

INMED HUMANITARIAN HEALTH CONFERENCE

TROPICAL DISEASES OF SIGNIFICANCE

DENGUE – THE POTENTIAL LULL BEFORE THE STORM

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SESSION OBJECTIVES

- ❖ Understand the Epidemiology and some Pathophysiology
- ❖ Know the criteria for Diagnosing this widespread tropical disease
- ❖ Know the Triage Criteria for patients who risk suddenly decompensating while seemingly recovering
- ❖ Implement only appropriate Treatment Options to avoid iatrogenic complications
- ❖ Know the Preventive Measures available for yourself and the local population

DISCLOSURE

- ❖ There are no relevant financial relationships with ineligible companies to disclose.

OVERVIEW

- ❖ Dengue – also known as "Break-Bone Fever"
 - Caused by 1 of the 4 viruses called the "Dengue Viruses" (DENV)
 - An infection spread by mosquitoes during the taking of a blood meal
 - May be asymptomatic or present with a broad range of clinical manifestations
 - ✧ Ranging from a mild Febrile Illness to a life-threatening Shock Syndrome
 - Numerous viral, host, and vector factors impact the risk of infection and disease severity
 - Dengue is the most widespread mosquito-borne disease among humans
 - ✧ ~4 Billion people – nearly half of the world's population – live where at risk of contracting Dengue
 - ✧ Thus, Dengue remains important arthropod-borne viruses from medical and public health perspectives

WORLDWIDE DISEASE BURDEN

- Dengue is endemic in >130 countries across all 6 WHO (World Health Organization) regions
 - ✧ 70% of the disease burden is in Asia according to the WHO
 - ◆ In 2024 (the WORST Dengue year ever): reported 14.4 Million cases; 7.7 Million laboratory-confirmed; ~53,000 severe cases; 11,200 deaths...roughly double 2023
 - The Americas, especially Brazil, accounted for >13 Million of those reported cases
 - WHO declared "Grade 3 Emergency" (highest tier) in 2024...which continues to the present
- The emergence of Severe Dengue as a public health problem has largely been a result of human behaviors
 - ✧ Esp. population growth, poor urban planning (with overcrowding and poor sanitation), modern transportation, and lack of effective mosquito control

[SEE: PAGE 11 – WORLD MAP OF DENGUE]

EPIDEMIOLOGY

- ❖ Distribution overlaps with Yellow Fever, West Nile, Chikungunya, & Zika
 - All carried by the *Aedes* mosquitoes [see below]
- ❖ "Dengue-endemic" regions: Tropical Asia, Central & South America, sub-Saharan Africa, & Western Pacific
 - Where DENV transmission occurs year-round with seasonal surges
 - More densely populated urban areas are particularly affected
- ❖ Prior scant information from sub-Saharan Africa (where Malaria masked it) is now changing
 - A sharp rise in Dengue cases was recognized and reported in 2024
- ❖ Of significance, Dengue is now seasonally present in the southern continental U.S., many U.S. territories, as well as southern Europe
 - Due to *Aedes albopictus* mosquitoes [see below] now becoming well-established in temperate zones
- ❖ "Epidemic Dengue" transmission occurs when DENV is introduced into a region as an isolated event involving a single virus strain
 - If sufficiently large populations of susceptible hosts, and certain mosquito species are present:
 - ✦ Transmission of DENV is explosive with the infection incidence often exceeding 25–50%
- ❖ "Hyperendemic" transmission refers to the continuous circulation of **multiple DENV serotypes** in the same area
 - Requires the year-round presence of competent vector mosquitoes and a large population of susceptible individuals
 - All 4 DENV types are present in Southeast and South Asia, South America (except Chile), Central America, the Caribbean, and Mexico
- ❖ Transmission of DENVs between mosquitoes and nonhuman primates has been demonstrated, but no evidence this is an important reservoir for transmission to humans

ETIOLOGIC AGENTS

- ❖ DENV are members of the family *Flaviviridae*, genus *Orthoflavivirus*
 - They are small, enveloped viruses containing a single-stranded RNA genome
- ❖ The DENV include 4 antigenically related but distinct virus "serotypes"
 - These serotypes are designated DENV types 1 through 4 [i.e., DENV-1; DENV-2; DENV-3; DENV-4]
- ❖ All DENV are mosquito-borne human pathogens

THE VECTOR – MOSQUITOES

- ❖ As noted, both epidemic and endemic transmissions of DENV are maintained through a human-mosquito-human cycle involving mosquitoes of the genus *Aedes*
 - *Aedes aegypti* mosquitoes are widely distributed in tropical and subtropical areas from latitude 45° North to 35° South
 - *Aedes albopictus* mosquitoes are more tolerant of the cold and have a wider geographic distribution
 - ✦ However, they transmit DENV less effectively due to being less efficient natural vectors
- ❖ An uninfected female *Aedes* mosquito acquires the virus by feeding while the human's viremia titer is sufficient
 - After the necessary "extrinsic" incubation period, i.e., inside the mosquito, (8–12 days) the mosquito remains infectious for its lifetime
- ❖ *Aedes* mosquitoes typically breed in or close to houses, laying eggs in both man-made and natural water collections – even soft drink bottle caps
 - Biting throughout the daytime and at twilight at daybreak and dusk, esp. indoors/near houses
 - Prefer to bite humans, (notorious "ankle-biters"), frequently go unnoticed, are easily interrupted in their feeding, often moving on to another host
 - ✦ Thus, an infected *Ae. aegypti* mosquito may transmit DENV to several individuals in the same household

