

登革熱、屈公病之診斷及治療

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東南亞地區逐漸進入登革熱好發季節，提醒赴前述地區民眾應注意防範

資料來源: 公關室 Public Relations Office

日期: 2011/4/8

 SHARE

隨氣候逐漸回暖，病媒蚊漸趨活躍，東南亞地區逐漸進入登革熱好發季節。依據衛生署疾病管制局監測資料，今（100）年迄今共37例登革熱病例，其中22例為境外移入，皆來自東南亞國家（越南7例、菲律賓4例、印尼4例、泰國2例、馬來西亞2例、緬甸2例、新加坡1例）。據歷年疫情監測，我國幾乎每年之登革熱本土疫情均由境外移入病例在國內再傳染他人所致；因歷年登革熱境外移入病例皆以東南亞國家為主，且國際監測顯示部分東南亞國家今年疫情可能比往年嚴重，該局呼籲近期欲前往該地區的旅客或商務人士，應確實做好防蚊措施，避免蚊蟲叮咬，防範感染登革熱，以維護自身健康安全。

依國際監測資料，菲律賓今年由於雨季過長，定點醫院於1-2月間共監測13,281例登革熱病例，病例數較往年提前出現並快速增加，無緩和跡象，該國衛生部推測今年疫情可能較去年嚴重；柬埔寨今年截至3月底累計通報231例登革熱，並造成2例死亡（5歲與10歲兒童），高於去年同期的193例（1例死亡）。泰國截至3/26累計通報5,723例登革熱，其中7例死亡；馬來西亞截至4/2累計通報5,496例登革熱，其中9例死亡；寮國截至3/26累計通報226例登革熱，無死亡；新加坡截至4/2累計通報886例登革熱。

疾病管制局提醒民眾，前往登革熱流行地區探親、旅遊或工作時，務必做好防蚊措施，包括穿著淺色長袖衣褲、身體裸露部位塗抹衛生署核可防蚊劑。回國後如有發燒、頭痛、出疹、肌肉或關節痠痛等症狀，應儘速就醫，並告知旅遊史，作為醫師診治之參考。計劃出國的民眾可至疾病管制局網站（<http://www.cdc.gov.tw>）的「國際旅遊資訊」專區取得國際最新疫情與旅遊傳染病資訊，並可自行下載「帶著口袋醫師去旅行」、「健康走天涯」等衛教宣導手冊，或撥打免付費民眾疫情通報及諮詢專線1922洽詢。

Patient Profile

- Name: 周 X 軒
- DOB: 1996/2/11
- Age: 15 years old
- Chart No: 42140837
- Admission Date: 2010/8/22

Chief Complaint

- Mild fever and general malaise for 4 days

Present Illness-1

- This 15-year-old girl has no significant past medical history.
- She went to Cambodia on 8/10~8/17 with her church group for a mission trip.
- After coming back, she started to have mild fever with temperature of 37.5~38.0 degrees. The fever was accompanied by rhinorrhea and a mild cough with sputum.

ER Initial Evaluation 8/21

- Influenza rapid test: negative
- Hb: 13.1 g/dL Ht: 38.8%
- **WBC: 1300 μ L ANC: 728**
 - DC: (0-56-0-0-16-28)
- **PLT: $43 \times 10^3 / \mu$ L**
- CRP: 0.57 mg/dL

8/23 CBC, WBC/DC, Chemistries

- Hb: 14.7 g/dL Hct: 43.3% (↑11%)
- Reticulocyte: 1/1000 RBCs
- **WBC: 1300 μ L**
DC: (2-37-0-0-11-47-Atypical-Lym: 3)
- **PLT: $19 \times 10^3 / \mu$ L**
- ANC: 507
- **ASL(GOT): 200 U/L**
- **ALT(GPT): 59 U/L**
- **LDH: 501 IU/L**

- 8/25



• 8/25



• 8/25



- 8/25



• 8/27



• 8/27



• 8/27













Arboviruses

Disease	Vector	Host	Distribution	Disease
Alphaviruses				
Chikungunya	<i>Aedes</i>	Humans, monkeys	Africa, Asia	Fever, arthralgia, arthritis
Eastern equine encephalitis	<i>Aedes, Culiseta</i>	Birds	North and South America, Caribbean	Mild systemic ; encephalitis
Western equine encephalitis	<i>Culex, Culiseta</i>	Birds	North and South America	Mild systemic ; encephalitis
Venezuelan equine encephalitis	<i>Aedes, Culex</i>	Rodents, Horses	North, South, Central America	Mild systemic ; severe encephalitis
Flaviviruses				
Dengue	<i>Aedes</i>	Humans, monkeys	Worldwide, especially tropics	Mild systemic; break-bone fever, DHF, DSS
Yellow fever	<i>Aedes</i>	Humans, monkeys	Africa, South America	Hepatitis, hemorrhagic fever
Japanese encephalitis	<i>Culex</i>	Pigs, birds	Asia	Encephalitis
West Nile encephalitis	<i>Culex</i>	Birds	Africa, Europe, central Asia, North America	Fever, encephalitis, hepatitis
St. Louis encephalitis	<i>Culex</i>	Birds	North America	Encephalitis

登革熱 (Dengue fever)

- 由蚊子傳播的急性病毒性熱疾
 - 埃及斑蚊 *Aedes aegypti*
 - 白線斑蚊 *Aedes albopictus*
- 以高熱、頭部、肌肉、骨頭、關節的奇痛，後眼窩痛以及發疹為主要症狀。



登革熱 (Dengue fever)

- 由黃病毒科 (*Flaviviridae*)
 - 黃病毒屬 (*Flavivirus*)
 - 登革熱病毒亞屬
- 在登革熱病毒亞屬裡共有四種登革熱病毒，它們依抗原性的不同分別稱為第一、二、三、四型。

登革病毒

- 造成登革熱/登革出血熱/登革休克症候群
- 單股RNA病毒，依血清抗原性可分為四型，均具有感染致病的能力
- 再次感染不同型別登革病毒，可能發生較嚴重的登革出血熱

