

REVIEW OF DENGUE FEVER

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Summary

Dengue virus infections are a serious cause of morbidity and mortality in most tropical and subtropical areas of the world, mainly Southeast and South Asia, Central and South America. It causes more illness and death than any other arboviral infections, and its control is a priority for the WHO. The causative agent is a mosquito-borne RNA virus belonging to the family of Flaviviridae, is related to the viruses that cause dengue and Japanese encephalitis. Dengue is an acute mosquito-transmitted disease characterized by fever, headache, muscle and joint pain, rash, nausea, vomiting, hepatitis, renal failure, cardiovascular collapse and bleeding. Some infections result in dengue haemorrhagic fever (DHF), a syndrome that in its most severe form can threaten the patient's life, primarily through increased vascular permeability and shock. A major challenge for public health officials in all tropical areas of the world is to develop and implement sustainable prevention and control programmes that will reverse the trend of emergent DHF. However, Understanding of the dengue infection pathogenesis is not complete. We still have a long way to go.

Keywords: Dengue (DF), Mosquitoes, *Aedes aegypti*, Dengue haemorrhagic fever (DHF)

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Introduction

Dengue fever (DF) is a viral infection spread through the bite of infected female mosquito (*Aedes aegypti* and *Aedes albopictus*). Dengue viruses belong to the family Flaviviridae. There are four serotypes, dengue virus types 1,2,3 and 4 [1]. Dengue fever occurs in tropical and sub-tropical regions and usually increases in the hot and humid months. Dengue fever is not a new disease. It was discovered several hundred years ago. In recent years, dengue fever has become a major international public health concern[2].

Dengue fever is an infectious disease carried by mosquitoes and caused by any of four related dengue viruses. Classic DF is primarily a disease of older children and adults. It is characterized by the sudden onset of fever and a variety of nonspecific signs and symptoms, including frontal headache, retro-orbital pain, body aches, nausea and vomiting, joint pains, weakness, and rash [3, 4, 5, 6, 7]. This disease used to be called "break-bone" fever because it sometimes causes severe joint and muscle pain that feels like bones are breaking, hence the name. Health experts have known about dengue fever for more than 200 years [8]. Benjamin Rush from Philadelphia, US, first described "break bone fever" in 1780 [9]. Slaves who developed dengue fever in the West Indies were said to have "dandy fever" because of their posture and gait. Yellow fever was a significant problem until the early 20th century, and remains endemic and epidemic in tropical regions of South America and Africa.

Survey:

Dengue fever is found mostly during and shortly after the rainy season in tropical and subtropical areas of Africa, Southeast Asia and China, India, Middle East, Caribbean, Central & South America, Australia and the South and Central Pacific [10]. In 1990–1999, 11,297 cases of yellow fever and 2648 deaths were officially reported to the World Health Organization (WHO); 9358 cases (83%) occurred in Africa [11]. The largest number was reported from Nigeria, which sustained a series of epidemics between 1986 and 1994. In 1992, the disease was reported in East Africa (Kenya) for the first time in 26 years. Since 2000, notable outbreaks of yellow fever have occurred in Guinea, Sierra Leone, Liberia and Burkina Faso.

In 1996–2002, there were five fatal cases of yellow fever in unvaccinated travelers from the USA and Europe, to Brazil and Venezuela. It is estimated worldwide that 50-100 million individuals are infected with dengue virus each year. Most cases imported into the UK are acquired in South Asia. Dengue is uncommon in travelers' to Africa. Mosquito bite avoidance is currently the only available protection against infection.

The incidence of dengue has grown dramatically around the world in recent decades. Some 2.5 billion people – two fifths of the world's population – are now at risk from dengue. In 2007 alone, there were more than 890 000 reported cases of dengue in the Americas, of which 26000 cases were (DHF). The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia and the Western Pacific [12]. South-east Asia and the Western Pacific are the most seriously affected.

Pathogenesis:

Dengue is caused by an arbovirus of the family Flaviviridae, a positive sense single-stranded RNA virus. Human infection begins after deposition of viral particles through the skin from infected arthropod saliva. The mosquitoes involved are *A. simpsoni*, *A. africanus*, and *A. aegypti* in Africa, the *Haemagogus* genus in South America [13] and the *Sabethes* genus in France. Dengue is frequently severe but moderate cases may occur as the result of previous infection by another flavivirus. After infection the virus first replicates locally, followed by transportation to the rest of the body via the lymphatic system. Following systemic lymphatic infection, the virus proceeds to establish itself throughout organ systems, including the heart, kidneys, adrenal glands, and the parenchyma of the liver; high viral loads are also present in the blood [14]. Necrotic masses (Councilman bodies) appear in the cytoplasm of hepatocytes [15].

