# Dengue Infection

## Recent Diagnosis & Treatment

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# Global burden of dengue

- Global incidence of dengue has grown dramatically in recent decades.
- About two fifths of the world's population are now at risk.
- Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas.
- There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with the more serious disease
- The only way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes.

(WHO media center 2009)

# Dengue, countries or areas at risk, 2009


The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of Aedes aegypti, the principal mosquito vector of dengue viruses.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

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# Dengue fever in Indonesia
## Incidence Rate (per 100 000 population) by Provinces

1 January to 27 March 2004


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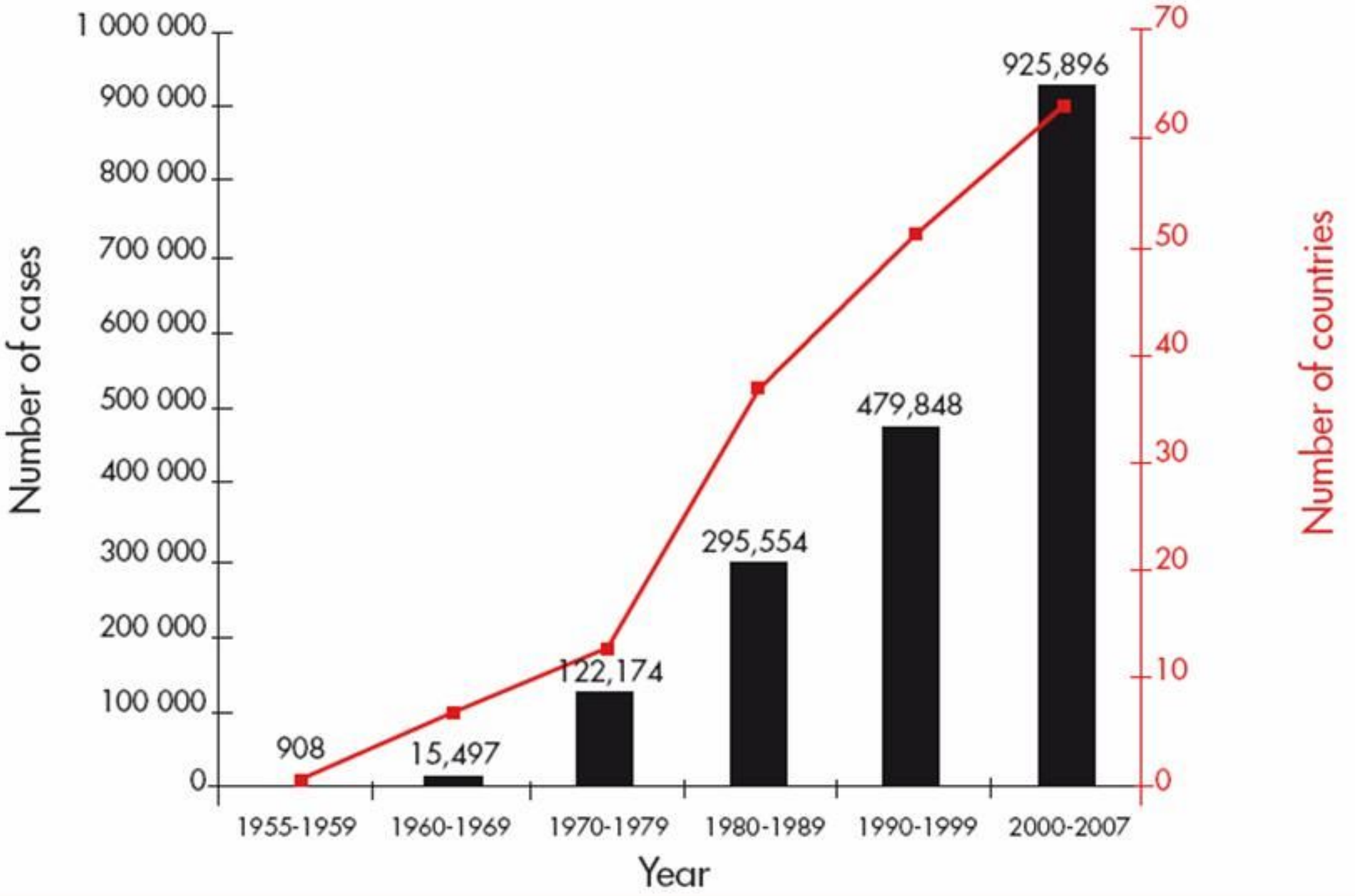
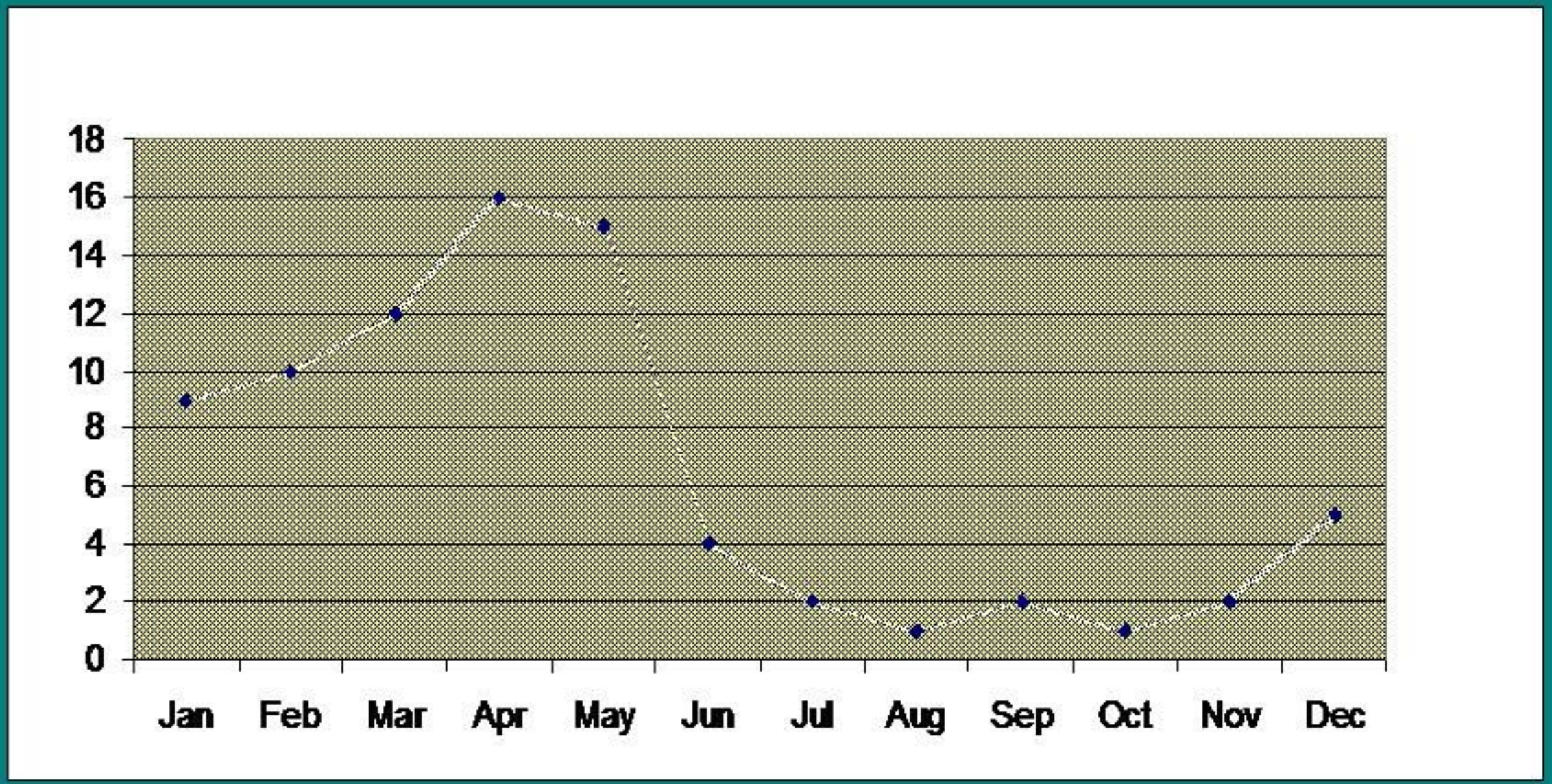
**Source : Ministry of Health, Indonesia**