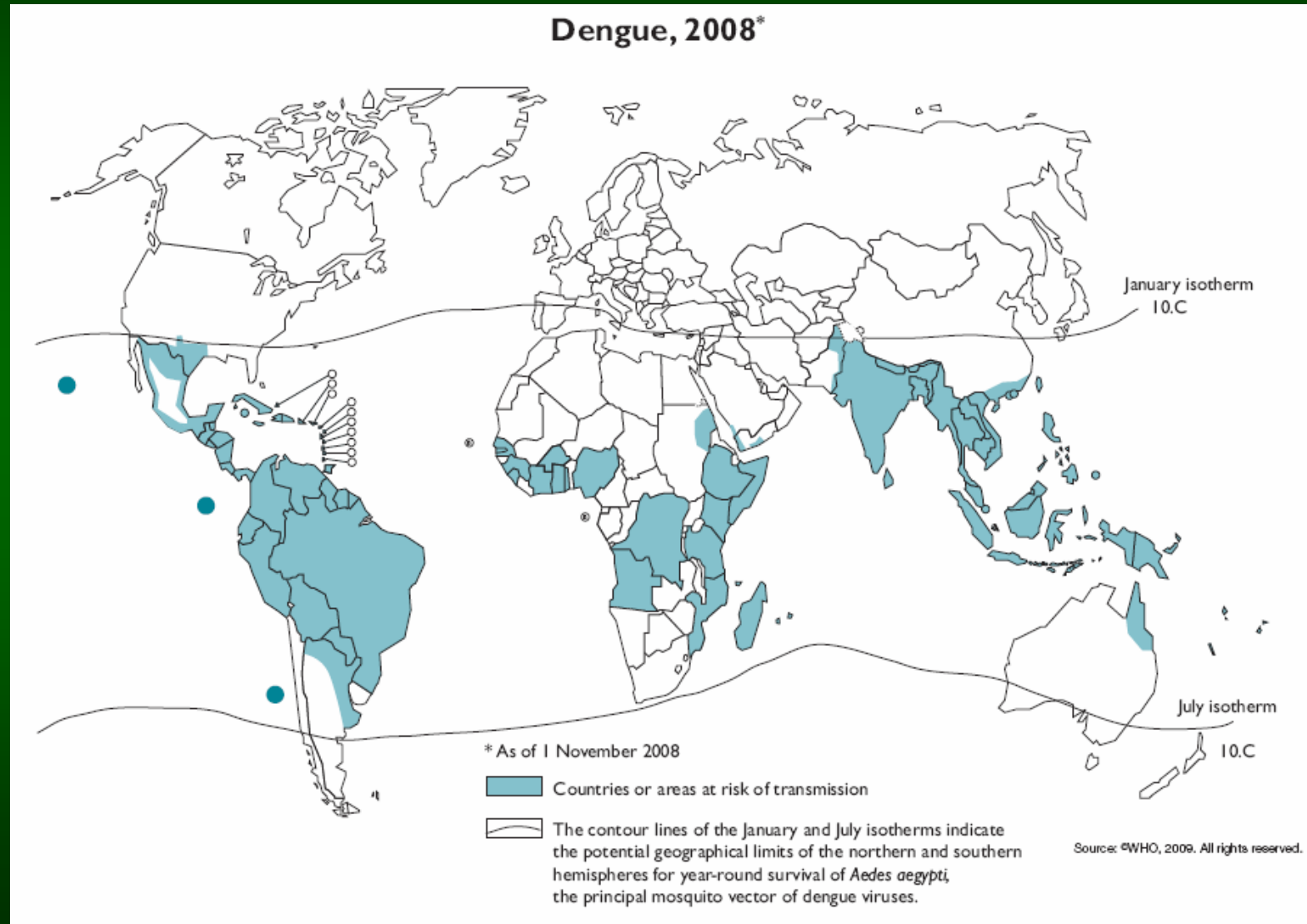
登革熱

- 傳染方式：人被帶有登革病毒的病媒蚊叮吮而受到感染。
- 潛伏期：約3~14天，通常約5~8天。
- 可傳染期：病人在發病前一天及發病後約5天內，血液裡就會有病毒，此時期若蚊蟲吸取病人的血液，病毒會在蚊體內繁殖，經8~12日後蚊蟲才有感染力。此後其終生皆具傳染力。

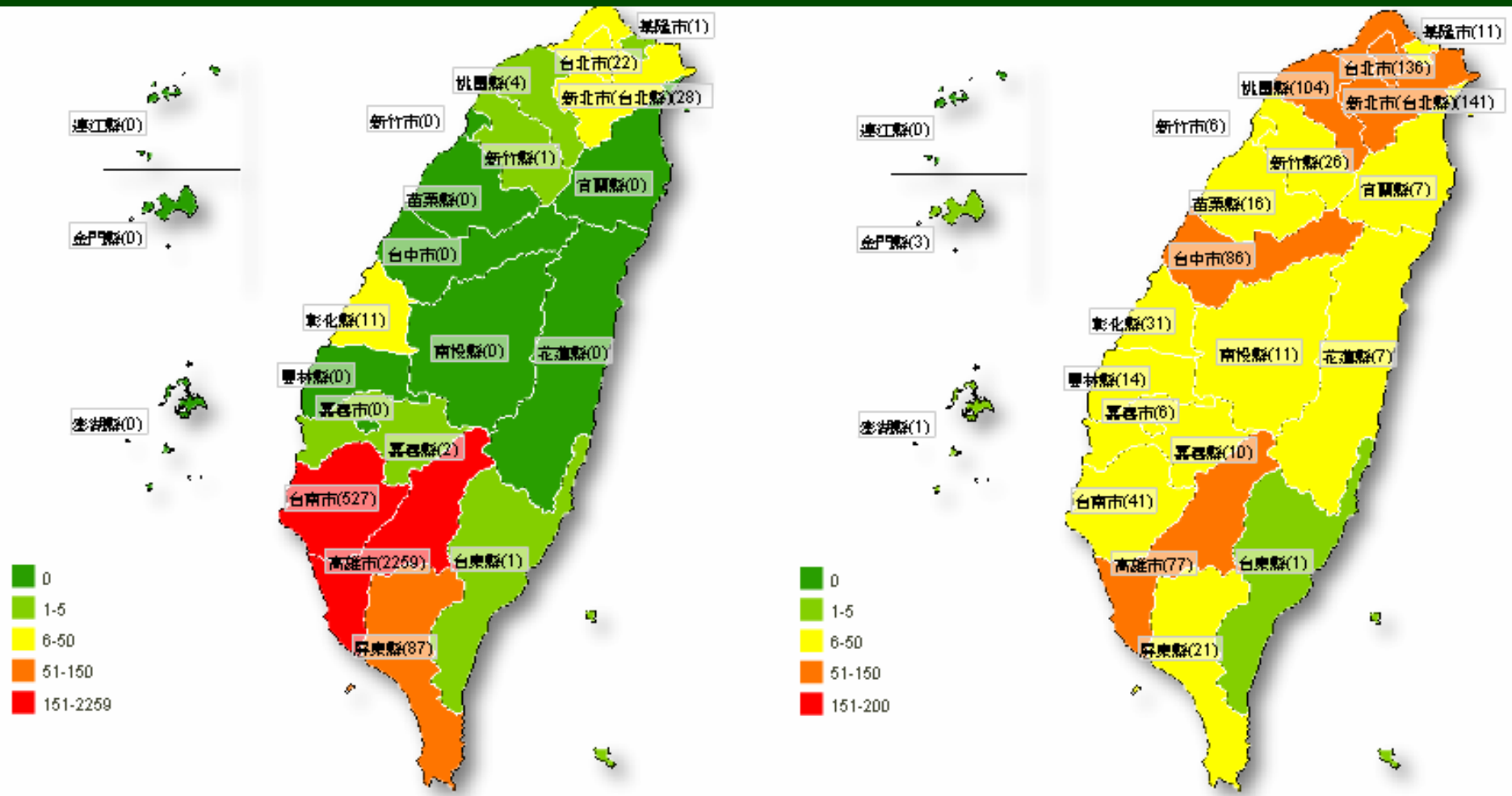
典型登革熱的臨床症狀

- 第一期(第一天到第三天):急性前期,畏寒.全身無力.骨頭酸痛.後眼球痛.關節痛.喉嚨痛像流行性感冒,食慾不振.乾嘔.嘔吐,睡不著
- 第二期(第四天):緩解期,燒退(danger),症狀減輕
- 第三期(第五天到第六天):急性後期,體溫回升(雙峰型的發燒),症狀重現
- 第四期(第六天以後):恢復期,燒退,病人出紅疹,2-4週後才完全恢復

