

DENGUE



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DENGUE



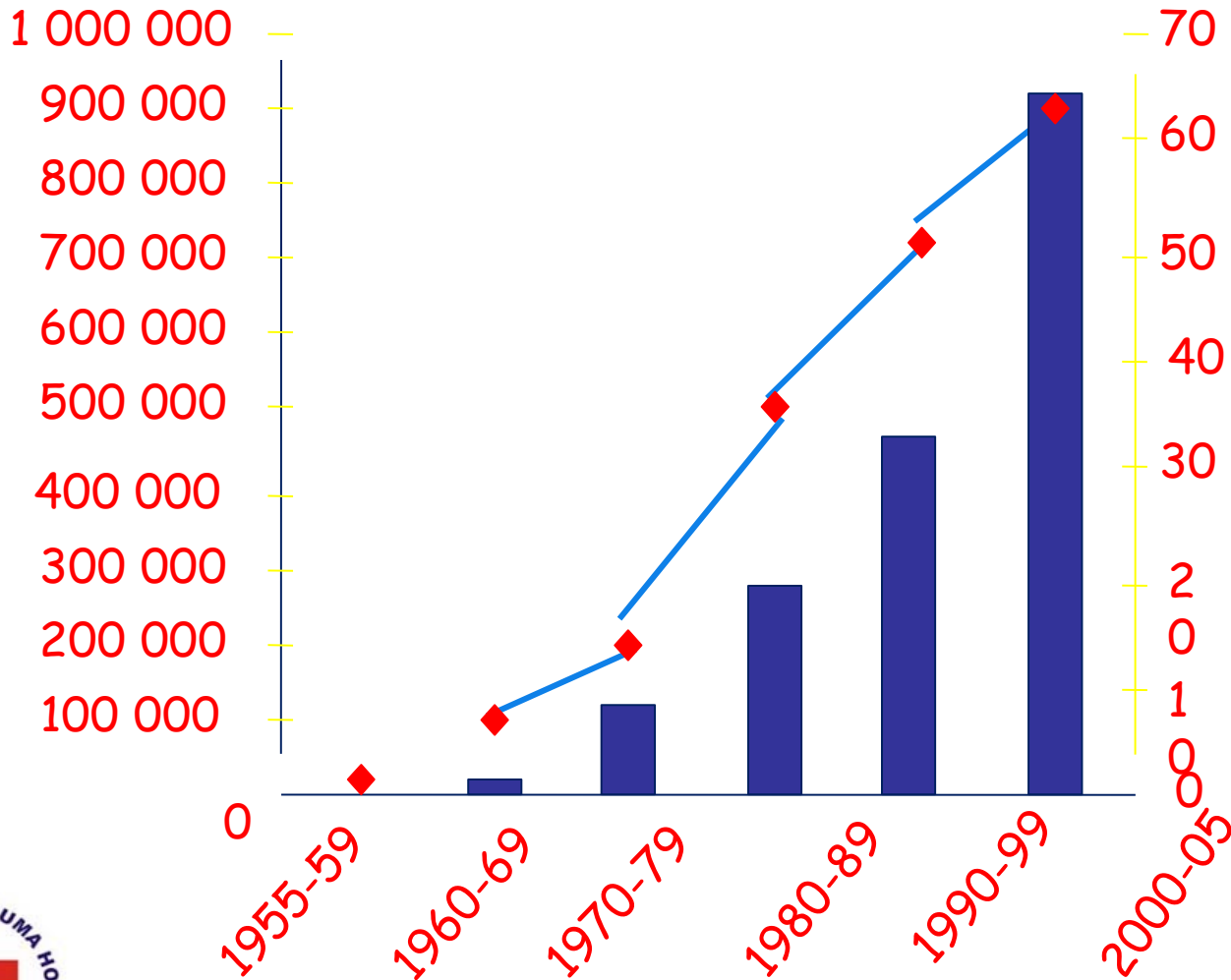
Million