Figure 1.2 Average annual number of dengue fever (DF) and dengue haemorrhagic fever (DHF) cases reported to WHO, and of countries reporting dengue, 1955–2007

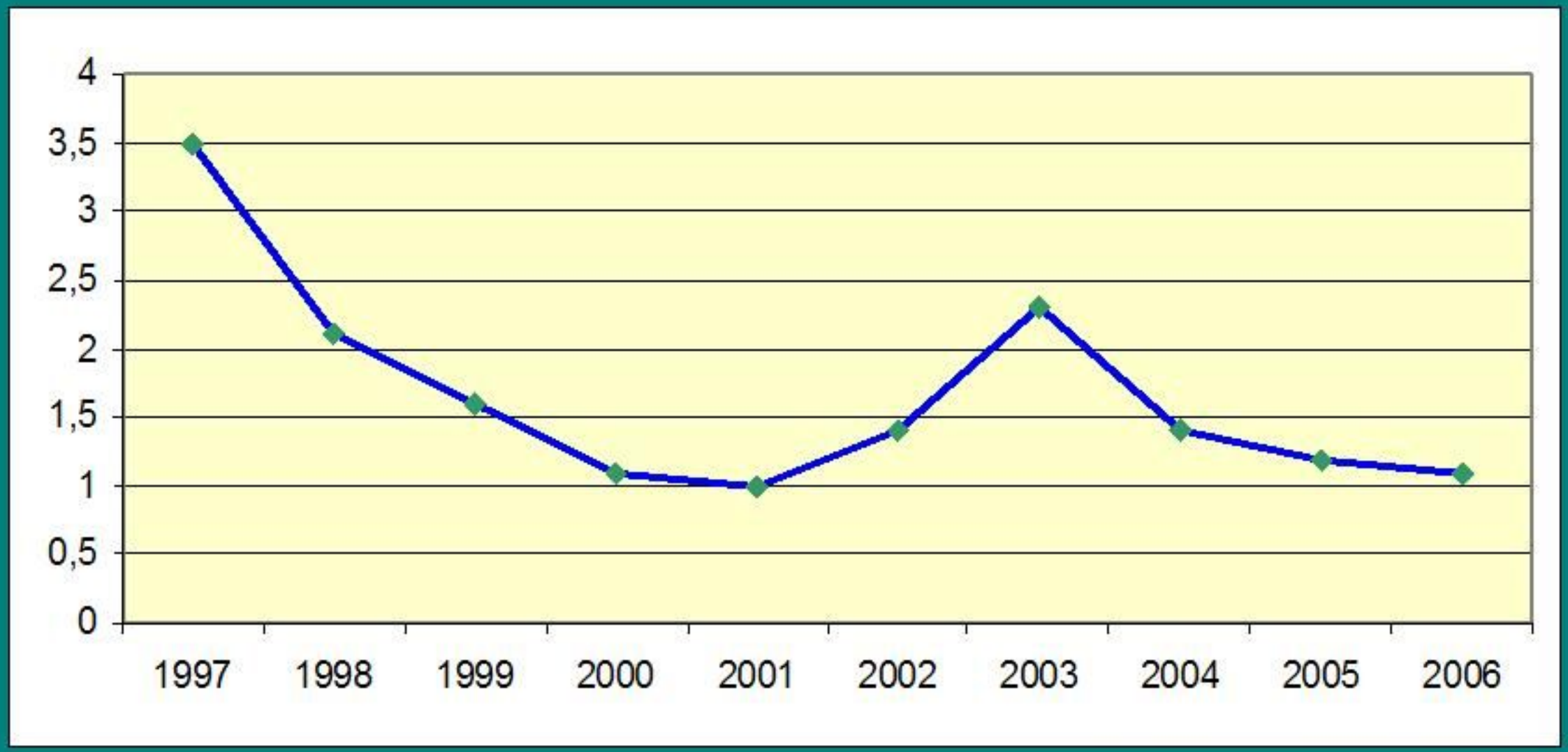


# Jogjakarta Province
# Average of monthly incidence rate / 100,000
# (1997-2006)




Wijisaksono *et al.*, 2007

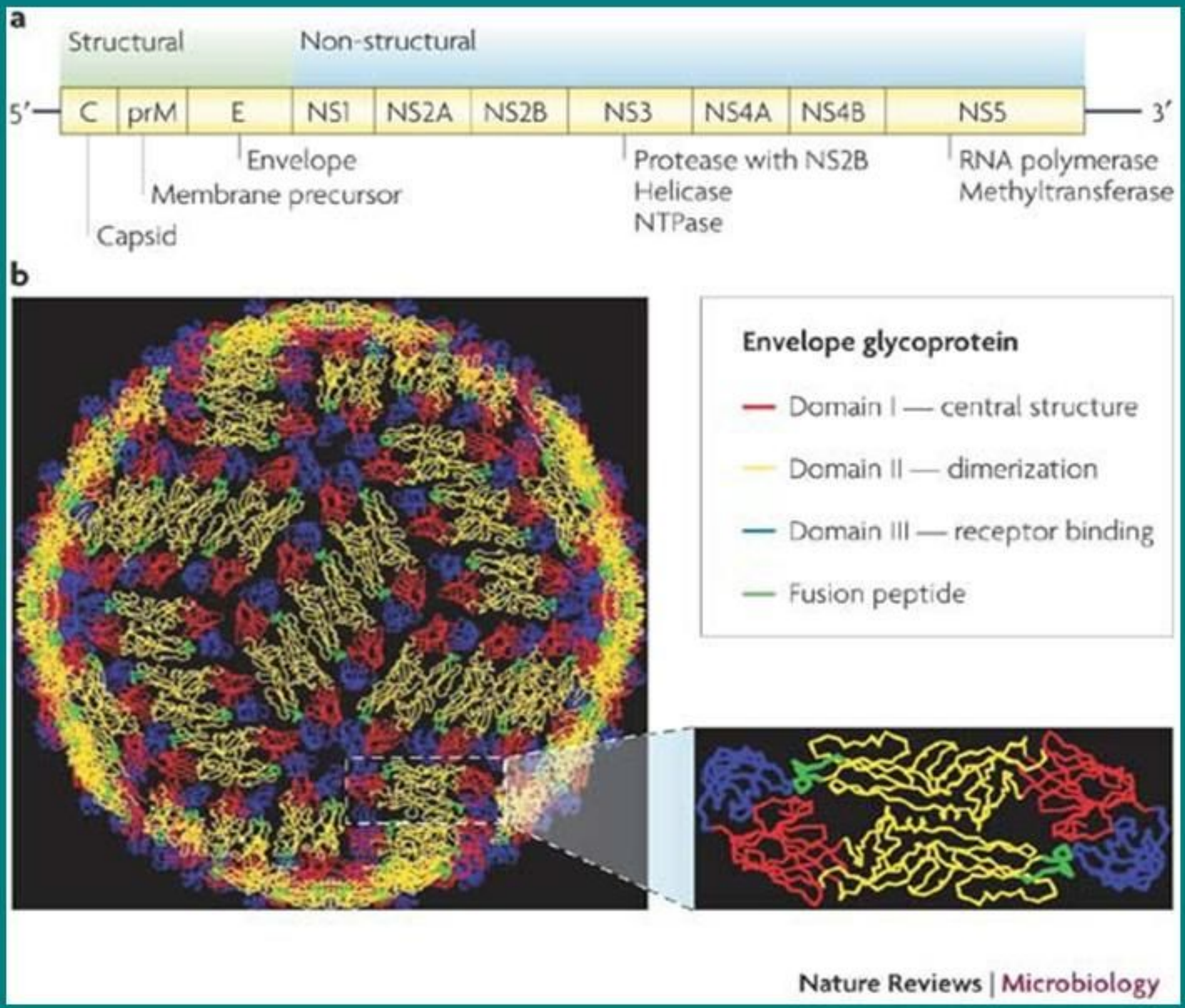
# Jogjakarta province
## DHF mortality rate (%)




Wijisaksono *et al.*, 2007

# Dengue Virus

- Causes dengue infection (mild⇒severe)
- Is an Flavivirus / Arbovirus
- Transmitted by mosquitoes (Aedes aegypti)
- Composed of single-stranded RNA
- Has 4 serotypes (DEN-1, 2, 3, 4)