全球登革熱流行分布圖



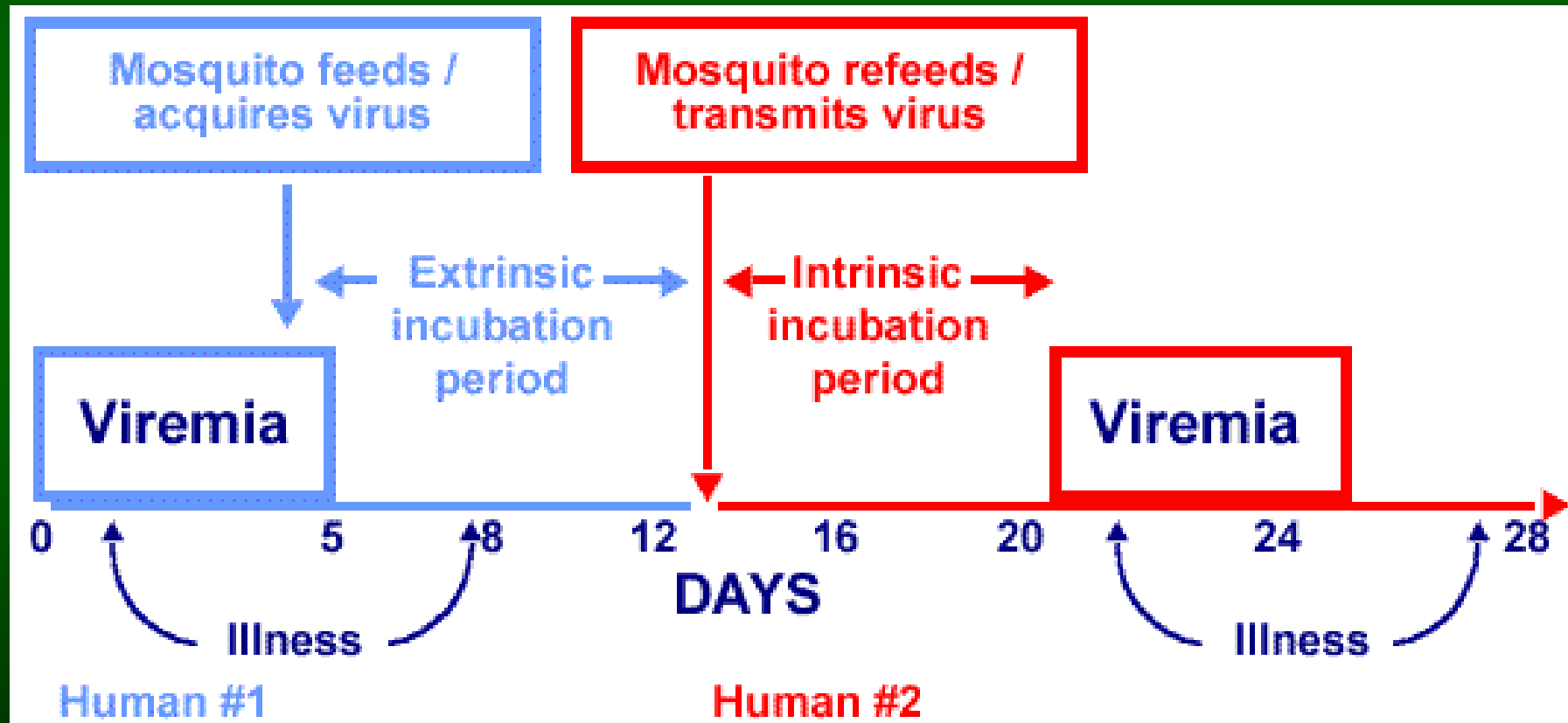
全國登革熱病例地理分布 (2008 – 2011)



本土病例

境外移入病例

Transmission of Dengue Virus by *Aedes aegypti*



Aedes aegypti

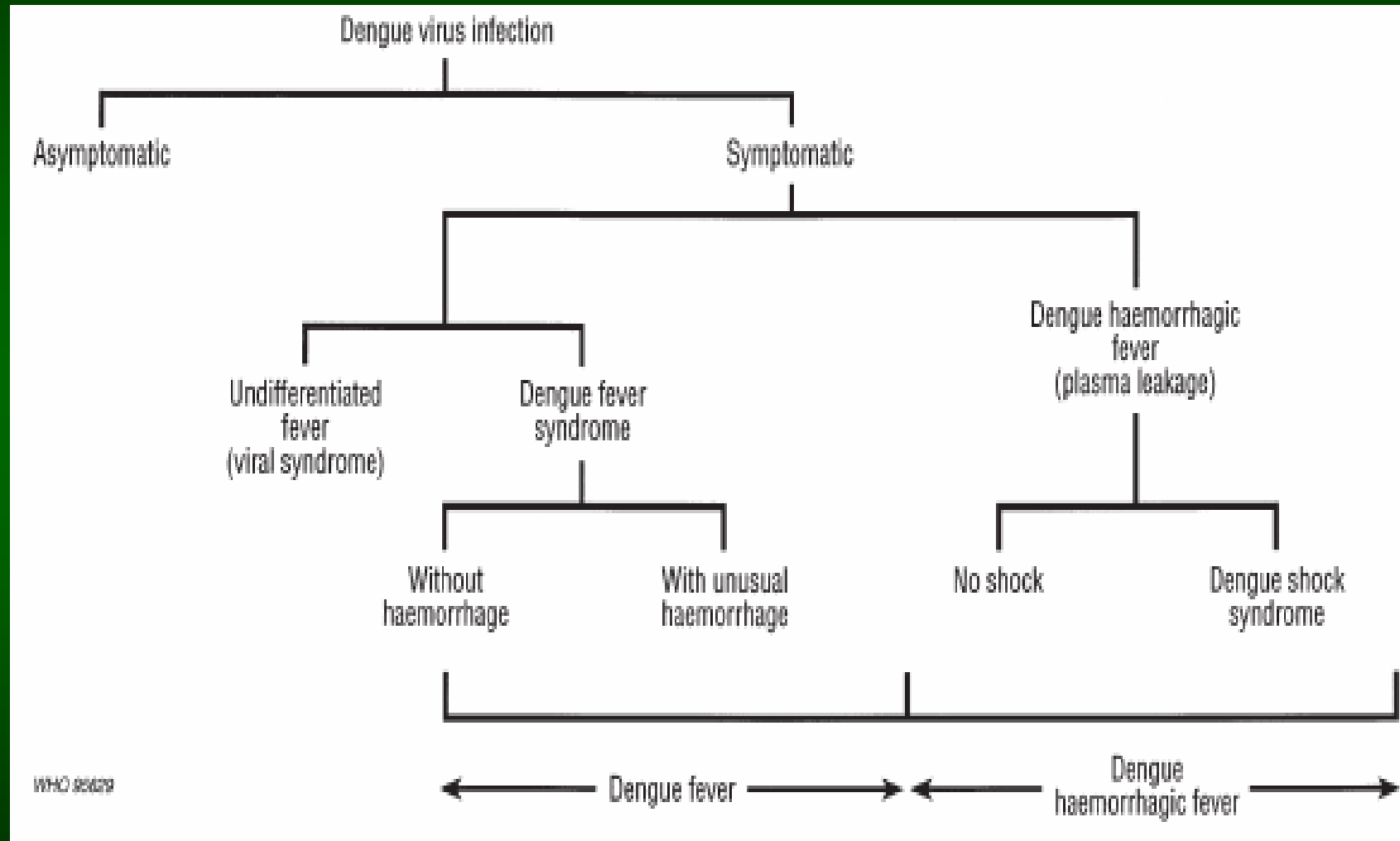
- Dengue transmitted by infected female mosquito
- Primarily a daytime feeder
- Lives around human habitation
- Lays eggs and produces larvae preferentially in artificial containers



