DEPARTMENT OF HEALTH AND HOSPITALS
Public Health

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DENGUE

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Dengue is a mosquito-borne infection which in recent years has become a major international public health concern. Dengue is found in tropical regions around the world, predominately in urban and peri-urban areas. A more lethal complication, dengue hemorrhagic fever (DHF), was first recognized during the 1950s and is today a leading cause of childhood deaths in many countries. There are four distinct viruses which cause dengue, and infection by one does not offer protection against subsequent infection by the other three. Indeed, there is good evidence that infection by a second dengue virus increases the risk of more serious disease resulting in DHF.

While uncomplicated dengue is not a severe disease, dengue hemorrhagic fever (DHF) leads to disseminated intravascular coagulation with 50% case fatality rate without early treatment. Dengue which was confined to tropical areas, is now considered an Emerging Infectious Disease and which may spread beyond its original geographical range. Every year there are some 100 millions of cases of dengue worldwide.

Dengue is caused by a Flavivirus (RNA virus of the family that includes yellow fever, West Nile encephalitis, Saint Louis encephalitis, Japanese encephalitis and Murray Valley fever). There are four serotypes of dengue (originally named 1 to 4).

Epidemiology

The dengue virus is transmitted worldwide by *Aedes aegypti* and in each area by other local *Aedes*. Viremic humans are the main reservoir of virus. Mosquitoes can become infected by feeding on viremic patients (generally only from the day before to the end of the febrile period). There is multiplication of the virus in the mosquito. This phase lasts 8 to 10 days.

Once infected, a mosquito remains infective for life, transmitting the virus to susceptible individuals during probing and blood feeding. Infective female mosquitoes may also transmit the virus to the next generation of mosquitoes by transovarial transmission. After a blood meal, mosquitoes usually do not feed again for three to five days, depending upon temperature. It is during this second (or, rarely, third) feeding that a susceptible person is inoculated with the virus. The adult life span of dengue vector mosquitoes is generally very short (a few days), although some can survive 14 days or longer. Accordingly, it is amazing that dengue virus transmission occurs at all. However, mosquito populations are so large that even though most females die before feeding a second time, enough individuals survive long enough to keep virus transmission going.

Humans are the main host of the virus. Infected humans circulate the virus in their blood at approximately the same time as they have fever. *Aedes* mosquitoes may acquire the virus if they feed on an individual at this time. There is no person to person transmission. Vertical transmission from mother to fetus has occasionally been reported.

Ae. aegypti and *Ae. albopictus* are the mosquito vectors of dengue in the Western Hemisphere. They are somewhat similar in appearance, although the markings on the thorax (the "back" of the mosquito, where the wings are attached) are different. Both species are similar in habits and breeding sites, feeding in the daytime (mostly early and late in the day) and breeding in artificial containers around the home. Prime sites include paint cans, old tires, clogged rain gutters, pet watering dishes and similar venues.

Aedes aegypti is a mosquito breeding in peridomestic waters (flower pots, tin cans, discarded tires, barrels, buckets, cisterns and all kinds of small collection of water around the houses). *Aedes aegypti* usually bites in the early morning (few hours after daybreak), and late afternoon (few hours before dark). In shaded areas or when it is overcast, *Aedes aegypti* may bite at any time during the day.

Aedes albopictus, known as the Asian tiger mosquito, was accidentally introduced from Japan in 1985 into the Houston, Texas, area. Since then it has rapidly spread over much of the central and southern U.S., often replacing the native *Ae aegypti*. Today, the Asian tiger mosquito is the primary pest mosquito in many towns and cities and is extremely difficult to control by standard mosquito spraying (truck or airplane) because of its close proximity to houses and daytime feeding habit.

Dengue is distributed world wide in the tropical and subtropical areas. The main areas of endemicity are Southeast Asia (Indian subcontinent, Indochinese peninsula, Indonesia, Philippines), the South Pacific Islands (from Papua New Guinea to French Polynesia), limited foci in Africa, the Caribbean Islands and the eastern coast of Central and South America bordering the Gulf of Mexico and the Caribbean Sea.

