



What Clinicians Need to Know about Dengue in the United States

Clinician Outreach and Communication Activity (COCA) Call
Thursday, September 29, 2022

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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Describe current dengue epidemiology and the populations who are at greatest risk for dengue and severe dengue in the United States.
2. Recognize the three phases (febrile, critical, convalescent) and the three severity levels of symptomatic dengue (dengue, dengue with warning signs, severe dengue) based on a patient's clinical and laboratory findings.
3. Identify the indicated treatment group (A, B, C), including hospital admission and intravenous fluids management recommendations, based on dengue phase and severity.

To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov

Today's Presenters

- **Laura Adams, DVM, MPH**
Epidemiologist
Dengue Branch, Division of Vector-Borne Diseases
Centers for Disease Control and Prevention
- **Liliana Sánchez-González, MD, MPH**
Epidemiologist
Dengue Branch, Division of Vector-Borne Diseases
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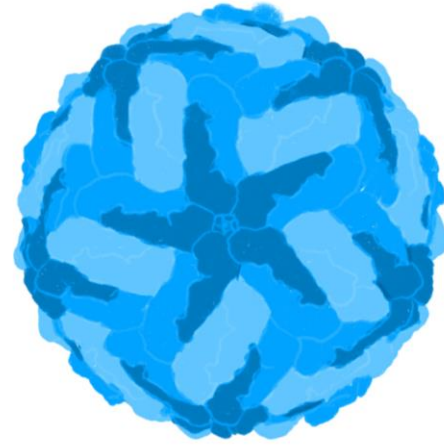
Dengue Epidemiology

Laura Adams

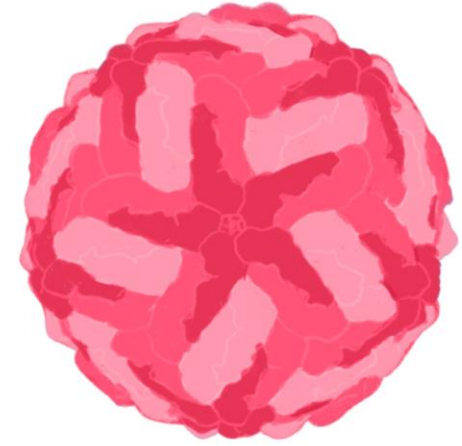
Dengue

Dengue Virus

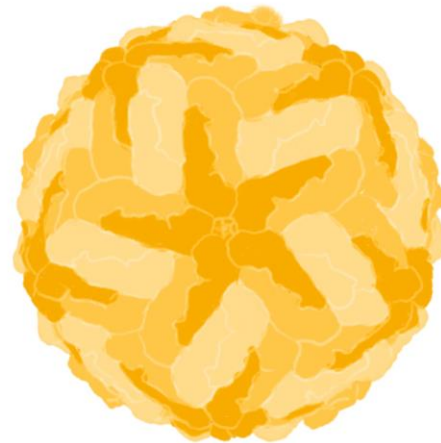
- DENV-1, 2, 3, 4
 - Lifelong DENV type-specific immunity
 - Short-term cross-immunity (~1–3 years)



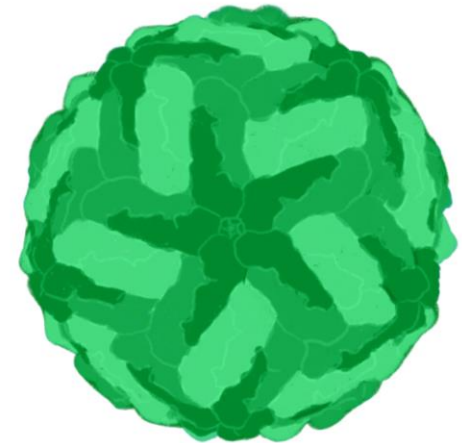
Dengue 1



Dengue 2



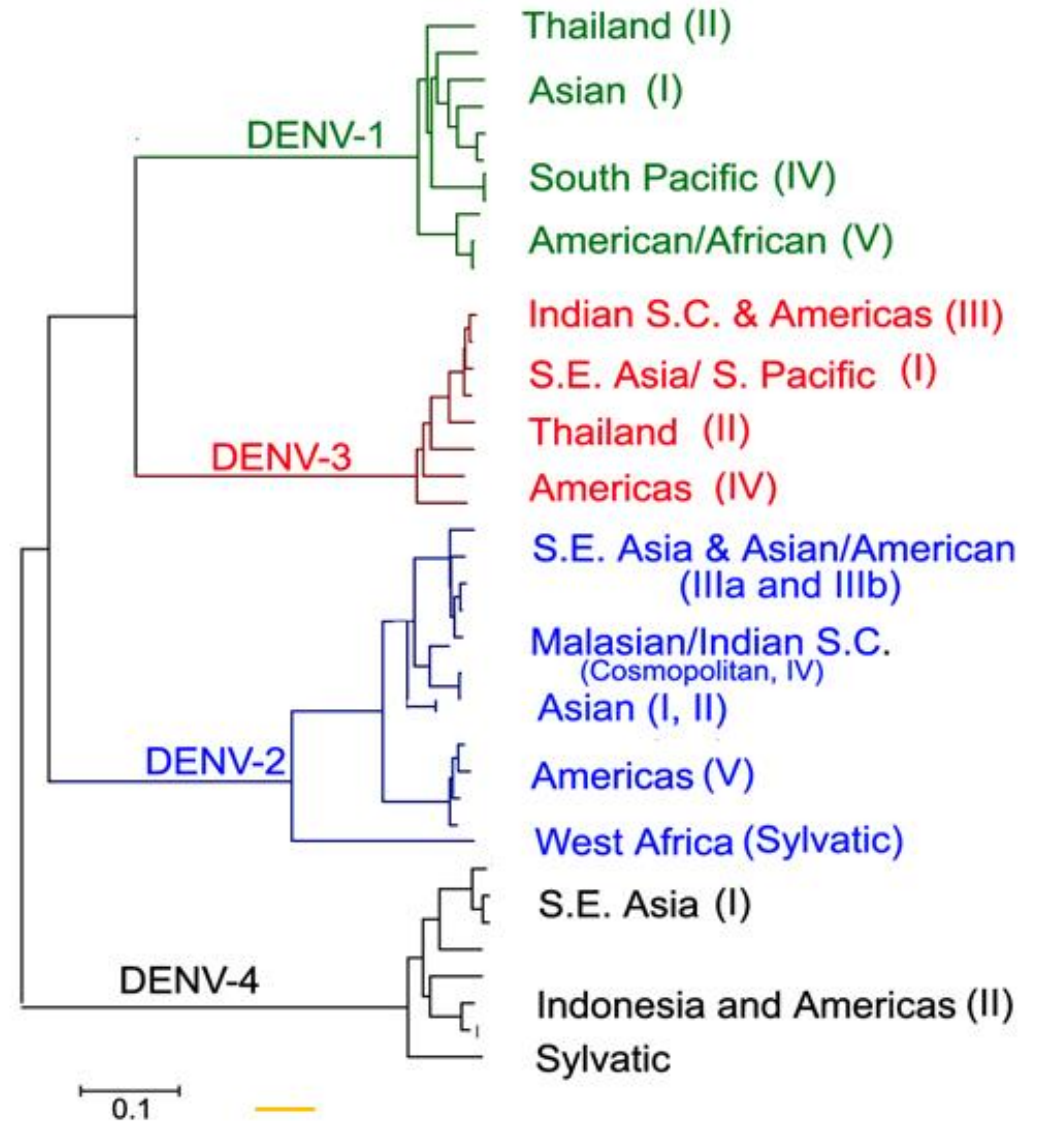
Dengue 3



Dengue 4

Dengue Virus Types

- Genetic variation within DENV types
 - Some variants may be more virulent, but many factors involved (e.g., age, timing between infections, order of infections)



DENV Transmission

- Vector-borne
 - Saliva of infected *Aedes spp* mosquito
- Other modes
 - Vertical from mother to baby
 - Blood transfusion or organ transplantation
 - Needle stick, mucocutaneous, or hospital/laboratory accident
 - Breast milk
 - Sexual

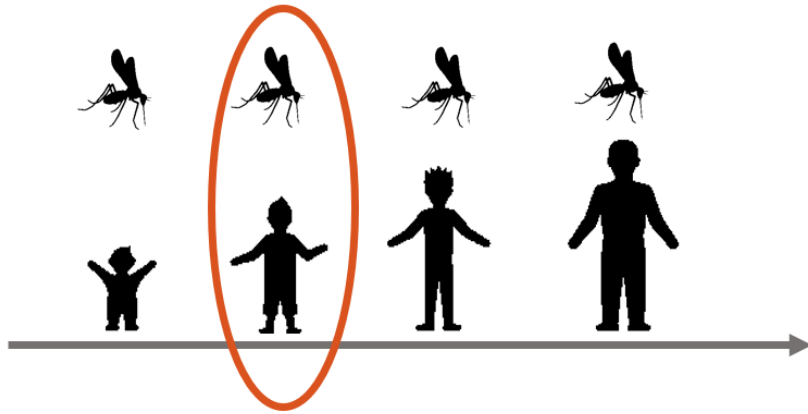
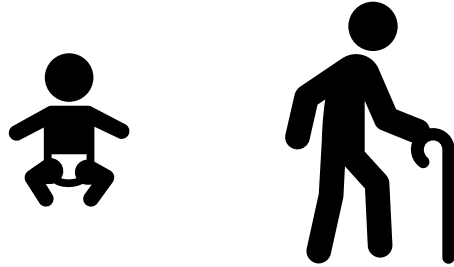