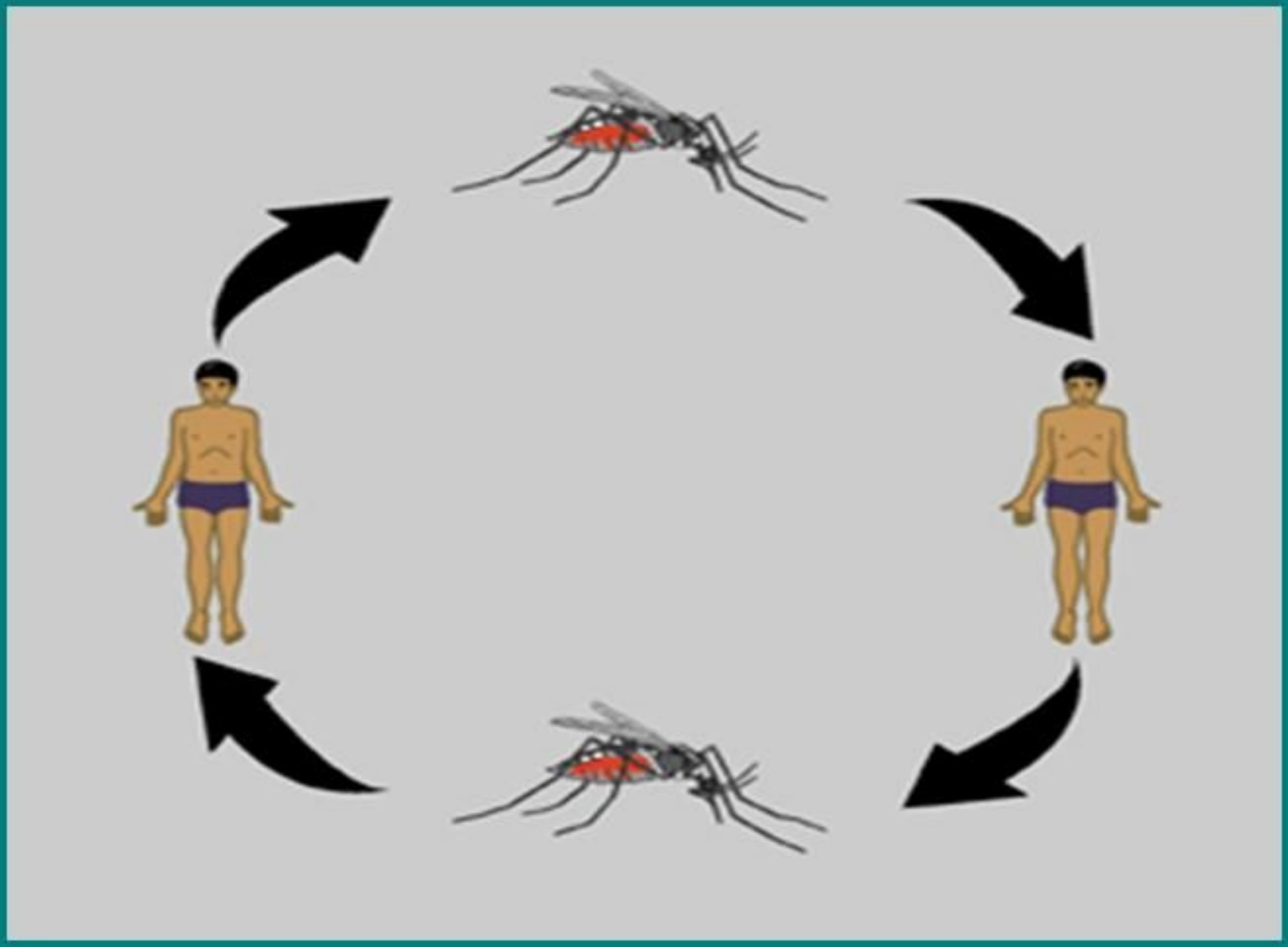



Nature Reviews | Microbiology

# 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


Aedes aegypti



# Dengue Clinical Syndromes (WHO, 1997)

- Undifferentiated fever
- Classic dengue fever
- Dengue hemorrhagic fever

# Undifferentiated Fever

- May be the most common manifestation of dengue
- Prospective study found that 87% of students infected were either asymptomatic or only mildly symptomatic

# Dengue Fever

is an acute febrile illness of 2-7 days duration (sometimes with two peaks) with two or more of the following manifestations:

- headache
- retro-orbital pain
- myalgia/arthralgia
- rash
- haemorrhagic manifestation (petechiae and positive tourniquet test) and,
- leukopenia.

## WHO guidelines for the diagnosis of dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS).

| DHF grade | Duration of fever, d | Hemorrhage | Thrombocytopenia: platelets/mm$^3$ | Increased vascular permeability |
