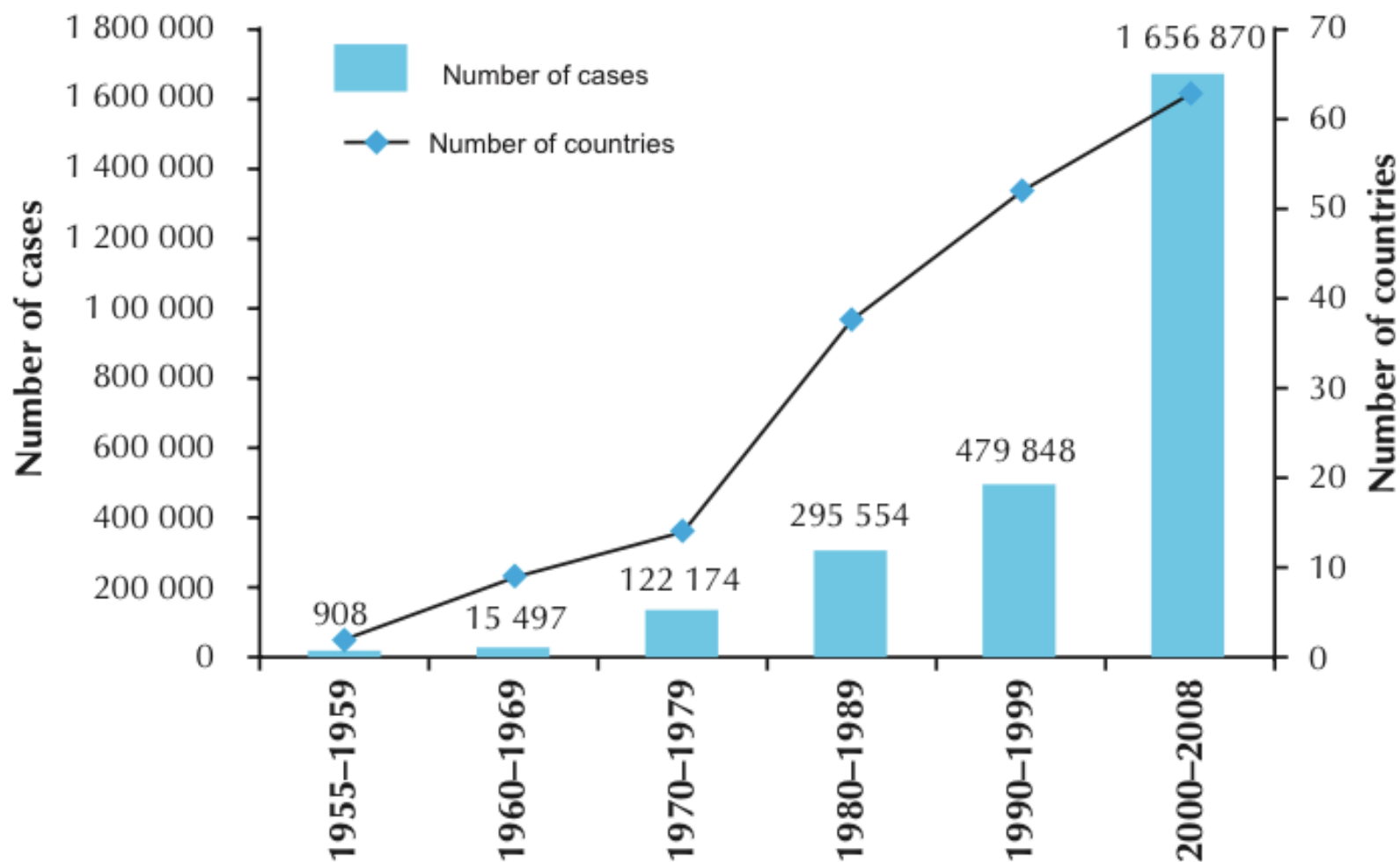


# Dengue fever - update

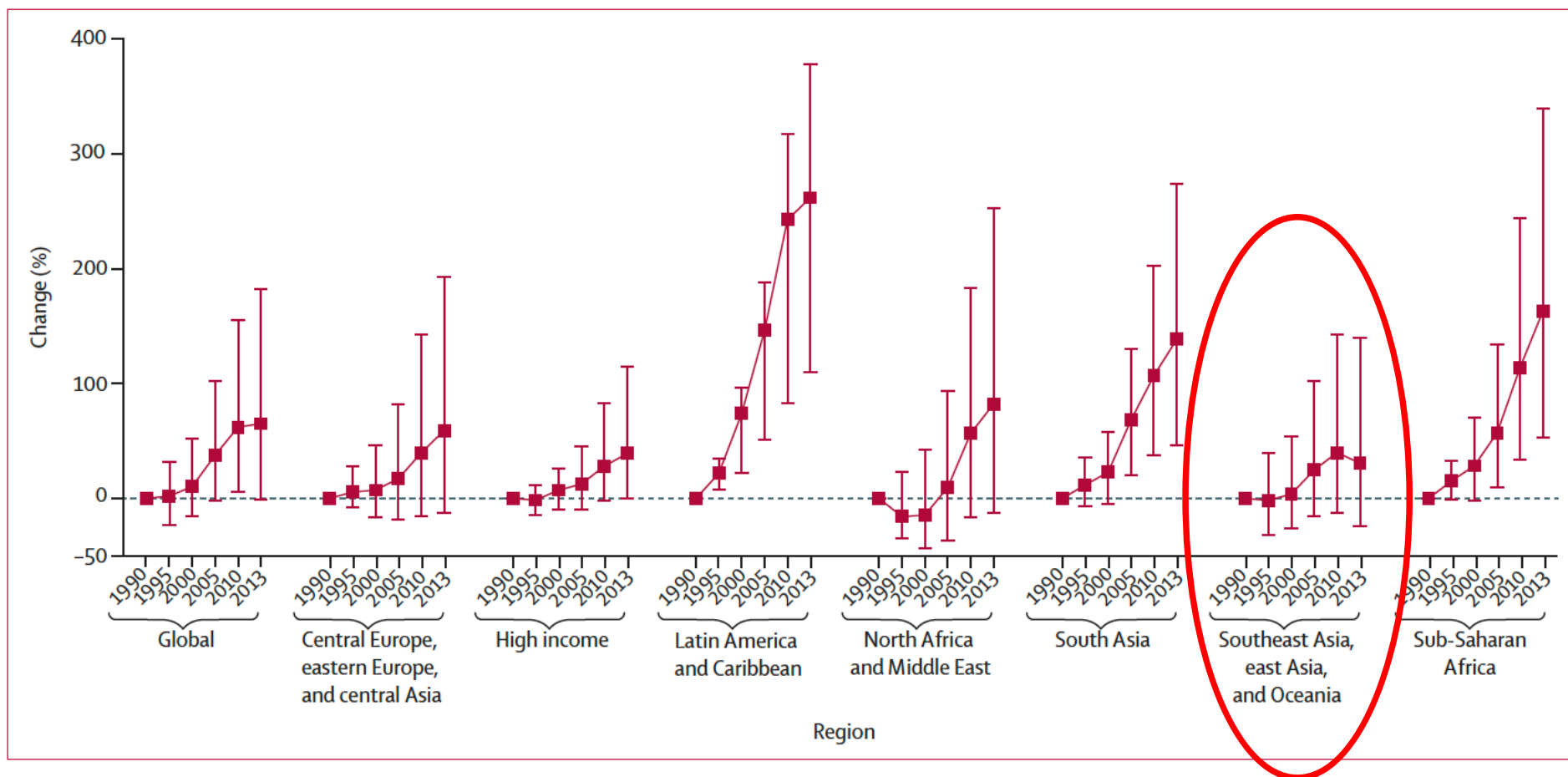


Dr Owen Tsang  
Princess Margaret Hospital  
13 July 2017  
IC forum

# World figures







**Figure 3: Change in disability-adjusted life-years for dengue since 1990 in dengue-endemic countries**

Dengue-endemic countries are those with a non-zero probability of dengue transmission based on Bhatt and colleagues.<sup>7</sup>

# Epidemiology

- WHO reports **30x increase** in cases since 1960
- No. of countries reporting epidemic dengue has **increase > 4x** since 1970
- **Half** the world population are at risk
- **~ 50-100 millions** new infections per year
- **Case fatality 1-5%**
- **~ 75%** global population exposed to dengue are in **Asia-pacific** region