Aedes aegypti



Aedes albopictus

Risk Factors for Severe Dengue



■ Age

- Infants born to seropositive mothers
- Elderly

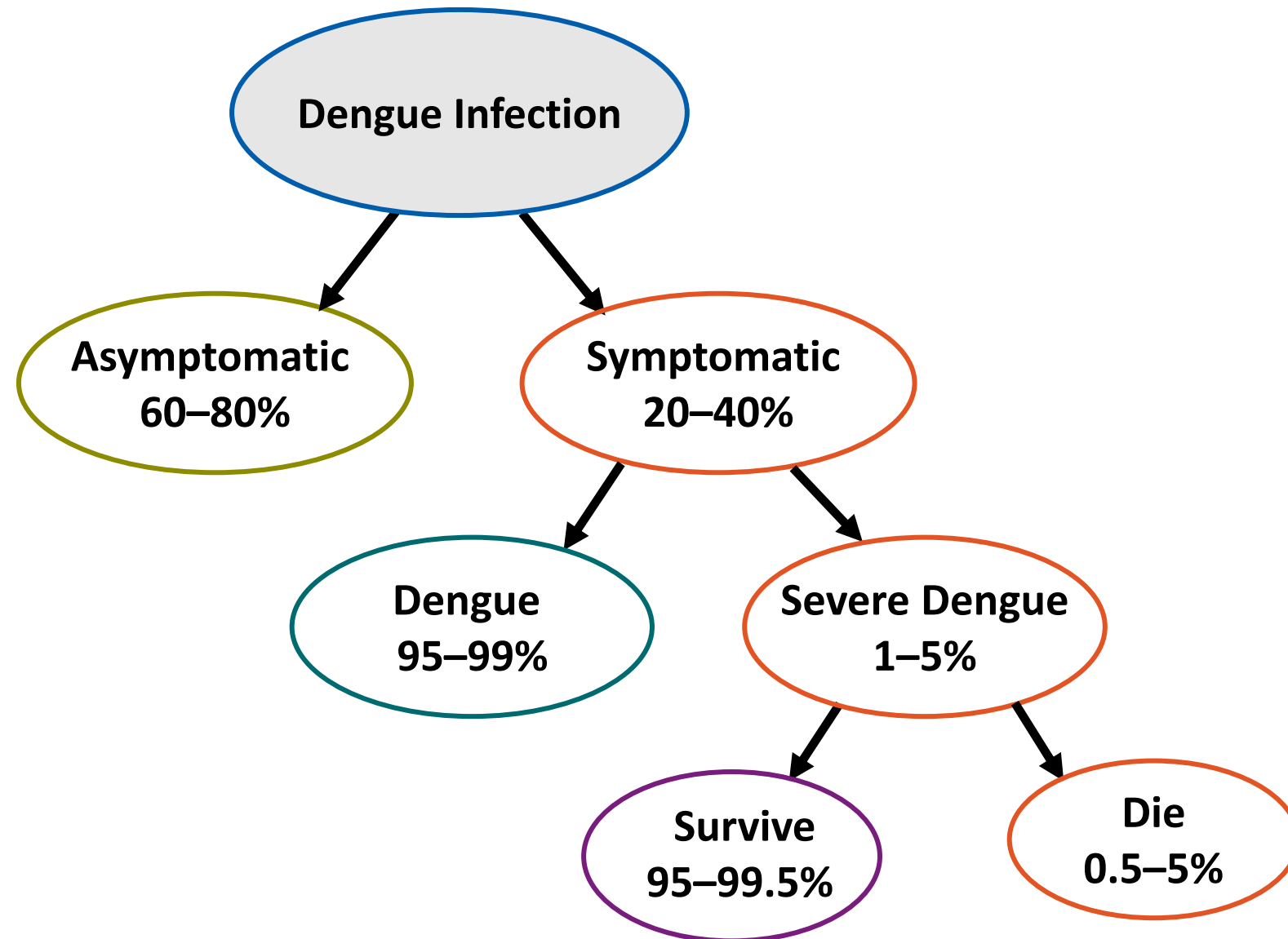
■ Number of dengue infections

- 2nd >> 1st, 3rd, 4th infection

■ Comorbidities

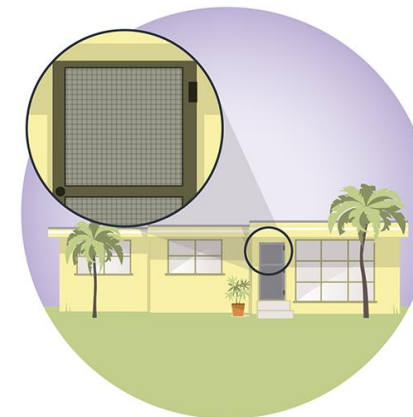
- Asthma, diabetes, obesity, hypertension, sickle cell disease

Dengue Outcomes



Dengue Prevention

- Use EPA-registered insect repellents:
 - DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, 2-undecanone
- Wear long-sleeved shirts and long pants
- Control mosquitoes in and around the home
 - Screens
 - Empty and clean water-holding items



Dengvaxia™ Dengue Vaccine: ACIP Recommended in 2021

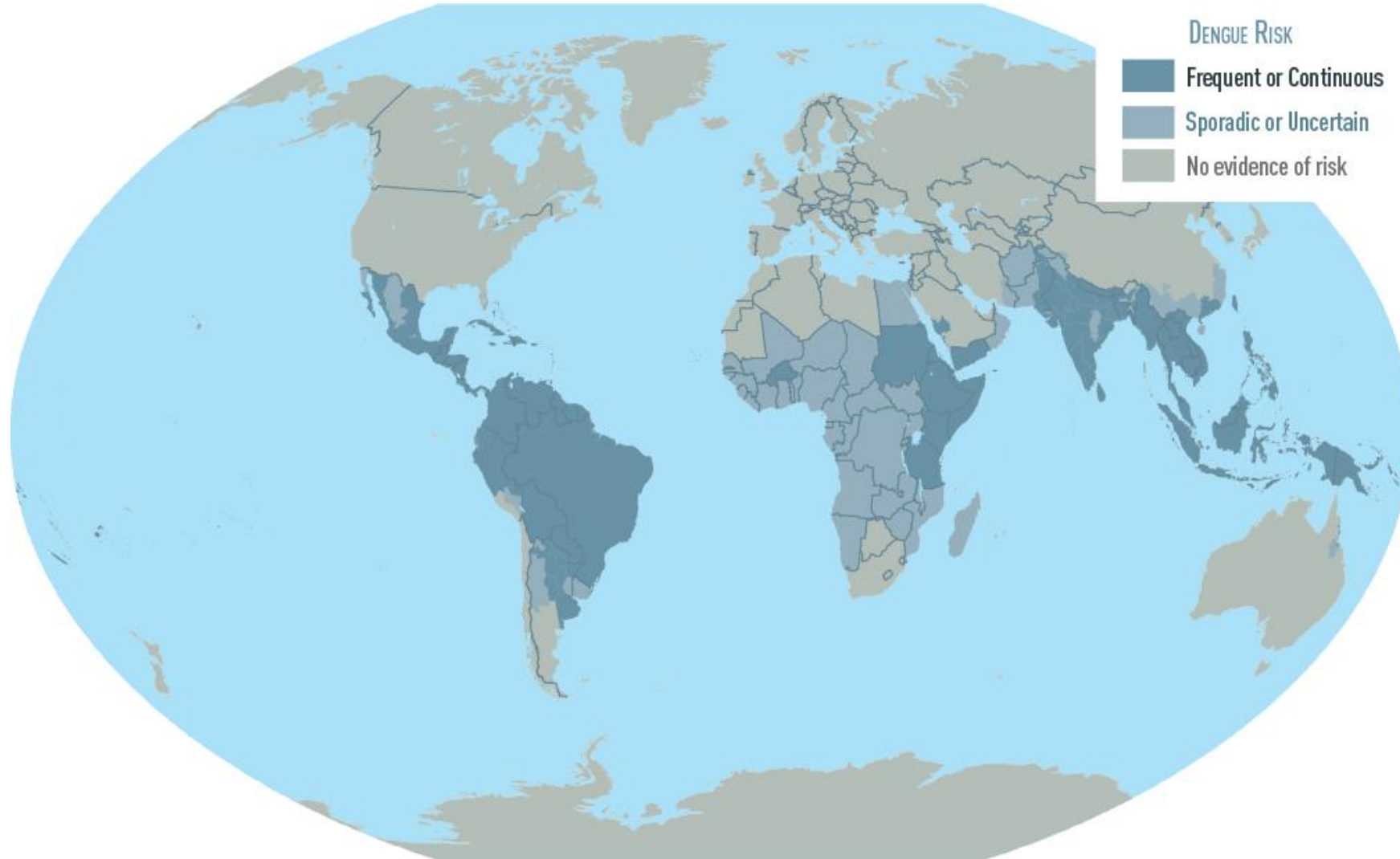


Three doses of Dengvaxia are indicated for the prevention of dengue in:

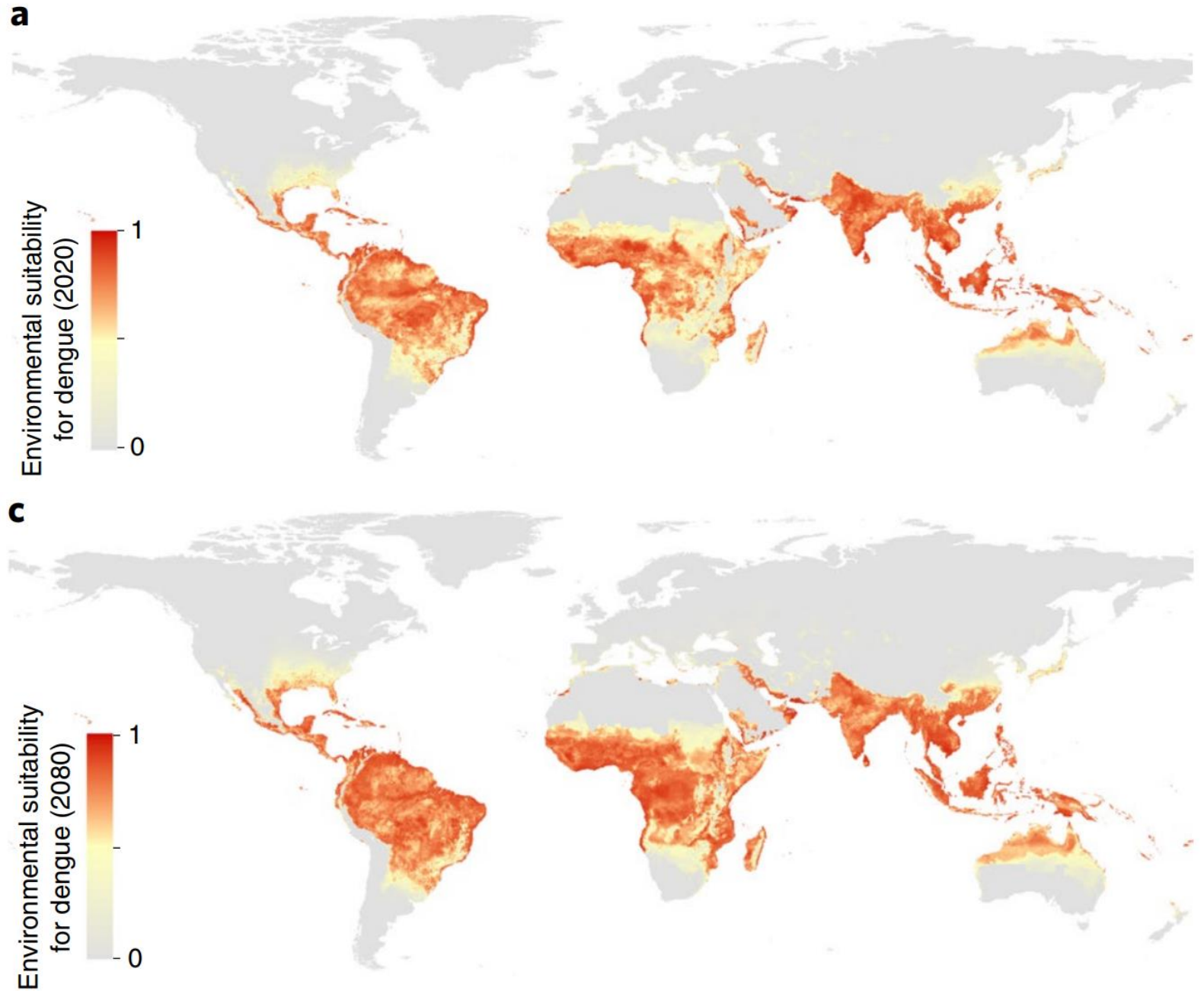
- People 9–16 years old WITH
 - laboratory confirmation of previous dengue virus infection AND
 - living in endemic areas.