Dengue Clinical Syndromes

- Undifferentiated fever
- Classic dengue fever
- Dengue hemorrhagic fever
- Dengue shock syndrome

Manifestations of dengue virus infection



Undifferentiated Fever

- May be the most common manifestation of dengue
- Prospective study found that 87% of infection were either asymptomatic or only mildly symptomatic
- Other prospective studies including all age-groups also demonstrate silent transmission

Clinical Characteristics of Dengue Fever

- Fever
- Headache
- Muscle and joint pain
- Nausea/vomiting
- Rash
- Hemorrhagic manifestations

Hemorrhagic Manifestations of Dengue

- Skin hemorrhages:
petechiae, purpura, ecchymoses
- Gingival bleeding
- Nasal bleeding
- Gastrointestinal bleeding:
hematemesis, melena, hematochezia
- Hematuria
- Increased menstrual flow

Encephalitis/Encephalopathy of Acute Dengue Infection

- Decreased level of consciousness: lethargy, confusion, coma
- Seizures
- Nuchal rigidity
- Paresis

Clinical Case Definition for Dengue Hemorrhagic Fever

4 Necessary Criteria:

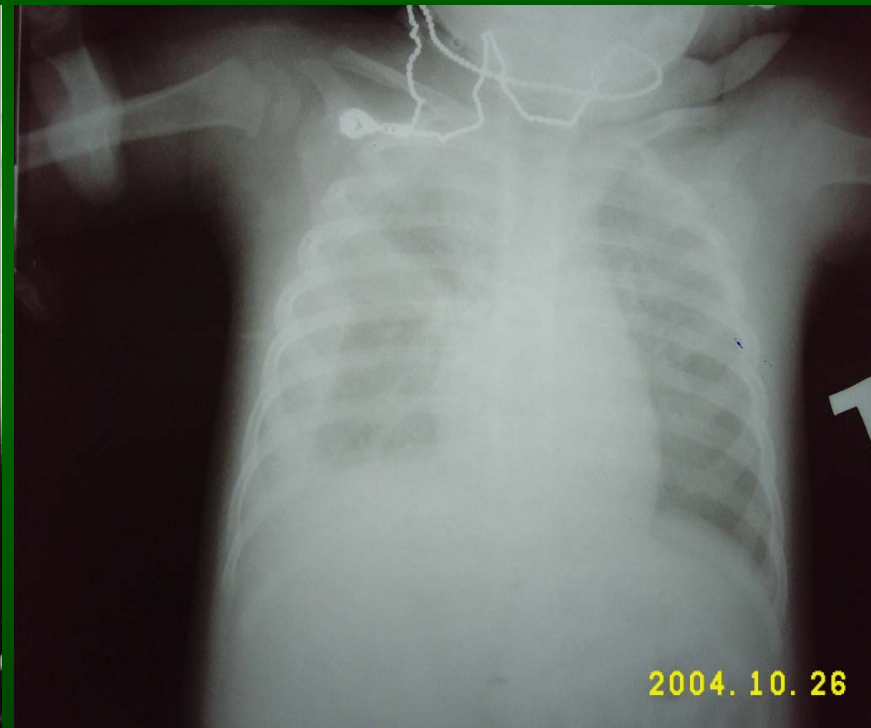
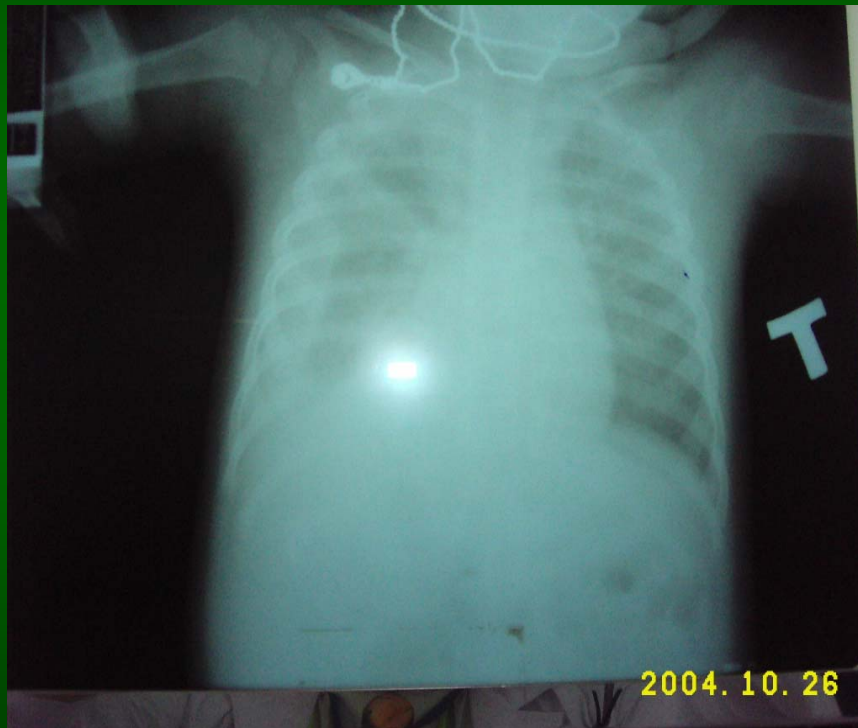
- Fever, or recent history of acute fever
- Hemorrhagic manifestations
- Low platelet count ($100,000/\text{mm}^3$ or less)
- Objective evidence of weaky capillaries:
 - elevated hematocrit ($\geq 20\%$)
 - low albumin
 - pleural or other effusions

Elevated Hematocrit ($\geq 20\%$)

[HCT (max) - HCT (min)]

$$\frac{\text{[HCT (max) - HCT (min)]}}{\text{HCT (min)}} \times 100\% \geq 20\%$$

Dengue pleural effusion



Clinical Case Definition for Dengue Shock Syndrome

- 4 criteria for DHF
- Evidence of circulatory failure manifested indirectly by all of the following:
 - Rapid and weak pulse
 - Narrow pulse pressure (≤ 20 mm Hg) OR hypotension for age
 - Cold, clammy skin and altered mental status
- Frank shock is direct evidence of circulatory failure

Four Grades of DHF

- Grade 1
 - Fever and nonspecific constitutional symptoms
 - Positive tourniquet test is only hemorrhagic manifestation
- Grade 2
 - Grade 1 manifestations + spontaneous bleeding
- Grade 3
 - Signs of circulatory failure (rapid/weak pulse, narrow pulse pressure, hypotension, cold/clammy skin)
- Grade 4
 - Profound shock (undetectable pulse and BP)