# Guangzhou 2014 outbreak

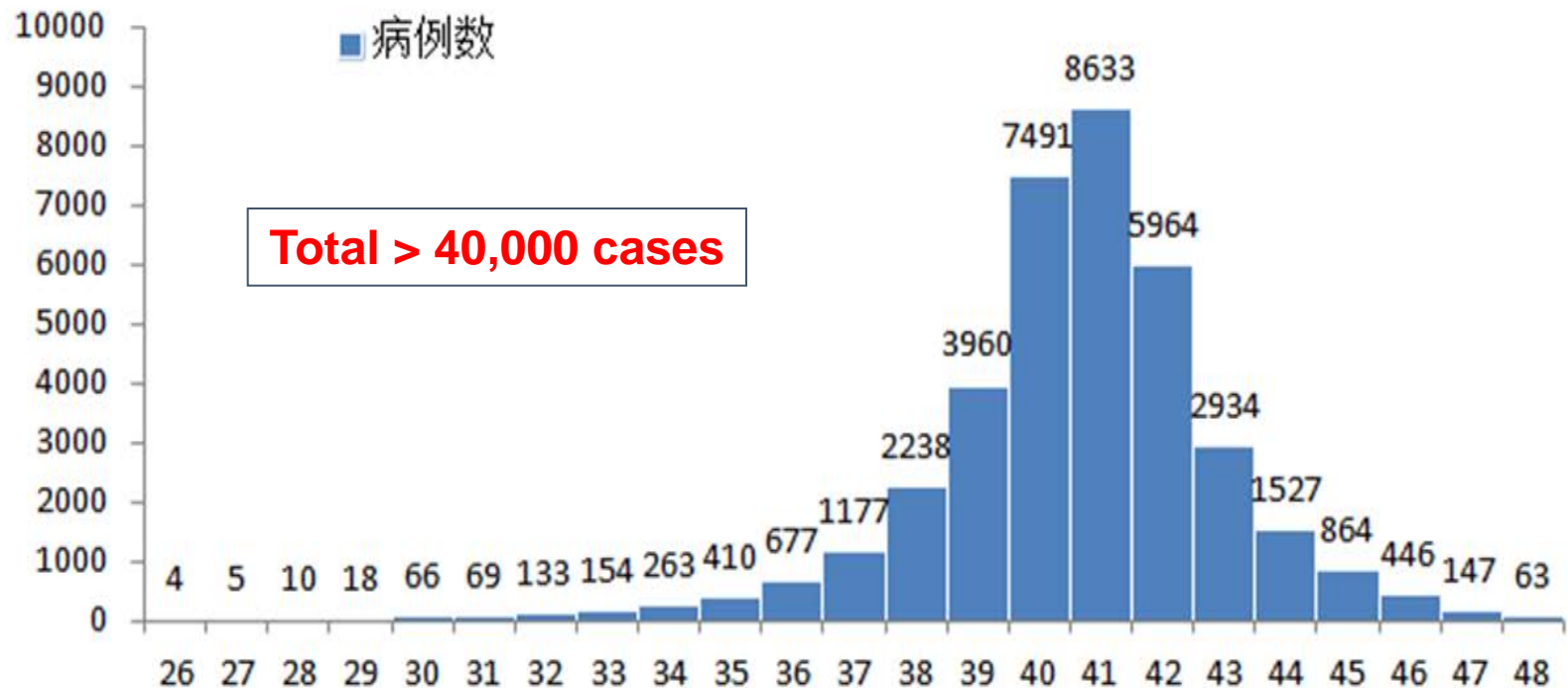
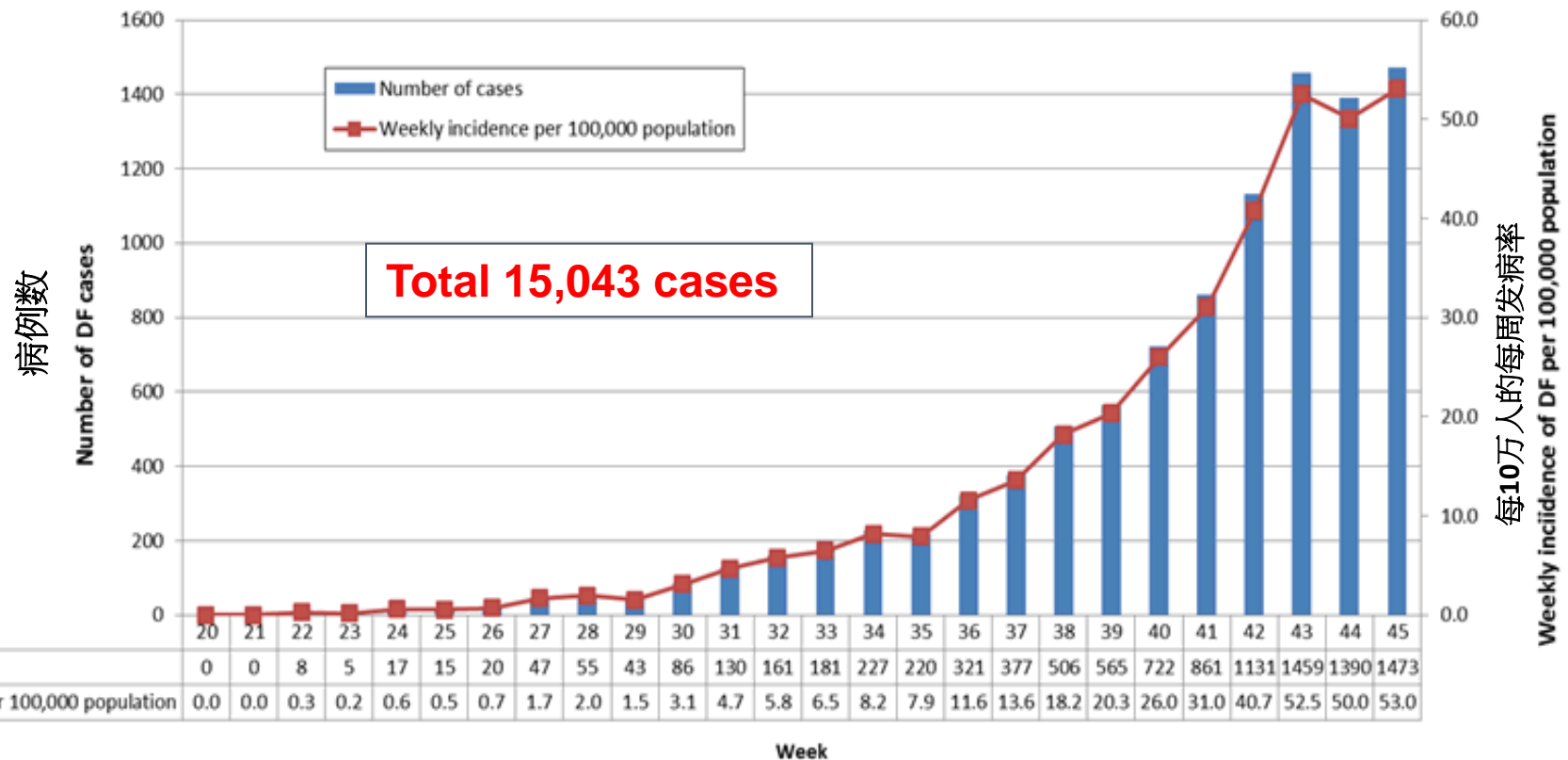


图 2 2014 年登革热病例按周报告曲线

# Taiwan Kaohsiung 2014 outbreak

Weekly number of cases and incidence of DF  
in Kaohsiung, Taiwan, 2014



# Taiwan 2015 outbreak

## 登革熱入夏以來本土病例統計

| 縣市  | 新增病例 | 較前日新增病例增減 | 確定病例  |
|-----|------|-----------|-------|
| 全 國 | 302  | (-45)     | 38369 |
| 台南市 | 16   | (1)       | 22608 |
| 高雄市 | 283  | (-38)     | 15022 |
| 屏東縣 | 4    | (-3)      | 273   |
| 新北市 | 0    | (1)       | 77    |
| 台北市 | 0    |           |       |
| 台中市 | 0    |           |       |
| 桃園市 | 0    |           |       |
| 彰化縣 | -1   |           |       |
| 嘉義縣 | 0    |           |       |
| 新竹縣 | 0    | (0)       | 24    |
| 雲林縣 | 0    | (0)       | 19    |
| 新竹市 | 0    | (0)       | 18    |
| 嘉義市 | 0    | (0)       | 17    |
| 澎湖縣 | 0    | (0)       | 11    |
| 台東縣 | 0    | (0)       | 11    |
| 花蓮縣 | 0    | (0)       | 9     |
| 基隆市 | 0    | (0)       | 7     |
| 南投縣 | 0    | (0)       | 7     |
| 宜蘭縣 | 0    | (0)       | 5     |
| 苗栗縣 | 0    | (0)       | 5     |
| 金門縣 | 0    | (0)       | 3     |
| 連江縣 | 0    | (0)       | 1     |

**Total 42,572 cases  
Death > 200 cases**

## 奪命好凶！台灣這波登革熱致死率 多新加坡10倍

NOWnews - 2015年10月13日 下午3:02

-A +A

相關內容



台灣這一波登革熱致死率高，奪命凶過國外！衛福部疾管署防疫醫師研究發現，比較同樣使用登革熱快篩、疫情規模相當的新加坡2013年疫情之後，台南引爆的這一波疫情迄今死

千分之3至4，足足比新加坡死亡率的萬分之4，多出，其中最大差異在於，台灣4成以上感染者都是逾55危險族群。

行疫情指揮中心今（13）天最新統計，台南市昨僅新增217例本土登革熱病例，較上周同日已減少105例，疫情已經明顯趨緩。疾管署署長郭旭崧樂觀的說，台南疫情已大勢底定，將會慢慢降溫。