Global Dengue Epidemiology

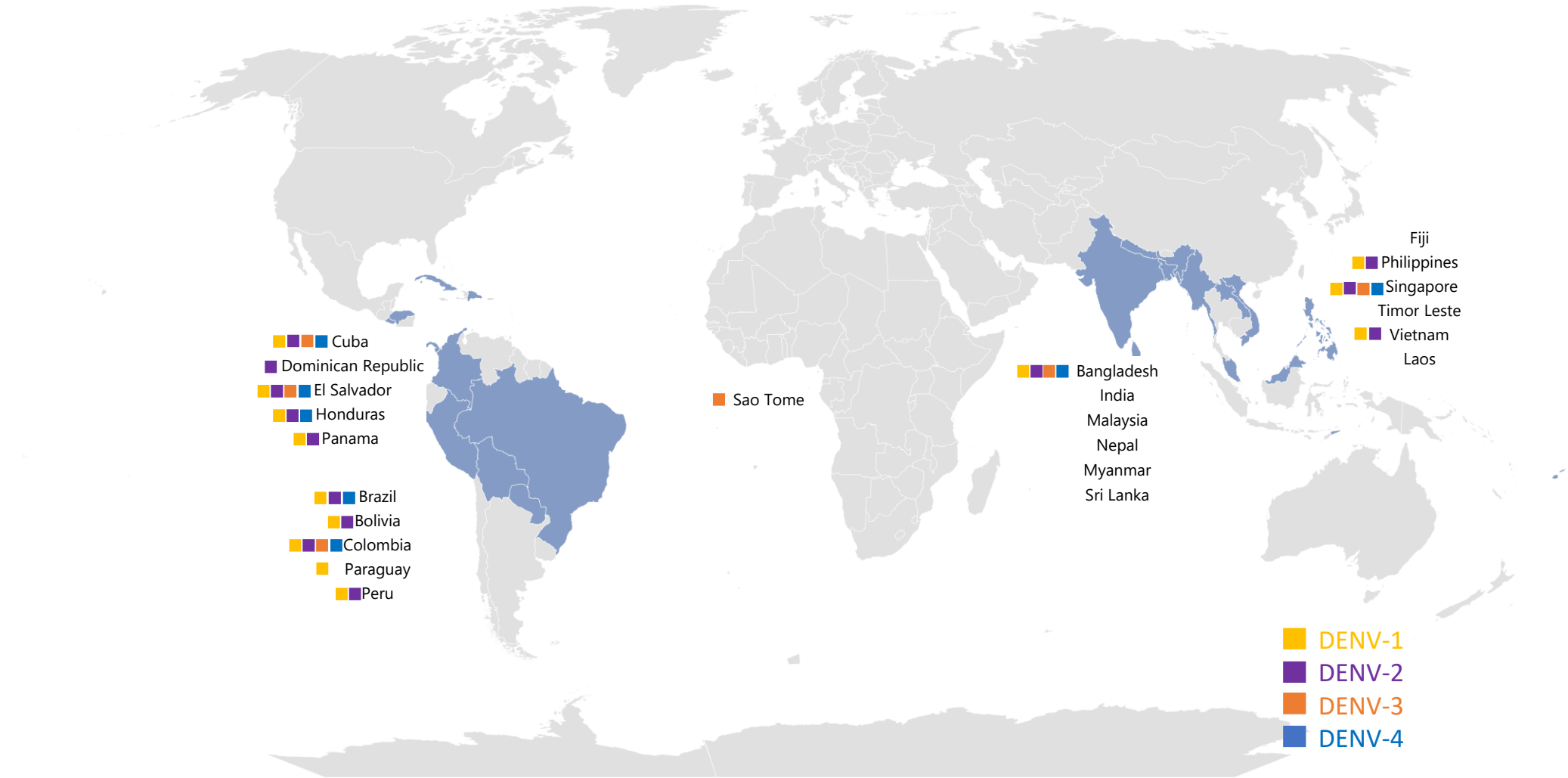
Dengue is the most important virus transmitted by mosquitos worldwide.



