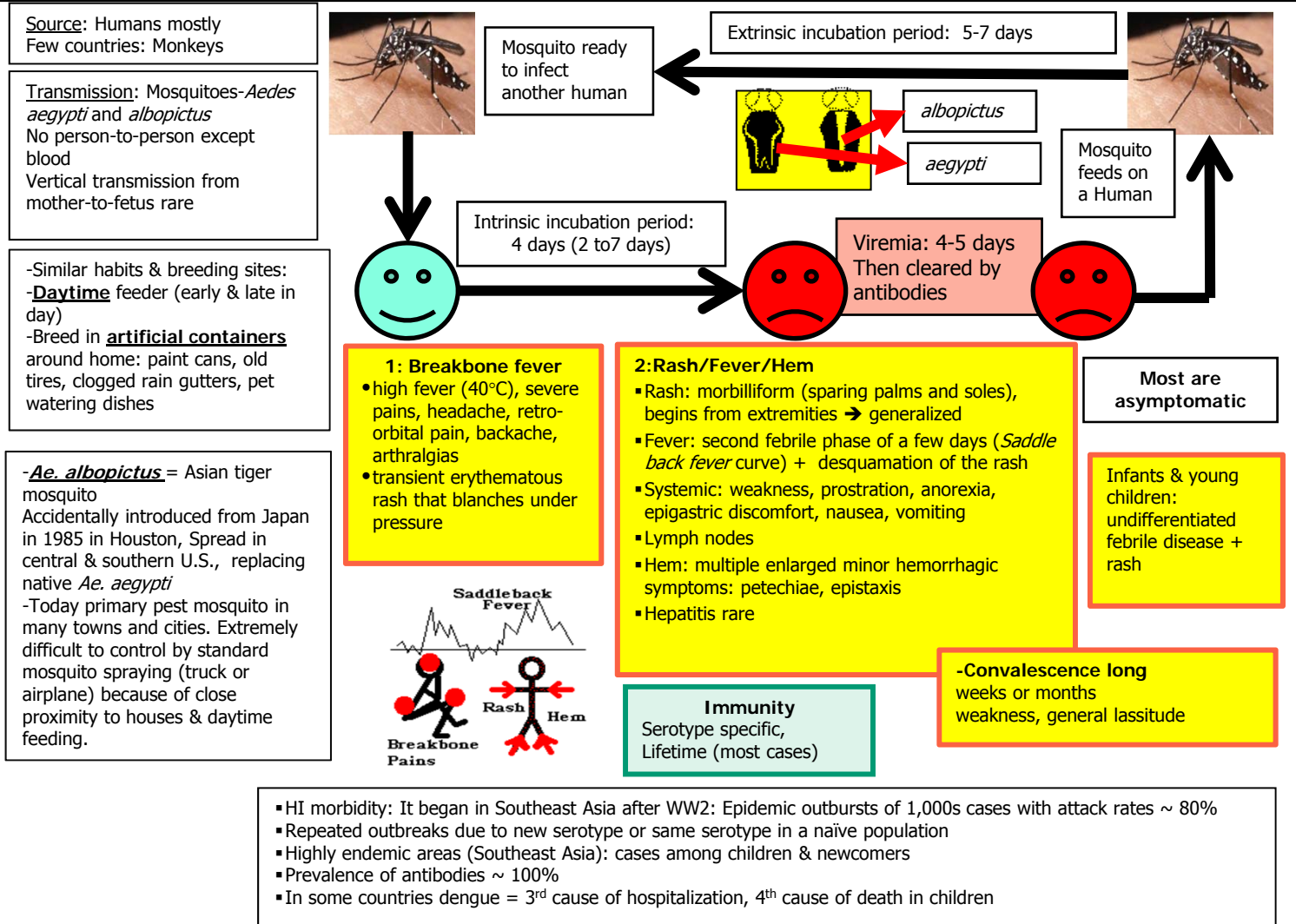


Dengue

Epidemiology



Diagnosis

FLAVI virus: RNA, E envelope protein, C capsid protein, M membrane protein; 4 Serotypes: 1, 2, 3, 4

Dengue can be diagnosed by:

1- Isolation of the virus, for **Acute infection with DENV**

- confirmed by **virus isolated** (DENV antigen or RNA in tissue specimens) by immunofluorescence or immunohistochemical analysis, **from serum or tissue specimens**, or **specific dengue virus genome** identified by RT-PCR from serum or plasma, CSF, or tissue specimens during acute febrile illness. One-step, real time RT-PCR or nested RT-PCR widely used to detect dengue genes in acute-phase serum samples. This detection coincides with viremia and the febrile phase of illness onset.
- confirmed by **identification of DENV RNA** in tissue specimens by immunofluorescence or immunohistochemical analysis,

2-Serological tests: acute/recent dengue infection with serum samples during the first 5 days of sx or early convalescent phase (>5 days of sx).

- **Seroconversion** from negative to positive IgM antibody to dengue (IgM antibody capture enzyme-linked immunosorbent assay MAC-ELISA) or demonstration of a fourfold or greater increase in IgG antibody titers in paired (acute and convalescent) serum.

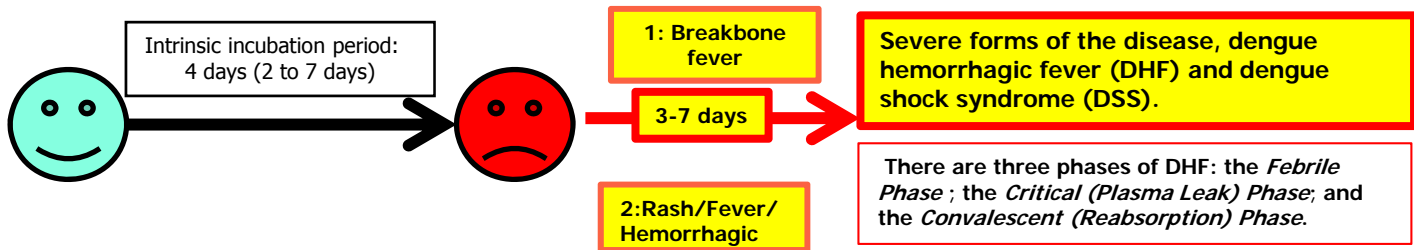
Patients who have IgM antibodies to dengue detected in their serum specimen via an and had either 1.) A negative RT-PCR result in the acute phase specimen or 2.) Did not submit an acute phase specimen, are classified as having a recent probable dengue infection. This is due to the fact that IgM antibodies for dengue may remain elevated for 2 to 3 months after the illness. There is cross reactivity with other flaviviruses WNV, SLE, JEV, YFV. Review past medical hx, travel hx, vaccination record (YF vaccine). Often times both an acute and convalescent phase specimens are needed to make a diagnosis of dengue infection. This is especially true for those who submit a day 5 acute specimen because the virus and IgM antibodies may be at undetectable levels. So if a patient with suspected dengue infection submits a late acute phase specimen that is negative (e.g., by RT-PCR and MAC-ELISA), and they do not submit a convalescent specimen, they are classified as a laboratory-indeterminate case.

Treatment

Treatment is **symptomatic or supportive**, -Rest and the use of:

- To relieve fever- acetaminophen or paracetamol
- To relieve arthritic component-ibuprofen, naproxen, or another non-steroidal anti-inflammatory agent (NSAID) to relieve the arthritic component
- Aspirin is NOT advised because of bleeding risk and risk of developing Reye's syndrome in children younger than 12 years
- In patients with severe joint pains not relieved by NSAID, narcotics (e.g., morphine) or short-term corticosteroids can be used
- Drink plenty of fluids to replenish fluid lost from sweating, vomiting, and other insensible losses

Dengue Hemorrhagic Fever



The Febrile Phase: Early in the course of illness, patients with DHF can present much like DF, but they may also have hepatomegaly without jaundice (later in the Febrile Phase). The hemorrhagic manifestations that occur in the early course of DHF most frequently consist of mild hemorrhagic manifestations as in DF. Less commonly, epistaxis, bleeding of the gums, or frank gastrointestinal bleeding occur while the patient is still febrile (gastrointestinal bleeding may commence at this point, but commonly does not become apparent until a melanic stool is passed much later in the course). Dengue viremia is typically highest in the first three to four days after onset of fever but then falls quickly to undetectable levels over the next few days. The level of viremia and fever usually follow each other closely, and anti-dengue IgM anti-bodies increase as fever abates.