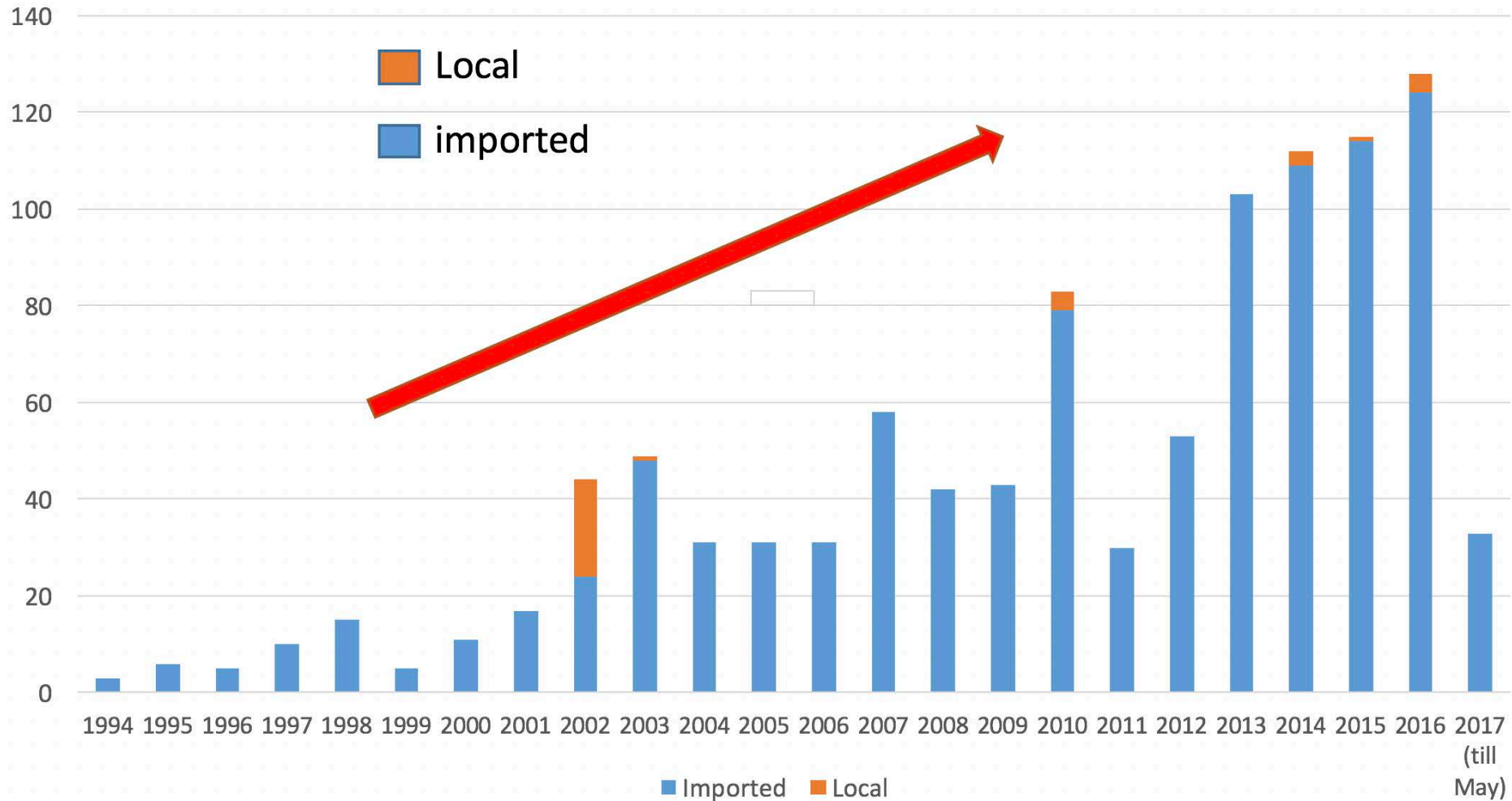


全國今年入夏以來登革熱本土病例已累計2萬3456例，目前已造成89人死亡，仍有43例疑似死亡個案待審，外界普遍預估，死亡人數恐破百人，創下有史以來的新高。

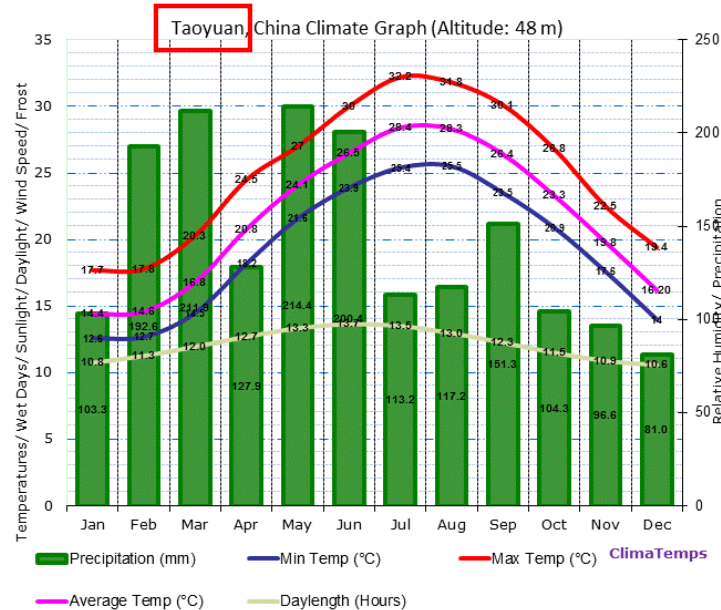
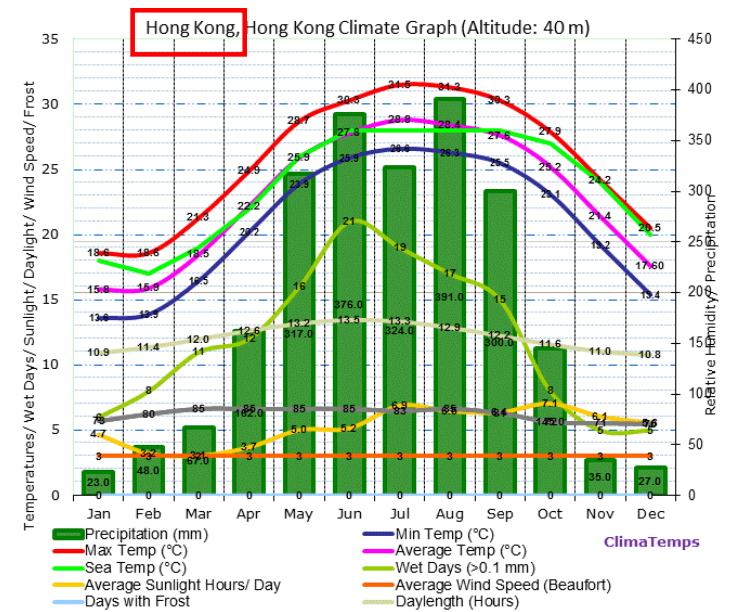
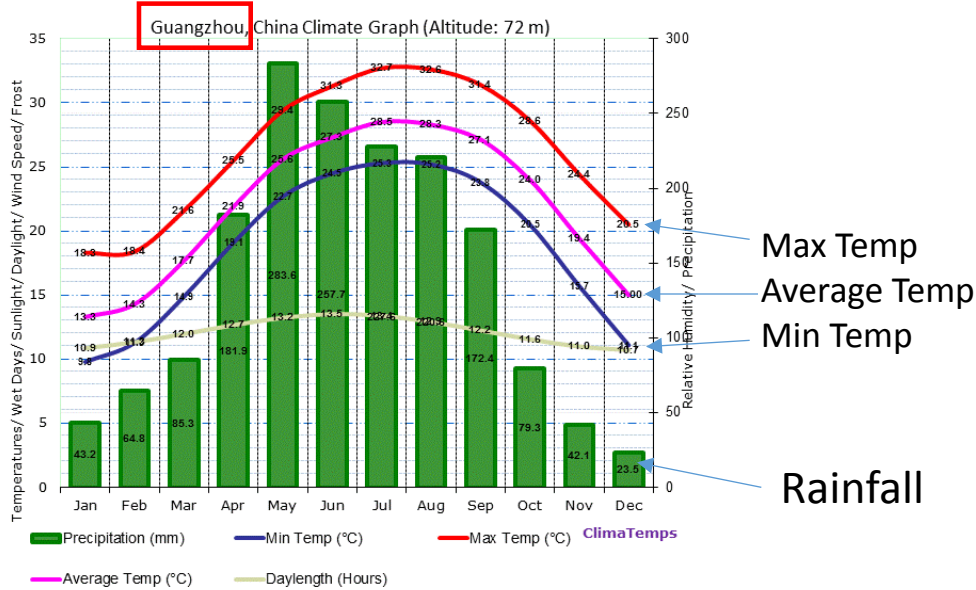
疾管署首席防疫醫師羅一鈞表示，國內這波疫情，死亡個案年齡中位數為77歲，相較之下，新加坡2013年疫情的死亡個案年齡中位數僅52歲，且台灣4成以上確診患者年齡超過55歲，但新加坡比率只有14%，近8成都是15至50歲的青壯人口，顯示年齡是造成台灣致死率多出新加坡8至10倍的主要因素。

截止日期:2015/11/26 18:00

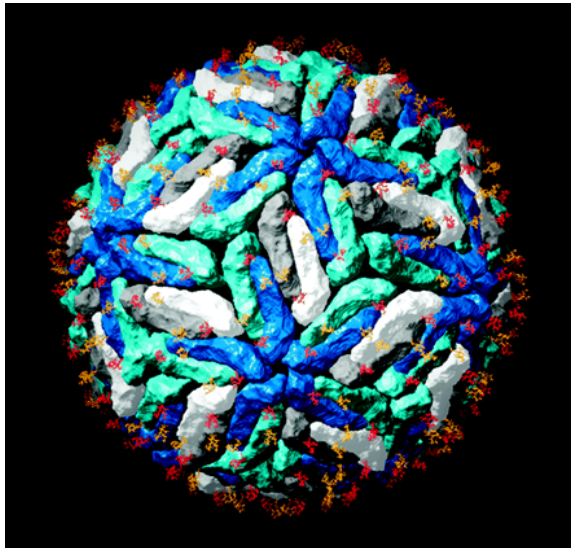
# Dengue cases in Hong Kong (1994 – 5/2017)