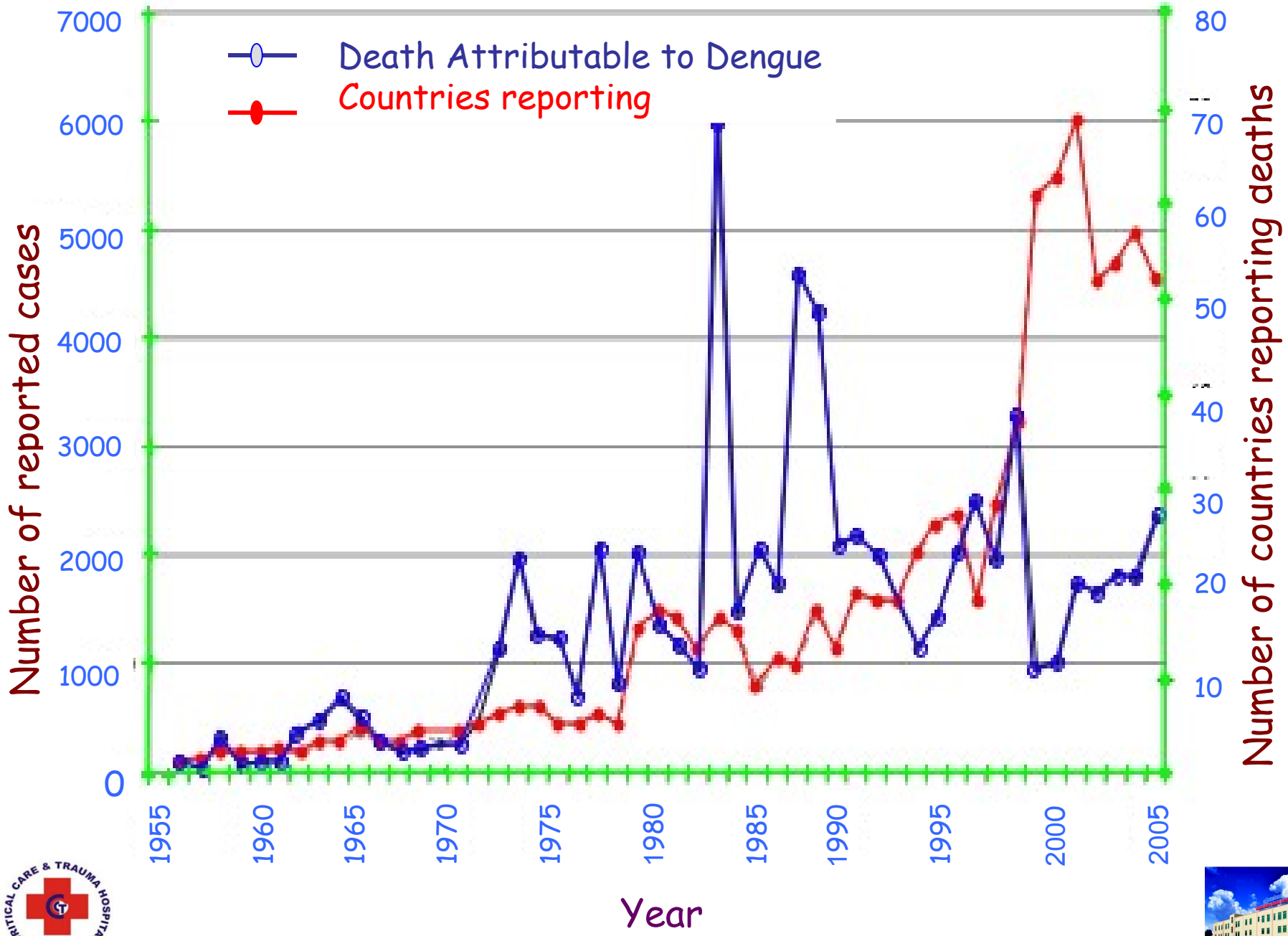
Million

500 000 cases of DHF require hospitalisation and at least 2.5% of cases die, every year.