The Critical (Plasma Leak) Phase: About the time when the fever abates, the patient enters a period of highest risk for developing the severe manifestations of plasma leak and hemorrhage. At this time, it is vital to watch for evidence of hemorrhage and plasma leak into the pleural and abdominal cavities and to implement appropriate therapies replacing intravascular losses and stabilizing effective volume. If left untreated, this can lead to intravascular volume depletion and cardiovascular compromise. Evidence of plasma leak includes sudden increase in hematocrit ($\geq 20\%$ increase from baseline), presence of ascites, a new pleural effusion on lateral decubitus chest x-ray, or low serum albumin or protein for age and sex. Patients with plasma leak should be monitored for early changes in hemodynamic parameters consistent with compensated shock such as increased heart rate (tachycardia) for age especially in the absence of fever, weak and thready pulse, cool extremities, narrowing pulse pressure (systolic blood pressure minus diastolic blood pressure < 20 mmHg), delayed capillary refill (> 2 seconds), and decrease in urination (i.e., oliguria). Patients exhibiting signs of increasing intravascular depletion, impending or frank shock, or severe hemorrhage should be admitted to an appropriate level intensive care unit for monitoring and intravascular volume replacement. Once a patient experiences frank shock he or she will be categorized as having DSS. Prolonged shock is the main factor associated with complications that can lead to death including massive gastrointestinal hemorrhage. Interestingly, many patients with DHF/DSS remain alert and lucid throughout the course of the illness, even at the tipping point of profound shock.

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 > 2 cm
- ▶ Clinical fluid accumulation
- ▶ Lethargy; restlessness
- ▶ Increase in HCT concurrent with rapid decrease in platelet count

No warning signs

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

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

For patients with any of

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

Group A
Outpatient management

Group B
Inpatient management

Group C
Inpatient management

Dengue Management DO's and DON'Ts

- X DON'T use corticosteroids.** They are not indicated and can increase the risk of GI bleeding, hyperglycemia, and immunosuppression.
- X DON'T give platelet transfusions for a low platelet count.** Platelet transfusions do not decrease the risk of severe bleeding and may instead lead to fluid overload and prolonged hospitalization.
- X DON'T give half normal (0.45%) saline.** Half normal saline should not be given, even as a maintenance fluid, because it leaks into third spaces and may lead to worsening of ascites and pleural effusions.
- X DON'T assume that IV fluids are necessary.** First check if the patient can take fluids orally. Use only the minimum amount of IV fluid to keep the patient well-perfused. Decrease IV fluid rate as hemodynamic status improves or urine output increases.
- ✓ DO tell outpatients when to return.** Teach them about warning signs and their timing, and the critical period that follows defervescence.
- ✓ DO recognize the critical period.** The critical period begins with defervescence and lasts for 24-48 hours. During this period, some patients may rapidly deteriorate.
- ✓ DO closely monitor fluid intake and output, vital signs, and hematocrit levels.** Ins and outs should be measured at least every shift and vitals at least every 4 hours. Hematocrits should be measured every 6-12 hours at minimum during the critical period.
- ✓ DO recognize and treat early shock.** Early shock (also known as compensated or normotensive shock) is characterized by narrowing pulse pressure (systolic minus diastolic BP approaching 20 mmHg), increasing heart rate, and delayed capillary refill or cool extremities.
- ✓ DO administer colloids (such as albumin) for refractory shock.** Patients who do not respond to 2-3 boluses of isotonic saline should be given colloids instead of more saline.
- ✓ DO give PRBCs or whole blood for clinically significant bleeding.** If hematocrit is dropping with unstable vital signs or significant bleeding is apparent, immediately transfuse blood.