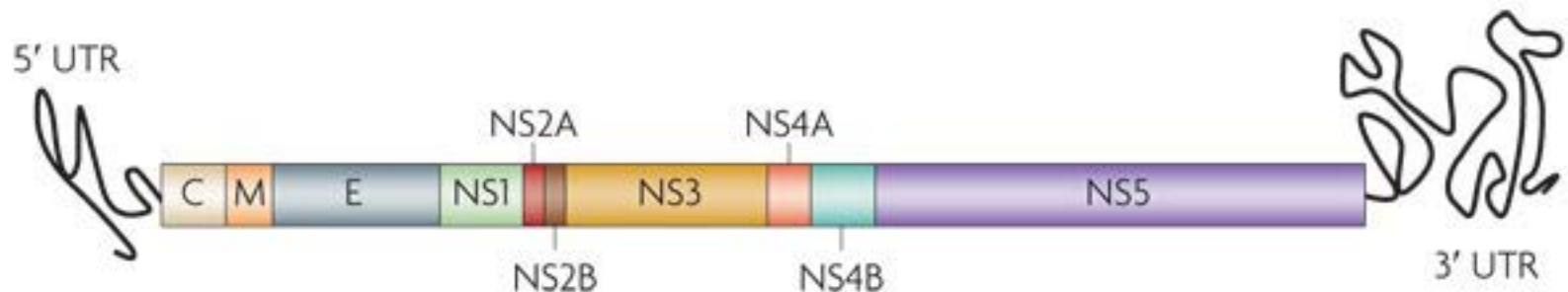
# Temperature & humidity of 3 cities

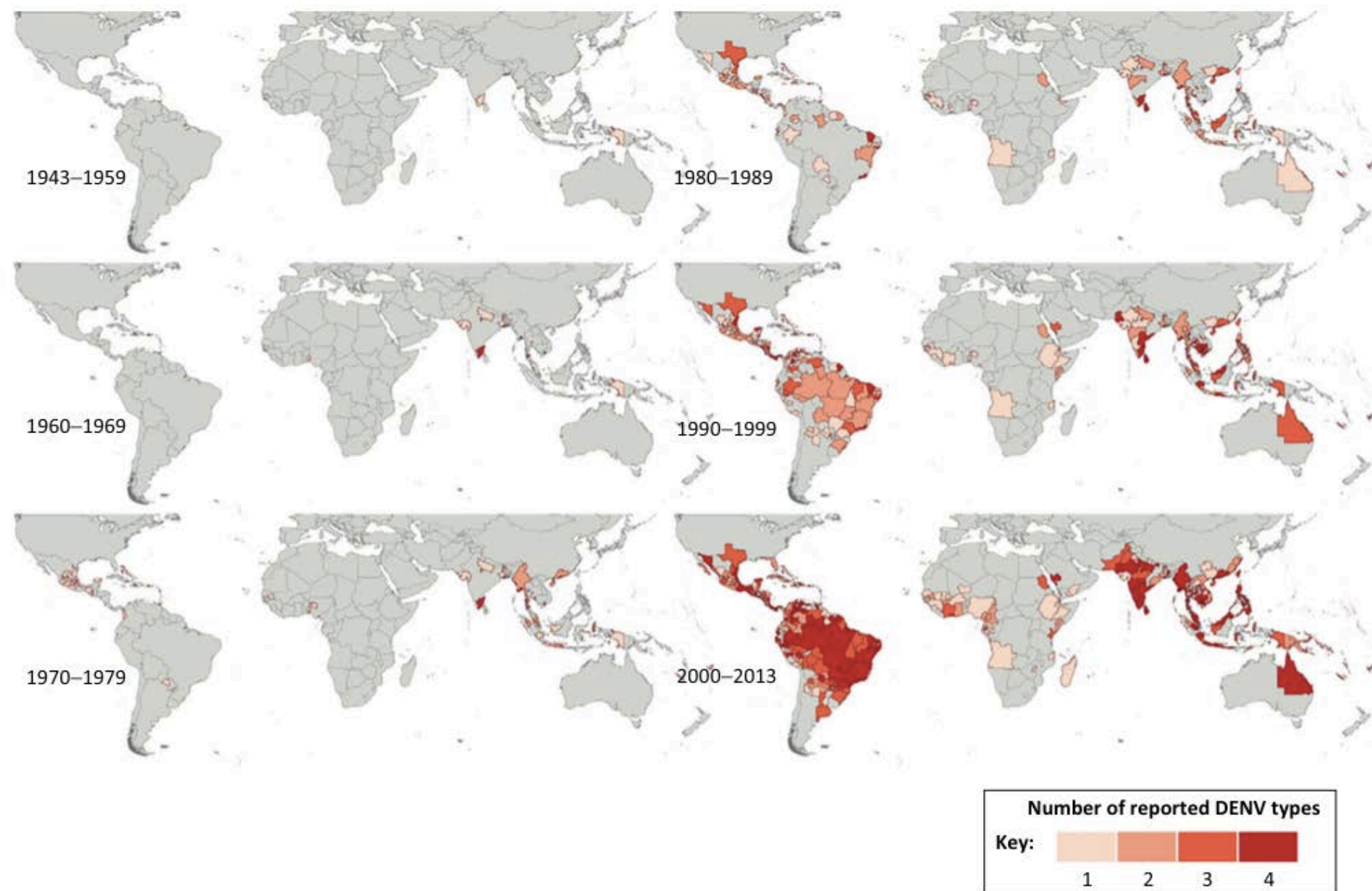


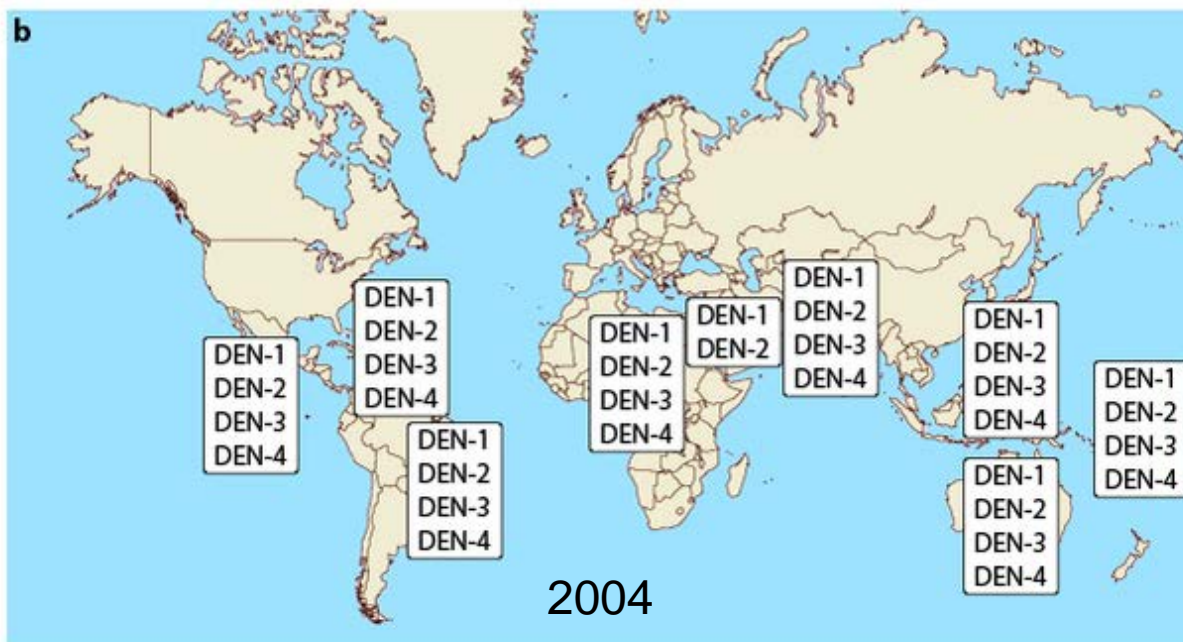
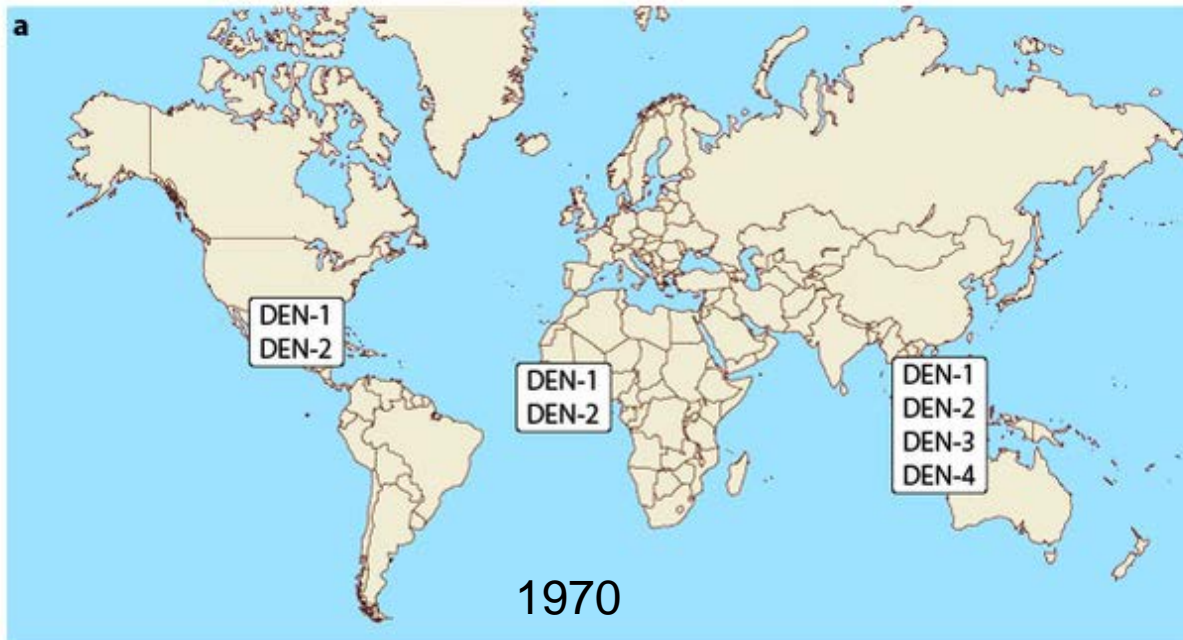
# Dengue virus



- Single stranded Enveloped RNA virus
- Genus *Flavivirus*
- Arbovirus: transmitted by mosquito, no human to human transmission except for blood transfusion
- 4 serotypes: DEN-1, 2, 3, 4
- Same group: Yellow fever virus, Hepatitis C virus, JEV, Tick-borne encephalitis virus
- Infection with one serotype provides lifelong immunity to that virus
- No cross-protective immunity to the other serotypes



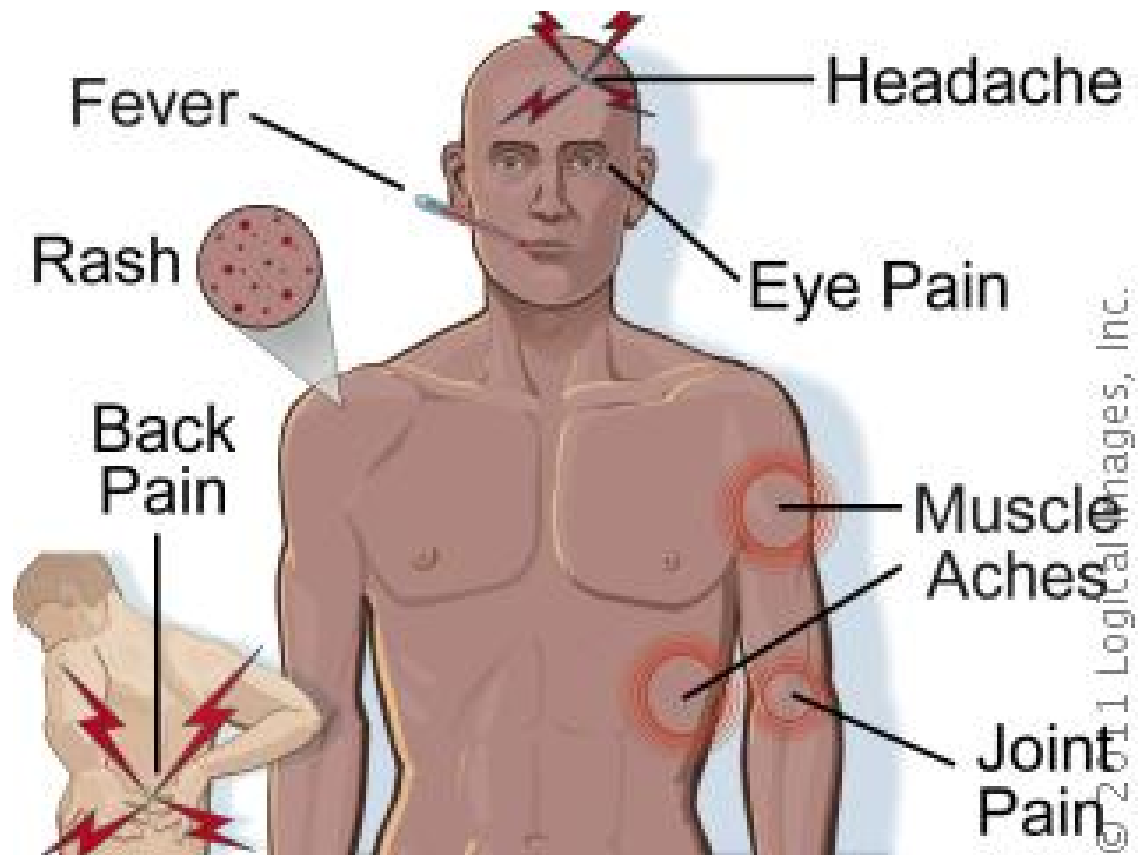




# Classical Clinical Syndromes

1. **Undifferentiated fever:** most common: > 80%
2. **Classical Dengue fever:**
  - Fever, headache, M & Jt pain, Nausea/vomiting, rash, hemorrhagic manifestation
3. **Dengue hemorrhagic fever:**
  - Fever, hemorrhagic manifestation
  - Low platelet < 100
  - Evidence of leakage capillaries: ↓ Alb, ↑ hemotocrit > 20%, Pleural or other effusions
4. **Dengue shock syndrome:**
  - Sign of circulatory failure

# Classical Dengue fever



ORIGINAL  
ARTICLE

## Review of dengue fever cases in Hong Kong during 1998 to 2005

Vivien WM Chuang 莊慧敏  
TY Wong 黃天佑  
YH Leung 梁耀康  
Edmond SK Ma 馬紹強  
YL Law 羅育龍  
Owen TY Tsang 曾德賢  
KM Chan 陳啟明  
Iris HL Tsang 曾愷玲  
TL Que 郭德麟  
Raymond WH Yung 翁維雄  
SH Liu 劉少懷

**Objective** To describe the epidemiology, clinical and laboratory findings, and outcomes of patients presenting locally with dengue.

**Design** Retrospective review of case records.

**Setting** Public hospitals, Hong Kong.

**Patients** Medical records of all laboratory-confirmed dengue patients admitted to public hospitals during 1998 to 2005 were reviewed retrospectively.

**Results** A total of 126 cases were identified, 123 (98%) being dengue fever and three (2%) dengue haemorrhagic fever. One patient who had blood transfusion-acquired dengue fever was highlighted. A total of 116 (92%) cases were 'imported', while 10 (8%) were local. Among the 56 serotypes confirmed by reverse transcription-polymerase chain reaction, dengue virus type 1 was the most

# Clinical features of cases in HK

| Symptoms                         | Percentage (N= 124) |
|----------------------------------|---------------------|
| Fever                            | <b>98%</b>          |
| Myalgia                          | 83%                 |
| Headache                         | 65%                 |
| Skin rash                        | <b>60%</b>          |
| Fatigue                          | 59%                 |
| Dizziness                        | 45%                 |
| Retrobulbar pain                 | <b>34%</b>          |
| GI (nausea, vomiting, diarrhoea) | 35%                 |
| URT (Dry cough, sore throat)     | 29%                 |
| Epistaxis                        | 10%                 |
| Gum bleeding                     | 12%                 |
| Hematemesis                      | 2%                  |
| Tarry stool                      | 1%                  |
| Petechiae                        | <b>45%</b>          |
| Lymphadenopathy                  | 16%                 |

# Laboratory findings

| Laboratory findings  | Percentage |
|----------------------|------------|
| Thrombocytopenia     | 86%        |
| Lymphopenia          | 69%        |
| Neutropenia          | 78%        |
| Atypical lymphocytes | 75%        |
| Prolonged APTT       | 51%        |
| Elevated AST         | 91%        |
| Elevated ALT         | 80%        |
| Hypoalbuminaemia     | 28%        |