Danger Signs in Dengue Hemorrhagic Fever

- Abdominal pain - intense and sustained
- Persistent vomiting
- Abrupt change from fever to hypothermia, with sweating and prostration
- Restlessness or somnolence

Warning Signs for Dengue Shock

Four Criteria for DHF:

- Fever
- Hemorrhagic manifestations
- Excessive capillary permeability
- $\leq 100,000/\text{mm}^3$ platelets

Initial Warning Signals:

- Disappearance of fever
- Drop in platelets
- Increase in hematocrit

Alarm Signals:

- Severe abdominal pain
- Prolonged vomiting
- Abrupt change from fever to hypothermia
- Change in level of consciousness (irritability or somnolence)

When Patients Develop DSS:

- 3 to 6 days after onset of symptoms



Risk Factors Reported for DHF

- Virus strain
 - DHF risk is greatest for DEN-2, followed by DEN-3, DEN-4 and DEN-1
- Pre-existing anti-dengue antibody
 - Previous infection
 - Maternal antibodies in infants
- Host genetics
- Age

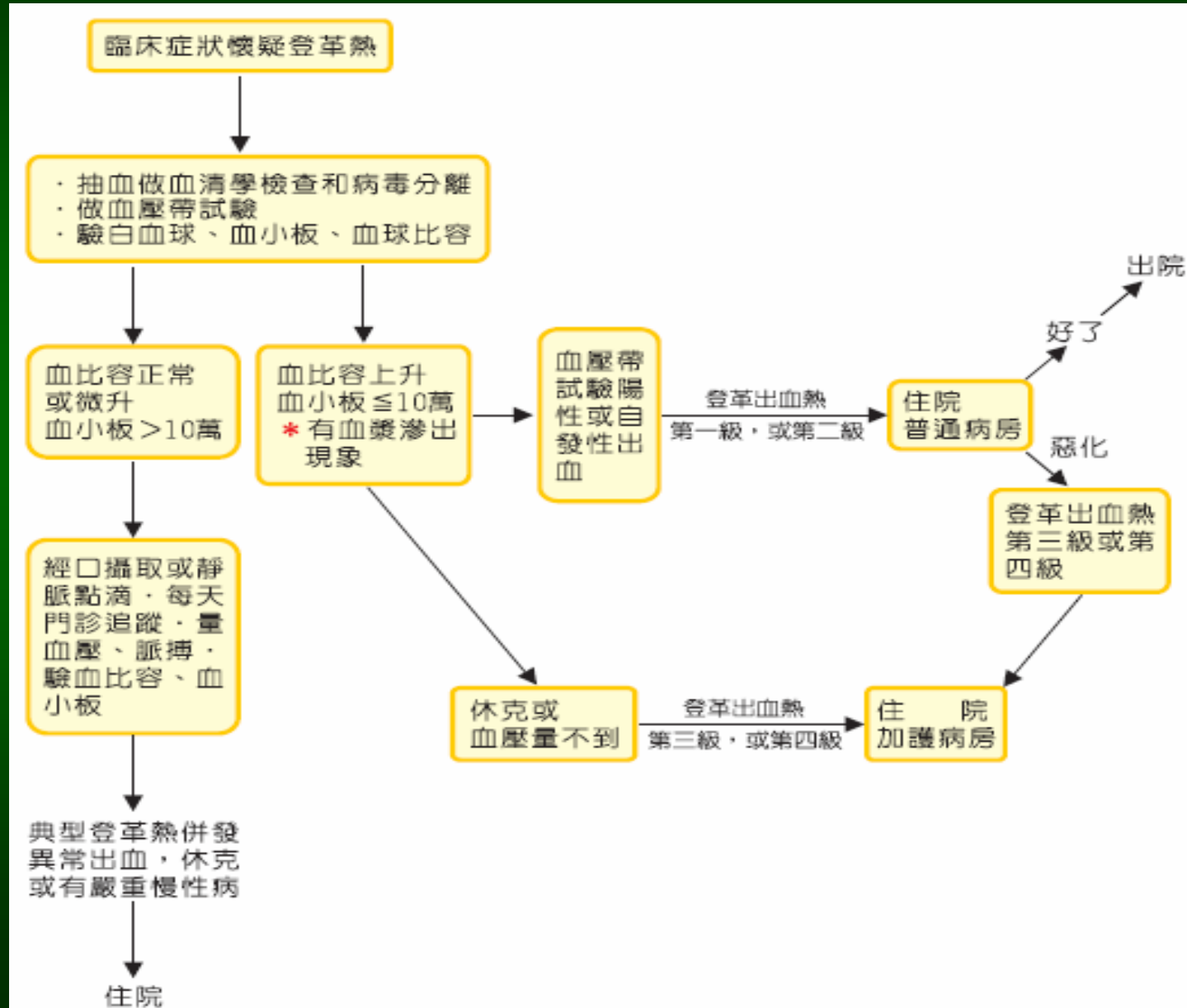
Clinical Evaluation in Dengue Fever

- Blood pressure
- Evidence of bleeding in skin or other sites
- Hydration status
- Evidence of increased vascular permeability—pleural effusions, ascites
- Tourniquet test

Laboratory Tests in Dengue Fever

- Clinical laboratory tests
 - CBC—WBC, platelets, hematocrit
 - Albumin
 - Liver function tests
 - Urine—check for microscopic hematuria
- Dengue-specific tests
 - Virus isolation
 - Serology

臨床上懷疑登革熱處理流程



Positive Tourniquet Test



Tourniquet Test

- Inflate blood pressure cuff to a point midway between systolic and diastolic pressure for 5 minutes
- Positive test: 20 or more petechiae per 1 inch² (6.25 cm²)

Dengue Fever Scoring System

Table 2. Proposed dengue scoring system

Characteristics	Score
(I) Epidemiology	
Recent travel to Southeast Asia or endemic dengue fever in Taiwan within 1 week	4
(II) Clinical symptom	
Skin rash	3
Bleeding sign*	3
Fever	2
Headache, retrobulbar pain, bone pain, myalgia	1
GI symptoms [†]	1
Absence of cough and rhinorrhea	1
(III) Differential diagnosis	
Fever > 7 days	-8
Identified infection focus (e.g. eschar of scrub typhus and upperrespiratory infection)	-10