OTHER MODES OF TRANSMISSION

- ❖ Nosocomial transmission
 - DENV may be transmitted via blood products, needlestick injury, and mucocutaneous exposure
- ❖ Vertical transmission
 - I.e., passage of the pathogen from mother to baby during the period immediately before and after birth, whether across the placenta, in the breast milk, or through direct contact
- ❖ Congenital Dengue
 - Increasingly recognized when maternal infection occurs near term
 - ✦ Risk of fetal loss, preterm delivery, neonatal symptomatic disease
- ❖ Organ donor-derived cases
 - Recognized since 2018 in endemic areas

PATHOGENESIS

- ❖ Substantial gaps remain in understanding the pathogenesis of DENV infections
 - Especially due to a lack of a suitable animal models of disease
- ❖ Most DENV infections are asymptomatic, while some patients experience a mild nonspecific illness or “Classic Dengue” [see below]
- ❖ “Severe Dengue” (previously known as Dengue Hemorrhagic Fever and Dengue Shock Syndrome)
 - Occurs in <1% of all DENV infections (i.e., including those with or without symptoms)
 - Some of the factors causing Severe Dengue remain elusive
 - The risk of developing Severe Dengue is highest among individuals who develop a second Dengue infection caused by another DENV serotype
 - ✦ Known as “secondary” or “heterotypic” infection
 - ✦ Thus, Severe Dengue occurs primarily among individuals in areas where multiple DENV types circulate concurrently
 - ✦ Likely factors include different immune responses between primary and secondary DENV probably mediated via a “Cytokine Storm” triggered by the patient’s immune system
 - ◆ Antibody-dependent enhancement of infection
 - ◆ Enhanced immune complex formation
 - ◆ Accelerated T lymphocyte responses and cytokine production
- ❖ Recent research reports:
 - Genetic analyses of DENV strongly suggest that Severe Dengue only occurs with specific “virulent” genotypes within each of the 4 DENV serotypes
 - Unfortunately, these “virulent” genotypes have disseminated globally

IMMUNITY

- ❖ Long-lasting protection **does occur** against a DENV infection of the **same** serotype
 - However, cross-immunity against infections by the other 3 DENV serotypes wanes over subsequent months
- ❖ In the setting of “Hyperendemic” transmission, the prevalence of antibody against the several local DENV serotypes rises with age
 - However, hyperendemicity, i.e., multiple circulating DENV serotypes, is a major factor contributing to the occurrence of Severe Dengue

HUMAN INCUBATION PERIOD

- ❖ The incubation period of DENV infection has a broad range: 3–14 days
- ❖ Symptoms onset is typically 4–7 days after the infected *Aedes* mosquito bite
- ❖ Viremia in humans – thereby able to infect new biting mosquitoes – closely mirrors the onset of symptoms
 - Then persists until the fever abates

CLINICAL PRESENTATION

- ❖ Overall, ~25% of people infected with DENV will become symptomatic with Dengue
 - Only ~5% of those symptomatic (~1% of all infections) will develop Severe Dengue
- ❖ Symptoms
 - Symptoms can range from mild to severe, usually lasting 5–7 days
 - Children and Young Adults
 - ✧ May have high fever but are generally less symptomatic during the Febrile Phase vis-à-vis Adults
- ❖ **"Classic Dengue"** is an acute febrile illness sometimes known as "Break-Bone Fever" accompanied by:
 - Marked bone, joint, and muscle pains
 - Retro-orbital pain
 - Headache

[SEE: PAGE 12 – DENGUE SYMPTOMS]

SIGNIFICANCE OF "PRIMARY" AND "SECONDARY" TERMINOLOGY

- ❖ A "primary DENV infection" is the first wild-type infection for a patient
- ❖ A "secondary infection" is the second wild-type infection
 - Typically caused by a different DENV serotype
- ❖ Secondary infections separated by >18 months represent the highest risk for a severe clinical outcome

WHO'S 2009 REVISED "SEVERITY CLASSIFICATION" AND "CLINICAL PHASES"

- ❖ In an effort to improve case management, in 2009 the WHO published a revised Classification Scheme
- ❖ This new classification has clearer descriptors and essentially replaced the 1997 scheme
- ❖ The Dengue Severity Classification is used as a Clinical Triage Tool
 - Answers the question: **"How sick is this patient RIGHT NOW"**
- ❖ The Phases of the Dengue illness provides a Disease Timeline
 - ✧ Answers the question: **"Where is this patient in the course of illness?"**
- ❖ The best way to think of these: **"The Classification tells you WHAT to do; the Phase tells you WHEN to worry most."**
- ❖ And the answers to BOTH questions should be documented at every patient encounter
- ❖ However, be advised that some authors still use the outdated terminology – which can be confusing
 - E.g., "Dengue Hemorrhagic Fever", "Dengue Shock Syndrome"...even in the NEJM in late 2025!