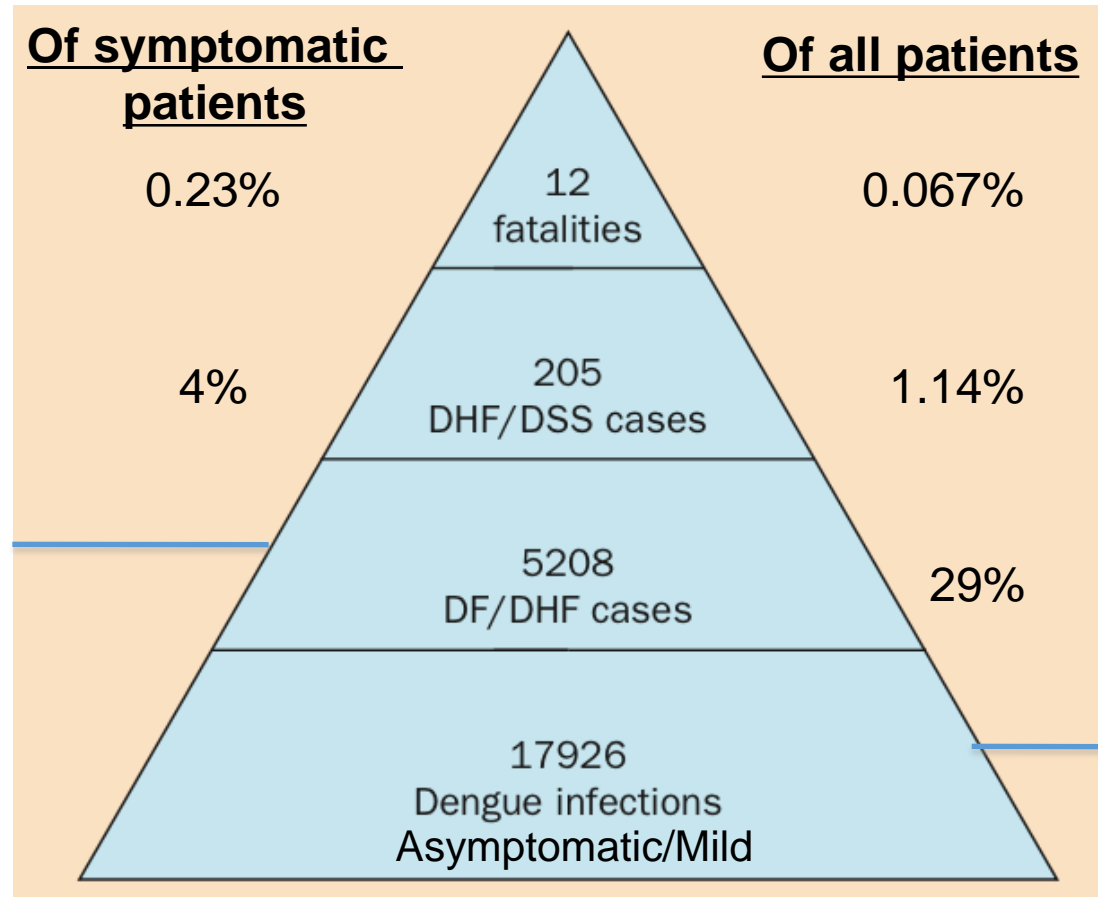
# PMH cases



# PMH case

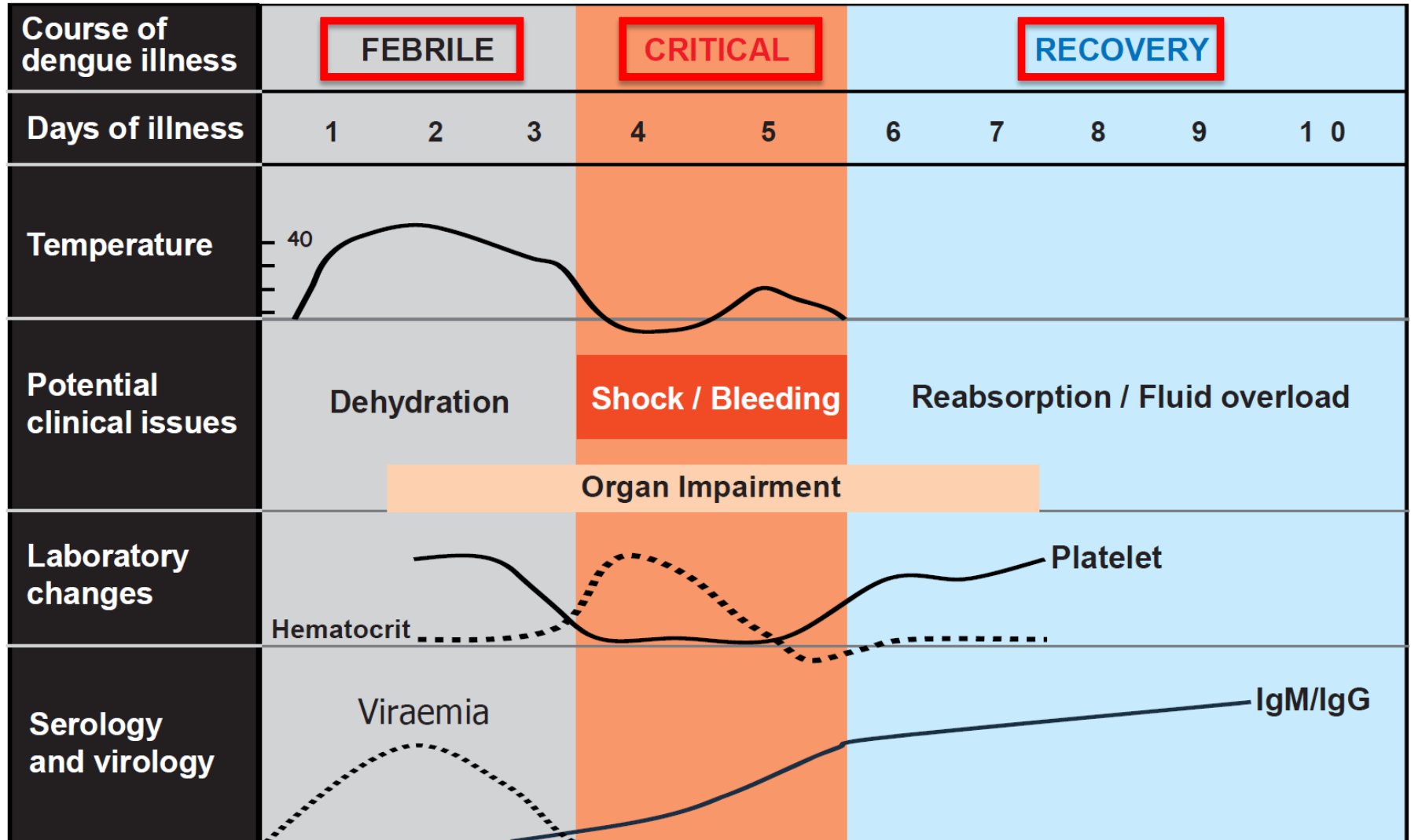


# Clinical course



*Reported and estimated DF/ DHF and dengue-2 infections during the 1997 DHF Cuban epidemic*

# New Clinical course



# Symptoms of Dengue fever

## Febrile phase

sudden-onset fever

headache

mouth and nose  
bleeding

muscle and  
joint pains

vomiting

rash

diarrhea

## Critical phase

hypotension

pleural effusion

ascites

gastrointestinal  
bleeding

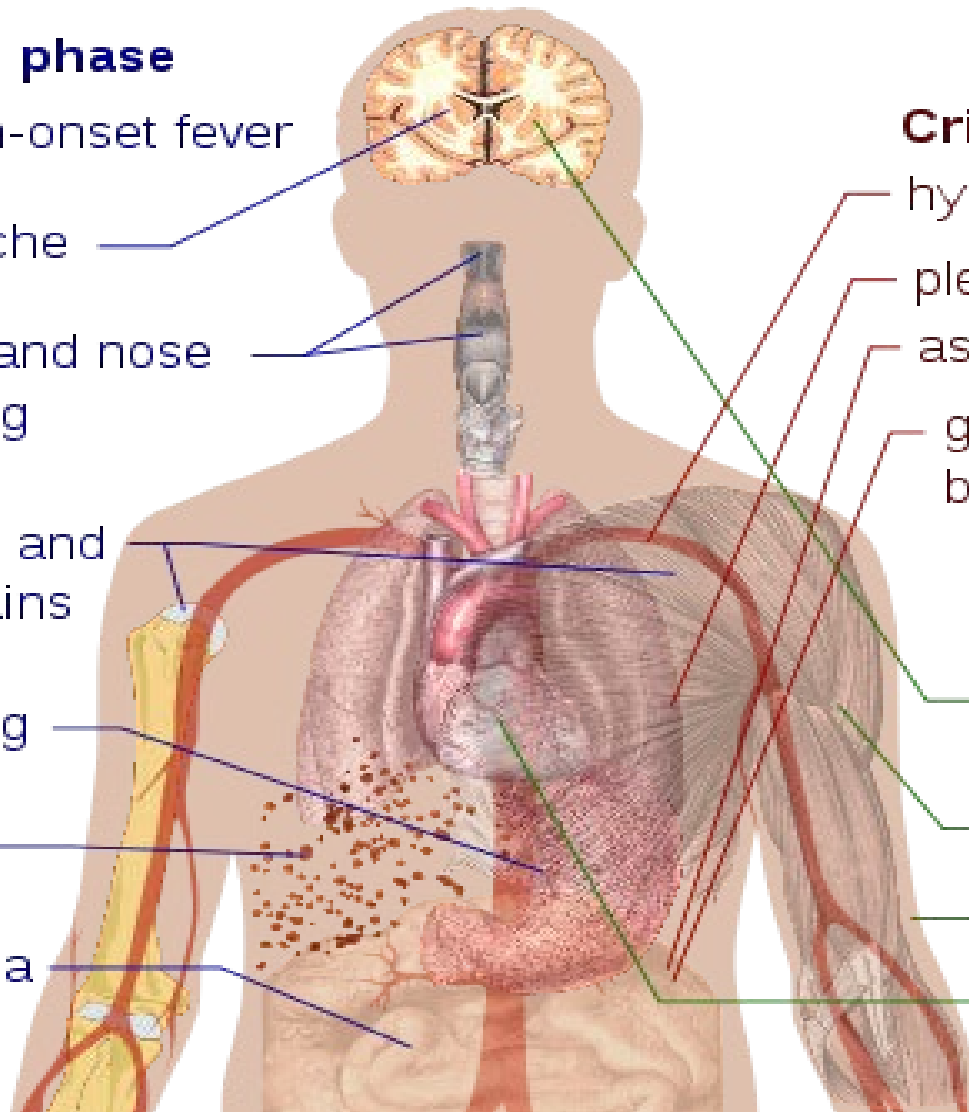
## Recovery phase

altered level of  
consciousness

seizures

itching

slow heart rate



# Febrile phase

| Clinical syndrome          | Differential diagnoses  |
|----------------------------|---|
| Flu-like syndrome          | Influenza<br>Measles<br>Chikungunya<br>Adenovirus<br>Infectious mononucleosis<br>Acute HIV seroconversion illness |
| Rash                       | Rubella<br>Measles<br>Scarlet fever<br>Meningococcal infection<br>Chikungunya<br>Drug                             |
| Diarrhea                   | Rotavirus<br>Food poisoning   |
| Neurological manifestation | Meningoencephalitis<br>Febrile seizures   |

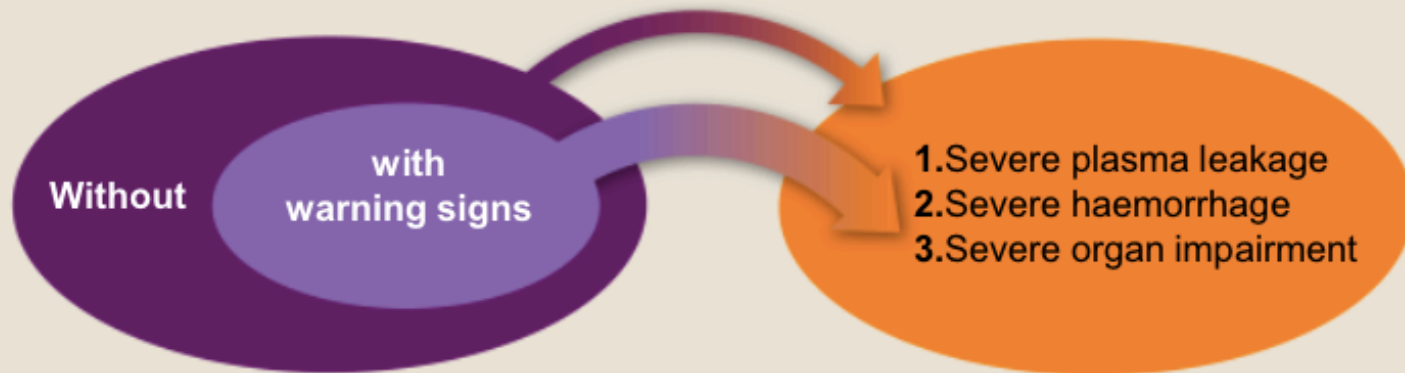
# Critical phase

| Clinical syndrome                              | Differential diagnoses  |
|--|---|
| Acute abdomen                                  | Acute appendicitis<br>Acute cholecystitis<br>Perforated viscus<br>Viral hepatitis<br>Diabetic ketoacidosis  |
| Shock  | Septic shock  |
| Respiratory distress<br>(Kussmaul's breathing) | Diabetic ketoacidosis<br>Renal failure<br>Lactic acidosis   |
| Leucopaenia &<br>thrombocytopenia ± bleeding   | Acute leukaemia<br>Immune thrombocytopaenia purpura<br>Thrombotic Thrombocytopenic purpura<br>Malaria / Leptospirosis / Typhoid / Typhus<br>Bacterial sepsis<br>SLE<br>Acute HIV seroconversion illness |

# Dengue case classification by severity

## Dengue ± warning signs

## Severe dengue



### Criteria for dengue ± warning signs

#### Probable dengue

Live in/travel to dengue endemic area. Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leucopenia
- Any warning sign

#### Laboratory confirmed dengue

(important when no sign of plasma leakage)

#### Warning signs\*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy; restlessness
- Liver enlargement >2cm
- *Laboratory*: Increase in HCT concurrent with rapid decrease in platelet count

*\* Requiring strict observation and medical intervention*

### Criteria for severe dengue

#### 1. Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

#### 2. Severe bleeding

as evaluated by clinician

#### 3. Severe organ involvement

- Liver: AST or ALT ≥ 1000
- CNS: Impaired consciousness
- Heart and other organs