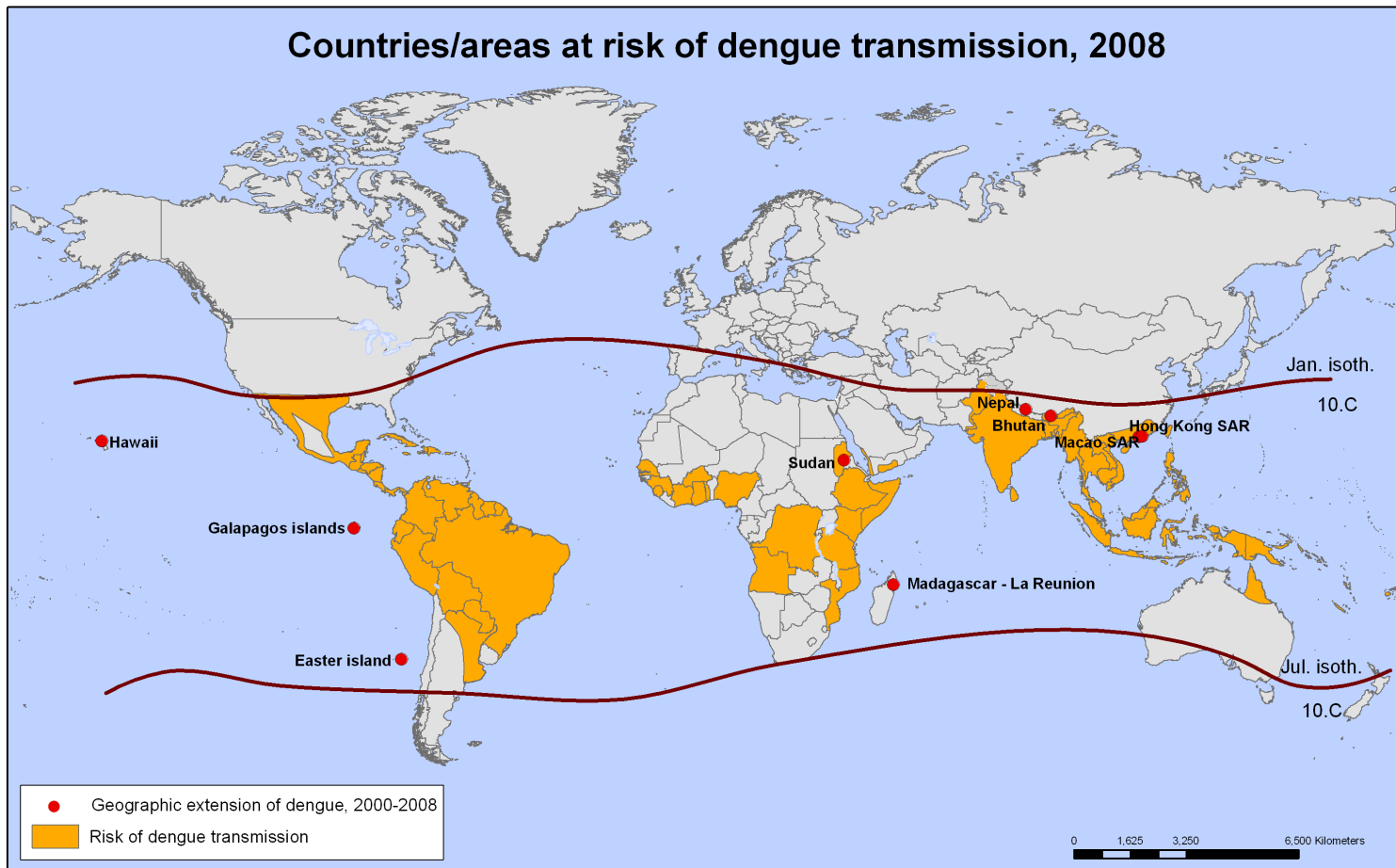


WHO report of countries reporting Dengue





Countries / Areas at risk of Dengue Transmission, 2008



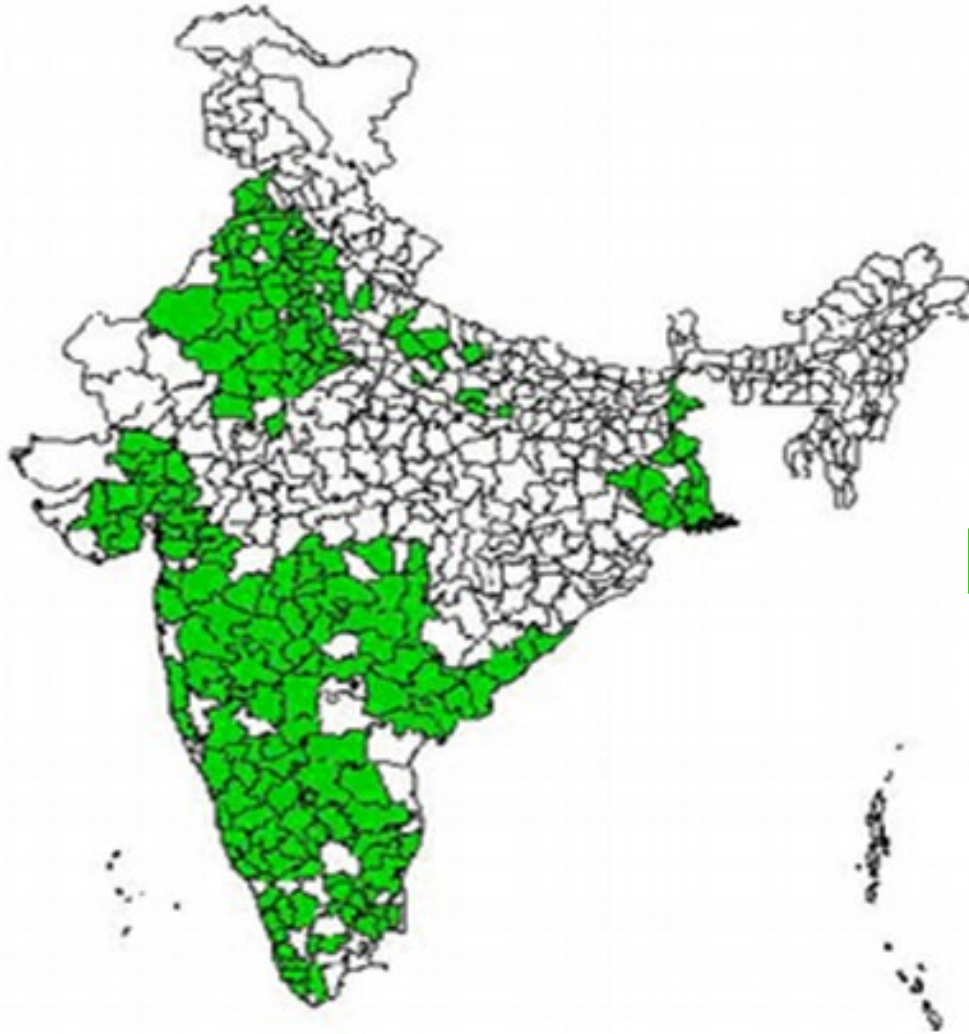
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers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

