)** Capsid protein (12 kDa) of mature DENV is highly basic
2. **Membrane protein (prM/M)** prM, also termed as precursor-membrane protein,
3. **Envelope protein (E)** Envelope protein is a glycoprotein belonging to class II viral membrane fusion protein
4. **Non-structural protein (NS)** The seven non-structural proteins include NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5. NS1 plays important role in structural stability and secretion of NS1 in dimeric

# 2023臺灣登革熱 一定要了解

全國登革熱本土病例及境外移入病例統計表-依發病日

最近一例發病日	臺灣 2018 年-2022 年登革熱之疫情					2024/02/04
2024年5週 (上週累計數)	發病年份	確定病例	本土登革 重症	主要流行地區 (本土病例數)	備註	10
2024年6週 (本週累計數)	2018	533	1	臺中市(113)、新北市(44)、高雄市(12)、彰化縣(8)、臺北市(2)、嘉義縣(2)、桃園市(1)、臺南市(1)	本土(183)、境外(350)	2
2024年02月 (本月累計數)	2019	640	0	高雄市(58)、臺南市(31)、新北市(7)、臺北市(2)、桃園市(1)、臺中市(1)	本土(100)、境外(540)	5
2024年 (今年累計數)	2020	137	0	新北市(50)、桃園市(23)	本土(64)、境外(73)	125
2023年(去年總數)	2021	12	0	-	本土(0)、境外(12)	<b>@@@ 26703</b>
上週與前三週平均數比較 (病例數)	2022	88	0	高雄市(18)、臺中市(2)	本土(20)、境外(68)	△16.33
上週與過去三年同期平均數比較 (病例數)						△8.67
今年累計死亡數						0

聯合新聞網  
<https://udn.com> 生活 :

8年來最嚴峻！登革熱攻陷西台灣病例暴增醫療恐崩盤

2023年9月10日 — 氣候暖化改變本土登革熱地圖。前疾管局局長蘇益仁表示，過去埃及斑蚊僅在現在嘉義以南，位在嘉義以北的雲...

賴人包 / 台灣登革熱疫情創十年新高 已出現9例重症！醫師揭兩關鍵防蚊

三立新聞網  
更新時間：2023年8月6日

2023.08.06

據疾管署統計，今年本土登革熱病例截至2023.09.09為止，共有五九一三例、廿四例重症、九例死亡。2023.09.24 破1萬例。

疾管署2023.12.05新聞文稿：疾管署指出，國內整體疫情呈下降趨勢，今年截至12月4日累計25,470例本土病例。判斷錯誤或疫情不透明

# 2024年臺灣登革熱病例數降低

全國登革熱本土病例及境外移入病例統計表-依發病日

最近一例發病日	2024/09/25
2024年38週 (上週累計數)	14
2024年39週 (本週累計數)	9
2024年09月 (本月累計數)	39
2024年 (今年累計數)	398
2023年(去年總數)	26706
上週與前三週平均數比較 (病例數)	△6
上週與過去三年同期平均數比較 (病例數)	▽672
今年累計死亡數	0

截至11月20日累計24,287例本土病例今年(2023)累計本土重症病例124例，年齡介於未滿10歲至90歲以上，分別為臺南市99例、雲

林縣15例、高雄市8例及屏東縣2例，另**累計死亡病例52例.** (2023.01.01-2023.11.20)

# 2024.台灣登革熱疫情明顯升高

- 2024年台灣登革熱疫情明顯升高，根據高雄市政府衛生局統計，截至2024年10月19日（第42週）：
  - 全台登革熱通報與確診情況
    - 總通報病例數：35,155例
    - 陽性病例數：466例
    - 本土確診個案：237例
    - 境外移入個案：229例
  - 其中高雄市疫情最為嚴重：
    - 高雄市通報病例數：25,386例
    - 陽性病例數：166例
    - 本土個案：137例
    - 境外移入個案：29例
- 截至2024年9月11日，台灣累計登革熱死亡病例數為9例。
  - □ 死亡個案特徵
    - 年齡介於40多歲至70多歲。
    - 多數具潛在疾病（如糖尿病、腎病、慢性病等）。
    - 發病後1至7日內病情惡化，不幸過世。
    - 死亡個案主要集中在南部疫情熱區，尤其臺南市。
  - ✅ 疾管署提醒