# Dengue Case Management

## Assessment

### Presumptive Diagnosis:

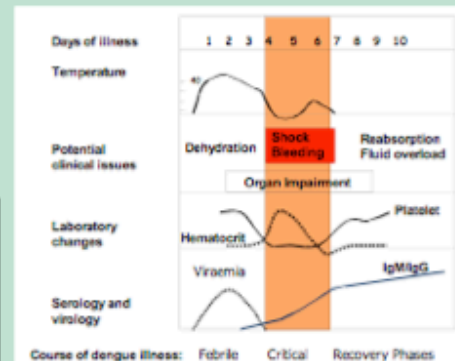
Live in / travel to endemic area plus  
Fever and two of the following:

- Anorexia and nausea
- Rash
- Aches and pains
- Warning signs
- Leucopenia
- Tourniquet test positive

Lab.confirmed dengue  
(important when no sign  
of plasma leakage)

### Warning signs:

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy; restlessness
- Liver enlargement >2cm
- Laboratory: Increase in HCT concurrent with rapid decrease of platelet count



## Classification

negative

Co-existing conditions  
Social circumstances

negative

**Dengue without  
warning signs**

**Group A**  
May be sent home

positive

**Dengue with  
warning signs**

**Group B**  
Referred for in-hospital care

positive

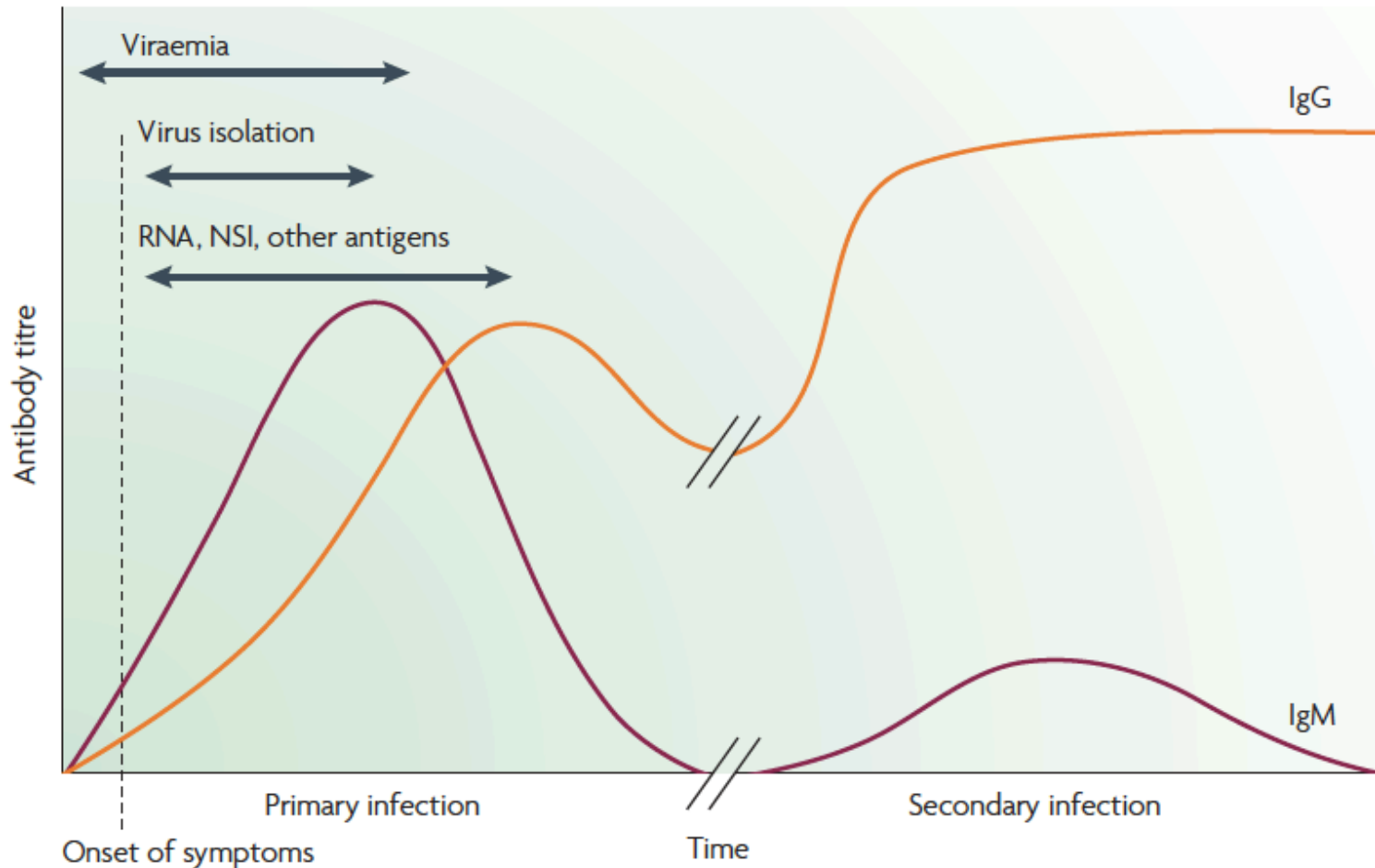
**Severe Dengue**

**Group C**  
Require emergency treatment

# Clinical pearls

- Place of travel **within 14 days** should raise suspicion
- **Leucopenia** followed by progressive **thrombocytopenia** is suggestive
- **Atypical lymphocyte** is common in dengue infection
- A rising **HCT** accompanying **progressive thrombocytopenia** is critical phase.
- In the absence of a baseline HCT, a HCT > **40%** in **female** & > **46%** in **male** should raise the suspicion of **plasma leakage**.
- Evidence of **increased vascular permeability**: pleural effusions, ascites

# Laboratory diagnosis



# Diagnostic tests

| Tests                          | Sensitivity  | Specificity   |
|--------------------------------|--------------|---------------|
| IgM test                       | 61.5 – 100%  | 52 – 100%     |
| IgG test                       | 46.3 – 99%   | 80 – 100%     |
| Rapid IgM detection            | 20.5 – 97.7% | 76.6% - 90.6% |
| NS1 Ag detection               | 54.2 – 93.4% | 92.5 – 100%   |
| RT-PCR                         | 59 – 100%    | 100%          |
| Virus isolation (Cell culture) | 40.5%        | 100%          |

# Specific anti-virals in clinical trials

| Drug                               | Developer  | Phase  | Trial site | Current status (end date)               |
|------------------------------------|--|--------|------------|---|
| Ivermectin                         | Mahidol University   | II/III | Thailand   | Yet to initiate                         |
| UV-4B                              | Unither<br>Virology  | I      | ?          | Yet to initiate                         |
| Ribavirin                          | Guangzhou 8th People's Hospital                              | II     | China      | Ongoing (December 2015)                 |
| Lovastatin                         | Oxford University Clinical<br>Research Unit & Wellcome Trust | I      | Vietnam    | Ongoing [90] (January 2015)             |
| <del>Chloroquine</del>             | University of Sao Paulo                                      | I/II   | Brazil     | ? (June 2009)                           |
| <del>Chloroquine</del>             | Oxford University Clinical<br>Research Unit & Wellcome Trust | I      | Vietnam    | Completed [91] (July 2008)              |
| <del>Prednisolone</del>            | Oxford University Clinical<br>Research Unit & Wellcome Trust | I      | Vietnam    | Completed [92] (January 2011)           |
| <del>Carica folia</del><br>extract | Fr. Muller Homeopathic<br>Medical College                    | I      | India      | Completed <sup>NR</sup> (December 2013) |
| <del>Balapiravir</del>             | Hoffmann-La Roche  | I      | Vietnam    | Completed [93] (April 2011)             |
| <del>Celgosivir</del>              | Singapore Gen Hospital &<br>Duke-NUS Graduate Med School     | I/II   | Singapore  | Completed [94] (July 2013)              |

# Vaccines for Dengue virus

## Dengue

Acambis and Sanofi Pasteur

Live, attenuated chimeric dengue–yellow fever

WRAIR and GlaxoSmithKline

Live, attenuated

NIH, Biologicals E (India), Panacea (India)

Live, attenuated chimeric dengue–dengue

Mahidol University (Bangkok)

Live, attenuated

CDC, Inviragen, Shantha (India)

Live, attenuated chimeric dengue–dengue

Hawaii Biotech

Recombinant, subunit

U.S. Navy

DNA



Annee Sabchareon, Derek Wallace, Chukiat Sirivichayakul, Kriengsak Limkittikul, Pornthep Chanthavanich, Saravudh Suvannadabba, Vithaya Jiwariyavej, Wut Duangjai, Kikana Benwan, T.Akh.Mutal, Annick Maureau, Melanie Souille, Alain Bouckenooghe, Simonette Vissani, Nadia G Tornieporth, Jean La

**Background** Roughly h  
investigated the efficac

**Methods** In this observational study, 100 schoolchildren aged 4–10 years (rabies vaccine or placebo) and participants were followed up for 25 months. All acute febrile and non-structural protein-positive cases were confirmed, symptomatic rabies cases received intravenous injection (per-protocol).

**Findings** 4002 participants  
analysis (2452 vaccine



# Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial

Maria Rosario Capeding, Ng  
Mary Noreen Chua, Chan Qi  
In-Kyu Yoon, Diane van der  
Melanie Saville, Alain Bouck

## Summary

**Background** An estimate of the impact of a phase 3 vaccine efficacy trial on the burden of vaccine against symptomatic COVID-19.

**Methods** We did an observational study in the Pacific region. Between 2007 and 2010, computer-generated randomised injections of a recombinant dengue vaccine (DENVax 12). Randomisation was done for the preparation and follow-up of the participants and their guardians. Our primary outcome was dengue, irrespective of primary or secondary infection. The primary endpoint was the proportion of participants with dengue, with intention to treat and per protocol analyses.

Lancet 2014; 384: 1358-65  
Published Online  
July 11, 2014  
[http://dx.doi.org/10.1016/S0140-6736\(14\)61060-6](http://dx.doi.org/10.1016/S0140-6736(14)61060-6)  
See Comment page 1327

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University of Indonesia, Cipto  
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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Efficacy of a Tetravalent Dengue Vaccine in Children in Latin America

Luis Villar, M.D., Gustavo Horacio Dayan, M.D., José Luis Arredondo-García, M.D.,  
Doris Maribel Rivera, M.D., Rivaldo Cunha, M.D., Carmen Deseda, M.D.,  
Humberto Reynales, M.D., Maria Selma Costa, M.D.,  
Javier Osvaldo Morales-Ramírez, M.D., Gabriel Carrasquilla, M.D.,  
Luis Carlos Rey, M.D., Reynaldo Dietze, M.D., Kleber Luz, M.D., Enrique Rivas, M.D.,  
Maria Consuelo Miranda Montoya, M.D., Margarita Cortés Supelano, M.D.,  
Betzana Zambrano, M.D., Edith Langevin, M.Sc., Mark Boaz, Ph.D.,  
Nadia Torniepoorth, M.D., Melanie Saville, M.B., B.S.,