|---|---|---|---|---|
| I | >2, ≤7 | Positive tourniquet test only | ≤100,000 | Plasma leakage[a] |
| II | >2, ≤7 | Spontaneous bleeding[b] | ≤100,000 | Plasma leakage[a] |
| III (DSS) | >2, ≤7 | Positive tourniquet test and/or spontaneous bleeding[b] | ≤100,000 | Plasma leakage[a] and circulatory failure with pulse pressure ≤20 mm Hg or hypotension for age |
| IV (DSS) | >2, ≤7 | Positive tourniquet test and/or spontaneous bleeding[b] | ≤100,000 | Plasma leakage[a] and profound shock with undetectable pulse and blood pressure |

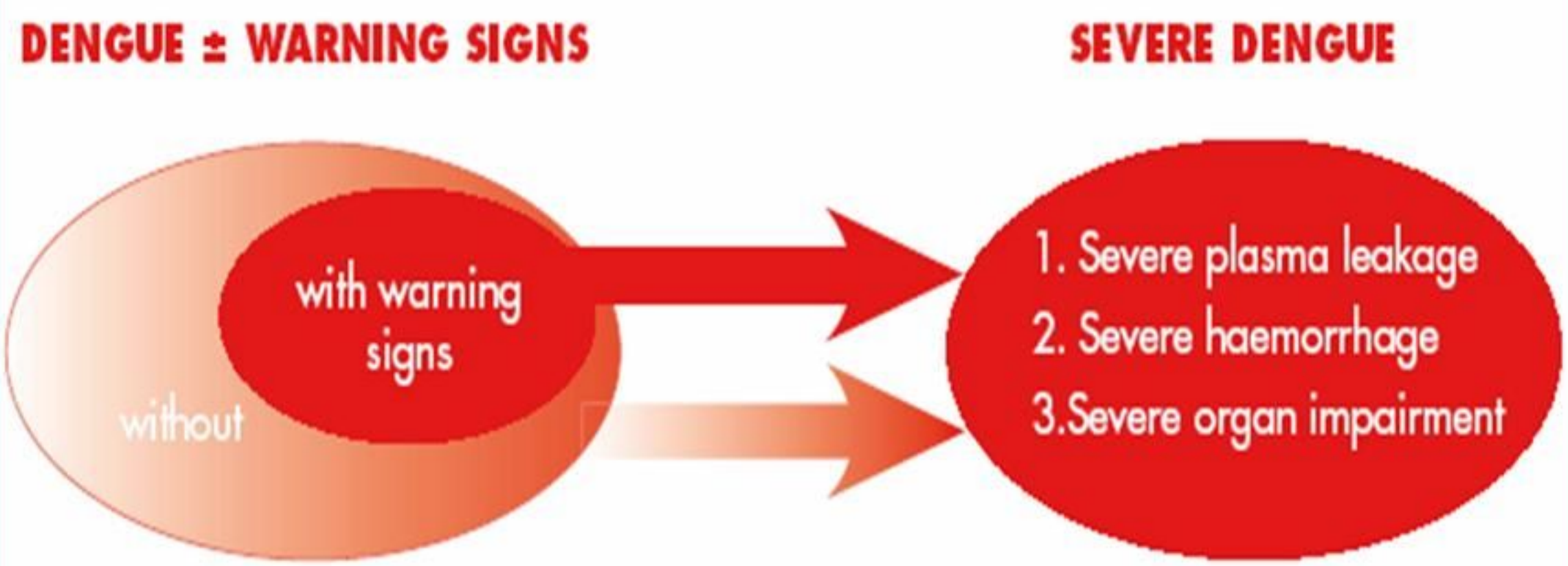
[a] As demonstrated by any of the following: elevation of the admission hematocrit to ≥20% above the expected mean for age, sex, and population; reduction of the hematocrit to ≥20% of the baseline value after fluid resuscitation; and clinical signs of plasma leakage, such as pleural effusion or ascites.