WHO "SEVERITY CLASSIFICATION" SCHEME

- ❖ WHO's revisions describe these 3 clinical categories:
 - Dengue Without Warning Signs
 - Dengue With Warning Signs
 - Severe Dengue
- ❖ **"Dengue WITHOUT Warning Signs"**
 - "Presumptive diagnosis of Dengue infection" with (a) patient is a resident of [or] traveled from an endemic area within the past 2 weeks, PLUS (b) Fever, PLUS (c) any 2 of the following:
 - ✧ Nausea/vomiting
 - ✧ Headache, Retro-orbital or ocular pain, myalgias, or arthralgias (~70% of cases)
 - ✧ Transient macular, maculopapular, or petechial rash of the face, thorax, abdomen, extremities (~50%)
 - ✧ Positive tourniquet test [see below]
 - ✧ Leukopenia (if laboratory available)

- ❖ **“Dengue WITH Warning Signs”** (requires close observation and typically inpatient management)
 - Possible development of a severe case includes the criteria for Dengue infection (as defined above) PLUS at least one of the following Warning Signs:
 - ✧ Severe Abdominal pain
 - ✧ Persistent vomiting
 - ✧ Clinical fluid accumulation
 - ◆ E.g., Ascites, Pleural Effusion
 - ✧ Mucosal bleeding / “Minor” hemorrhagic manifestations:
 - ◆ E.g., Purpura/Ecchymosis, Epistaxis, Gum Bleeding, Hematemesis, Hematuria, or atypical Vaginal Bleeding
 - ✧ Lethargy or restlessness
 - ✧ Hepatomegaly >2 cm
 - ✧ Rising hematocrit ($\geq 20\%$ above average for age and sex), due to hemoconcentration
 - ◆ Concurrently with a falling platelet count (i.e., $< 100,000/\mu\text{L}$, even $< 20,000/\mu\text{L}$)
- ❖ **“SEVERE Dengue”** (requires ICU-level care)
 - Includes Dengue infection (as described above) PLUS at least one of the following issues clinically:
 - ✧ Severe plasma leakage manifesting as:
 - ◆ Shock
 - ◆ Fluid accumulation with Respiratory Distress
 - ✧ Severe hemorrhaging
 - ✧ Severe organ involvement:
 - ◆ Liver with markedly elevated AST/ALT
 - ◆ Impaired consciousness
 - ◆ Organ failure

RISK FACTORS FOR SEVERE DENGUE

- ❖ Include these:
 - Immunity: History of a prior episode of Dengue, esp. DENV-2
 - Pregnant women
 - Babies, esp. ages 6m–12m [described below]
 - Adults
 - Obesity
 - Diabetes
 - Kidney failure

WHO “CLINICAL PHASES” OF INFECTION

- ❖ There are 3 “Phases” that can be seen in the setting of DENV infections:
 - [#1] Febrile Phase
 - [#2] Critical Phase
 - [#3] Convalescent Phase
- ❖ Patients move through all 3 Phases of infection sequentially IF they have either “Dengue WITH Warning Signs” or “SEVERE Dengue”
- ❖ However, in patients classified as “Dengue WITHOUT Warning Signs,” they only experience the [#1] Febrile and [#3] Convalescent Phases, but not the [#2] Critical Phase
- ❖ **[#1] FEBRILE PHASE**
 - Characterized by sudden high-grade fever $\geq 38.5^{\circ}\text{C}$ ($\geq 101.3^{\circ}\text{F}$) PLUS symptoms of Classic Dengue (as described above)