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

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DENGUE AREA- India



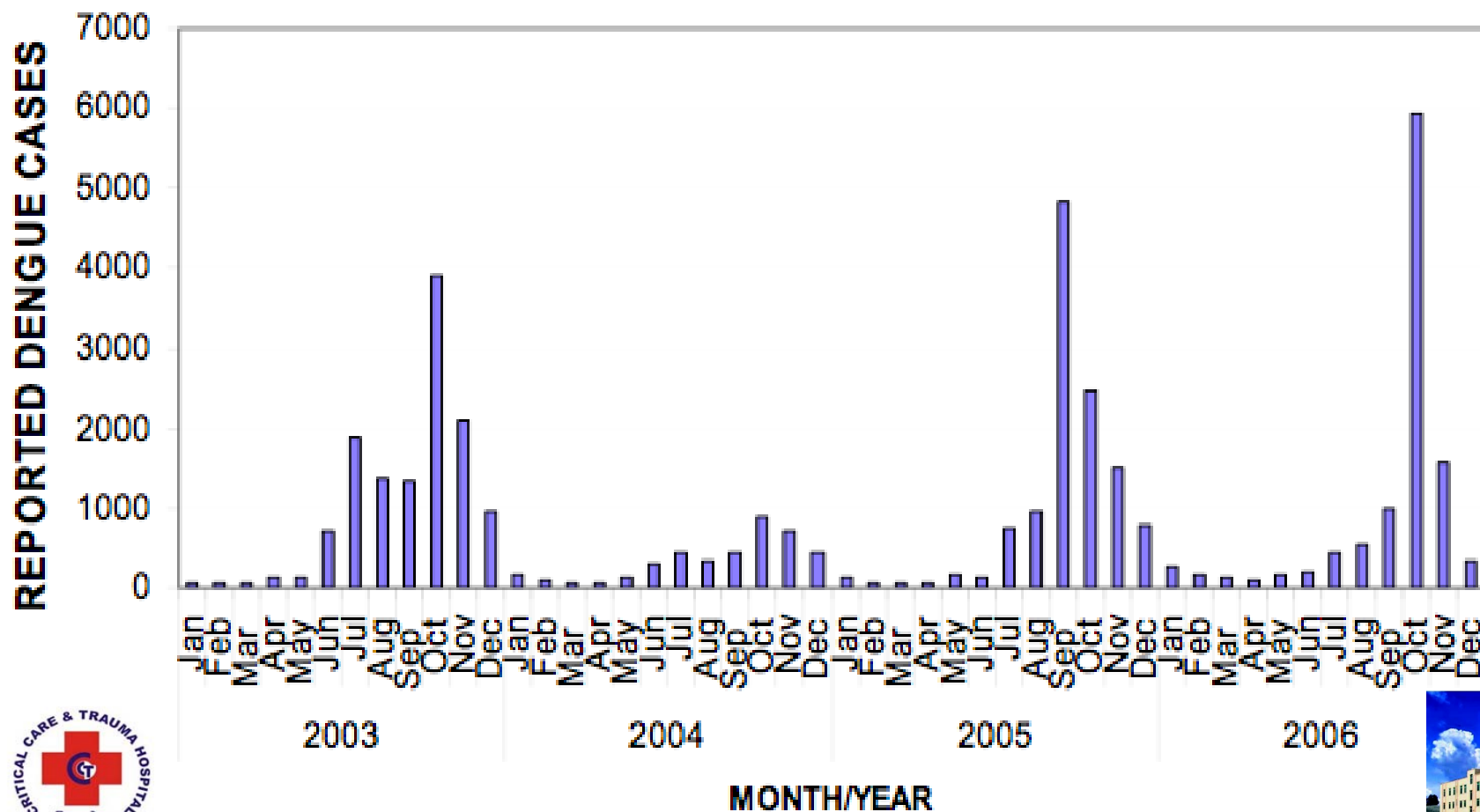