**Dengue
incidence is
likely to
increase as the
climate warms.**

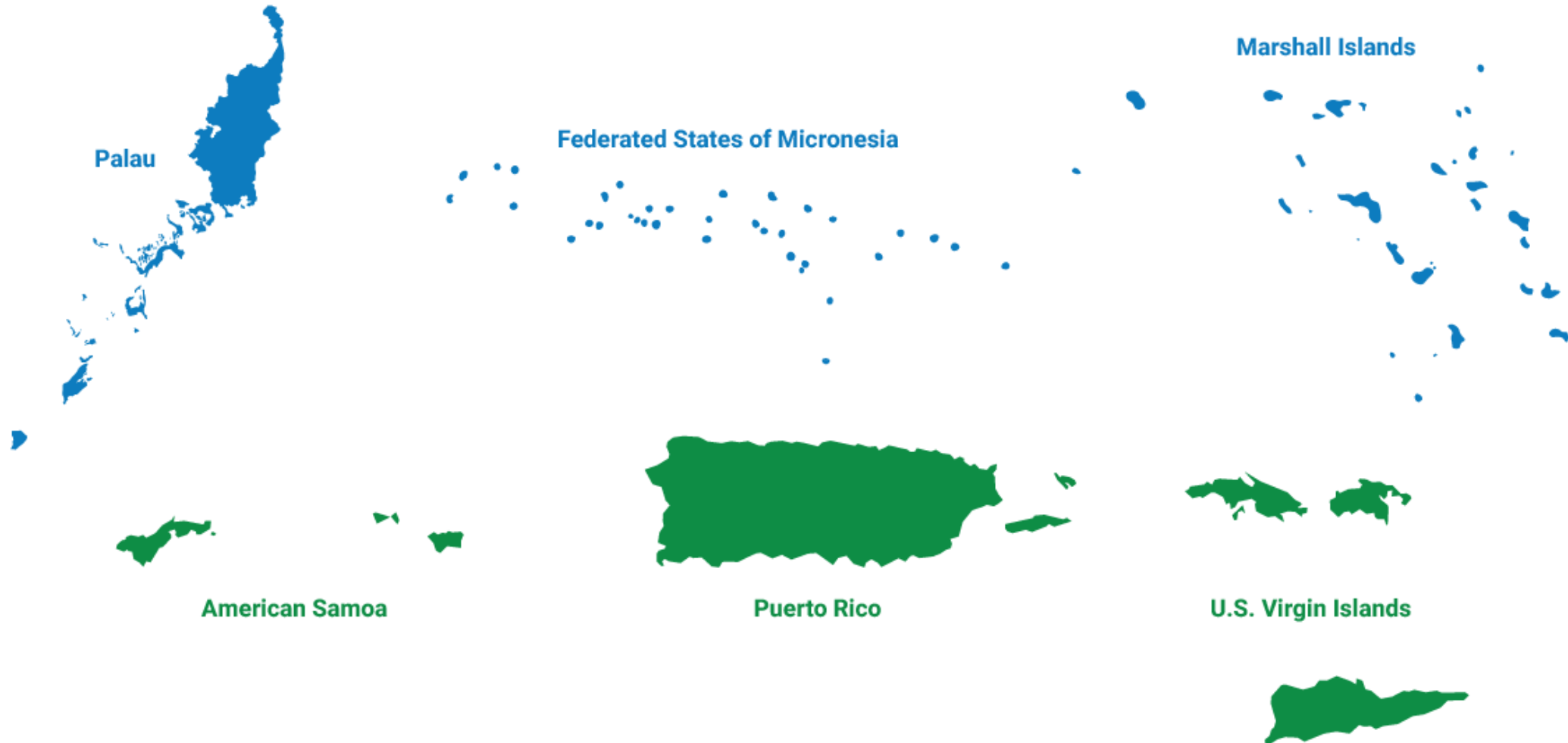


Global Dengue Outbreaks, 2022



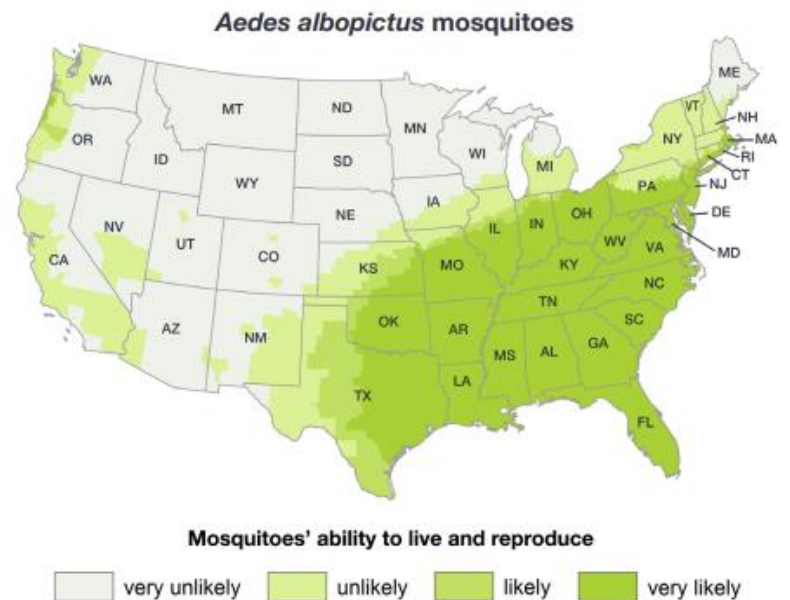
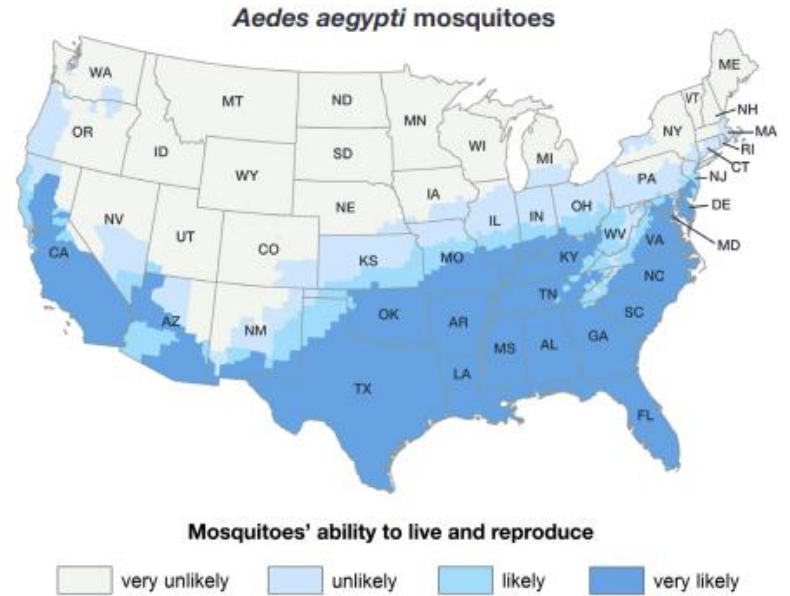
United States Dengue Epidemiology

Dengue is endemic in six U.S. territories and freely associated states.

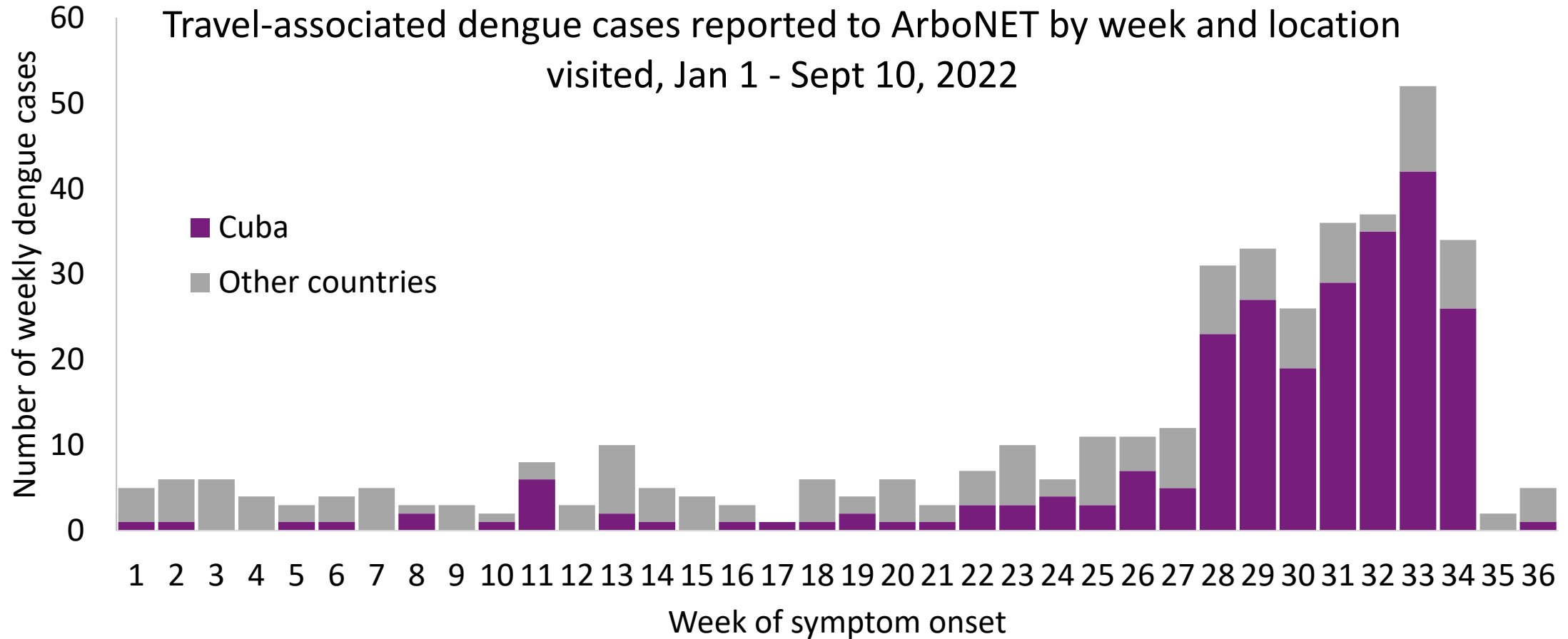


Dengue Cases in the United States

- Most cases (>90%) in states associated with travel to endemic areas
- Competent vectors (*Aedes* spp) present in many states



Recent increase in travel-associated cases reported to ArboNET* from Cuba



*ArboNET, unpublished data. 2022 numbers are preliminary and subject to change.



What Clinicians Need to Know about Dengue in the United States

Dengue: Clinical Classification, Diagnosis, and Management

Liliana Sánchez-González, MD, MPH

Epidemiologist

Dengue Branch, Division of Vector-Borne Diseases

Centers for Disease Control and Prevention

Content

- Clinical classification
- Course of disease
- Clinical assessment
- Laboratory diagnosis and workup
- Treatment

Think Dengue

- All febrile patients with potential exposure in the previous 2 weeks
- Unrecognized disease is a common cause of death
- If suspected, manage as dengue



Clinical Classification and Clinical Course

Dengue Clinical Classification – WHO (2009)

Dengue

Probable Dengue

Live in/travel to endemic area

Fever and **two** of the following criteria:

- Nausea/vomiting
- Rash
- Aches and pains (headache, retro-orbital pain, myalgia, arthralgia)
- Tourniquet test positive
- Leukopenia

Dengue with warning signs

One or more of the following warning signs:

- Abdominal pain or tenderness
- Persistent vomiting ($\geq 3/h$, or $\geq 4/6$ h)
- Clinical fluid accumulation (ascites, pleural effusion)
- Mucosal bleeding
- Lethargy, restlessness
- Postural hypotension
- Liver enlargement > 2 cm
- Progressive increase in hematocrit

Severe dengue

One or more of the following manifestations:

- Severe plasma leakage leading to Shock
Respiratory distress
- Severe bleeding
- Severe organ involvement
Liver (AST or ALT $> 1,000$)
Brain
Heart

Dengue Clinical Classification – WHO (2009)

Dengue

Probable Dengue

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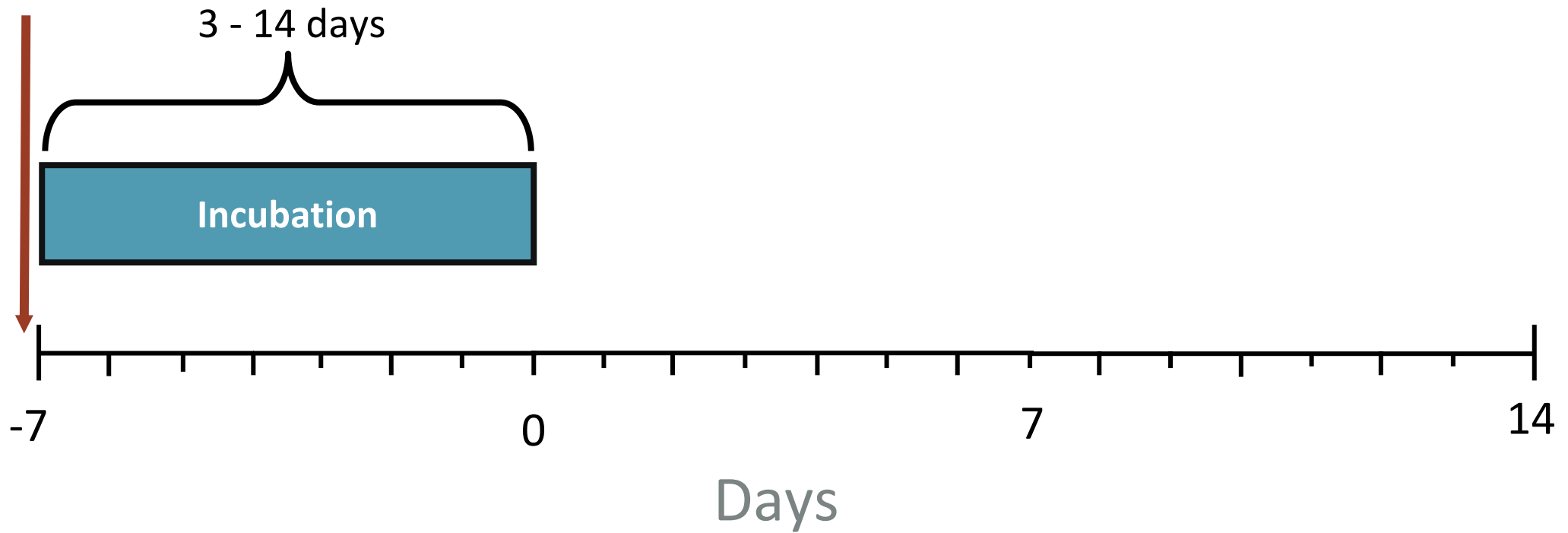
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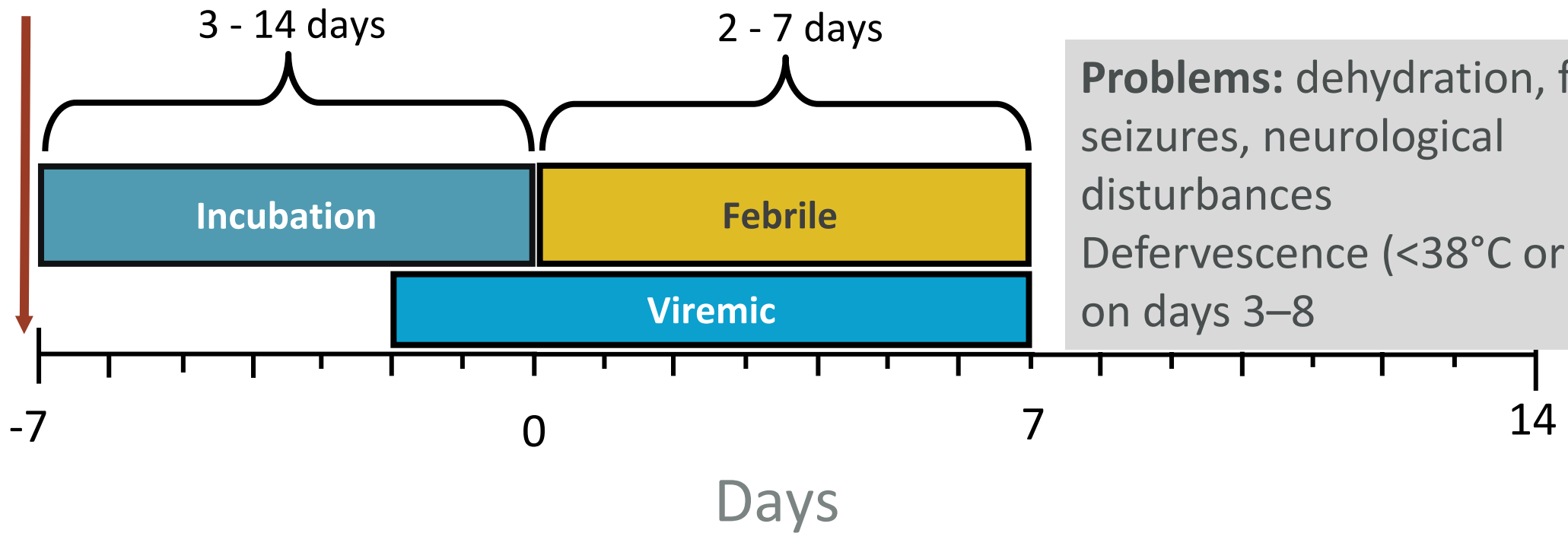
Clinical Course