2014

# Efficacy of Recombinant live-attenuated tetravalent Dengue vaccines

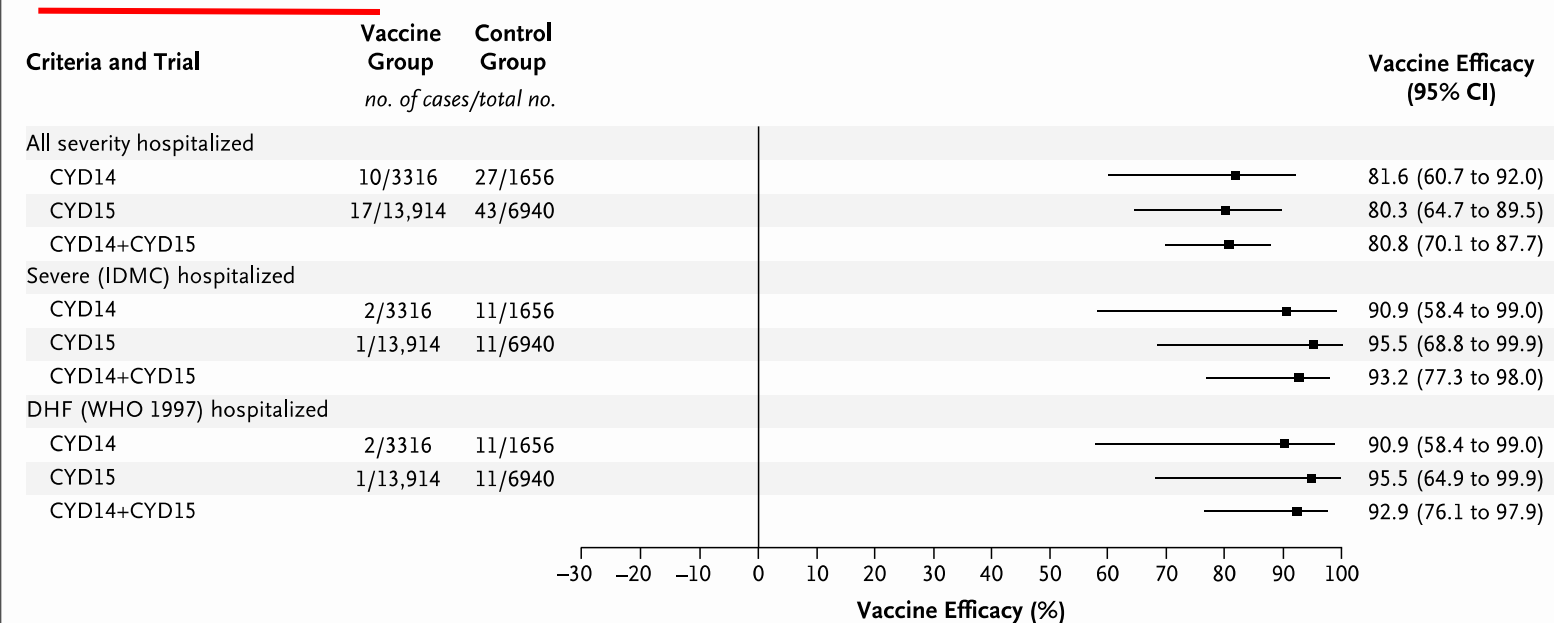
| Year | Phase | Setting                    | Cases                | Dose                     | FU  | Vaccine Efficacy (VE)  |
|------|-------|----------------------------|----------------------|--------------------------|-----|--|
| 2012 | 2b    | Thailand                   | 4002 cases, 4-11 yo  | Injection at 0, 6 & 12 m | 25m | <b>Overall: 30.2%</b><br>DEN-1: 55.6%<br>DEN-2: 9.2%<br>DEN-3: 75.3%<br>DEN-4: 100%  |
| 2014 | 3     | 5 Asian countries          | 10275 cases, 2-14 yo | Injection at 0, 6 & 12 m | 25m | <b>Overall: 56.3%</b><br>DEN-1: 54.5%<br>DEN-2: 34.7%<br>DEN-3: 65.2%<br>DEN-4: 72.4%<br><b>Vs DHF: 80%</b><br><b>Vs severe disease: 70%</b>         |
| 2014 | 3     | 5 Latin American countries | 20869 cases, 9-16 yo | Injection at 0, 6 & 12 m | 25m | <b>Overall: 64.7%</b><br>DEN-1: 50.3%<br>DEN-2: 42.3%<br>DEN-3: 74%<br>DEN-4: 77.7%<br><b>Vs severe disease: 95.5%</b><br><b>Vs admission: 80.3%</b> |

**VE in individuals who were seropositive at baseline: 78.2%**

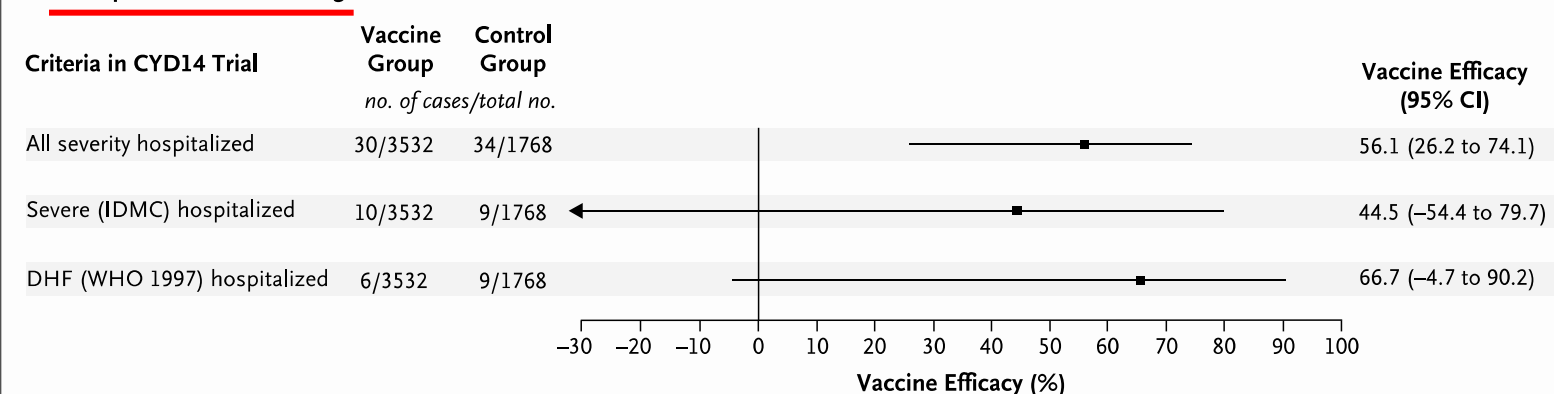
**VE in individuals who were seronegative at baseline: 38.1%**

# Year 3 studies of 35,000 children of Asian & Latin America

## A Participants 9 Yr of Age or Older



## B Participants under 9 Yr of Age



## Year 3 studies of 35,000 children of Asian & Latin America

**Table 1.** Annual Incidence of Hospitalization for Virologically Confirmed Dengue, According to Trial, Age Group, and Study Period.\*

| Trial, Age Group,<br>and Study Period | Vaccine Group      |                        |                           | Control Group      |                        |                           | Relative Risk<br>(95% CI) |
|---------------------------------------|--------------------|------------------------|---------------------------|--------------------|------------------------|---------------------------|---------------------------|
|                                       | Cases of<br>Dengue | Total<br>Participants† | Annual Incidence<br>Rate‡ | Cases of<br>Dengue | Total<br>Participants† | Annual Incidence<br>Rate‡ |                           |
|                                       |                    |                        |                           |                    |                        |                           |                           |
|                                       | <i>no.</i>         |                        | % (95% CI)                | <i>no.</i>         |                        | % (95% CI)                |                           |
| CYD14                                 |                    |                        |                           |                    |                        |                           |                           |
| All participants§                     | 27                 | 6,778                  | 0.4 (0.3–0.6)             | 13                 | 3387                   | 0.4 (0.2–0.7)             | 1.04 (0.52–2.19)          |
| 2–5 yr                                | 15                 | 1,636                  | 1.0 (0.6–1.6)             | 1                  | 813                    | 0.1 (0.0–0.7)             | 7.45 (1.15–313.80)        |
| 6–11 yr                               | 10                 | 3,598                  | 0.3 (0.1–0.6)             | 8                  | 1806                   | 0.5 (0.2–1.0)             | 0.63 (0.22–1.83)          |
| 12–14 yr                              | 2                  | 1,544                  | 0.1 (0.0; 0.5)            | 4                  | 768                    | 0.6 (0.2–1.4)             | 0.25 (0.02–1.74)          |
| <9 yr                                 | 19                 | 3,493                  | 0.6 (0.4–0.9)             | 6                  | 1741                   | 0.4 (0.1–0.8)             | 1.58 (0.61–4.83)          |
| ≥9 yr                                 | 8                  | 3,285                  | 0.3 (0.1–0.5)             | 7                  | 1646                   | 0.5 (0.2–1.0)             | 0.57 (0.18–1.86)          |

- Waning immunity?
- Antibody dependent enhancement?

## WHO position statement on Dengue vaccine

- The 1<sup>st</sup> Dengue vaccine: Dengvaxia® (CYD-TDV) has been licensed
- Use in individuals 9-45 years of age living in endemic areas, > 50% seroprevalence rate.
- live recombinant tetravalent dengue vaccine, given as a 3-dose series on a 0/6/12 month schedule
- No recommendation in pregnant and lactating women due to lack of sufficient data in this population. However, the limited data collected during the clinical trials on inadvertent immunization of pregnant women have yielded no evidence of harm to the fetus or pregnant woman
- No recommendation in HIV-infected or immunocompromised individuals.
- No recommendation for vaccination of travellers or health-care workers

## RESEARCH ARTICLE

### INFECTIOUS DISEASE

# The live attenuated dengue vaccine TV003 elicits complete protection against dengue in a human challenge model

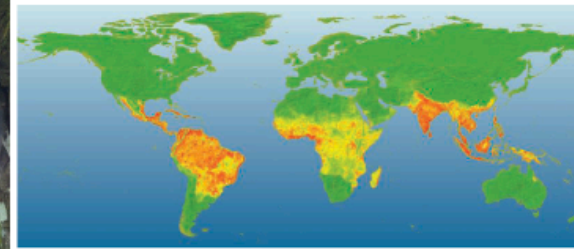
Beth D. Kirkpatrick,<sup>1\*</sup> Stephen S. Whitehead,<sup>2\*</sup> Kristen K. Pierce,<sup>1</sup> Cecilia M. Tibery,<sup>3</sup> Palmtama L. Grier,<sup>3</sup> Noreen A. Hynes,<sup>4</sup> Catherine J. Larsson,<sup>1</sup> Beulah P. Sabundayo,<sup>3</sup> Kawsar R. Talaat,<sup>3</sup> Anna Janiak,<sup>3</sup> Marya P. Carmolli,<sup>1</sup> Catherine J. Luke,<sup>4</sup> Sean A. Diehl,<sup>1</sup> Anna P. Durbin<sup>3†</sup>

- Phase II study
- 100% protection vs dengue 2 viremia, rash & neutropenia after Den 2 virus challenge

# Some concern: the 5<sup>th</sup> Dengue



## NEWS&ANALYSIS



**Jungle fever.** Even as dengue spreads (*inset*, redder colors indicate higher infection risk), a new serotype is likely circulating among macaques on Borneo.

## TROPICAL MEDICINE

### Surprising New Dengue Virus Throws A Spanner in Disease Control Efforts

**BANGKOK**—Dispatches from the frontlines of the war on dengue are growing more and more dispiriting. In September 2012, pharmaceuticals giant Sanofi Pasteur revealed that a vaccine against the centuries-old tropical malady had stumbled in clinical trials. Meanwhile, dengue's toll is heavier than thought. According to an April report based on modeling, the annual global incidence, close to 390 million, is about three times higher than the number of cases estimated by the World Health Organization (WHO) for 2009. At a meeting here earlier this

expands, possibly thanks to climate change, efforts to control it by eliminating standing water and spraying aren't keeping pace.

Malaysia is a case in point. The nation used to suffer major dengue outbreaks once or twice a decade. "Since 1991, we have had yearly outbreaks," says Mohd Zaki, a vector-borne disease specialist with Malaysia's Ministry of Health. "Dengue is spreading from urban to rural areas and to countries, such as Nepal, where it has not been seen before," adds Samlee Plianbangchang, WHO's Southeast Asia regional director. A 2010 outbreak in

The fifth serotype, which almost escaped detection, clouds the picture even more. In 2007, when a dengue outbreak struck Malaysia's Sarawak state, on Borneo, blood and serum samples from a severe case labeled "dengue 4" were collected through a surveillance network set up by Jane Cardosa, a virologist now retired from Universiti Malaysia Sarawak. Later, a researcher found that the samples did not respond to dengue 4 diagnostic tests. Nikos Vasilakis, a virologist at the University of Texas Medical Branch in Galveston, sequenced its entire genome and found that the virus occupies a new branch on the dengue family tree. Vasilakis and his collaborators then determined that antibodies elicited in monkeys and humans by the Malaysian virus differ significantly from those elicited by the other four strains. When injected into monkeys previously stricken with types 1, 2, and 3, the new strain replicated like mad.