## 為什麼差距大？

- **症狀相似疾病多**：流感、腸病毒、其他病毒感染也會發燒、肌肉痛，容易被懷疑為登革熱。
- **防疫策略保守**：台灣採「疑似就通報」原則，寧可多報也不漏報，尤其在高風險地區。
- **檢驗排除率高**：通報後經檢驗排除者占多數，尤其在疫情初期或非流行季節。

## 延伸思考：這種差距其實是好事

- 顯示防疫系統「警覺性高」。
- 有助於早期介入、環境清理、病媒蚊監測。
- 也能作為社區衛教的切入點：讓民眾理解「通報不等於確診」，避免恐慌。

# 通報數字被績效導向扭曲，不僅會影響防疫判斷，更可能削弱整體公共衛生信任與行動力。

## ⚠️ 多報少爭 vs 防疫真相：潛在影響

面向	負面影響
疫情評估失真	通報數過高但陽性率低，可能誤導資源分配或誤判疫情趨勢。
基層疲勞與冷漠	若通報被視為績效壓力，基層人員可能產生「報了也沒用」的倦怠感。
社區信任流失	民眾若察覺通報與實際風險不符，可能對防疫指令產生懷疑。
政策失焦	上層若只看通報數字而忽略現場情境，可能制定出不符實際的措施。

### 💡 如何避免這種偏差？

- 1. 通報品質指標化**：不只看數量，也看「通報後是否有後續處置」、「是否為高風險族群」等。
- 2. 回饋機制透明化**：讓基層知道通報後的檢驗結果與後續行動，建立正向循環。
- 3. 教育與動員並重**：通報不只是績效，而是社區參與防疫的具體行動。

「通報後是否有後續處置」

# 「通報後是否有後續處置」

■ 登革熱的通報若沒有後續處置，就會淪為「形式上的警覺」，無法真正阻止疫情擴散。以下是理想的「通報後續處置流程」

## 1. 檢驗確認

- 快速檢驗：NS1抗原、PCR、IgM抗體等。
- 結果回報時效：理想在24–48小時內通知通報單位與病人。

## 2. 病媒蚊調查與環境處置

- 病人家住與活動地點調查：是否有積水容器、病媒蚊孳生源。
- 病媒密度監測：使用誘蚊燈、誘卵器等工具。
- 立即清除積水：動員社區或環保單位進行「巡、倒、清、刷」。
- 必要時化學防治：噴藥滅蚊，但須搭配社區溝通與風險告知。

## 3. 個案追蹤與衛教

- 病人衛教：避免被蚊子叮咬、居家休息、警覺重症徵象。
- 接觸者提醒：家人、鄰居若出現症狀應儘速就醫。
- 社區通報與動員：透過里長、社區幹部進行環境清理與宣導。