DENGUE AREA



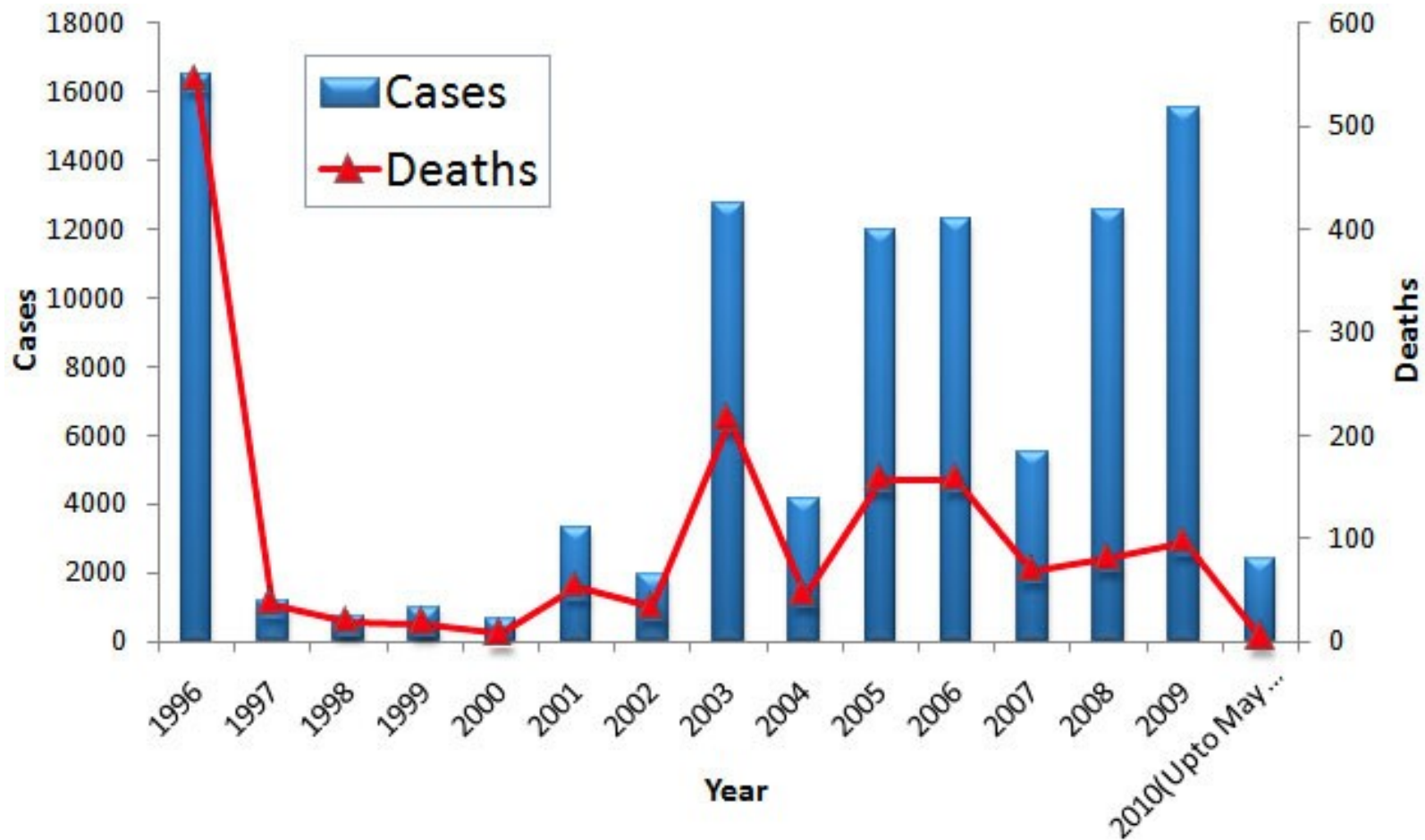
DENGUE CASES

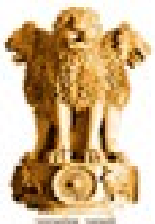


INDIA: seasonal trend of reported dengue cases (2003-2006)