The emergence of dengue/DHF as a major public health problem has been most dramatic in the American region. A large increase in size and distribution of dengue outbreaks occurred in the 1980's involving serotypes 1, 2 and 4 in countries where it was not previously documented or had been absent for several decades. For example in 1977 there was resurgence of dengue type 1 throughout the Caribbean which spread towards Mexico in 1978-80. In 1994 type 3 caused outbreaks in Nicaragua and Panama, this serotype had not been seen in the Americas for 15 years.

Louisiana is at a significant risk for importation of dengue. There is a small, but significant, risk for dengue outbreaks in the continental United States. Two competent mosquito vectors, *Aedes aegypti* and *Aedes albopictus*, are present and, under certain circumstances, each could transmit dengue viruses. This type of transmission has been detected twice in the last 15 years in south Texas (1980 and 1986) and has been associated with dengue epidemics in northern Mexico. Moreover, numerous viruses are introduced annually by travelers returning from tropical areas where dengue viruses are endemic. From 1977 to 1994, a total of 2,248 suspected cases of imported dengue were reported in the United States. Although some specimens collected were not adequate for laboratory diagnosis, preliminary data indicate that 481 (21%) cases were confirmed as dengue. Many more cases probably go unreported each year because surveillance in the United States is passive and relies on physicians to recognize the disease, inquire about the patient's travel history, obtain proper diagnostic samples, and report the case. These data underscore the fact that southern Texas and the southeastern United States, where *Aedes aegypti* is found, are at risk for dengue transmission and sporadic outbreaks.

The incubation period is two to seven days.

Clinical Description

Classical Dengue**:**
At onset the patient experiences high fever (40 °C) with severe pains (hence the name *Breakbone fever*): headache, retro-orbital pain, backache, arthralgias. These early symptoms are accompanied by a transient erythematous rash that blanches under pressure.

A few days later, a more intense scarlatiniform or morbilliform rash (sparing palms and soles) begins from the extremities and becomes generalized. There is also weakness, prostration, anorexia, epigastric discomfort, nausea and vomiting. At this stage, multiple enlarged lymph nodes can be found. The liver is

slightly enlarged. Leukopenia is profound (1,500 /mm^3). There may be some minor hemorrhagic symptoms such as petechiae and epistaxis. A second febrile phase of a few days (*Saddle back fever* curve) is accompanied by desquamation of the rash. Convalescence may be very long (weeks or months) and characterized by weakness and general lassitude.

The clinical features of dengue fever vary according to the age of the patient. Infants and young children may have an undifferentiated febrile disease with rash. Older children and adults may have either a mild febrile syndrome or the classical incapacitating disease with abrupt onset and high fever, severe headache, pain behind the eyes, muscle and joint pains, and rash.

Dengue Hemorrhagic Fever /Dengue Shock Syndrome**:**
The disease usually starts as classical dengue. During the first week, the patient's condition deteriorates very rapidly: sweating, hypotension and disseminated hemorrhagic symptoms (petechiae, ecchymoses, spontaneous hemorrhages, thrombocytopenia, alteration in clotting factors, reduced fibrinogen). DHF is defined by the following criteria:

1-fever,
2-hemorrhagic symptoms (minor or major)
3-platelet count <100,000 /mm^3
4-objective evidence of increased capillary permeability (e.g. hematocrit increased by ≥ 20% or pleural effusion or hypoproteinemia).

DSS includes DHF and hypotension or a narrow pulse pressure (≤ 20 mmHg). Capillary leakage may result in hypovolemic shock. Without treatment the prognosis is severe (50% case fatality rate), with adequate treatment the case fatality rate may be reduced to 1% to 5%.

Asymptomatic cases are frequent as shown by positive serologies in individuals who did not have any clinically evident disease.

Health-care providers should consider dengue in the differential diagnosis for all patients who have fever and a recent (i.e., preceding 2 weeks) history of travel to tropical areas.