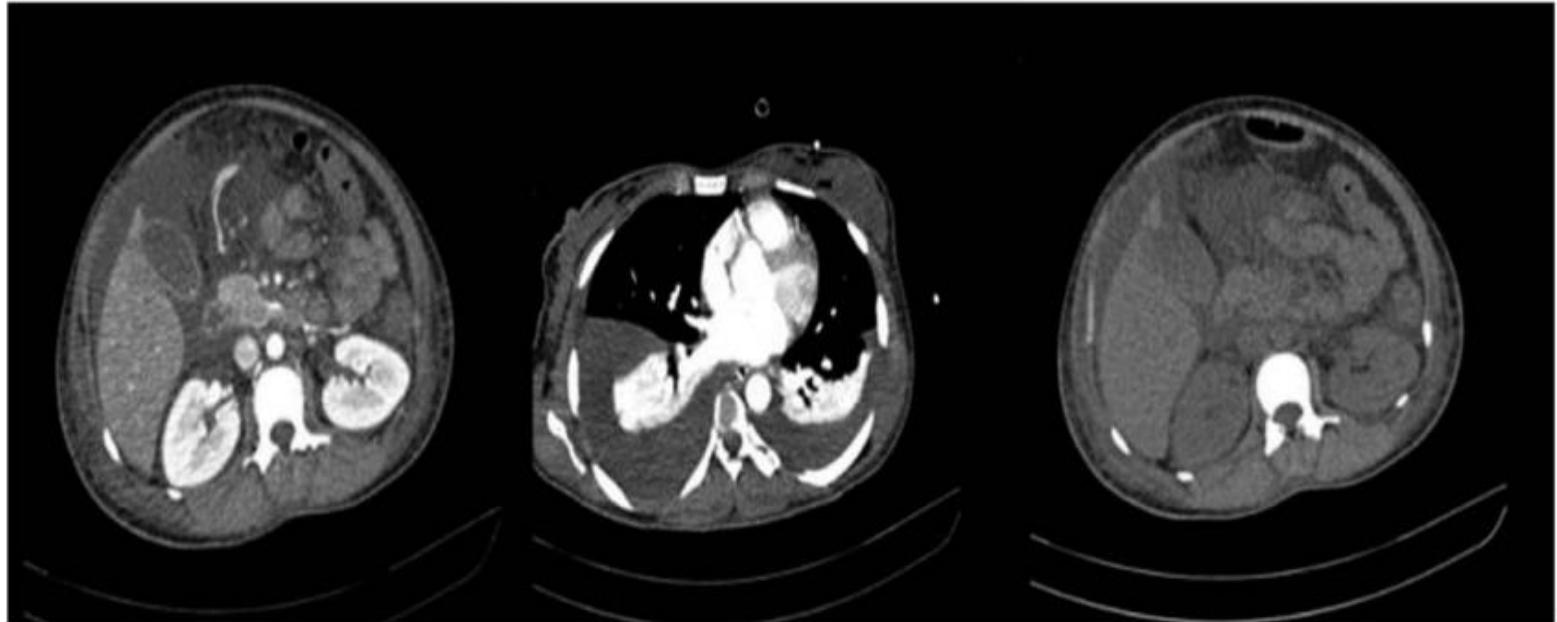
## 4. 資料回饋與系統學習

- 通報結果回饋基層：讓通報者知道是否確診、是否有後續處置。
- 統計分析：通報陽性率、處置完成率、病媒密度變化。
- 制度調整：若發現通報品質偏低，應加強教育或修正通報指引。

# 2025臺灣登革熱病例數更低

- 截至2025年9月中旬，台灣已累計報告登革熱本土病例約12例。這個數字相較於過去幾年屬於偏低水準，並未出現大規模流行。
-  與過往比較：2024年：登革熱本土病例數明顯偏高，部分地區（如臺南、高雄）曾出現群聚疫情。
- 今年受到「櫂加沙颱風」影響，疾管署曾示警登革熱風險增加，提醒民眾落實「巡、倒、清、刷」等防蚊措施。
  - 南台灣都市巷弄密集、人群移動頻繁，仍是病媒蚊擴散的潛在風險。

# Clinical course-1



**Figure 1.** Computed tomography scan of whole abdomen: Gross ascites with large amount of bilateral pleural effusion with bilateral lower lobe atelectasis.

The ultrasound of the abdomen and pelvic done on the day of admission showed moderate ascites with bilateral pleural effusion. The following day after the admission, she had four to five episodes of nausea and vomiting, for which she was kept nil per oral. She was started on intravenous fluids and antiemetic due to worsening lactate levels and persistent tachycardia; later that day, she complained of severe abdominal pain and respiratory difficulty, for which she was shifted to the ICU.

- Medical images 提示啦很多臨床狀況.很可能是照顧上的重點所以要好好的注意看有哪些變化.又代表臨床什麼意義
- **bilateral pleural effusion**→
- →hypoalbuminemia
- -→respiratory problems.--<tachypneic

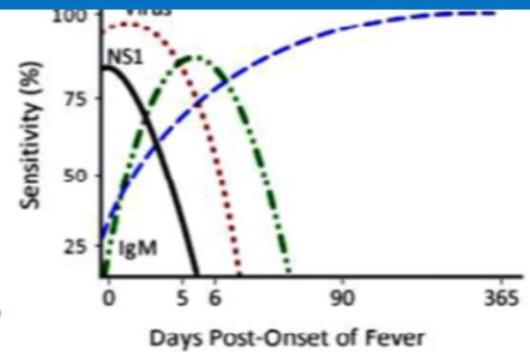
# Clinical course-2

- During the third day, her abdominal distension progressively increased, and she became tachypneic, confused, drowsy, and restless. She was subsequently **diagnosed with Dengue shock syndrome with ALF and grade III Hepatic Encephalopathy** evidenced by altered liver biochemistry with coagulopathy, severe lactic acidosis, and altered level of the sensorium.