Mosquito
bite



Clinical Course – Febrile phase

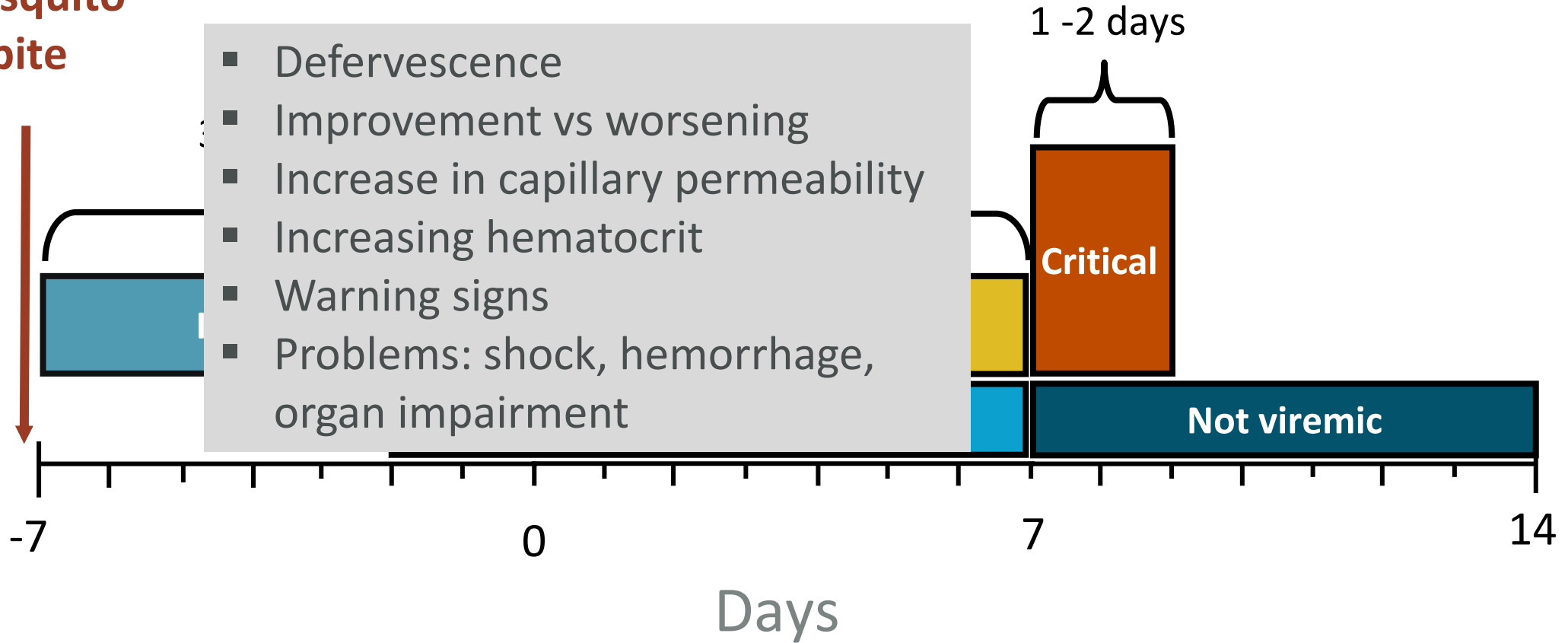
Mosquito bite



Problems: dehydration, febrile seizures, neurological disturbances
Defervescence (38°C or $100.4^{\circ}\text{F}</math>) on days 3–8$

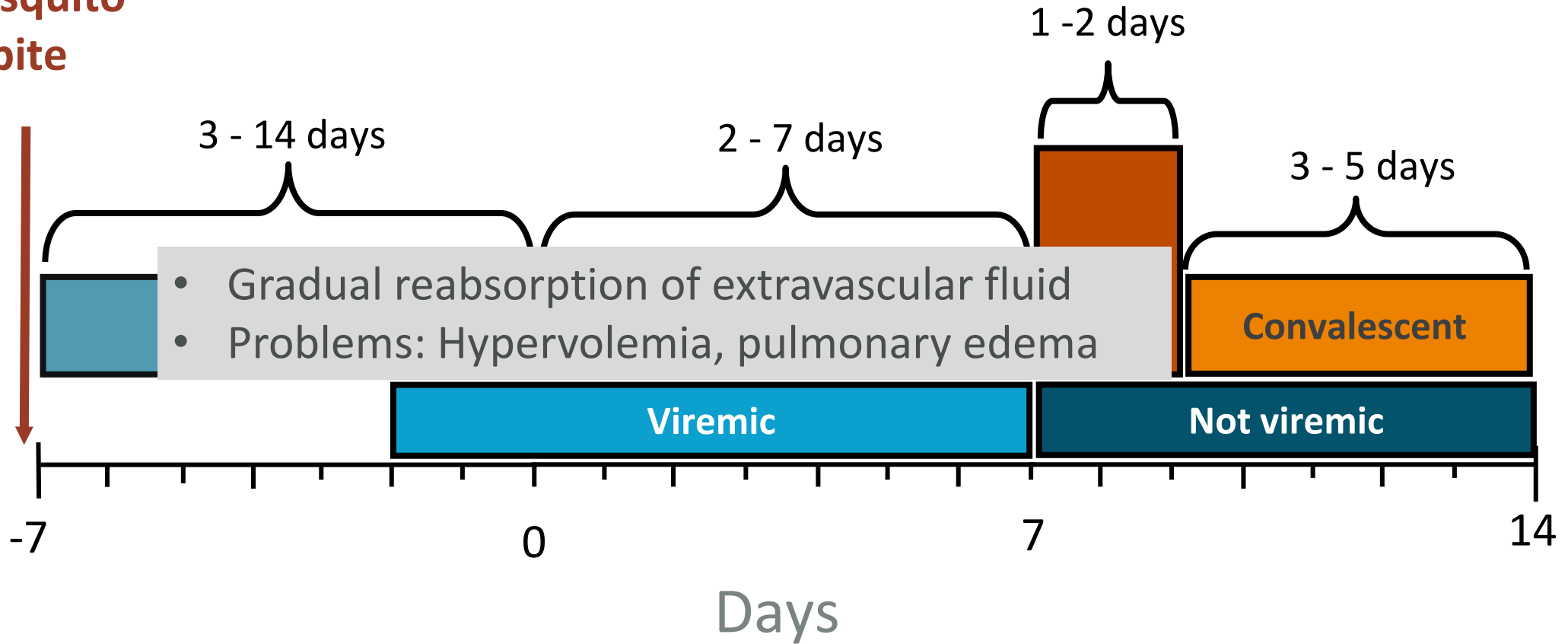
Clinical Course – Critical phase

Mosquito bite



Clinical Course – Convalescent phase

Mosquito bite




Key Messages

- Dengue is a dynamic disease
 - Presentation can change quickly
- Monitoring and identification of warning signs and severe criteria are key to classification and management of dengue patients
- Plasma leakage and progression to severe dengue, usually occurs in the critical phase
- Shock (not bleeding) is the most common severe dengue manifestation

Clinical Assessment



Overall Assessment

- Diagnosis
 - Classification (Severity)
 - Phase (Course of disease)
 - Comorbidities/other conditions
 - Intervention category
- 

History and Physical Exam

Criteria	Assessment
Fever	Onset, defervescence
Other symptoms	Cough, runny nose, sore throat, anorexia, diarrhea, dysgeusia, lymphadenopathy, conjunctival injection
Hydration status	Oral intake, urine output
Warning signs	Abdominal pain/tenderness, persistent vomiting, clinical fluid accumulation, mucosal bleeding, lethargy, postural hypotension, hepatomegaly, hemoconcentration
Rash and bleeding manifestations	Examine skin for rashes, mild mucosal bleeding. Melena and hematuria
Change in mental status	Dizziness, seizures, restlessness
Comorbidities/other conditions	Chronic conditions, pregnancy, infants, social conditions

A microscopic illustration of a blood vessel. The vessel is shown in cross-section, with a thick, orange-colored wall. Inside the vessel, there are several red blood cells, depicted as red, biconcave discs. The plasma is shown as a light orange fluid. There are small, pink, Y-shaped structures on the vessel wall, which appear to be leaking plasma into the surrounding tissue. The background is a dark, reddish-brown color.