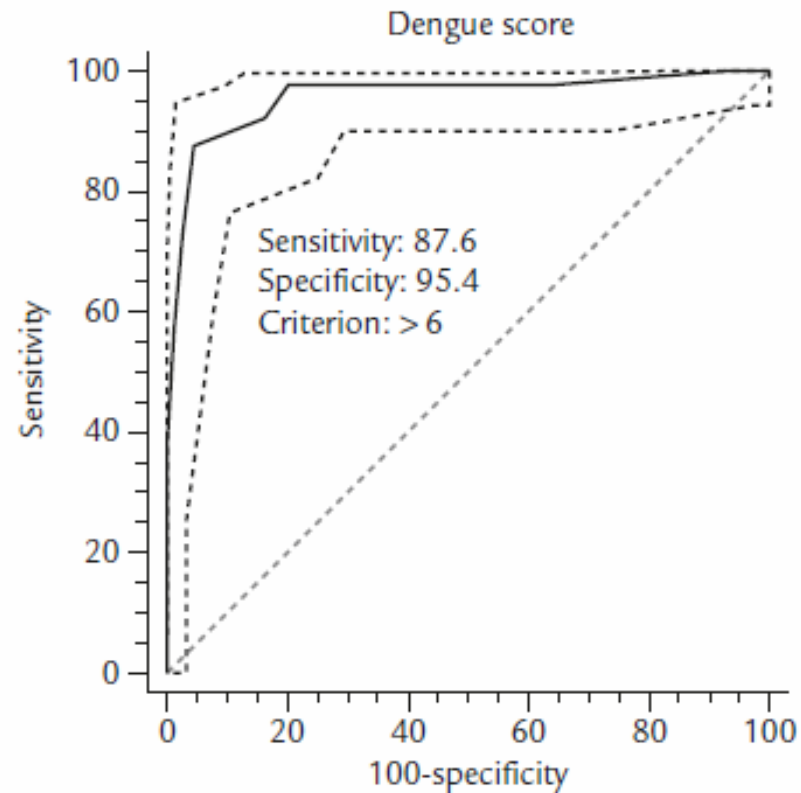


Figure. Receiver operating characteristic curve for dengue scoring system. The dotted lines indicate the 95% confidence interval.



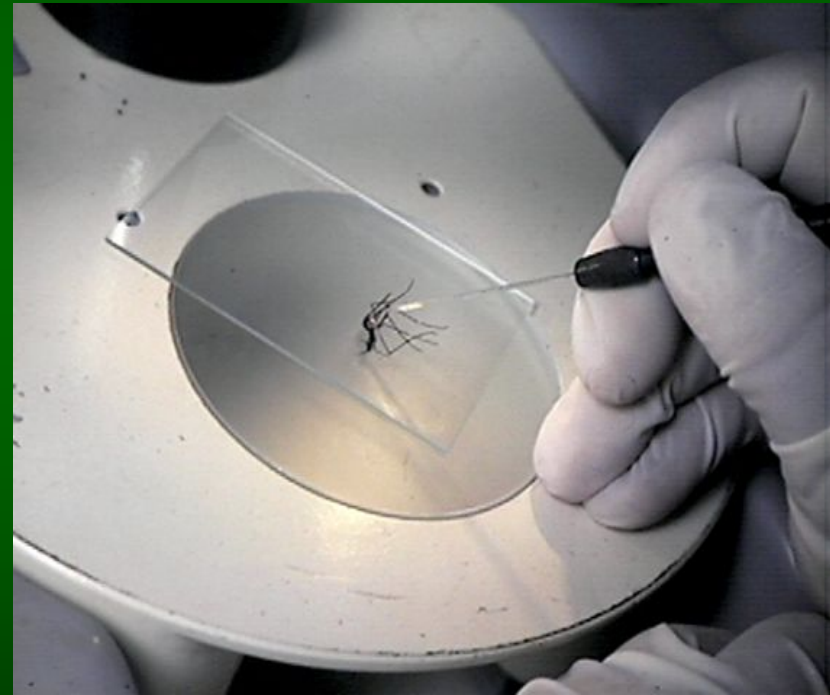
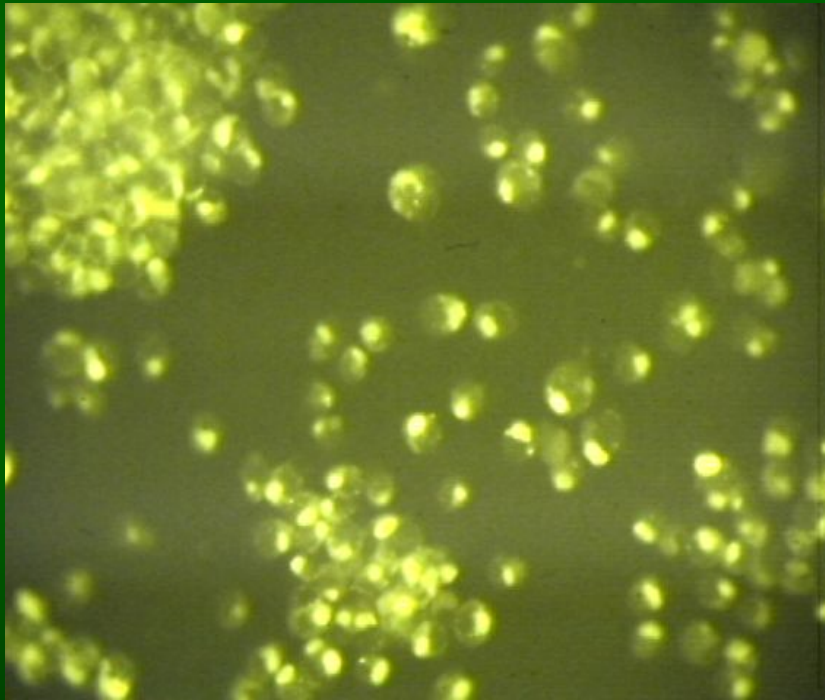
Differential Diagnosis of Dengue

- Influenza
- Measles
- Rubella
- Malaria
- Typhoid fever
- Leptospirosis
- Meningococemia
- Rickettsial infections
- Bacterial sepsis
- Other viral hemorrhagic fevers

Laboratory Methods for Dengue Diagnosis

- Virus isolation to determine serotype of the infecting virus
- IgM ELISA test for serologic diagnosis