[b] For example, skin petechiae, bruising, or mucosal/gastrointestinal bleeding.

Expert consensus groups in Latin America (Havana, Cuba, 2007), South-East Asia (Kuala Lumpur, Malaysia, 2007), and at WHO headquarters in Geneva, Switzerland in 2008 agreed that:

"dengue is one disease entity with different clinical presentations and often with unpredictable clinical evolution and outcome";

## Suggested dengue case classification and levels of severity



# Suggested dengue case classification and levels of severity

## 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
- Leukopenia
- Any warning sign

### Laboratory-confirmed dengue

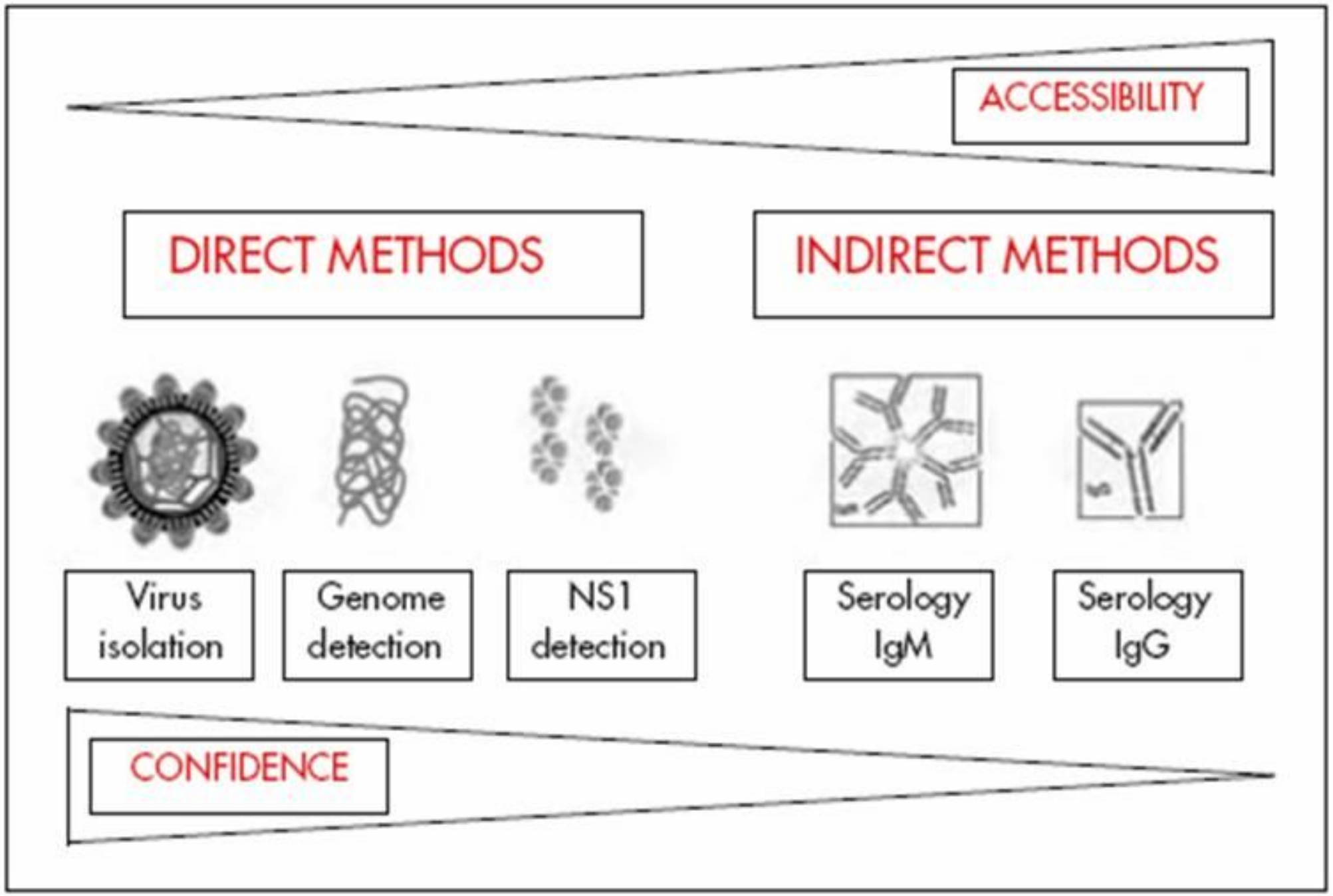
(important when no sign of plasma leakage)

### Warning signs*

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

*(requiring strict observation and medical intervention)