DENGUE CASES





Dengue Cases & Deaths since 2007



Government of India



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DENGUE VIRUS



- Dengue virus belongs to the family Flaviviridae which also includes :
 - Yellow fever
 - Japanese encephalitis
 - West Nile encephalitis

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DENGUE VIRUS



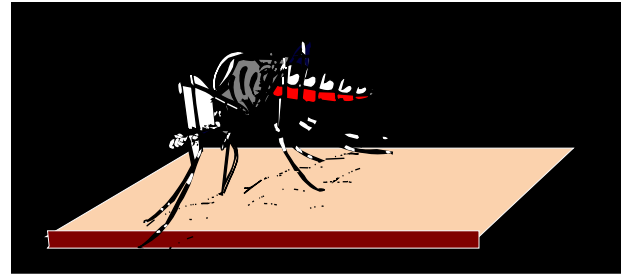
- Causes dengue & dengue hemorrhagic fever
- Is an arbovirus
- Transmitted by mosquitoes:- *Aedes aegypti*
- Composed of single-stranded RNA
- Has 4 serotypes (DEN-1, 2, 3, 4)

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Replication & Transmission of Dengue Virus

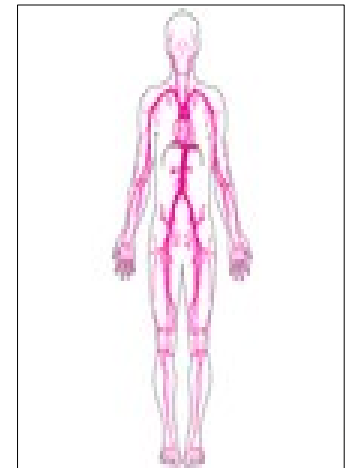
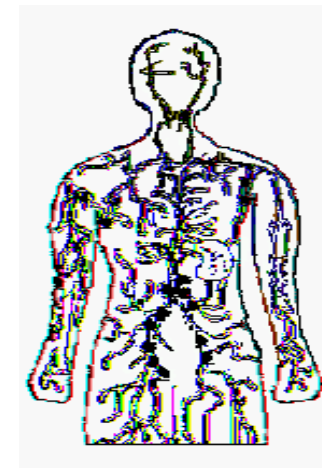
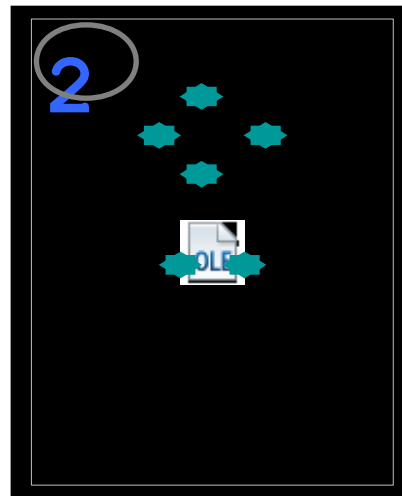


1. Virus transmitted to human in mosquito saliva



2. Virus replicates in target organs

3. Virus infects white blood cells and lymphatic tissues



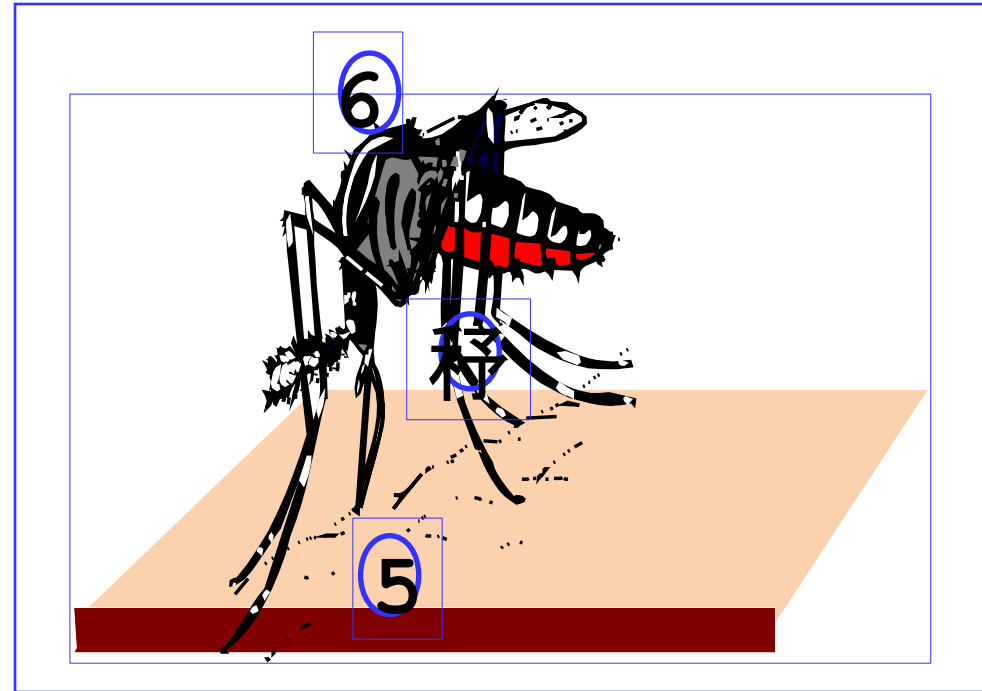
4. Virus released and circulates in blood