- Physical examination may demonstrate:
 - ✧ Conjunctival injection
 - ✧ Pharyngeal erythema
 - ✧ Lymphadenopathy
 - ✧ Hepatomegaly
 - ✧ Variably a transient macular rash
 - A **Tourniquet Test** should also be performed:
 - ✧ Examine the volar forearm skin just below antecubital crease
 - ✧ Make note of any pre-existing petechiae
 - ✧ Inflate a blood pressure cuff on the upper arm to midway between systolic and diastolic blood pressures and hold for 5 minutes
 - ✧ Then 1–2 minutes after deflating the cuff, examine the skin below the cuff for new petechiae
 - ◆ The presence of ≥ 10 new petechiae in a square inch is considered a positive test
 - ✧ While useful in a Resource-Limited Area, the diagnostic performance is only modest
 - ◆ Sensitivity ranges from 30–60% depending on several variables (age, hydration, timing, etc.)
 - ✧ Reminder: a negative test does not rule out Dengue
 - Duration of this Febrile Phase is 3–7 days
 - ✧ After which MOST patients move directly to the Convalescent Phase and recover without complications
 - However, if the Critical Phase is destined to occur, the warning signs typically emerge in the LATE Febrile Phase, around defervescence
- ❖ **[#2]CRITICAL PHASE**
- Almost all DENV infections that progress to a Critical Phase are due to a secondary infection
 - ✧ The difference reflects different immune responses of secondary DENV infections
 - ◆ Including enhanced immune complex formation, etc. (as above)
 - However, a subset of Critical Phase infections occurs in Infants ages 6m–12m in endemic areas
 - ✧ Having acquired DENV-specific antibodies transplacentally, they become susceptible to a Severe (secondary) DENV infection when antibody levels decline below the neutralization threshold
 - ✧ Thereafter, the Child experiences a DENV-infected mosquito bite but may react as if this were a secondary infection
 - In ALL patients: Between days 3–7 of illness, must be monitored for signs of vascular leakage of plasma
 - ✧ Plasma leakage is the most specific and life-threatening feature of Severe Dengue
 - ◆ Usually occurs during the period of 24 hours pre/post the time of defervescence!
 - ✧ Significant vascular leakage reduces intravascular volume, decreasing organ perfusion, i.e., shock-like
 - ✧ Corresponding symptomatic manifestations of the Critical Phase may include:
 - ◆ Persistent vomiting
 - ◆ Severe abdominal pain
 - ◆ Tender hepatomegaly
 - ◆ Lethargy or restlessness
 - ✧ Possible manifestations: Severe plasma leakage with minimal hemorrhaging...OR **vice versa**
 - ✧ This Critical Phase typically lasts for 24–48 hours
- ❖ **[#3]CONVALESCENT PHASE**
- During the Convalescent Phase, plasma leakage and hemorrhage resolve, vital signs stabilize, and accumulated fluids are resorbed
 - Usual duration is 2–4 days
 - ✧ Although Adults may experience profound fatigue for even weeks thereafter

[SEE: PAGE 13 – COURSE OF ACUTE DENGUE VIRUS INFECTION]

DIAGNOSTIC LABORATORY TESTS

- ❖ FYI: Laboratory diagnostic tests are available for Dengue
 - Directly: detection of viral components in the serum
 - Indirectly: by serology
- ❖ In settings where serologic assays are available
 - An acute-phase serum sample for an immunoglobulin (Ig)M immunoassay is the laboratory test of choice
- ❖ Of course, these tests may not be available in the Majority World

[SEE: PAGE 14 – LABORATORY TESTS FOR THE DIAGNOSIS OF DENGUE]

DIFFERENTIAL DIAGNOSIS

- ❖ Early clinical presentations of Dengue, Chikungunya, and Zika virus infection may be indistinguishable
 - Chikungunya
 - ✧ Dengue more commonly includes abdominal pain and leukopenia and less prominent arthralgias
 - Zika virus infection
 - ✧ Unlike Dengue, Zika is commonly associated with conjunctivitis
- ❖ Oropouche virus infection majorly emerged in 2023-2024 and is nearly indistinguishable from Dengue acutely
 - Severe headache with photophobia is more prominent with Oropouche
 - Cases confirmed in 11 countries of the Americas in 2024 (including South and Central America and the Caribbean)
 - Testing for both is increasingly available
- ❖ Additional differential diagnostic possibilities include (some depending on the region of the world):
 - Other viral hemorrhagic fevers – Ebola virus, Marburg virus, Lassa virus, Yellow Fever virus, Hantavirus, and Crimean-Congo Hemorrhagic Fever (CCHF – regionally important)
 - Malaria
 - Typhoid Fever
 - Leptospirosis – characterized by fever, rigors, myalgia, conjunctival suffusion, and headache
 - Viral Hepatitis – including Hepatitis A, B, C, D, and E
 - Rickettsial infection – including African Tick Bite Fever and Relapsing Fever
 - Mayaro virus – in South American settings
 - Acute HIV infection
 - COVID-19

TREATMENTS

- ❖ **General Management**
 - Management is primarily supportive – and sometimes requiring even aggressive efforts
 - ✧ E.g., maintaining adequate intravascular volume when indicated medically
- ❖ **Antiviral Drugs**
 - ✧ New (first-ever reported) oral drug (JNJ-1802) / Mosnodenvir by Johnson & Johnson
 - ◆ Blocks DENV replication against all 4 serotypes
 - Mutations in DENV-2 and -3 are now limiting its effectiveness
 - ✧ Novartis has another molecule (NITD-688) that reportedly retains its potency
 - ✧ However, currently there is NO licensed antiviral against Dengue virus infection
- ❖ **Outpatient Management**
 - Appropriate for patients with presumptive diagnosis of Dengue in the **absence** of Warning Signs and the **absence** of ALL of these “Coexisting Conditions”:

[Continued on the Next Page]