Q6, 診斷的依據是什麼？

# Dengue fever診斷的依據

- (一) 臨床檢體(血液)分離並鑑定出登革病毒。
- (二) 臨床檢體分子生物學核酸檢測陽性。
- (三) 血清學抗原(登革病毒的非結構蛋白**non-structural protein 1**，簡稱**NS1**)檢測陽性。
- (四) 急性期(或初次採檢)血清中，登革病毒特異性**IgM**或**IgG**抗體為陽性者。
- (五) 成對血清(恢復期及急性期)中，登革病毒特異性**IgM**或**IgG**抗體(二者任一)有陽轉或 $\geq 4$ 倍上升。

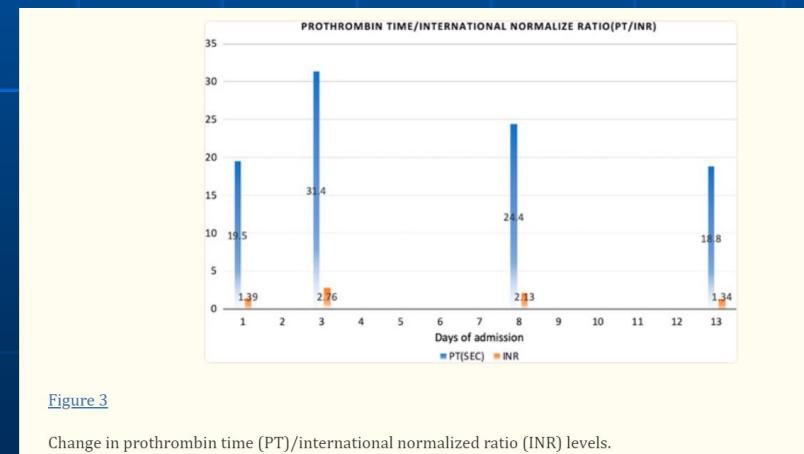
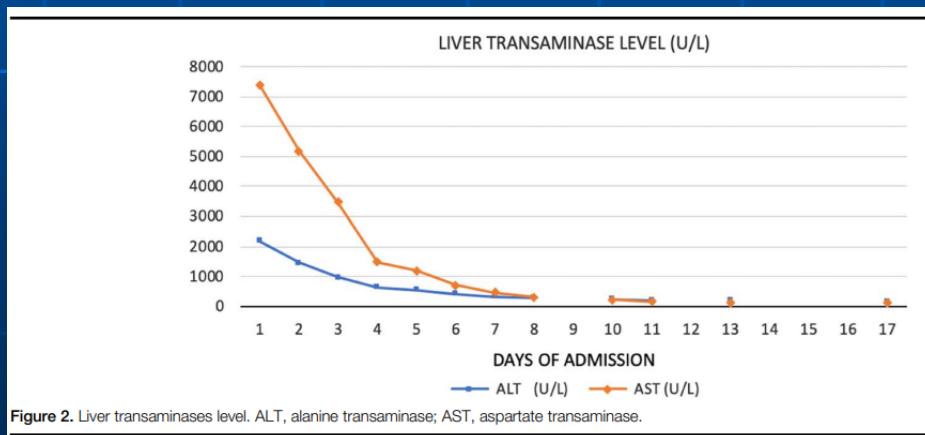


# Clinical course-3

- She was started on antibiotics, enema, diuretics, proton pump inhibitors, methylprednisolone, lactulose, 20% albumin infusion, N-acetylcysteine, and was kept on total parenteral nutrition. Hepatotoxic medications were avoided. She was intubated due to altered level of consciousness to protect her airway. The computed tomography scan of whole abdomen was done on the third day of hospital admission (Fig. 1). Therapeutic tapping of ascitic fluid was done to provide relief to the patient. Over time, her deranged transaminases (Fig. 2) level was improved. Her coagulopathy which was deranged (Fig. 3), was appropriately managed with fresh frozen plasma and vitamin K. Slowly her clinical status as well as biochemical profiles was improved.

# Clinical course-4

- She was completely weaned off the ventilator on the fifth day of intubation. After 20 days, she was discharged from the hospital. Later during a follow-up visit, her transaminase levels were within normal range.



Q7,Clinical course:要看出臨床經過的變化是否改善或惡化常需要依據一些評估指標(assessment parameters).