Replication and Transmission of Dengue Virus



5. Second mosquito ingests virus with blood
6. Virus replicates in mosquito midgut and other organs, infects salivary glands
7. Virus replicates in salivary glands



Dengue Clinical Syndromes



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

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Clinical Characteristics of Dengue Fever



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



Signs and Symptoms of Encephalitis/Encephalopathy Associated with Acute Dengue Infection



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

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Hemorrhagic Manifestations of Dengue



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

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Clinical Case Definition for Dengue Hemorrhagic Fever



4 Necessary Criteria:

- Fever, or recent history of acute fever
- Hemorrhagic manifestations
- Low platelet count (100,000/mm³ or less)
- Objective evidence of "leaky capillaries:"
 - elevated hematocrit (20% or more over baseline)
 - low albumin
 - pleural or other effusions

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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

Unusual Presentations of Severe Dengue Fever



- Encephalopathy
- Hepatic damage
- Cardiomyopathy
- Severe gastrointestinal hemorrhage
- GBS Like syndrome
- Multiorgan failure
- Compartmental syndrome

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Dengue - Manifestations



Epidemic in Delhi

- Special ward created for dengue fever
- 560 patients were admitted to this ward

Lymphadenopathy 31%

Hematemesis 28%

Palatal rash 27%

Epistaxis 26%

Malena 14%

Thrombocytopenia 13%

Dengue shock syndrome 2.5%

11 Deaths, DIC- 3, IC bleed-1, GI bleed-7

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Risk Factors Reported for DHF



- Virus strain
- Pre-existing anti-dengue antibody
 - previous infection
 - maternal antibodies in infants
- Host genetics
- Age

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Clinical Evaluation in Dengue Fever



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

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Positive Tourniquet Test



Differential diagnosis of dengue fever & DHF

• Dengue Fever

- Malaria .
- Chikungunya
- Other viral Fevers .
- Rickettsial infections particularly Scrub Typhus
- Leptospirosis.
- Influenza.
- Typhoid Fever

• DHF

- Leptospirosis.
- Chikungunya
- Kawasaki disease.
- Yellow fever.
- Hanta viral infections.
- Other viral haemorrhagic fevers.
- Meningococcal septicaemia.

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

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Laboratory diagnosis: Dengue virus infection



- Confirmed dengue infection

- Virus isolation
- Genome detection
- Antigen detection
- IgM or IgG seroconversion

- Probable dengue infection

- IgM positive
- Elevated IgG titre (that is, 1,280 or greater by haemagglutination inhibition test)



Testing Algorithms for Dengue



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- NS1 ELISA
- The non-structural protein 1 (NS1) of the dengue viral genome has been shown to be useful as a tool for the diagnosis of acute dengue infections. Dengue NS1 antigen has been detected in the serum of DENV infected patients as early as 1 day post onset of symptoms (DPO), and up to 18 DPO



Thrombocytopenia



- Thrombocytopenia is almost always present in patients with dengue
- Mechanisms
 - Early bone-marrow suppression
 - Increased peripheral destruction
- Profound thrombocytopenia, with platelet nadirs as low as 5000 cells per μL
- During the recovery period, platelet numbers rise promptly in the hypercellular marrow
- In the absence of bleeding no evidence exists to show that prophylactic platelet transfusions improve outcome

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Lum LC, et al, J Pediatr 2002; 140: 629-31.