Identifying Plasma Leakage

Hemoconcentration

- Hematocrit $\geq 20\%$ higher than the person's baseline
- Drop of $\geq 20\%$ of baseline hematocrit following volume-replacement

Pleural effusion, Ascites

- Respiratory distress
- Chest X-rays
- Abdominal discomfort, flank pain
- Fluid wave and shifting dullness
- Abdominal ultrasound

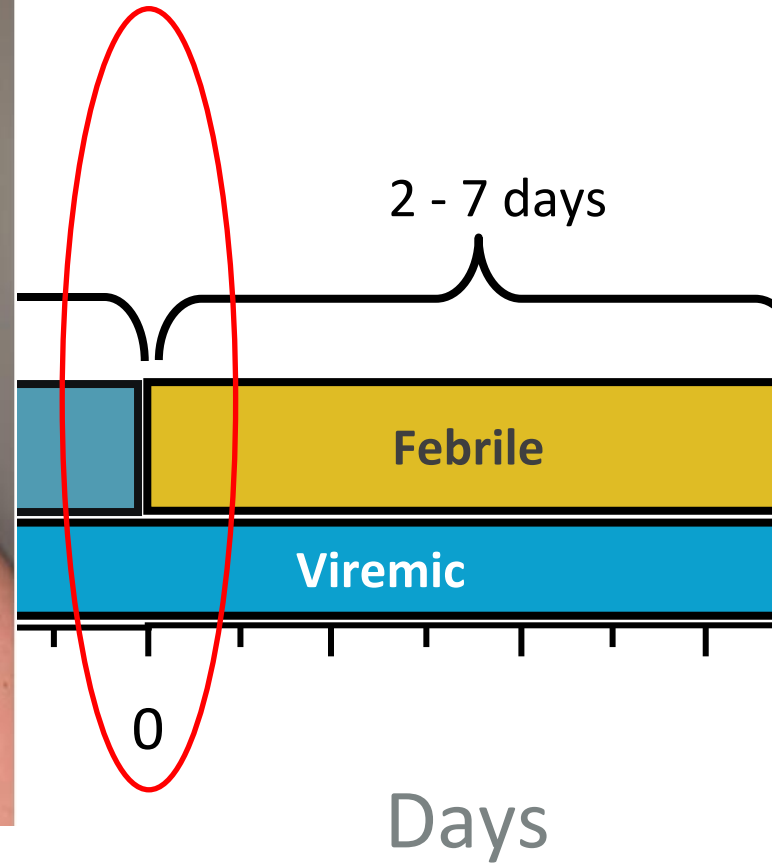
Identifying Shock

Important to identify early signs of shock including:

- Narrowing pulse pressure (≤ 20) with rising diastolic pressure
- Delayed capillary refill (>2 sec)
- Tachycardia in absence of fever



Rashes in Dengue – Early facial rash



With sudden onset of fever:

Flushing or erythema of face, neck and chest for 1- 2 days

May have injected pharynx and red lips.

Rashes in Dengue – Maculopapular rash

Mosquito
bite



-7



Febrile

Days 2 to 6:

Macular or maculopapular
truncal rash that spreads
to face and extremities

May become scaly

7

14

Rashes in Dengue – “Islands of white in a sea of red”



1 -2 days

Confluent (pruritic) rash with round “islands” of normal skin on lower extremities

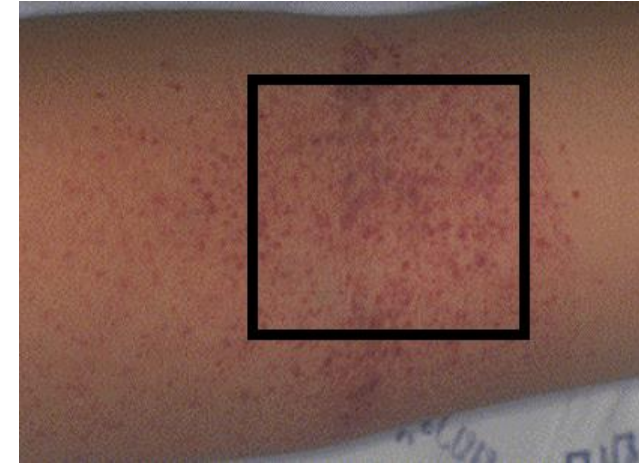
Picture 3 reproduced from Matsuura H, Kishida M, Nakata Y, et al Dengue rash: white islands in a sea of red *Postgraduate Medical Journal* 2019;95:676 with permission from BMJ Publishing Group Ltd

Hemorrhagic Manifestations

- Dengue

~30% of cases have minor bleeding

(petechiae, purpura, epistaxis, gingival bleeding, mild hematuria)



- Severe dengue

- Massive GI bleeding associated with prolonged shock and metabolic acidosis

- May be occult

- Site of venipuncture



Differential Diagnosis

- Febrile phase

Malaria, typhoid fever, influenza, chikungunya, rubella, measles, leptospirosis, meningococcal infection, Zika, Yellow Fever, mononucleosis, rickettsial infections, COVID-19

- Critical phase

Malaria, typhoid fever, leptospirosis, viral hepatitis, bacterial sepsis, acute abdomen, diabetic ketoacidosis, preeclampsia, platelet disorders, COVID-19

Clinical Clues for Dengue Infection

- Early facial rash
- Headache & retro-orbital pain
- Positive tourniquet test
- Warning signs, especially abdominal pain
- Pleural effusions in chest X-rays after defervescence
- Bradycardia after defervescence
- Shock after fever goes away
- Lucid patient despite impending shock

Self-knowledge Check

A 17-year-old female from Puerto Rico, who is visiting relatives in New York City, presents with a 4-day history of fever, highest measured at 103°F yesterday, accompanied by headache, generalized myalgia and arthralgia, sore throat, and 5 episodes of vomiting this morning.

Vital Signs: BP: 110/80 HR: 104 RR: 18 T: 100.4°F (38 °C)

Choose the **TRUE** statement

- A. Patients with dengue do not present with respiratory symptoms, therefore this patient does not have dengue.
- B. It is more likely that this patient has malaria than dengue.
- C. This patient is in the febrile phase, given her temperature.
Hence, there are no concerns for progression to severe disease yet.
- D. Dengue should be considered as the patient is from a dengue endemic area.
This patient has warning signs for severe dengue and should be hospitalized.

Self-knowledge Check - Response

The correct answer is D

A,B, C are false:

- A. Less common symptoms of dengue include respiratory symptoms like cough, sore-throat, and rhinorrhea.
- B. There is no malaria in Puerto Rico, but dengue is endemic.
- C. Defervescence can occur gradually, with the critical phase starting when the patient still has low fever.

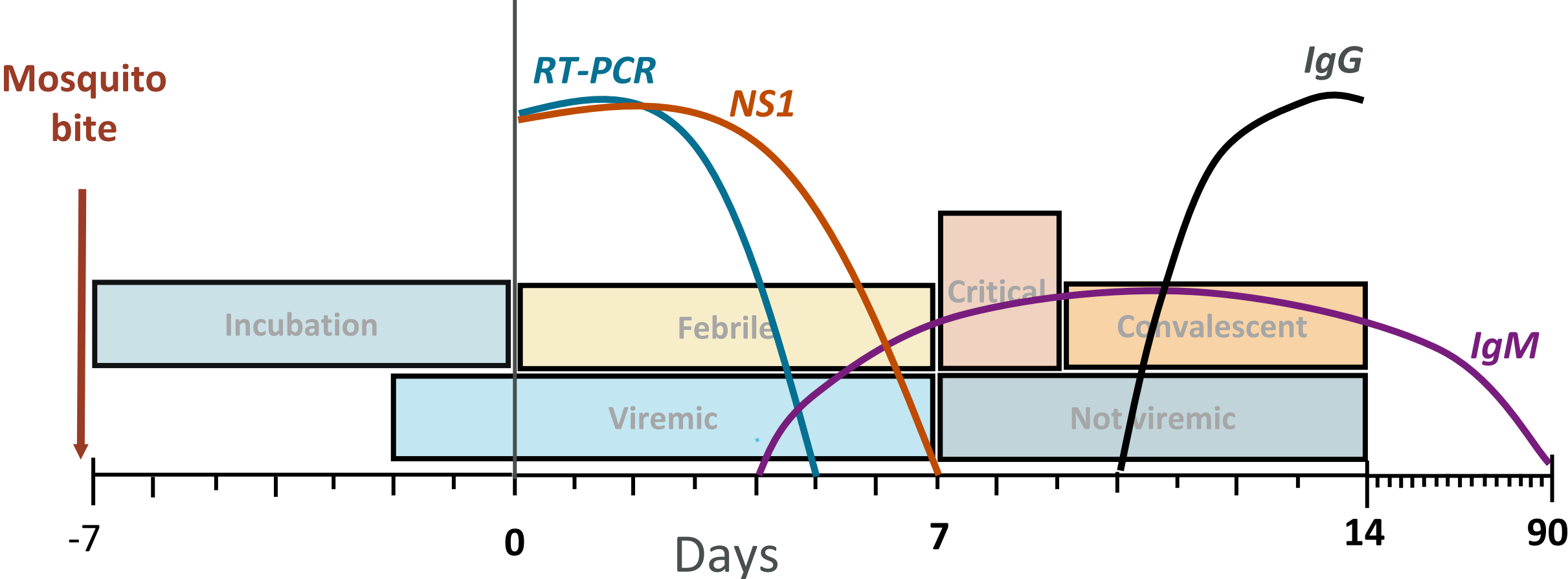
D is correct

Persistent vomiting is a dengue warning sign, this patient should be under medical observation/hospitalization.