- 這個案例的指標是放在肝功能上,還有肝昏迷的相關指數.
- The most common definition of ALF involves any degree of mental deterioration (encephalopathy) in a patient without underlying cirrhosis and an illness lasting less than 26 weeks<sup>10</sup>. **Evidence of coagulation irregularity**, often an international normalized ratio of 1.5, is also included.
- Degree of encephalopathy**
- Coagulation irregularity.**
- Blood ammonia. Serum bilirubin**

# Causes of hepatic coma

1. Dengue hemorrhagic fever is diagnosed by the presence of fever with signs of hemorrhages, thrombocytopenia, and plasma leakage<sup>4</sup>. Dengue shock syndrome is the most severe form of dengue, which can affect several organs, including the liver, brain, and kidney, and result in fatal outcomes.
2. Liver involvement in dengue is a crucial (關係重大)feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of ALF
3. 何時要思考肝臟受到影響
  - (a) Dengue patients who presented with abdominal pain, nausea, vomiting, and anorexia should be evaluated for liver involvement<sup>11</sup>.
  - (b) Liver function test and coagulopathy
4. Mechanism of ALF:
  - The exact pathophysiology behind liver failure in dengue is not clear. The possible hypothesis includes T-cell-mediated host immunity and the underlying cytokine storm, which is also known as cytokine “Tsunami”<sup>4,12,13</sup>. Interleukin-22 and interleukin-17 are particularly responsible for liver injury
  - ALF often results in multiorgan dysfunction including hemodynamic instability, renal failure, cerebral edema, and even death because of shock

# Dengue shock syndrome and ALF

- Dengue shock syndrome is the most severe form of dengue, which can affect several organs, including the liver, brain, and kidney, and result in fatal outcomes [Samanta and Sharma, 2015].
- Liver involvement in dengue is a crucial feature, and the effect ranges from an asymptomatic rise in liver enzymes to the development of ALF.

Samanta J, Sharma V. Dengue and its effects on liver. *World J Clin Cases* 2015;3:125. ( Department of Gastro-enterology, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India.)

登革熱已成為一種重要的蟲媒病毒疾病，對熱帶國家人口的疾病負擔產生重大影響。登革熱通過伊蚊叮咬傳播。該病毒似乎具有一些肝毒性作用。肝功能檢查中紊亂形式的肝臟疾病很常見，可能包括血清膽紅素輕度升高、轉氨酶升高和血清白蛋白紊亂。雖然在大多數情況下無癥狀，但黃疸和急性肝衰竭（ALF）等臨床表現偶爾會使臨床表現複雜化。事實上，在流行國家，登革熱被認為是ALF的重要病因。

- ALF often results in multiorgan dysfunction including hemodynamic instability, renal failure, cerebral edema, and even death because of shock[4,12]. **Souza et al.[14] found that 74.2% of patients with serologically confirmed dengue had significantly elevated transaminase.** Many studies have point that the elevation of AST is more than alanine aminotransferase (ALT). The change in the ratio of aspartate aminotransferase (AST)/ALT is rarely observed in hepatitis A, B, or C viruses-induced acute hepatitis but only in Dengue fever[4]. Later Kuo et al.[15] and Nguyen et al.[16] found that the level of AST was higher than that of ALT.

# 如何去找引發急性肝衰竭之原因

- Infection? esp. hepatitis viruses.
- Dengue virus ?

找到登革熱病毒感染的證據就可以判斷這是急性肝衰竭的原因

- Q8,在疾病劇本裡好好敘述登革熱發生的肝臟變化—看看幾篇報告就可以了解
- *Souza et al.* 14 found that 74.2% of patients with serologically confirmed dengue had significantly elevated transaminase. Many studies have point that the elevation of AST is more than alanine aminotransferase (ALT). The change in the ratio of aspartate aminotransferase (AST)/ALT is rarely observed in hepatitis A, B, or C viruses-induced acute hepatitis but only in Dengue fever4.
- Later *Kuo et al.* 15 and *Nguyen et al.* 16 found that the level of AST was higher than that of ALT. Damaged striated muscle, cardiac muscle, and erythrocytes release the AST, which could be the reason for the high level of AST as compared with ALT17,18.
- The prothrombin time and activated partial thromboplastin time are prognostic variables used to evaluate the degree of liver damage and serve as indicators of bleeding in individuals with ALF19.
- Severe coagulopathy-like disseminated intravascular coagulation, severe sepsis, renal impairment, increased intracranial pressure resulting in cerebral edema, and cardiopulmonary collapse resulting in multiple organ failure are all complications of ALF20,21.