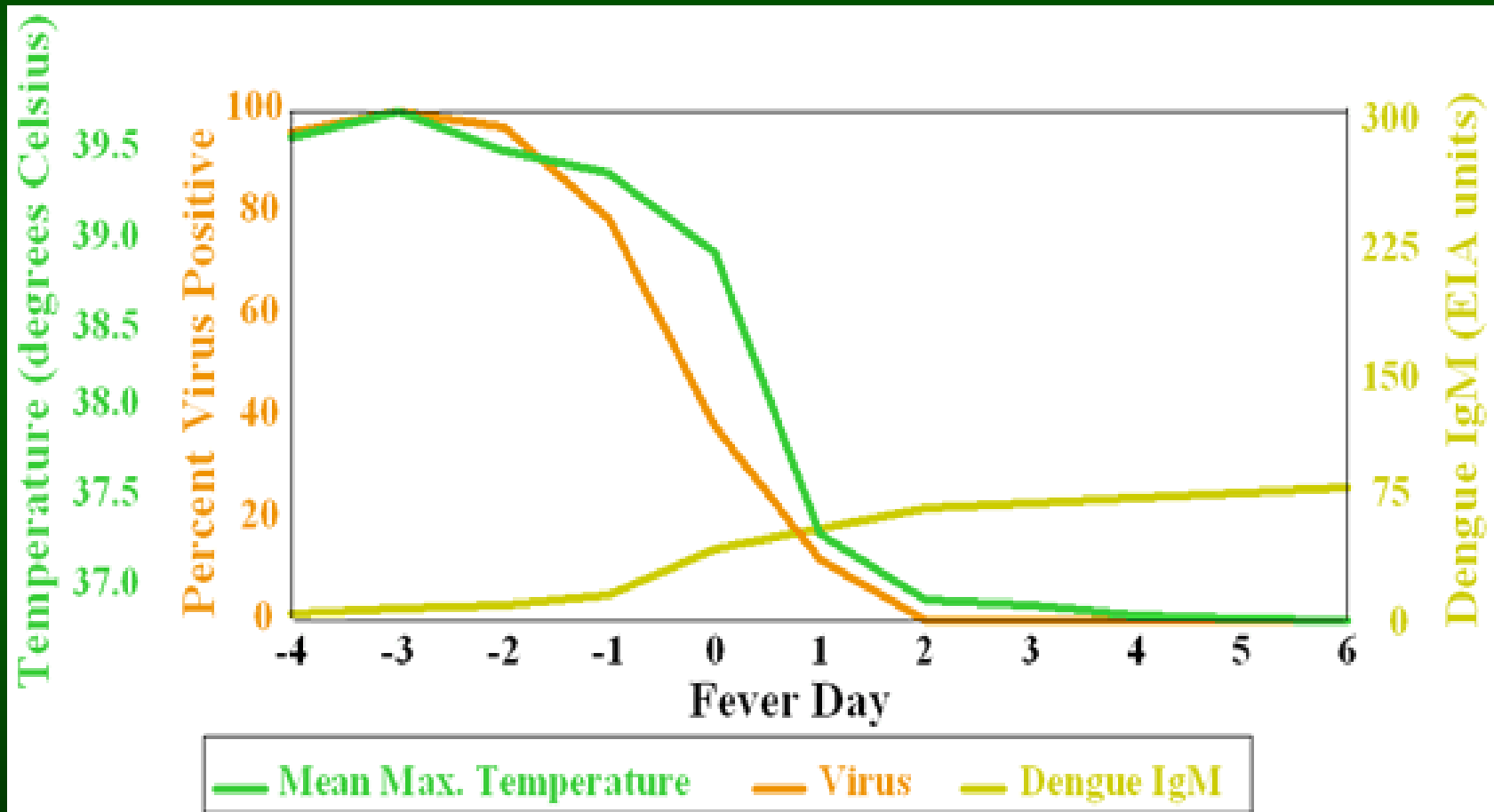
Virus Isolation: Cell Culture



ELISA Test for Serologic Diagnosis



Temperature, Virus Positivity, and Anti-Dengue IgM, by Fever Day



Adapted from Figure 1 in Vaughn et al., **Fever day 0 is the day when the BT < 38°C.** J Infect Dis, 1997; 176:322-30.

TREATMENT

- No specific treatment
- To treat shock due to the loss of plasma from the vascular compartment
- Avoid aspirin, ibuprofen
- Supportive care
- Adequate fluid supply
- Fluid (water, fruit juice, etc)

TREATMENT

- Avoid giving **IV fluids** unless the patient is bleeding or the haematocrit level is rising progressively.
- Avoid rushing into giving **blood transfusion** unless the haematocrit is falling dangerously.
- Do not give **platelet transfusion** unless the platelet count is very low or unless there is bleeding.

輸血適應症

	適應症	劑量
新鮮的全血	腸胃道出血合併血比容小於35% 或血比容快速降低大於20%	20ml/kg
新鮮冷凍血漿	腸胃道出血合併瀰漫性血管內凝血症	10-20ml/kg
血小板	大量或明顯持續性出血合併血小板小於兩萬	1U/5-10kg
Cryoprecipitate	腸胃道出血加上fibrinogen小於1g/kg	1U/6kg

屈公病

DIAGNOSIS AND MANAGEMENT OF IMPORTED CHIKUNGUNYA FEVER IN TAIWAN: A CASE REPORT

Ko Chang,¹ Hsiao-Chen Hsieh,¹ Jih-Jin Tsai,^{2,3,4} Wei-Ru Lin,^{2,3} Po-Liang Lu,^{2,3,5,6} and Yen-Hsu Chen^{3,5,7}

¹Department of Internal Medicine, Kaohsiung Municipal Hsiao-Kang Hospital, ²School of Medicine, ⁵Graduate Institute of Medicine and ⁷Tropical Medicine Research Center, College of Medicine, Kaohsiung Medical University; ³Division of Infectious Disease, Department of Internal Medicine, Department of ⁴Tropical Medicine Center and ⁶Laboratory Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan.

Chikungunya virus, a mosquito-borne alphavirus, is endemic in Africa and Southeast Asia but is rarely reported in Taiwan. We report the case of a Taiwanese woman who developed Chikungunya fever, which was first diagnosed by a clinician rather than by fever screening at an airport. The woman presented with fever, maculopapular rash, and arthralgia, the triad for the disease, on the day she returned home after a trip to Malaysia. These symptoms are very similar to those of dengue fever, which is endemic in Southern Taiwan. Chikungunya infection was confirmed by reverse transcriptase-polymerase chain reaction and seroconversion on paired serum specimens. For approximately 40 years until 2006, no cases of Chikungunya fever had been found in Taiwan. Clinicians in Taiwan should consider Chikungunya fever as a possible diagnosis for a febrile patient with arthralgia, rash, and a history of travel to an endemic area, such as Africa or Southeast Asia.

Key Words: chikungunya fever, dengue fever, Taiwan
(*Kaohsiung J Med Sci* 2010;26:256–60)

屈公病

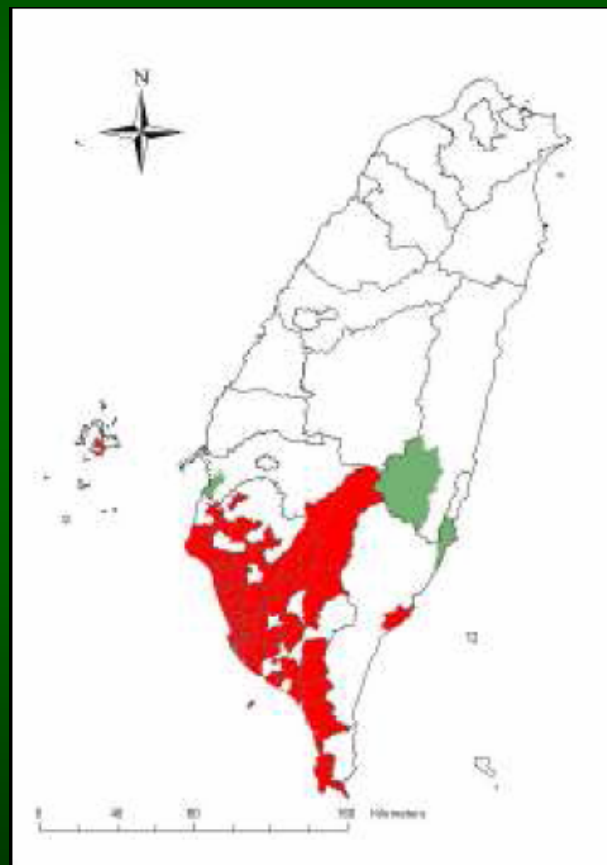
- 屈公病是一種經由蚊子傳遞病毒所引起的疾病，盛行於非洲、東南亞及印度
- 該病毒最早是在1952年從坦尚尼亞一位發燒病人的血清中分離出來
- “Chikungunya”為坦尚尼亞土語，原意為“身體彎曲形同摺疊狀”，係因嚴重的關節痛所引起的