Diagnosis and Laboratory Workup

Acute management of dengue should be based on clinical evaluation and NOT on lab confirmation

Diagnostic Testing



RT-PCR: Reverse Transcription Polymerase Chain Reaction
NS1: Non-structural protein

IgM: Immunoglobulin M
IgG: Immunoglobulin G

Diagnostic Testing in the United States



- Dengue is a nationally notifiable disease
- Rapid diagnostic tests are NOT widely available (none are FDA-approved)
- Testing can be arranged through the arboviral surveillance team at the State/Local Health Department
- Some laboratories offer DENV RT-PCR, NS1, and DENV IgM



Laboratory Tests

- Complete blood cell count (CBC)
- Metabolic panel
- Serum protein and albumin levels
- Liver panel
- Coagulation panel

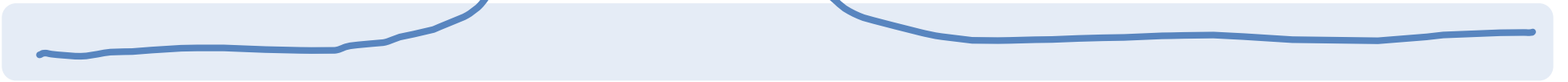
Common laboratory findings

Leukocytes
(neutrophils)

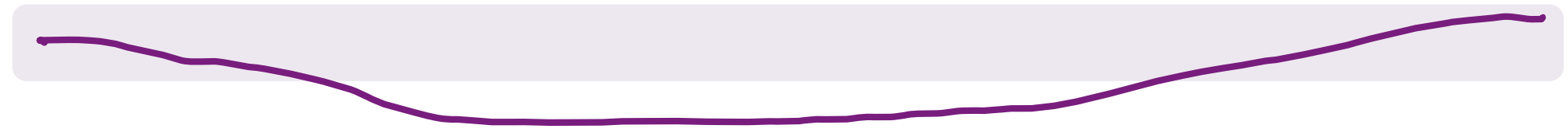
Lymphocytes



Hematocrit



Platelets



Febrile

Critical

Convalescent

Management

A decorative horizontal bar at the bottom of the slide, composed of several colored rectangular segments: orange, lime green, brown, teal, purple, and blue.

Dengue Management

- Standard of care is supportive management
- No curative treatment or antiviral available
- Proper treatment can reduce case-fatality rate to <1%

Management Groups

Depends mostly on clinical manifestations and patients may:

- Be sent home – **Group A**
- Be referred for in-hospital management – **Group B**
- Require emergency treatment and urgent referral – **Group C**

Dengue Case Management

ASSESSMENT

Presumptive Diagnosis

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

- ▶ Nausea and vomiting
- ▶ Rash
- ▶ Aches and pains (headache, eye pain, muscle ache or joint pain)
- ▶ Warning signs
- ▶ Tourniquet test positive
- ▶ Leukopenia

Warning Signs

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

No warning signs

Group A
Outpatient management

For patients with warning signs of severe dengue OR co-existing conditions

- ▶ Pregnancy
- ▶ Infancy
- ▶ Diabetes mellitus
- ▶ Poor social situation
- ▶ Old age
- ▶ Renal failure

Group B
Inpatient management

For patients with any of

- ▶ Severe plasma leakage with shock and/or fluid accumulation with respiratory distress
- ▶ Severe bleeding
- ▶ Severe organ impairment

Group C
Inpatient management



Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases

Group A Outpatient Management

During the febrile phase (may last 2-7 days) and subsequent critical phase (1-2 days), your clinic should

- ▶ Follow CBCs
- ▶ Watch for dehydration
- ▶ Watch for warning signs, including decreasing platelet count and increasing hematocrit
- ▶ Watch for defervescence (indicating beginning of critical phase)

Advise patient or their family to do the following

Control the fever

- ▶ Give acetaminophen every 6 hours (maximum 4 doses per day). Do not give ibuprofen, aspirin, or aspirin-containing drugs.
- ▶ Sponge patient's skin with tepid water when temperature is high.

Prevent dehydration which occurs when a person loses too much fluid (from high fever, vomiting, or poor oral intake). Give plenty of fluids (not only water) and watch for signs of dehydration. Bring patient to clinic or emergency room if any of the following signs develop:

- ▶ Decrease in urination (check number of wet diapers or trips to the bathroom)
- ▶ Few or no tears when child cries
- ▶ Dry mouth, tongue or lips
- ▶ Sunken eyes
- ▶ Listlessness, agitation, or confusion
- ▶ Fast heartbeat (>100/min)
- ▶ Cold or clammy fingers and toes
- ▶ Sunken fontanel in an infant

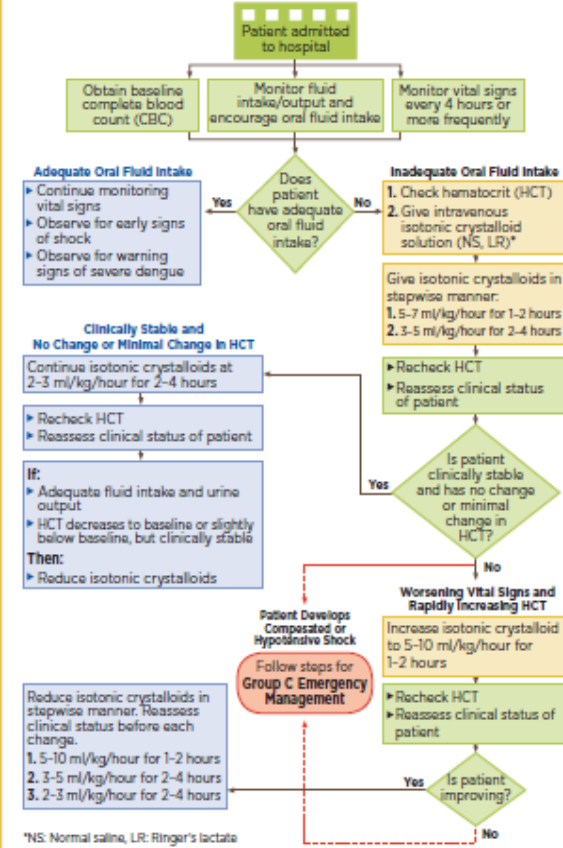
Prevent spread of dengue within your house

- ▶ Place patient under bed net or have patient use insect repellent while febrile to avoid infecting mosquitoes that can infect others within 2 weeks.
- ▶ KILL all mosquitoes in house.
- ▶ Empty containers that carry water on patio.
- ▶ Put screens on windows and doors to prevent mosquitoes from coming into house.

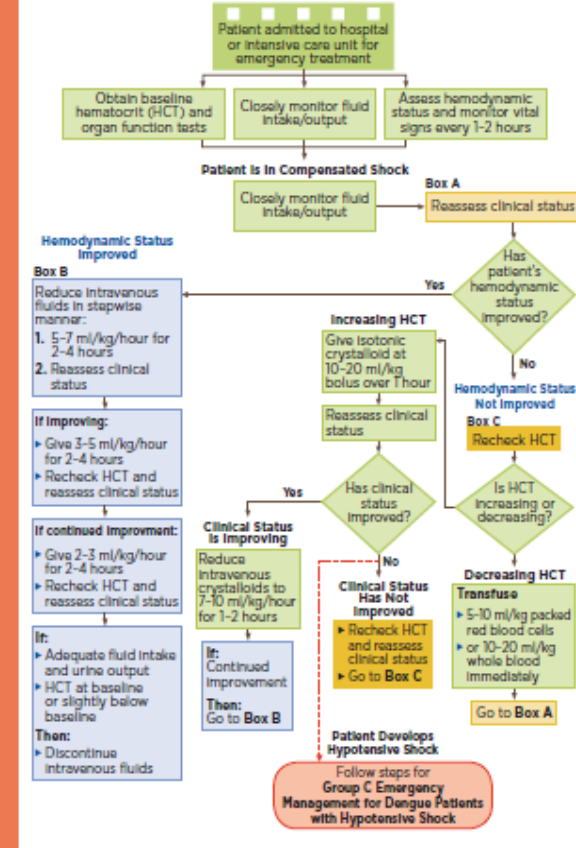
Watch for warning signs as temperature declines 3 to 8 days after symptoms began. Return IMMEDIATELY to clinic or emergency department if any of the following warning signs appear:

- ▶ Severe abdominal pain or persistent vomiting
- ▶ Red spots/patches on skin
- ▶ Bleeding from nose or gums
- ▶ Vomiting blood
- ▶ Black, tarry stools
- ▶ Drowsiness or irritability
- ▶ Pale, cold, or clammy skin
- ▶ Difficulty breathing

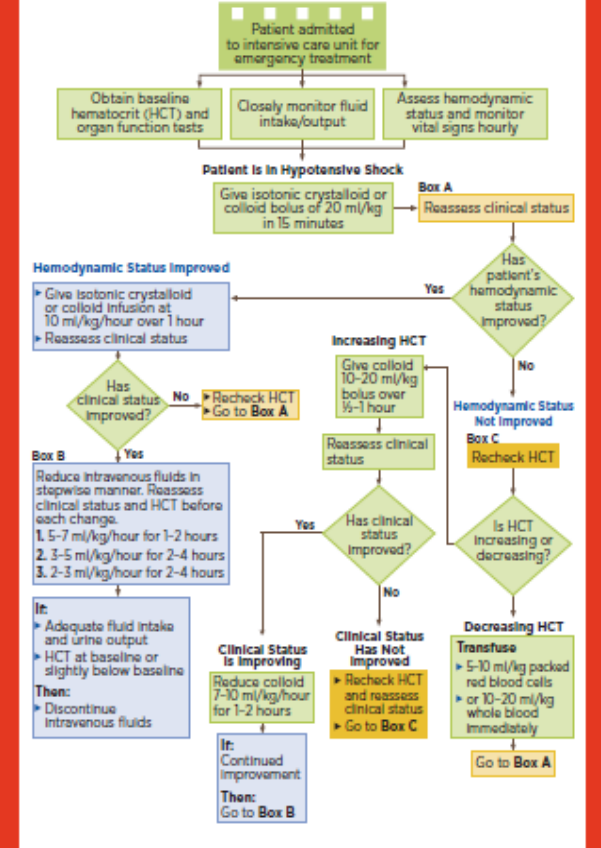
Group B – Inpatient Management for Dengue Patients with Warning Signs



Group C – Emergency Management for Dengue Patients with Compensated Shock



Group C – Emergency Management for Dengue Patients with Hypotensive Shock



Group A – Outpatient Follow-up

Patients with:

- No warning signs
- Ability to drink sufficiently
- Normal urine output

- **Should be reviewed clinically daily**
 - Daily CBC (until out of critical phase)
- **What to monitor for?**
 - Signs of dehydration in febrile phase
 - Disease progression and defervescence
 - Warning signs
- **Recommendations**
 - Mosquito net, bed rest, **oral fluids**, paracetamol
 - No aspirin or NSAIDS

Group B: Inpatient management (1)

Patients with:

- Warning signs
- Co-existing conditions (pregnancy, infancy, obesity, diabetes mellitus, renal failure, chronic hemolytic diseases)
- Social circumstances

- Observation/Hospitalization
- Bed rest, mosquito net
- Baseline labs
- IV line
- Monitor ins and outs
- If inadequate oral fluids intake or warning signs:
 - Give isotonic crystalloids in a stepwise manner
 - Monitor hematocrit every 4-6 h