Laboratory Tests

The diagnosis is confirmed by serologic testing or viral isolation. The presence of IgM antibodies against dengue is the most simple confirmatory test. IgG antibodies (detected by hemagglutination inhibition or ELISA) are present in the circulation years after infection and therefore their presence does not indicate a recent infection. Viremia occurs very early in the infection (before the 5^{th} day), by the time the second symptomatic period occurs, the virus may be difficult to isolate.

A case of dengue is confirmed by*

- Isolation of the virus from blood, or
- Identification of specific IgM in appropriately timed serum sample(s) (obtained between 5 and 90 days after onset of illness), or
- A fourfold rise in IgG antibody titer between acute and convalescent serum specimens.

The state laboratory will test paired specimens for Dengue antibodies to the different dengue virus types by EIA.

**It is important to determine whether the patient has ever received a yellow fever immunization, as this will interfere with the test results. If so, please make a note of it somewhere on the lab slip, or notify the Infectious Disease Epidemiology Section.*

Surveillance

Dengue is a reportable condition with reporting required within five business days.

Case Definition

Clinical description

An acute febrile illness characterized by frontal headache, retro-ocular pain, muscle and joint pain, and rash.

Dengue hemorrhagic fever is defined as an acute febrile illness with minor or major bleeding phenomena, thrombocytopenia (less than or equal to 100,000/mm^3), and evidence of plasma leakage documented by hemoconcentration (hematocrit increased by greater than or equal to 20%), or other objective evidence of increased capillary permeability.

The definition of dengue shock syndrome follows all of the above criteria for dengue hemorrhagic fever and also includes hypotension or narrow pulse pressure (less than or equal to 20 mm Hg).

Laboratory criteria for diagnosis

- Isolation of dengue virus from serum and/or autopsy tissue samples, or
- Fourfold or greater rise or fall in immunoglobulin G (IgG) in paired serum samples, or
- Immunoglobulin M (IgM) antibody titers to dengue virus antigens, or
- Demonstration of dengue virus antigen in autopsy tissue or serum samples by immunohistochemistry or
- Detection of dengue virus nucleic acid

Obtain from the patient both an acute-phase (0 to 5 days after symptom onset) serum sample for directly detecting dengue virus and a convalescent-phase serum sample for detecting anti-dengue antibody, preferably obtained one to two weeks after the first sample.

Serum samples obtained for viral identification and serologic diagnosis can be sent through the Office of Public Health laboratory to the Center for Disease Control and Prevention's Dengue Branch, Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, 1324 Calle Canada, San Juan, Puerto Rico 00920-3860; Serum samples should be accompanied by a summary of clinical and epidemiologic information, including date of disease onset, date of sample, collection, and detailed recent travel history.

Case classification

Probable: a clinically compatible case with supportive serologic findings (a reciprocal IgG antibody titer of greater than or equal to 1280 or a positive IgM antibody test on a single acute (late), or convalescent phase serum specimen to one or more dengue virus antigens)

Confirmed: a clinically compatible case that is laboratory confirmed.

Investigation

- Upon receipt of a report of dengue fever, contact the physician and/or hospital to confirm the diagnosis.
- Verify whether the diagnosis has been laboratory confirmed. Attempt to get a serum for IgM testing. If not, it is important to obtain a serum specimen as soon as possible after the onset of illness, and a second specimen approximately two to three weeks later to document the four-fold increase necessary to have a confirmed diagnosis of recent infection. Most single IgG results result from past infection.
- Investigate the source of exposure, i.e., recent travel history (within 15 days of onset of illness) or mosquito exposure.

- If the case has no recent travel history but does report exposure to mosquitoes, determine the place of residence. An entomological investigation will be considered.

Prevention of transmission

Mosquito control and personal protection are the two main prevention measures.

Case Management - Treatment

There is no specific treatment for dengue fever. However, careful clinical management by experienced physicians and nurses frequently save the lives of DHF patients.

Hospital precaution and isolation: Standard precautions to prevent transmission by blood and body fluids in the early period. Vector isolation is only relevant in tropical hospitals which are not mosquito proof; patients should be placed under a mosquito net.