# Comparison of diagnostic tests according to their accessibility and confidence



# Suggested dengue case classification and levels of severity

## CRITERIA FOR SEVERE DENGUE

### Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

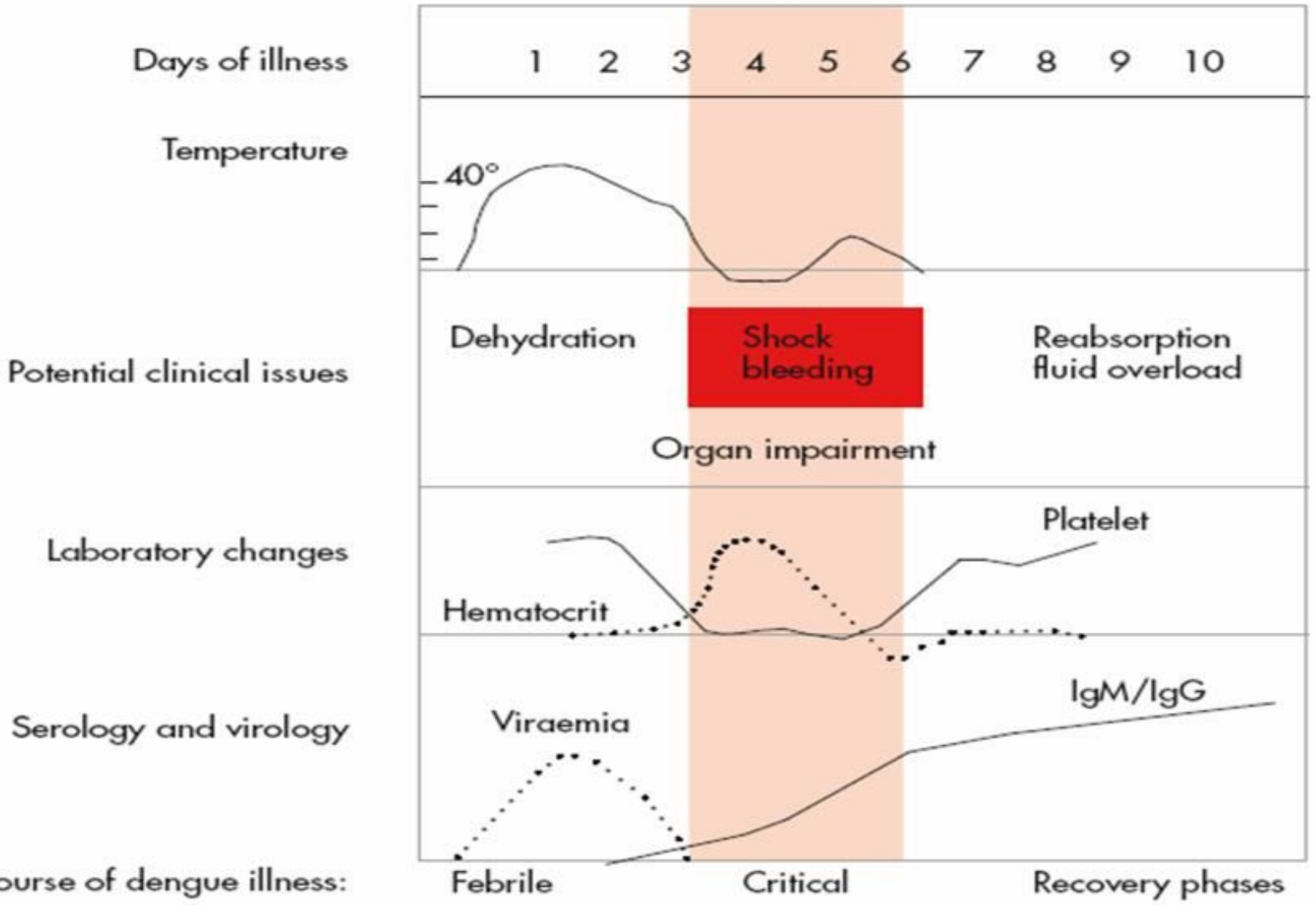
### Severe bleeding

as evaluated by clinician

### Severe organ involvement

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

## The course of dengue illness*




Yip, 2009

# A stepwise approach to the management of dengue

Step I. Overall assessment

I.1 History, including information on symptoms, past medical and family history

I.2 Physical examination, including full physical and mental assessment

I.3 Investigation, including routine laboratory and dengue-specific laboratory

Step II. Diagnosis, assessment of disease phase and severity

Step III. Management

III.1 Disease notification

III.2 Management decisions. Depending on the clinical manifestations and other circumstances, patients may:

- be sent home (Group A);
- be referred for in-hospital management (Group B);
- require emergency treatment and urgent referral (Group C).

# Group A – patients who may be sent home

These are patients who are able to tolerate adequate volumes of oral fluids and pass urine at least once every six hours, and do not have any of the warning signs, particularly when fever subsides.

Give paracetamol for high fever if the patient is uncomfortable.

Instruct the care-givers that the patient should be brought to hospital immediately if any of the following occur: no clinical improvement, deterioration around the time of defervescence, severe abdominal pain, persistent vomiting, cold and clammy extremities, lethargy or irritability/restlessness, bleeding (e.g. black stools or coffee-ground vomiting), not passing urine for more than 4–6 hours.

# Group B – patients who should be referred for in-hospital management

Patients may need to be admitted to a secondary health care centre for close observation, particularly as they approach the critical phase. These include patients with warning signs, those with co-existing conditions that may make dengue or its management more complicated (such as pregnancy, infancy, old age, obesity, diabetes mellitus, renal failure, chronic haemolytic diseases), and those with certain social circumstances (such as living alone, or living far from a health facility without reliable means of transport).

# If the patient has dengue without warning signs

Encourage oral fluids. If not tolerated, start intravenous fluid therapy of 0.9% saline or Ringer's lactate with or without dextrose at maintenance rate (Textbox H). For obese and overweight patients, use the ideal body weight for calculation of fluid infusion (Textboxes J and K). Patients may be able to take oral fluids after a few hours of intravenous fluid therapy. Thus, it is necessary to revise the fluid infusion frequently. Give the minimum volume required to maintain good perfusion and urine output. Intravenous fluids are usually needed only for 24–48 hours.

# If the patient has dengue with warning signs

Obtain a reference haematocrit before fluid therapy. Give only isotonic solutions such as 0.9% saline, Ringer's lactate, or Hartmann's solution. Start with 5–7 ml/kg/hour for 1–2 hours, then reduce to 3–5 ml/kg/hr for 2–4 hours, and then reduce to 2–3 ml/kg/hr or less according to the clinical response (Textboxes H, J and K).