- "Coexisting Conditions":
 - ✧ Pregnancy
 - ✧ Infancy
 - ✧ Old age
 - ✧ Diabetes
 - ✧ Renal failure
 - ✧ Underlying Hemolytic disease
 - ✧ Obesity
 - ✧ Poor social situation
 - Homecare Instructions should include:
 - ✧ An outpatient should be able to tolerate oral fluids and urinate at least Q6 hours
 - ✧ Plenty of **rest**; only light activities – avoid any exertion, especially if having joint symptoms
 - ✧ Drink **2–3 Liters** [Adults] of clean water daily (adding a pinch of salt to each 8 oz./250 mL glass)
 - ✧ Patients and their families should be instructed to **watch for signs of dehydration**
 - ◆ I.e., decrease in urination, few or no tears, dry mouth or lips, sunken eyes, listlessness or confusion, cold or clammy extremities, sunken fontanel in an Infant
 - Medications
 - ✧ Fever and myalgias should be managed with **Acetaminophen / Paracetamol** (name worldwide)
 - ◆ Max. Adult dosage 3000 mg/24hrs (or less in elderly or with hepatic impairment)
 - **AVOID: Aspirin or any NSAIDs** (Nonsteroidal Anti-Inflammatory Agents) due to the risk of serious bleeding
 - ✧ E.g., Ibuprofen, Naproxen, Diclofenac, etc.
 - As fever declines (3–7 days after onset of symptoms), patients are in the period of maximum risk for complications
 - ✧ Essential instructions: **Seek medical attention promptly for any of the following:**
 - ◆ Severe abdominal pain
 - ◆ Persistent vomiting
 - ◆ Bleeding from nose or gums
 - ◆ Vomiting blood
 - ◆ Very dark/even tarry/black feces
 - ◆ Drowsiness or irritability
 - ◆ Pale or cool skin
 - ◆ Difficulty breathing
 - Consider daily medical visits which may be warranted to monitor for serious complications
- ❖ **Management of High-Risk Patients for Severe Dengue – Hospital Inpatient Management**
- Warranted for patients with (a) "Dengue With Warning Signs", (b) "Severe Dengue", or (c) Dengue with "Coexisting Conditions" (as above)
 - ✧ Thereby, providing closer monitoring, access to IV fluids, and blood transfusions as needed
 - ◆ Avoiding rapid large fluid boluses unless the patient is frankly hypotensive (pulmonary edema risk)
 - ◆ Also, prophylactic platelet transfusion is NOT recommended in Dengue with thrombocytopenia (even if very low platelet counts) in the absence of significant bleeding
 - As noted, plasma leakage, if it occurs, typically becomes evident during the 24 hours pre/post defervescence
 - ✧ Because dramatic plasma leakage can develop suddenly with minimal hemorrhagic manifestations
 - ✧ Thus, early identification of patients at increased risk for shock and other complications is critical
 - The issue of "Secondary HLH" (hemophagocytic lymphohistiocytosis) as a fatal complication is beyond the scope of this document

PROGNOSIS

- ❖ Severe Dengue can be life-threatening if not treated aggressively in the hospital (usually in the ICU)
- ❖ The WHO reports:
 - Case Fatality Rates (CFR) can be <1% with proper case management
 - In its absence, the CFR can be >20% in patients with Severe Dengue

PREVENTION – PUBLIC HEALTH

- ❖ Prevention of Dengue infection in endemic areas includes mosquito control and vaccine development
- ❖ **Mosquito control** includes:
 - **Remove any standing water** where mosquitoes can breed (esp. in the rainy season)
 - ✧ Empty/remove both inside & outside of the residence, e.g., vases, plant saucers, trash cans, wading pools, spare tires, even soda bottle caps, etc.
 - ✧ Cover all water storage containers / barrels / cisterns to prevent access by mosquitoes
 - **Minimize mosquito bites** (indoors & outdoors) as much as possible
 - ✧ Apply Mosquito Repellent (e.g., DEET 30–50%) on all exposed skin – esp. *ankles* – 3–4 times daily
 - ◆ Safe for all patients including Pregnant Women
 - ◆ EXCEPTION: avoid for Infants <2m
 - ◆ If also using Sunscreen, apply Sunscreen first, Repellent second
 - ✧ Mosquito-proof by installing fine mesh screens on all windows & doors
 - ✧ If possible, regularly spray the home & work areas with effective insecticides against flying insects
 - ✧ Bednets, esp. long-lasting insecticidal pre-treated (Permethrin, etc.)
 - ◆ Anyone with a fever – to prevent mosquitoes from spreading the possible viral agent to others
 - ◆ Chronically ill or inactive Adults
 - ◆ Daytime napping Children
 - ✧ Wear long-sleeved tops and long pants / dresses – more effective if light-colored clothing
- ❖ **“Endosymbiotic Control”** reported in 2021 in the *New England Journal of Medicine*
 - A novel DENV infection control strategy consists of releasing male and female *Ae. Aegypti* mosquitoes infected with *Wolbachia pipientis* – an obligate intracellular bacterium
 - ✧ Which has a virus-blocking effect on the mosquitoes
 - ✧ These mosquitoes infected with *Wolbachia* are less susceptible to DENV infection than the wild-type
 - ✧ Another report in the NEJM in 2/2026 indicates that a program with male-only *Ae. aegypti* infected with *Wolbachia* cannot produce viable offspring thus reducing the wild-type populations
 - Many countries are now demonstrating benefit:
 - ✧ Indonesia: efficacy of 86% reduced Dengue hospitalizations from any of the 4 DENV serotypes!
 - ✧ Columbia: 90–94% reduction in Dengue incidence
 - ✧ World Mosquito Program in 2026 is releasing these treated mosquitoes across >14 countries