Treatment



- No specific therapeutic agents
- Steroids, antivirals, or carbazochrome (which decreases capillary permeability)
- Invasive procedures should be considered carefully because of the risk of haemorrhage.
- The choice of crystalloid or colloid solutions in dengue shock syndrome is under debate
- Component therapy
- Organ support

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Fluid Replacement in Dengue Shock Syndrome: A Randomized, Double-Blind Comparison of Four Intravenous-Fluid Regimens



- A double-blind, randomized trial comparing four intravenous-fluid regimens for acute resuscitation of 50 children with DSS
- Colloids (dextran 70 or gelafundin) restored CI & BP
- Colloids normalized hematocrit more rapidly than crystalloids (RL & NS).
- Dextran 70 rapidly corrected hematocrit and CI, without adverse effects
- Dextran 70 preferred solution for acute resuscitation in DSS.



Management of Dengue Shock Syndrome: 4 IV Fluid Regimens in the First Hour



- 230 Vietnamese children with DSS.
- A randomized blinded comparison of 4 fluids (dextran, gelatin, lactated Ringer's, and "normal" saline)
- All the children survived
- No clear advantage to using any of the 4 fluids
- Longest recovery times occurred in the Ringer's lactate group



Comparison of Three Fluid Solutions for Resuscitation in Dengue Shock Syndrome



- double-blind, randomized comparison of 3 fluids
- 383 children with moderately severe shock
 - Ringer's lactate (128)
 - 6 percent dextran 70 (126)
 - 6 percent hydroxyethyl starch (129)
- The primary outcome measure was requirement for rescue colloid at any time after administration of the study fluid.
- Only one patient died (<0.2 percent mortality).

Wills BA, et al N Engl J Med 2005;353:877-89.



Comparison of Three Fluid Solutions for Resuscitation in Dengue Shock Syndrome



RESULTS

- Requirement for rescue colloid — was similar for the different fluids.
- The RR of requirement for rescue colloid was :
 - In moderate shock RL vs either colloid 1.08 (95 % CI, 0.78 to 1.47; **P=0.65**)
 - In severe shock Dextran vs Starch 0.88 (95 % CI, 0.66 to 1.17; **P=0.38**)
- RL had less rapid improvement in the hematocrit longer time to initial recovery than colloids.
- Minor variation in efficacy between the 2 colloids.
- Dextran had more adverse reactions than starch .

Wills BA, et al N Engl J Med 2005;353:877-89.



Choice of colloidal solutions in dengue hemorrhagic fever patients.



- There are 104 DHF children enrolled in the study
 - 57 are assigned in dextran
 - 47 in haesteril group.
- No allergic reaction was found after the use of both colloidal solutions.
- 10% Haes-steril is as effective as 10% dextran-40 in the treatment of DHF patients

Kalyanarooj S J Med Assoc Thai. 2008 Oct;91 Suppl 3:S97-103.



Non-hematological organ dysfunction and fluid balance determines outcome in adults with severe dengue infection: a multi-center study in India



- Multicenter, observational study in adults with DHF & DSS in India.
- 184 adults with a dengue IgM positive test admitted in 3 ICU in Pune over a 2 year period. 43 (23%) had DHF or DSS
- Median platelet count - 16.000/mm³ (9.000 - 25.000/mm³)
- 20 (48%) had MODS
- Hematological (35 patients, 80%), renal (20 patients, 50%) and cardiovascular (5 patients, 12%) failure, were the most frequent types of organ dysfunction.
- ICU mortality was 19% (8/42),

Schmitz L, Prayag S et al SCCM 2010 Miami



Non-hematological organ dysfunction and fluid balance determines outcome in adults with severe dengue infection: a multi-center study in India



- Mortality in patients with ≥ 3 organ dysfunctions reached 67% (8/12 patients).
- Risk of death was 4 times higher with the combination of cardiovascular failure with CNS.
- Cumulative fluid balance at 72h was more positive in the non-survivors than in the survivors (6.2 vs. 3.5 liters, $p < 0.05$)

Schmitz L, Prayag S et al SCCM 2010 Miami



Corticosteroids for treating dengue shock syndrome



- Observational studies suggested corticosteroids may benefit people with dengue shock syndrome.
- Four trials involving 284 participants
- Corticosteroids were no more effective than placebo or no treatment for reducing the number of deaths (RR 0.68, 95% CI 0.42 to 1.11)

Conclusions:

There is insufficient evidence to justify the use of corticosteroids in managing DSS.

Corticosteroids can potentially do harm

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Panpanich R,, et aj, Cochrane Database of Systematic Reviews 2006, Issue 3.
Art. No.: CD003488.





THANK YOU



Jeevan Reha Critical Care & Trauma Hospital
Research and Training Institute