Reassess the clinical status and repeat the haematocrit. If the haematocrit remains the same or rises only minimally, continue with the same rate (2–3 ml/kg/hr) for another 2–4 hours. If the vital signs are worsening and haematocrit is rising rapidly, increase the rate to 5–10 ml/kg/hour for 1–2 hours. Reassess the clinical status, repeat the haematocrit and review fluid infusion rates accordingly.

A number of criteria may be used to decide when to transfer a patient to a high-dependency unit. These include:

- early presentation with shock (on days 2 or 3 of illness);
- severe plasma leakage and/or shock;
- undetectable pulse and blood pressure;
- severe bleeding;
- fluid overload;
- organ impairment (such as hepatic damage, cardiomyopathy, encephalopathy, encephalitis and other unusual complications).

Compensated shock (systolic pressure maintained but has signs of reduced perfusion)

Fluid resuscitation with isotonic crystalloid
5–10 ml/kg/hr over 1 hour

Improvement

NO

Check HCT

HCT ↑ or high

Administer 2nd bolus of fluid
10–20 ml/kg/hr for 1 hour

Improvement

YES

If patient improves, reduce to
7–10 ml/kg/hr for 1–2 hours
Then reduce further

HCT ↓

Consider significant occult/overt bleed
Initiate transfusion with fresh whole blood

NO

Compensated shock (systolic pressure maintained but has signs of reduced perfusion)

Fluid resuscitation with isotonic crystalloid
5–10 ml/kg/hr over 1 hour

Improvement

YES

IV crystalloid 5–7 ml/kg/hr for 1–2 hours, then:
reduce to 3–5 ml/kg/hr for 2–4 hours;
reduce to 2–3 ml/kg/hr for 2–4 hours.

If patient continues to improve, fluid can be further reduced.

Monitor HCT 6–8 hourly.

If the patient is not stable, act according to HCT levels:
if HCT increases, consider bolus fluid administration or increase fluid administration;
if HCT decreases, consider transfusion with fresh whole transfusion.

Stop at 48 hours.

Che

HCT ↑ or high

Administer 2nd bolus of fluid
10–20 ml/kg/hr for 1 hour

Improvement

YES

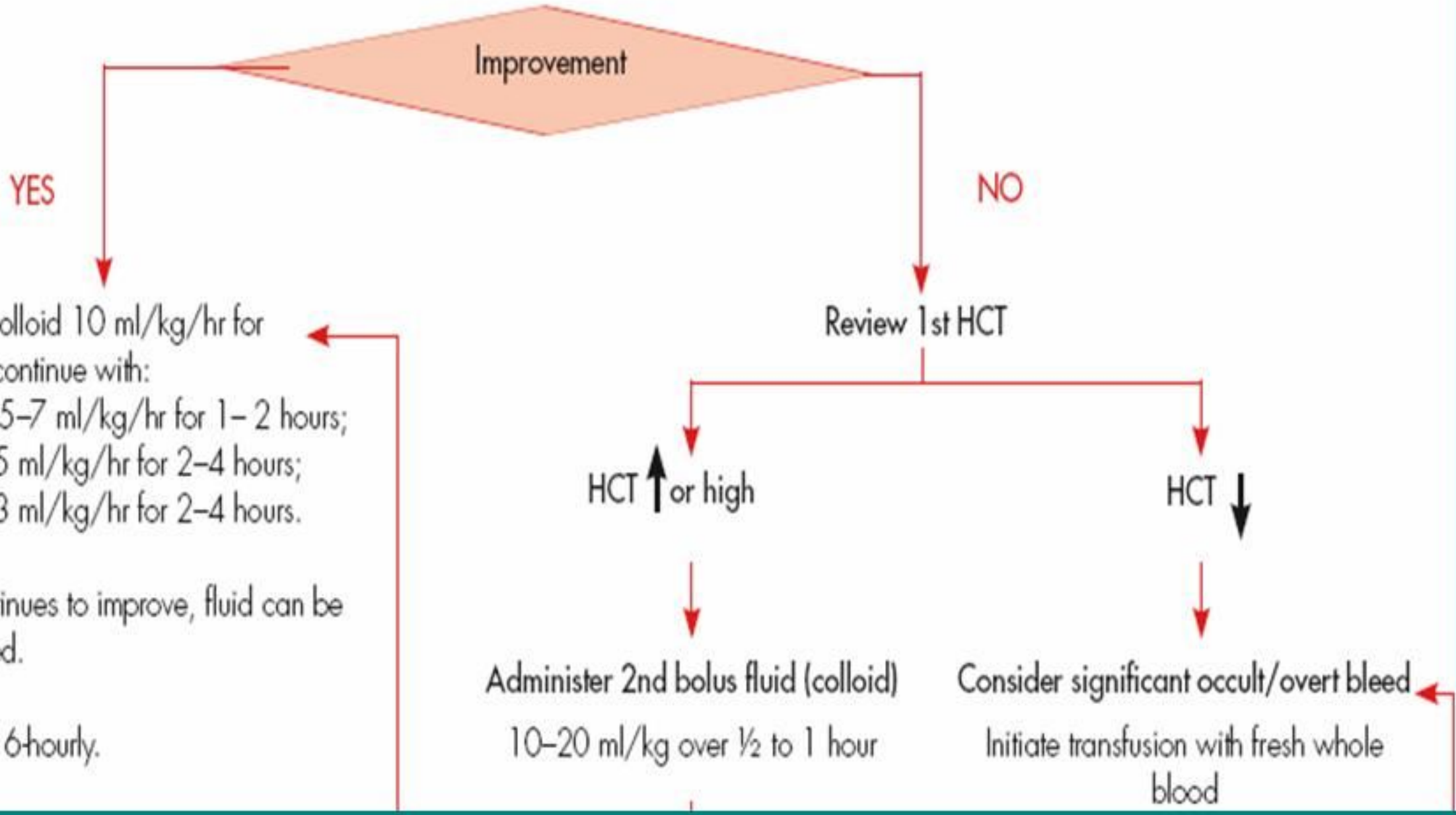
If patient improves, reduce to
7–10 ml/kg/hr for 1–2 hours
Then reduce further