PREVENTION – TRAVELERS & VOLUNTEERS

- ❖ Most travelers from nonendemic countries are at low risk for Severe Dengue (i.e., in the absence of prior Dengue illness)
 - Potential exceptions include:
 - ✧ Frequent international travelers, expatriates, frequently deploying military personnel, and immigrants from endemic areas returning to their countries of origin
- ❖ People with history of Dengue infection need not necessarily avoid subsequent travel to Dengue-endemic regions because:
 - Severe Dengue occurs in a very small (2–4%) percentage of secondary infections
 - Certainly, appropriate precautions (as above) to prevent mosquito bites are highly advisable

PREVENTION – VACCINES

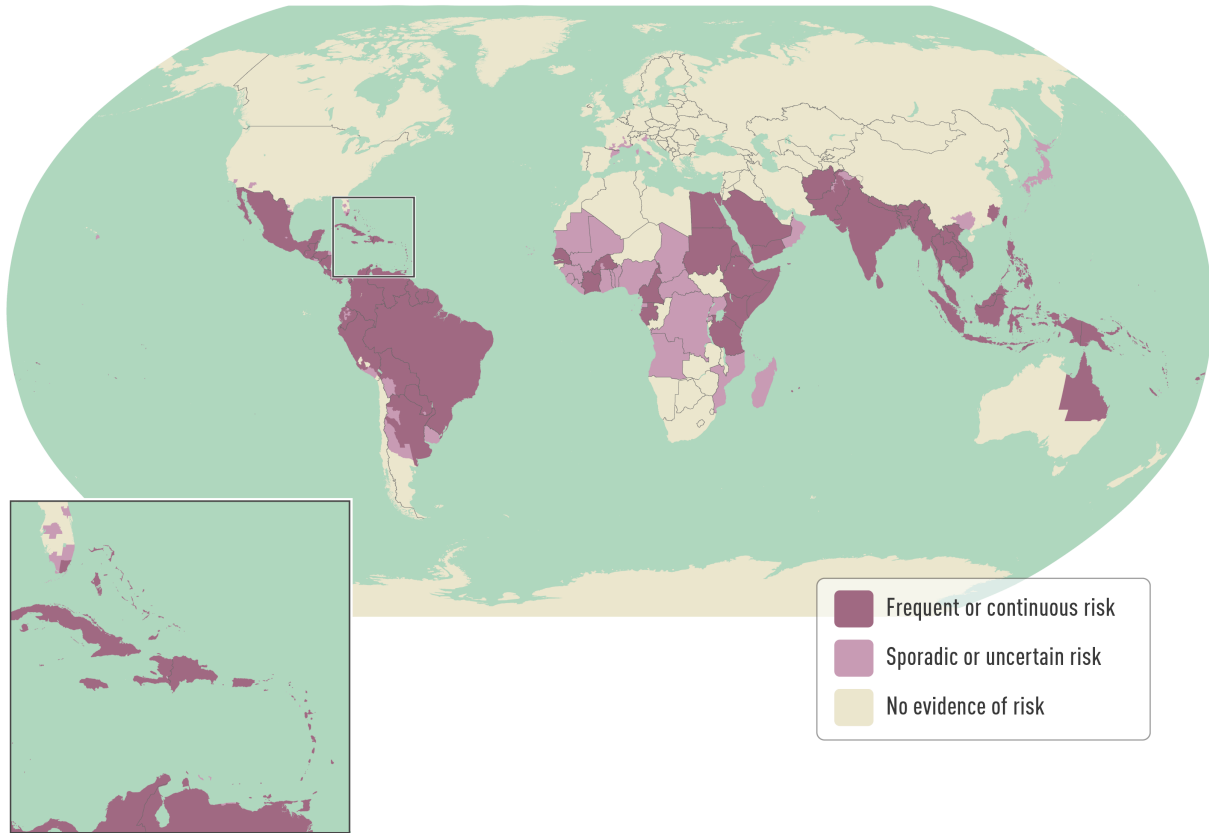
- ❖ A prior vaccine, **CYD-TDV (Dengvaxia®)**, is now being phased out by Sanofi citing low global demand
 - Will be terminating all distribution in the U.S. and globally in the summer of 2026
- ❖ A newer vaccine: **TAK-003 (Qdenga, Takeda)**
 - While not yet FDA approved, it has been approved in 40+ countries and WHO-qualified by late 2025
 - ✧ Brazil integrated Qdenga into its public health system in 2024 with ~19 Million doses administered
 - TAK-003 is a live attenuated tetravalent vaccine given subQ in a 2-dose schedule 3 months apart
 - ✧ Phase 3 trials: vaccine is safe and effective in both seropositive and seronegative persons
 - ✧ However, further efficacy data is needed for serotypes DENV-3 and -4 as questions remain
- ❖ And recently another arrival: **TV003 (Butantan-DV, Instituto Butantan, Brazil)**
 - While in earlier phases of development elsewhere, it is only licensed in Brazil at present
 - Excellent efficacy against DENV-1 and -2, but a paucity of information about DENV-3 and DENV-4
- ❖ Bottom line: There is currently NO Dengue vaccine available for routine use in the U.S. going forward