## Q9,急性肝衰竭處理的幾個重點-1

1. Severe coagulopathy-like disseminated intravascular coagulation, severe sepsis, renal impairment, increased intracranial pressure resulting in cerebral edema, and cardiopulmonary collapse resulting in multiple organ failure are all complications of ALF<sup>20,21</sup>.
  - Coagulations disorders should be addressed as well.
2. During ALF, complications like **metabolic abnormalities**, either due to infections or electrolyte abnormalities, should be corrected.
3. **Hepatic encephalopathy** is usually corrected by restricting protein intake along with the administration of lactulose and antibiotics like rifamixin and neomycin (nephrotoxic). However, lactulose is frequently prescribed to patients who have hepatic encephalopathy as a result of chronic liver illness. However, its utility in cases of sudden liver failure is debatable. According to one study, receiving lactulose helped patients with ALF live a small increase in survival time<sup>22</sup>

■ 4 Other treatment principles include the administration of N-acetyl cysteine, which has a crucial role in preventing free radicals-mediated hepatocyte damage

and prevention of hypoperfusion, dengue shock syndrome, or dengue hemorrhagic fever. Although this plays a specific role in mitigating the process, none is proven beneficial in all cases.

5. The last resort is a liver transplant in the case of ALF; however, it is not that feasible due to a limited number of donors.

6. Future: Preventive measures:

■ new methods should be developed to prevent as the dengue virus spread and new drugs should be discovered to prevent hepatotoxic injury 23,24.

# 治療

- 典型登革熱致死率低於1%
- 依據WHO資料，登革熱重症若無適當治療，**死亡率可能超過20%**，早期診斷並加以適當治療，死亡率可低於**1%**
- 登革熱沒有特效藥物可積極治療，一般採行支持性療法

- **2015年12月上市之活性減毒疫苗，可保護4種血清型**

- 法國Sanofi Pasteur藥廠生產，商品名為Dengvaxia® ( CYD-TDV )，目前已在墨西哥、菲律賓、印尼、泰國及新加坡等20多個國家核准上市，在台灣尚未上市
- 適用年齡為9-45歲的兒童及成人
- 感染過登革熱病毒的人接種疫苗有效且安全；但未曾感染過登革熱病毒的人於接種後倘自然感染登革熱，則發生登革熱重症風險增加。
- 針對接種前血清抗體陽性者，接種3劑（0/6/12個月）後之疫苗保護力約81.9% ( 95%CI : 67.2-90.0% )

Q10,找幾篇相關的臺灣報告了解過去我們在  
這一方面有多少認識

- 這是作業.

# Dengue fever with liver problems in Taiwan

## 3 cases died of acute liver failure.(1992)

### Total cases: 270

- 在1987年11月至1988年12月的疫期間，通過生化測試對125名男性和145名女性患者進行了登革熱對肝功能的影響。天冬氨酸轉氨酶（AST）、丙氨酸轉氨酶（ALT）、膽紅素、鹼性磷酸酶、γ-谷氨醯轉肽酶（G-GT）水平分別為93.3%、82.2%、7.2%、16.3%和83.0%。在大多數情況下，轉氨酶的升高為輕度至中度，但在11.1%和7.4%的患者中，轉氨酶的升高分別是AST和ALT正常上限的10倍。最初，AST水平高於ALT，在癥狀出現後9天增加到最高水準，然後在兩周內降至正常水準。生化檢查結果在有和沒有乙型肝炎或丙型肝炎病毒感染的病例之間沒有顯著差異，但在出血發作的患者中觀察到AST、ALT和G-GT的升高顯著升高。2例患者的肝活檢顯示小葉性肝炎的特徵。在五例死亡病例中，三例死於肝衰竭。結論是，登革熱可能引起與常規病毒性肝炎患者相似的肝損傷和轉氨酶升高。在流行或流行地區，在肝炎的鑑別診斷中應考慮登革熱感染。

**Chung-Huang Kuo et al (CGMH, Kaoshiung)** 肝臟生化檢查和登革熱 . Kuo CH, Tai DI, Chang-Chien CS, et al. Liver biochemical tests and dengue fever. Am J Trop Med Hyg 1992;47:265-270 (L1127)