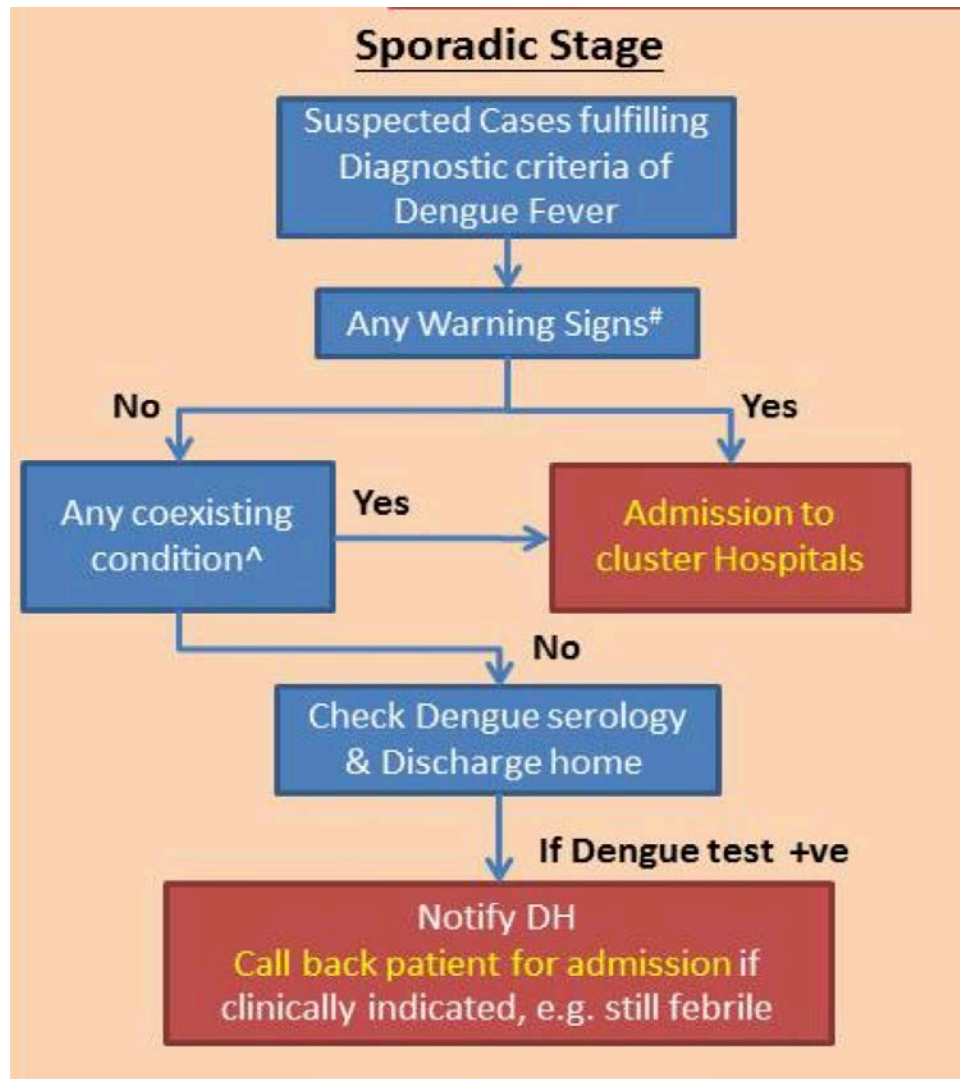
# Summary

- $> \frac{1}{2}$  of the world population is at risk for Dengue infection
- No of dengue infections & dengue endemic countries is increasing
- HK is at risk of being dengue endemic
- C/F of dengue is non-specific
- **Leucopenia** followed by **thrombocytopenia** with presence of **atypical lymphocytes** are suggestive
- NS1 Ag & RT-PCR aid early diagnosis
- Supportive management & organs support are important
- Live-attenuated tetravalent vaccines provide good efficacy in child  $> 9$ yo in endemic areas

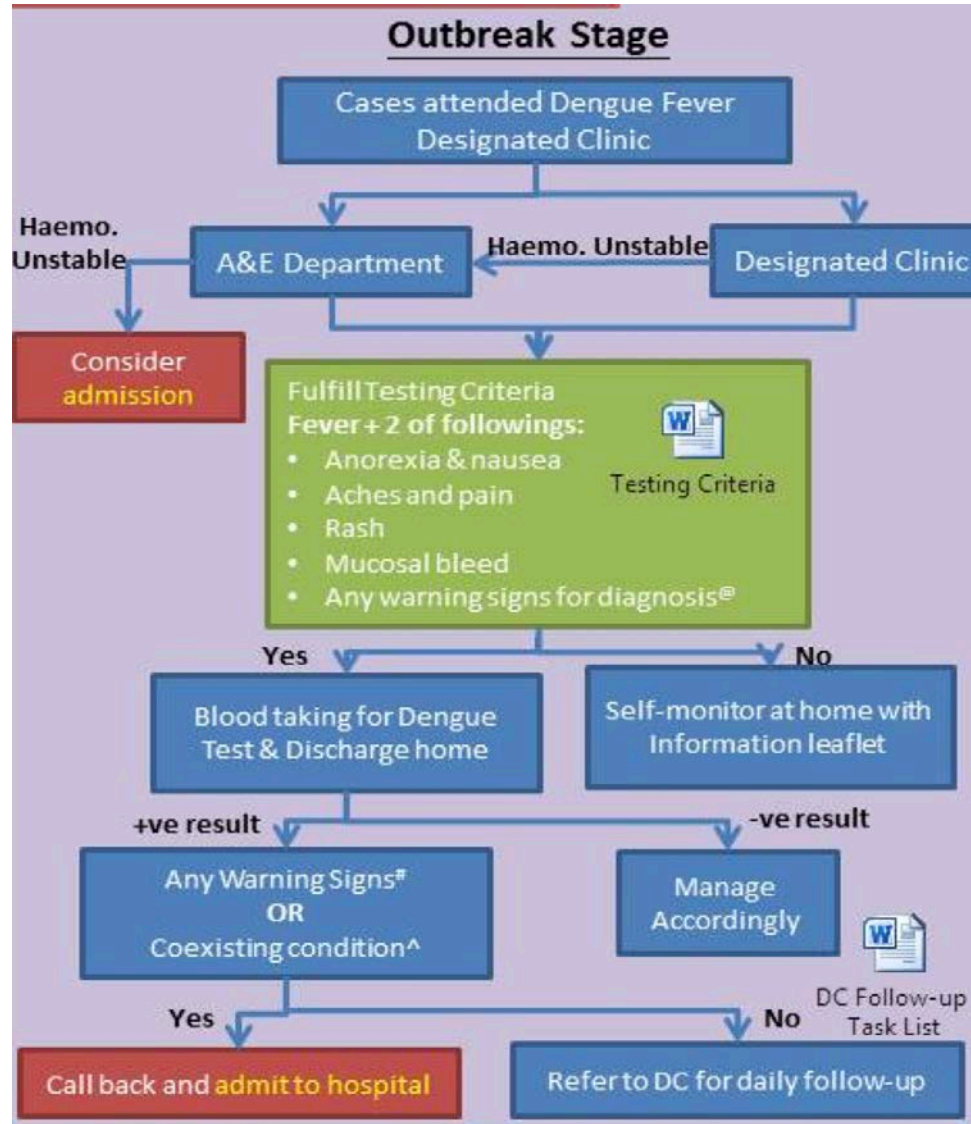
Thank you



# HAHO plan



# HAHO plan





## Appendix 2

### HA Checklist for patients with dengue fever during Epidemic (For AED & Designated Clinic)

| Diagnostic Criteria   |   |
|---|---|
| <input type="checkbox"/> Acute onset of fever (on-going local transmission)   |   |
| <b>Plus</b>   |   |
| Any <b>TWO</b> of the followings:   | * Warning signs for diagnosis:                        |
| <input type="checkbox"/> Anorexia & nausea  | <input type="checkbox"/> Abdominal pain or tenderness |
| <input type="checkbox"/> Aches and pain (e.g. Headache / Abdominal pain / Musculoskeletal pain / Retro-orbital pain / Myalgia / Arthralgia) | <input type="checkbox"/> Persistent vomiting          |
| <input type="checkbox"/> Rash   | <input type="checkbox"/> Clinical fluid accumulation  |
| <input type="checkbox"/> Mucosal Bleed  |   |
| <input type="checkbox"/> Any warning signs for diagnosis (*)  |   |

↓

| Constitute a Suspected Dengue case  |
|---|
| <input type="checkbox"/> Take blood for Dengue test (NS1 and IgM)+/- CBP                            |
| <input type="checkbox"/> Encourage adequate oral fluid intake, seek medical help if symptoms worsen |
| <input type="checkbox"/> Prescribe paracetamol prn, but avoid aspirin or NSAID                      |


↓

| Consider <b>hospital admission</b> if one of the followings   |
|---|
| <input type="checkbox"/> With any positive warning signs  |
| <input type="checkbox"/> With coexisting conditions including pregnancy, elderly, infant, DM, chronic renal or liver disease                  |
| <input type="checkbox"/> BP < 90/60, pulse pressure < 20mmHg or postural drop > 20mmHg  |
| <input type="checkbox"/> Platelets < 50K or HCT > 50%   |
| <input type="checkbox"/> Severe Dengue (severe bleeding, organ impairment, severe plasma leak + fluid accumulation with respiratory distress) |

↓

| If Dengue serology is <u>+ve</u>  |
|---|
| <input type="checkbox"/> Notify the case to CENO via NDORS / <u>eDENGUE</u>   |
| <input type="checkbox"/> Call back for clinical assessment and admit the patient if presence of warning signs or co-existing conditions.  |
| <input type="checkbox"/> For patient without warning signs or <u>co-existing</u> conditions, follow up the case at Designated Clinic. For patient attending AED, AED should refer the case to Designated clinic for FU. |

## Appendix 3

|   |                               |
|---|-------------------------------|
|  <p><b>HA Designated Dengue Clinic</b><br/> <b>Follow-up Assessment Task List</b><br/> <i>(2017-6-7 version)</i></p> | <p><b>Patient's Label</b></p> |
|---|-------------------------------|

### Follow-up Task List

1. Review Symptoms
2. Check Vital Signs:
  - Blood Pressure,
  - Pulse rate ,
  - Temperature
3. Blood taking for laboratory investigation:
  - 1<sup>st</sup> follow-up: CBP, L/RFT as a baseline
  - Subsequent follow-ups: CBP, consider L/RFT test if clinically indicated

### For patients **Consider** requiring admission, if any of the following condition appears:

- ☐ Blood Pressure: < 90/60 or pulse p'' < 20 or postural ↓ >20
- ☐ Pulse Rate: HR > 100/min
- ☐ Co-existing Condition
- ☐ Warning Signs
- ☐ Platelet (plt) (x10<sup>9</sup>/L): < 50 or Rapid ↓ Plt
- ☐ Hematocrit (Hct) (%): > 50% or ↑ Hct
- ☐ Deteriorating Creatinine or ALT
- ☐ Can't tolerate oral intake
- ☐ Acute confusion

### For patients **NOT** requiring admission, the following advices should be provided:

- ☐ Information home card to patient
- ☐ Adequate bed rest
- ☐ Adequate oral fluid intake
- ☐ Advice to attend medical care if deteriorates (e.g. warning signs)

### Discharge criteria / Not required daily clinic follow up (all are reached):

- ☐ Afebrile > 48 hours
- ☐ Clinical improvement
- ☐ Normal / Increasing trend of platelet count
- ☐ Stable Hct