Group B: Inpatient management (2)

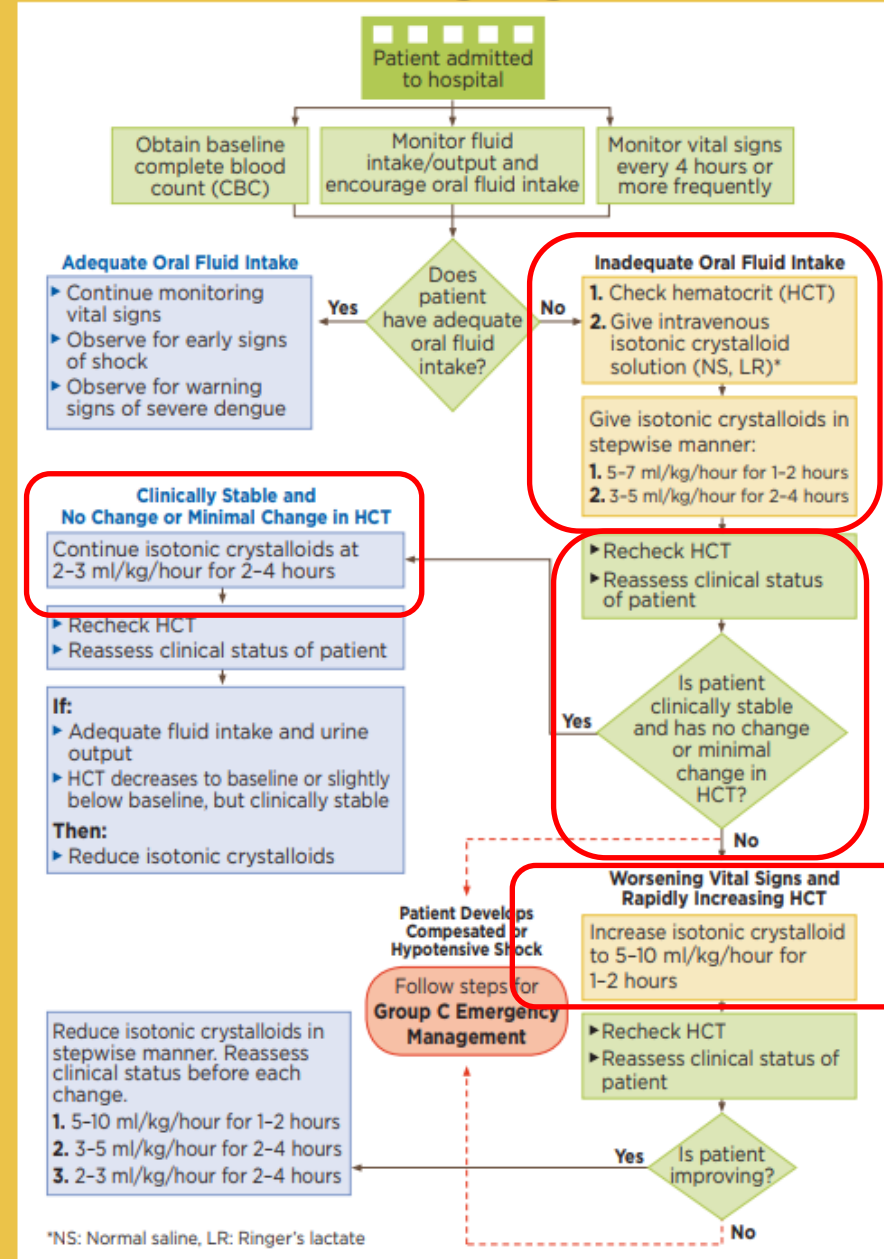
A 17-year-old female from Puerto Rico

- A 4-day history of fever
- Headache, generalized myalgia and arthralgia, sore throat
- **5 episodes of vomiting** this morning

Vital Signs:

BP: 110/80 HR: 104 RR: 18 T: 100.4°F (38 °C)

Group B – Inpatient Management for Dengue Patients with Warning Signs



Group C: Emergency Treatment

Patients who:

- Shock – Compensated and decompensated
 - Fluid accumulation with respiratory distress
 - Severe bleeding
 - Severe organ involvement
- Hospitalization/ICU
 - Mosquito net
 - Baseline labs
 - Oxygen
 - IV line – IV fluids in boluses (10-20 ml/kg)
 - Monitor hematocrit every 1-4 h
 - Monitor ins and outs
 - Monitor signs of fluid overload
 - Check for shock signs



Guiding Principles of Fluid Management (1)

- Limit IV fluids in febrile phase
- IV fluids usually needed for only 24–48 hr
- Give only isotonic solutions
- **Give minimum IV fluids required to restore intravascular volume, maintain good perfusion and urine output of at least 0.5 ml/kg/hr**
- Monitor signs of fluid response - **REASSESS**

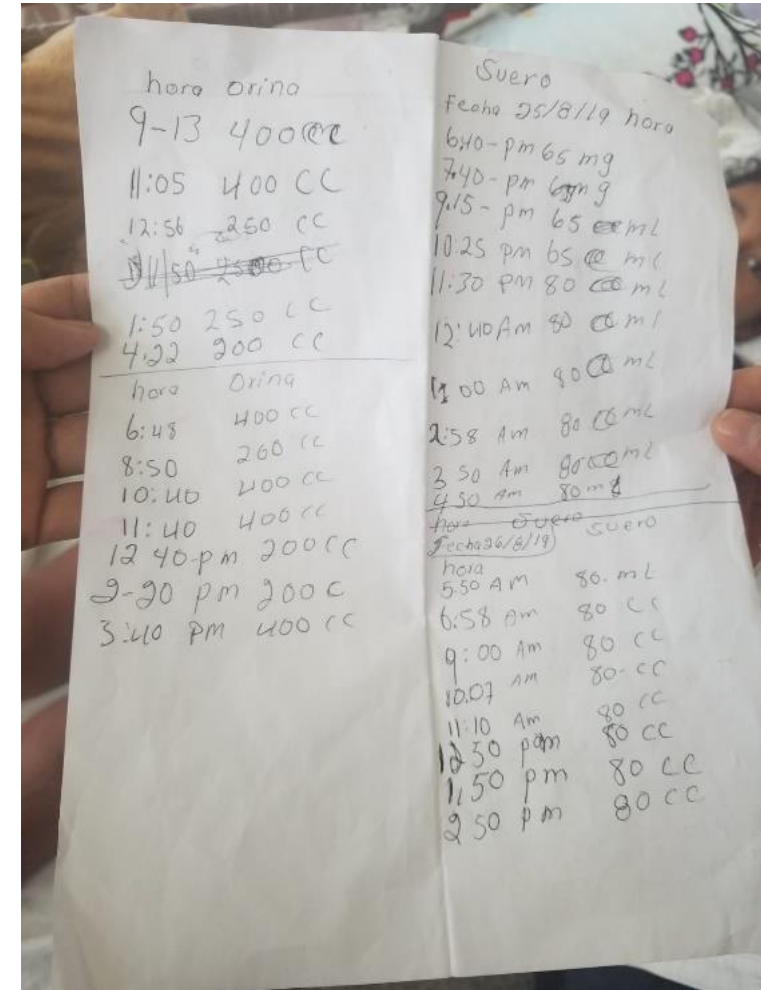
Guiding Principles of Fluid Management - 2

- Use ideal body weight (IBW) to calculate maintenance fluids in overweight/obese patients
- Extravasated fluids remain in body and need to be reabsorbed
- Monitor for fluid overload: other options for resuscitation include colloid and colloid plus furosemide (profound fluid overload)



Guiding Principles of Fluid Management - 3

- Colloids (albumin or Dextran 40) preferred if the blood pressure must be restored urgently (e.g. pulse pressure less than 10)
- Use blood products cautiously, preference for packed RBCs in setting of bleeding



Dengue Management Don'ts

- Do not use corticosteroids
- Do not use NSAIDS
- Do not give IM injections
- Do not give prophylactic platelet transfusions

Discharge Criteria

- No fever for 48 hours
- Improvement in clinical status (general well being, appetite, hemodynamic status, urine output, no respiratory distress)
- Increasing trend of platelet count
- Stable hematocrit without IV fluids

Remember, Think Dengue!

- Unrecognized disease is a common cause of death
- Early recognition of disease and appropriate clinical management with IV fluids can be life-saving



CDC Dengue Branch

Email: dengue@cdc.gov

Phone: (787)706-2399

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov

Continuing Education

- All continuing education for COCA Calls is issued online through the CDC Training & Continuing Education Online system at <https://tceols.cdc.gov/>.
- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **October 31, 2022**, with the course code **WC4520-092922**. The access code is **COCA092922**.
- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **November 1, 2022**, and **November 1, 2024**, and use course code **WD4520-092922**. The access code is **COCA092922**.
- Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CEs obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Today's COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage
https://emergency.cdc.gov/coca/calls/2022/callinfo_092922.asp

**A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*

Additional Resources

- Continue to visit <https://emergency.cdc.gov/coca/> to get more details about upcoming COCA Calls.
- Subscribe to receive notifications about upcoming COCA calls and other COCA products and services at emergency.cdc.gov/coca/subscribe.asp.

Join Us on Facebook



The screenshot shows the Facebook profile for COCA (CDC Clinician Outreach and Communication Activity). The profile picture features a diverse group of healthcare professionals. The cover photo shows a group of six people, including nurses and doctors, smiling. The page includes a navigation menu on the left with options like Home, About, Posts, Photos, Events, and Community, along with a 'Create a Page' button. The main content area shows the page name, a bio, and a recent post from October 31, 2017, announcing a free CE event on November 7, 2017. The right sidebar displays the location (Atlanta, Georgia), the number of likes (21,420) and followers (21,217), and a map of the location.

COCA
CDC Clinician Outreach and Communication Activity - COCA ✓
@CDCClinicianOutreachAndCommunicationActivity

Home
About
Posts
Photos
Events
Community
Create a Page

Liked Following Share ... Sign Up

Status
Write something on this Page...

Posts
CDC Clinician Outreach and Communication Activity - COCA shared their event.
October 31 at 1:18pm · 🌐
Clinicians, you can earn FREE CE with this COCA Call! Join us for this COCA Call November 7, 2017 at 2:00PM.

Government Organization in Atlanta, Georgia
Community See All
21,420 people like this
21,217 people follow this
About See All
Map showing location in Atlanta, Georgia near Clifton Rd NE and Houston St.

Thank you for joining us today!



emergency.cdc.gov/coca