# Abnormal liver functions in Dengue fever (Taiwan, 1992)

## ■Liver functions) % abnormality

■		
■		
■		
■	天冬氨酸轉氨酶 (AST)	93.
■	丙氨酸轉氨酶 (ALT)	82.2
■	膽紅素	7.2
■	齡性磷酸酶 10 fold greater than the normal upper limit for AST and ALT in 11.1% Remarks 10 fold greater than the normal upper limit for AST and ALT in 11.1% and 17.4% (G-GT)	16.3
■	γ-谷氨醯轉肽酶 (G-GT) <b>Acute liver failure---3 cases</b>	83.0
■	Mortality-----5/270 (1.1%)	

Chung-Huang Kuo et al (CGMH, Kaoshiung) Liver biochemical tests and dengue fever. Am J Trop Med Hyg 1992;47:265-270 (L1127)

# Conclusion

## ■ Q11,好好寫下這一篇這個討論的心得感想/或結論.

1. Dengue fever has been a significant burden in countries with poor resources. Since most dengue cases are better with conservative treatment, few develop serious complications.
2. Although liver involvement is mild in many cases, there are ALF cases associated with high morbidity and mortality due to complications such as encephalopathy, severe bleeding, renal failure, and metabolic acidosis. 3 People infected more than one time with different serotypes increase the risk of severe complications and mortality.
2. 4 To accurately diagnose dengue and prevent misdiagnosis as viral hepatitis in dengue-endemic areas, clinicians must be aware of the need for **early patient monitoring and measurement of suitable laboratory data**. The afflicted patient's health, bleeding, and laboratory-determined markers such as complete blood count, serum transaminase levels, prothrombin time, and international normalized ratio should thus be constantly monitored while assuring adequate supportive care and treatment. 疾病指標的重要性要案例個別考慮
3. 5. Resource-limited countries like many countries in Asia are facing an increasing case of dengue fever with increasing serious complications.

# 生病的故事→完成疾病劇本 應具備哪些內容

Cheng-Yi Wang  
2025.09.26

# 疾病劇本之主要內容

- 1.疾病的特色,--前言
- 2.流行病學, 特別是本土的相關報告
- 3.主要的症狀及徵象—problem list
- 4.診斷依據
- 5.處理原則(規範)guidelines
- 6.Outcome, 影響預後之重要因素.
- 7.居家醫療之重點事項(home care)

# 完整的疾病劇本必須包括：

- 1. 生病的原因,演變,就醫時的問題,含主訴
- 2. 診斷,診斷依據.
- 3. 治療方式以及治療反應
- 4. 住院醫療中的變化,有無改善有無惡化.  
臨床變動之原因.
- 5. 最后的結局. (Final outcome)

# 完整的疾病劇本

- 1. 劇情概要 - summary
- 2. 病因 - roots
- 3. 影響預後之重要因素 - risk factors
- 4. 臨床問題 problem list - 含主訴
- 5. 診斷, 診斷依據
- 6. 必須鑑別之其他疾病及鑑別重點
- 7. 治療規範
- 8. 故事主角接受之治療及效果評述
- 9. 故事末了一最後的結局
- 10. 劇作家的感言

# 分項敘述

- I. 流行病學探討即臺灣相關之報告
- II. 劇情變動之相關誘因
  - a. 為何惡化
  - b. 改善之相關要件, 及效果
- III. 疾病未來動向
  - a. 居家醫療之重點
  - b. 生活必要之改變
  - c. 收集眾多案件之報告, 敘述後果關鍵因素
- IV. 本病最新進展 -2020以後之報告提出之新觀點, 新治療方式或病因之發現
- V. 閉幕前主角要說的話以及劇作家的感言
- VI. 參考文獻(建議十篇以內, 不超過15篇)

# 結論(2025.09.26)

- 1. 我們提出一個案例說明登革熱會發生肝衰竭.這是一個值得重視的臨床問題
- 2. 請大家參考文獻后,提出報告.
- 3. 這個課題會完成會成為臨床推理這一本書的重要內容. 各位都將是這本書的作者
- 4. 請大家在2個星期內完成.  
學習肝衰竭之臨床處置.也練習如何去搜查文獻, 並做簡要的敘述

可能以單獨提出也可以四五個同學聯合提出,  
提出超過兩篇時,可以做一個專題討論分析各位報告或內容的優缺點