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

Surveillance

1-Determine if case was imported or autochthonous
2-Once an autochthonous case of Dengue is detected, an in-depth epidemiologic investigation must be conducted to:

- Track viral spread.
- Monitor for possible introduction into surrounding areas.
- Describe key epidemiologic and clinical features.
- Assess clinical severity and impact on society (e.g., days missed from work, school closures, etc.).
- Identify risk factors for infection or severe disease.
- Identify circulating DENV lineages.

Case Definition

Suspect case: patient with acute onset of fever $>38.5^{\circ}\text{C}$ (101.3°F) and severe arthralgia or arthritis not explained by other medical conditions, and who resides, or has visited epidemic or endemic areas within two weeks prior to the onset of symptoms.

Confirmed case: suspect case with any of the following Dengue specific tests:

- Viral isolation.
- Detection of viral RNA by RT-PCR.
- Detection of IgM in a single serum sample (collected during acute or convalescent phase).
- Four-fold increase in DENV-specific antibody titers (samples collected at least two to three weeks apart).

Case Detection

-Consider Dengue in the differential diagnosis for individuals who are presenting

• **fever and arthralgias that are not explained by another etiology**

- have an atypical presentation; atypical dengue with severe joint pain or conjunctivitis.
- Suspect if association with traveler recently returned from an area with ongoing Dengue
- Small clusters of disease (fever and arthralgia or arthritis)
- Increase in hospital visits for fever and arthralgia or arthritis occurring in a localized area in a short time.

Case Definition during an epidemic, all patients need not be subjected to confirmatory tests as above. An epidemiologic link can be sufficient.

Sensitivity and specificity for clinical criteria for DENV infection during outbreak of the disease: combination of fever and polyarthralgias

- sensitivity 84%
- specificity 89%,
- correct classification 87% of individuals with serologically confirmed DENV infection.

Vector Surveillance & Control

• For arboviruses with a human-mosquito-human transmission cycle, **the most important source of viral importation is the viremic traveler.**

Mosquito Control at Airport not useful

- Mosquito abatement activities at international airports
- Spraying adulticides in passenger cabins of arriving international flights
- ➔ virus-infected mosquitoes arriving in passenger aircraft are not considered as significant sources of most arboviral importations.
- No need to place any restrictions on baggage, cargo, containers, goods, or postal parcels beyond usual practices
- For arboviruses with a human-mosquito-human transmission cycle, **the most important source of viral importation is the viremic traveler.**
- **Travel Health Alert Notices (THANs)** to international travelers

1. Vector Surveillance and Identification of High Risk Areas

-Systematically collect surveillance data on relative densities of *Ae. aegypti* and *Ae. albopictus*. Surveillance methods for *Ae. aegypti* and *Ae. albopictus* are varied and include methods to monitor egg production, larval sites, pupal abundance, and adult abundance.

-Detect and identify hidden and difficult to control larval sites (e.g., cryptic locations such as septic tanks, storm drains, sump pumps, and vacant lots), and other productive sites, as well as the readily identified and commonly found larval habitats.

2. Personal Protection

-Personal repellents on skin or clothing. DEET (N,N-diethyl-m-toluamide) and picaridin (also known as KBR3023 or Bayrepel™) are effective

-Infants and others sleeping or resting during the day should use bed nets to avoid infection from *Ae. aegypti* and *Ae. albopictus*, both of which are day biting mosquitoes.

-Those potentially infected with DENV during an outbreak must **rest beneath an IT bed net** to avoid mosquito bites and further spread of infection. Use of IT bed nets has the additional benefit of killing mosquitoes that come into contact with the net.

3. Household Prevention

-**Screens on windows** and doors reduce entry of vectors into the home.

-**Mosquito proofing water storage vessels** reduce oviposition sites and local production.

-Use commercially available **pyrethroid-based aerosol sprays** and other products: mosquito coils and electronic mat vaporizers. Aerosol sprays may be applied throughout the home, but areas where adult mosquitoes rest (dark, cooler areas) must be targeted, including bedrooms, closets, clothing hampers, etc. Care should be taken to emphasize proper use of these products when advocating their application to the public, in order to reduce unnecessary exposure to pesticides.

4. Neighborhood and Community Prevention

Effective communication to the community and various stakeholders is crucial to avoid confusion and misinformation and to engage people in steps to reduce the risk of disease.