HCT = haematocrit

## Hypotensive shock

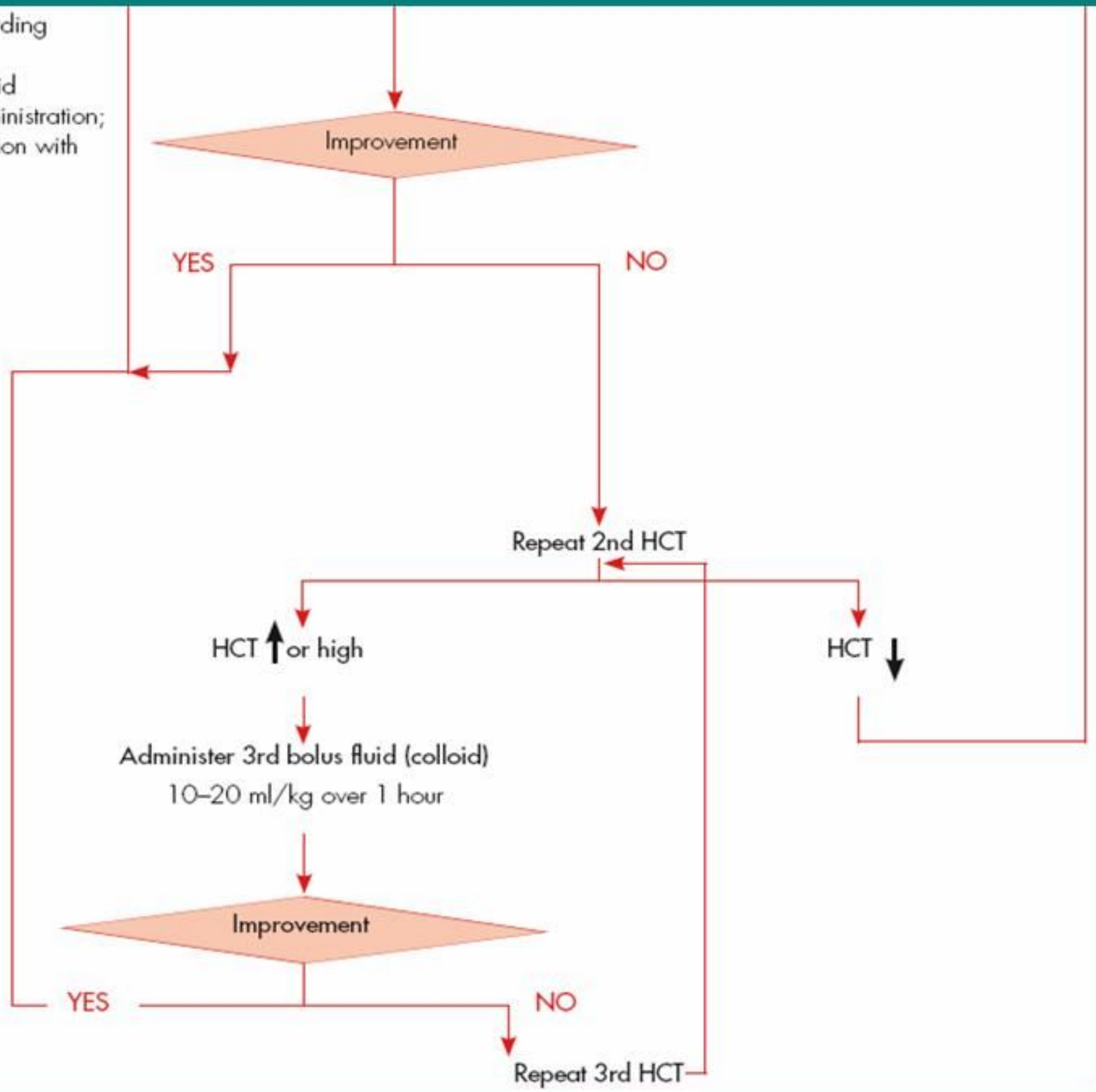
Fluid resuscitation with 20 ml/kg isotonic crystalloid or colloid over 15 minutes

Try to obtain a HCT level before fluid resuscitation



If the patient is not stable, act according to HCT levels:
if HCT increases, consider bolus fluid administration or increase fluid administration;
if HCT decreases, consider transfusion with fresh whole transfusion.

Stop at 48 hours.



Severe bleeding can be recognized by:

- persistent and/or severe overt bleeding in the presence of unstable haemodynamic status, regardless of the haematocrit level;
- a decrease in haematocrit after fluid resuscitation together with unstable haemodynamic status;
- refractory shock that fails to respond to consecutive fluid resuscitation of 40-60 ml/kg;
- hypotensive shock with low/normal haematocrit before fluid resuscitation;
- persistent or worsening metabolic acidosis ± a well-maintained systolic blood pressure, especially in those with severe abdominal tenderness and distension.

The action plan for the treatment of haemorrhagic complications is as follows:

- Give 5–10ml/kg of fresh-packed red cells or 10–20 ml/kg of fresh whole blood at an appropriate rate and observe the clinical response. It is important that fresh whole blood or fresh red cells are given. Oxygen delivery at tissue level is optimal with high levels of 2,3 di-phosphoglycerate (2,3 DPG). Stored blood loses 2,3 DPG, low levels of which impede the oxygen-releasing capacity of haemoglobin, resulting in functional tissue hypoxia. A good clinical response includes improving haemodynamic status and acid-base balance.

Mucosal bleeding may occur in any patient with dengue but, if the patient remains stable with fluid resuscitation/replacement, it should be considered as minor. The bleeding usually improves rapidly during the recovery phase. In patients with profound thrombocytopaenia, ensure strict bed rest and protect from trauma to reduce the risk of bleeding. Do not give intramuscular injections to avoid haematoma. It should be noted that prophylactic platelet transfusions for severe thrombocytopaenia in otherwise haemodynamically stable patients have not been shown to be effective and are not necessary (*14*).

# Thank you