INFORMATION RESOURCES

- ❖ From the U.S. Centers for Disease Control & Prevention (CDC) including a section for healthcare professionals
 - www.cdc.gov/dengue/hcp/index.html
- ❖ Information from the World Health Organization (WHO) on this important topic
 - www.who.int/health-topics/dengue-and-severe-dengue#tab=tab_1
 - www.who.int/publications/i/item/9789240111110 (clinical management of arboviral diseases)
- ❖ Frequently updated information on diseases across the globe from the CDC country-by-country
 - wwwnc.cdc.gov/travel/destinations/list
 - SEE: “Clinician Resources” (on the left side column)
 - SEE: (also on the left column): Advice for Travelers / Humanitarian Aid Workers
(listed alphabetically on a long list of topics)
- ❖ UpToDate® ©2026 – Licensed by subscription to Duane R Spaulding MD
 - www.uptodate.com

THANK YOU!

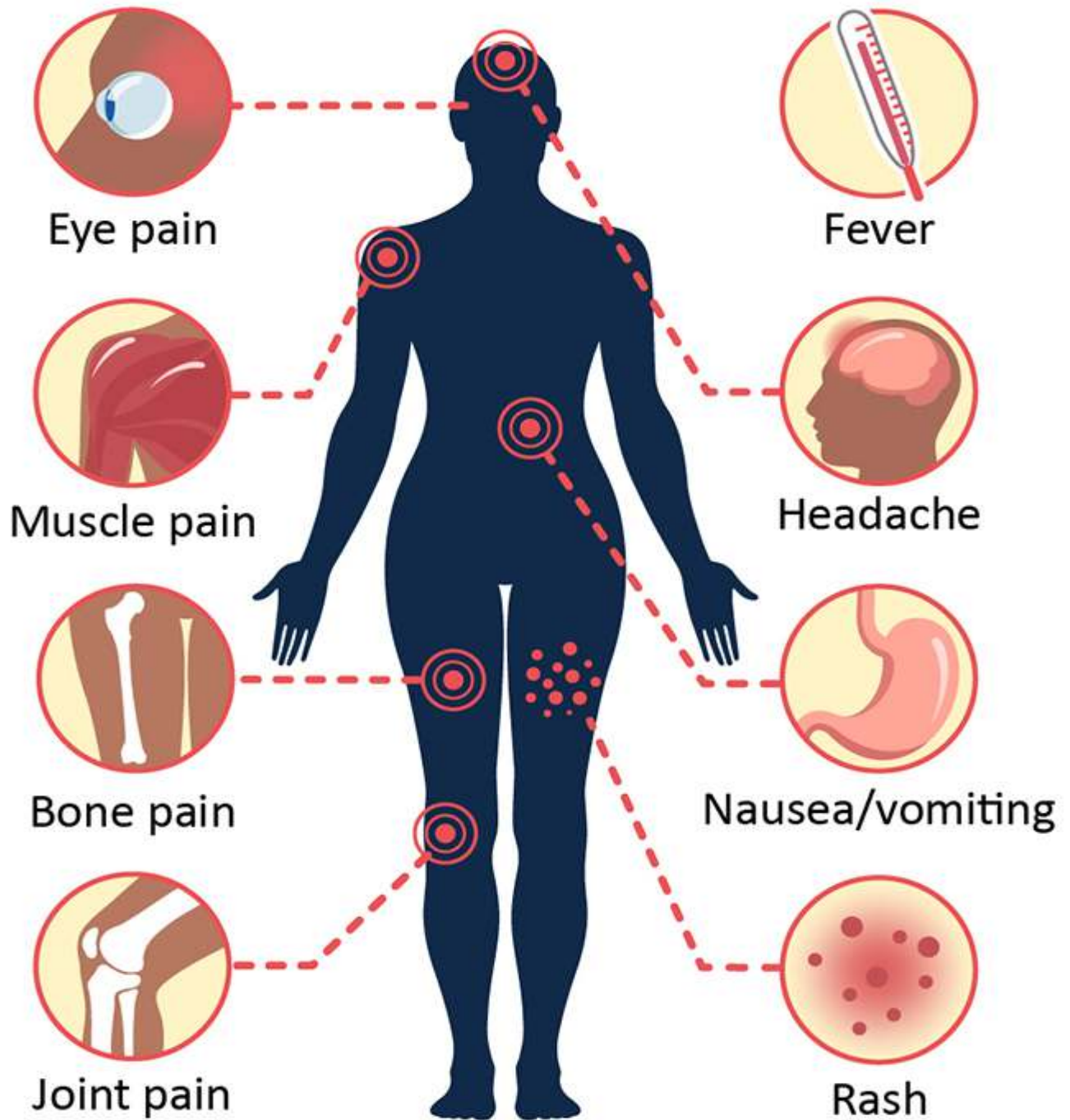
World Map Highlighting Areas of Dengue Risk - CDC