Arboviruses

Disease	Vector	Host	Distribution	Disease
Alphaviruses				
Chikungunya	<i>Aedes</i>	Humans, monkeys	Africa, Asia	Fever, arthralgia, arthritis
Eastern equine encephalitis	<i>Aedes, Culiseta</i>	Birds	North and South America, Caribbean	Mild systemic ; encephalitis
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West Nile encephalitis	<i>Culex</i>	Birds	Africa, Europe, central Asia, North America	Fever, encephalitis, hepatitis
St. Louis encephalitis	<i>Culex</i>	Birds	North America	Encephalitis

病媒蚊

- 埃及斑蚊
 - 分布於嘉義布袋以南各縣市
- 白線斑蚊
 - 分布於全島平地及1500公尺以下之山區
 - 埃及斑蚊：喜歡棲息在室內
 - 白線斑蚊：棲息場所多在室外



感染過程

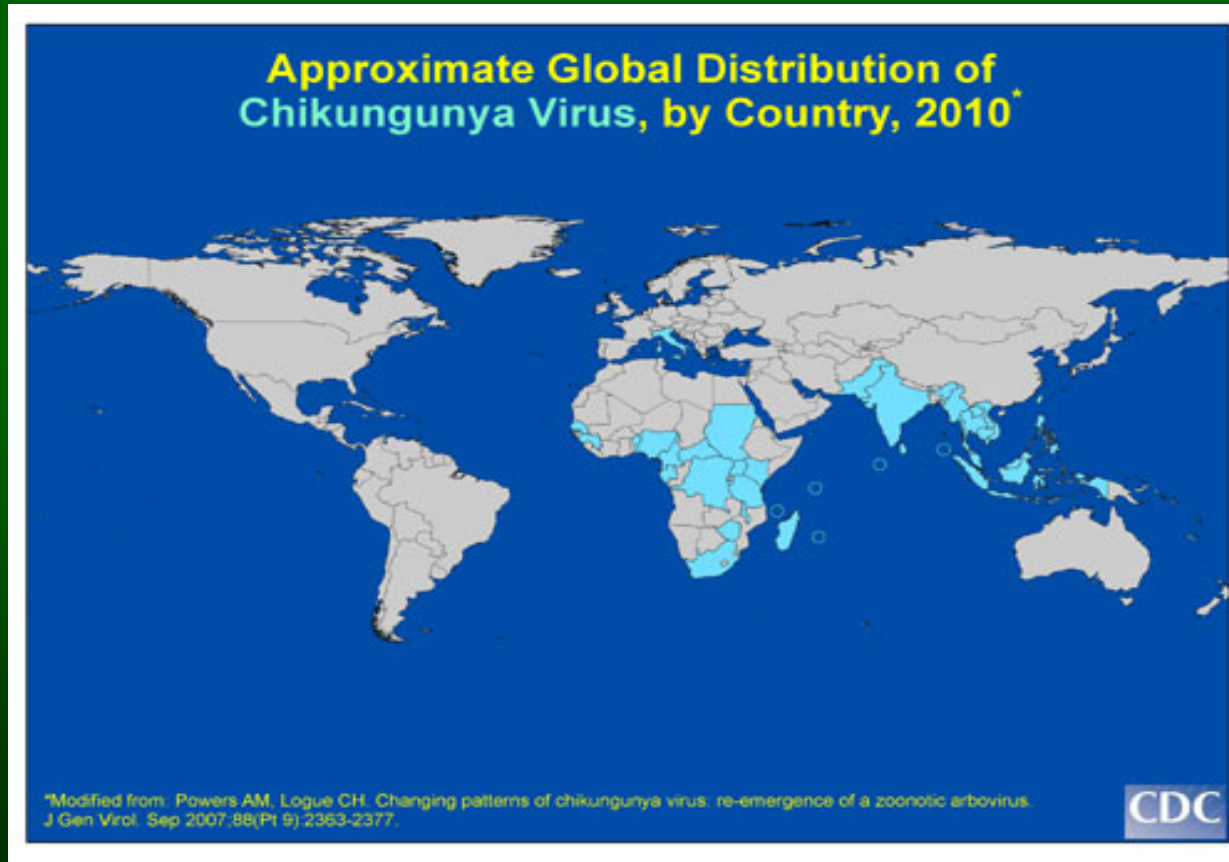
- 傳染方式
 - 經由病媒蚊叮咬傳播
- 潛伏期
 - 潛伏期2~12 天，平均3~7 天
- 可傳染期
 - 病人發病前2 天及發病後5 天為病毒血症期，此時期若蚊蟲吸取病人的血液，病毒會在蚊體內繁殖後具有感染力
- 感染性及抵抗力
 - 於性別及年齡無顯著差異

病例定義

- 屈公病：有「屈公病」相關流行地區旅遊史，且有下列症狀：
 - 發燒
 - 頭痛
 - 噁心
 - 嘔吐
 - 肌痛
 - 出疹
 - 關節痛

屈公病流行區域

- 屈公病全球流行區域涵蓋非洲撒哈拉沙漠以南（sub-Saharan Africa）、亞洲及南美洲的熱帶及亞熱帶區域



實驗室診斷

- 由臨床檢體分離出屈公病毒或證實有屈公病毒抗原或核酸
- 抗體有4倍以上之上升，或屈公病毒特異性IgM 抗體陽性

治療及預後

- 治療方式
 - 無針對屈公病毒之抗病毒藥物
 - 依病情給予支持療法
 - Relieve symptoms of fever and aching such as ibuprofen, naproxen, acetaminophen, or paracetamol.
 - Aspirin should be avoided.
- 預後
 - 感染後通常可以完全復原
 - 有些個案關節痛持續幾個月

Non-specific constitutional symptoms observed in haemorrhagic fever patients with dengue and chikungunya

Criteria	DHF(%)	Chikungunya Fever (%)
Injected pharynx	96.8	90.3
Vomiting	57.9	59.4
Constipation	53.5	40.0
Abdominal pain	50.0	31.6
Headache	44.6	68.4
Generalized lymphadenopathy	40.5	30.8
Conjunctival injection	32.8 ^b	55.6 ^b
Cough	21.5	23.3
Rhinitis	12.8	6.5
Maculopapular rash	12.1 ^b	59.4 ^b
Myalgia/arthralgia	12.0 ^b	40.0 ^b
Enanthema	8.3	11.1
Abnormal reflex	6.7	0.0
Diarrhoea	6.4	15.6
Palpable spleen	6.3 ^c	3.1 ^c
Coma	3.0	0.0

^a Modified from Nimmannitya S et al. *American journal of tropical medicine and hygiene*, 1969, 18: 954–971.

^b Statistically significant difference.

^c Infants under 6 months.

Criteria for differential diagnosis of dengue haemorrhagic fever and chikungunya fever

Criteria	Dengue haemorrhagic fever (%)	Chikungunya fever (%)
Duration of fever:		
2–4 days	23.6	62.5
5–7 days	59.0	31.2
>7 days	17.4	6.3
Haemorrhagic manifestations:		
positive tourniquet test	83.9	77.4
scattered petechiae	46.5	31.3
confluent petechial rash	10.1	0.0
epistaxis	18.9	12.5
gum bleeding	1.5	0.0
melaena/haematemesis	11.8	0.0
Hepatomegaly	90.0	75.0
Shock	35.2	0.0

^a Modified from Nimmannitya S et al. *American journal of tropical medicine and hygiene*, 1969, 18: 954–971.



THANK YOU !!