<https://tinyurl.com/294u328a>

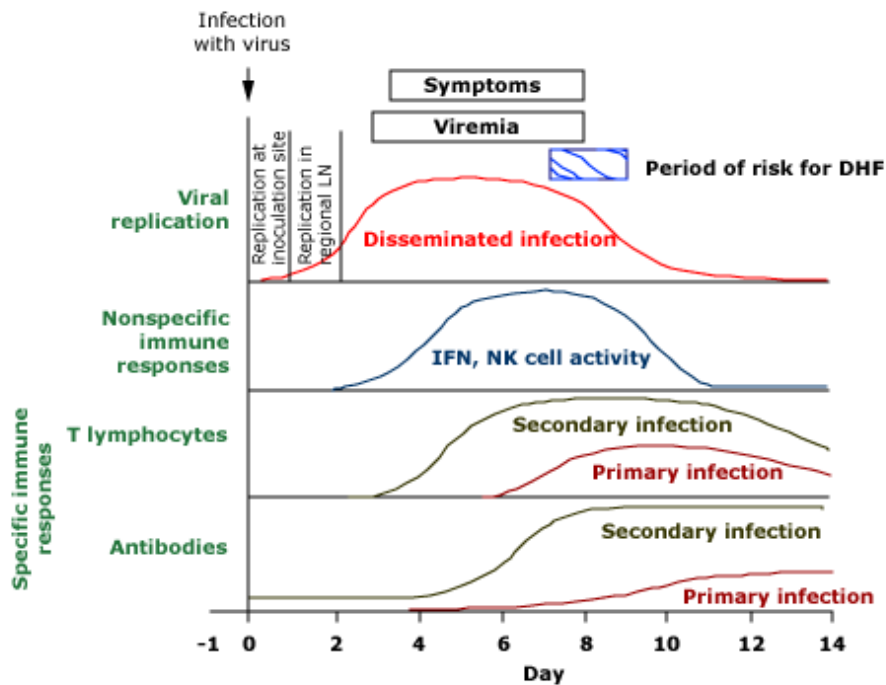
Dengue Symptoms

Fever with any of the following





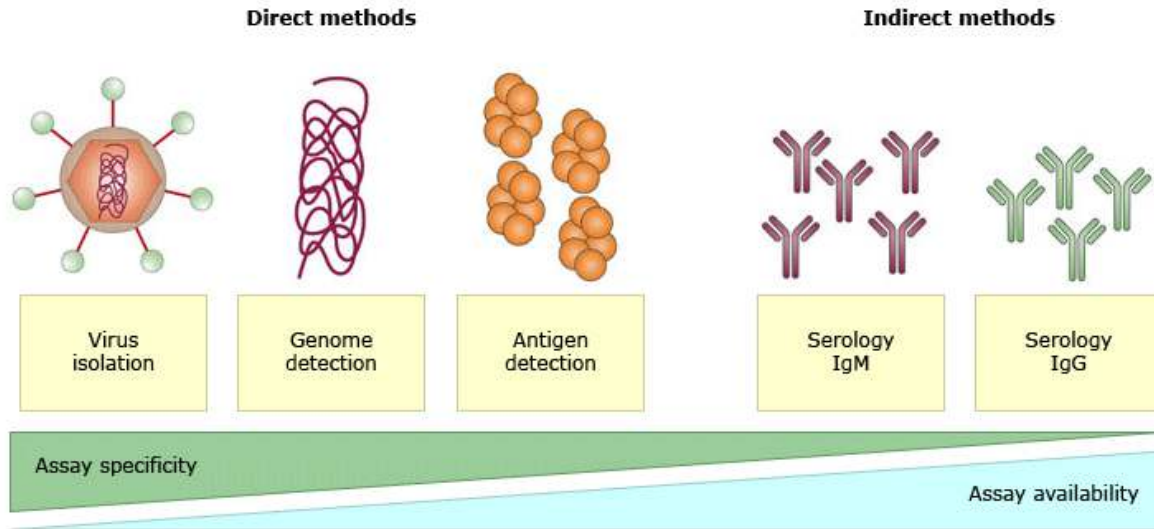
Acute dengue virus infection



Hypothetical schema of events in acute dengue virus infection. The kinetics and general location of viral replication are diagrammed in relation to the presence of detectable viremia, general symptoms (fever, myalgias, headache, rash), and the period of risk for plasma leakage, shock, severe thrombocytopenia, and bleeding in dengue hemorrhagic fever (DHF). Nonspecific immune responses include the production of interferons (IFN) and natural killer (NK) cell activity. The kinetics of dengue virus-specific T lymphocyte activation and the production of dengue virus-specific antibodies occur later and are of lesser magnitude in primary infections (first exposure to dengue viruses) than in secondary infections (later infection with a second dengue virus serotype).



Laboratory tests for diagnosis of dengue virus infection



Comparative merits of laboratory methods for diagnosis of dengue infection.

Ig: immunoglobulin.

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