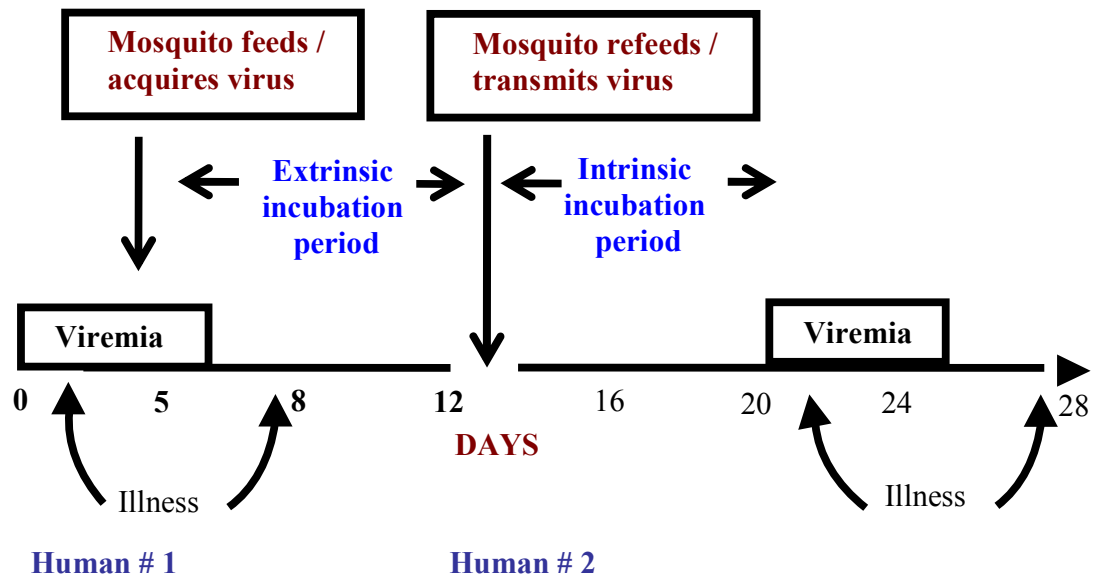
Dengue begins suddenly after an incubation period of three to five days in the human body. In mild cases only fever and headache may be present. The severe form of the disease commences with fever, chills, bleeding into the skin, rapid heartbeat, headache, back pains, and extreme prostration,

Nausea, vomiting, and constipation are common. Jaundice usually appears on the second or third day. After the third day the symptoms recede, only to return with increased severity in the final stage, during which there is a marked tendency to hemorrhage internally; the characteristic “coffee ground” vomitus contains blood. The patient then lapses into delirium and coma, often followed by death [16]. During epidemics the fatality rate was often as high as 85%. Although the disease still occurs, it is usually confined to sporadic outbreaks.

There is a difference between disease outbreaks in rural or forest areas and in towns. Disease outbreaks in towns and non-native people may be more serious because of higher densities of mosquito vectors and higher population densities [17].

Transmission:

Dengue viruses are transmitted to humans (host) through the bites of the female striped *Aedes aegypti* mosquito (vector). This variety of mosquito breeds easily during the rainy seasons but can flourish in peridomestic fresh water, e.g. water that is stored in plastic bags, cans, flowerpots and old tires. The dengue virus is transmitted to its host during probing and blood feeding. The mosquito may carry the virus from one host to another host and the mosquito is most active in the early morning and later afternoon. A mosquito bite can cause the disease. Incubation period occurs when the viruses has been transmitted to the human host. The period ranges from 3 to 15 days (usually lasting for 5-8 days) before the characteristics of dengue appear. During incubation time, the dengue viruses multiply [18].

Transmission of Dengue Virus by *Aedes aegypti*

The transmission cycle of dengue virus by the mosquito *Aedes aegypti* begins with a dengue-infected person. This person will have virus circulating in the blood a viremia that lasts for about five days. During the viremic period, an uninfected female *Aedes aegypti* mosquito bites the person and ingests blood that contains dengue virus. Although there is some evidence of transovarial transmission of dengue virus in *Aedes aegypti*, usually mosquitoes are only infected by biting a viremic person [19]. Then, within the mosquito, the virus replicates during an extrinsic incubation period of eight to twelve days.

The mosquito then bites a susceptible person and transmits the virus to him or her, as well as to every other susceptible person the mosquito bites for the rest of its lifetime. The virus then replicates in the second person and produces symptoms. The symptoms begin to appear an average of four to seven days after the mosquito bite this is the intrinsic incubation period, within humans. While the intrinsic incubation period averages from four to seven days, it can range from three to 14 days.

Symptoms:

- High fever (102-105 F)
- Chills

- Headache
- Retro-orbital pain
- Enlarged lymph nodes
- Deep muscle and joint pains
- Loss of appetite
- Nausea and vomiting
- Low blood pressure and heart rate
- Extreme fatigue

Basically, dengue commences with high fever and other signs appear for 2 to 4 days. Then, the temperature drops rapidly and intense sweating takes place. After about a day with normal temperature and a feeling of well-being, the temperature rises abruptly again. The rash may appear over most of the body 3 to 4 days after the fever begins and then subsides after 1 to 2 days. The palms of the hands and soles of the feet may be swollen and bright red. Although the patient may feel exhausted for several weeks, most cases of dengue take approximately one week to recover.

Symptoms of DHF include all of the symptoms of classic dengue including marked damage to blood and lymph vessels and bleeding from the nose, gums, or under the skin, causing purplish bruises. This form of dengue disease can cause death.

Prognosis:

Of patients who are jaundiced as a result of yellow fever, 20–50% dies, usually 6–9 days after onset. A poor prognosis is indicated by:

- Early appearance and deepening of jaundice
- Markedly elevated serum aminotransferase
- Increased prothrombin time
- Severe haemorrhage

Few patients survive shock and coma. Survivors recover rapidly from the acute intoxication, but may experience weakness and fatigue for several weeks. Bacterial pneumonia and parotitis may complicate recovery. Patients may survive the acute hepatitis, only to succumb to the late complications of renal tubular necrosis. Patients

who survive acute hepatitis exhibit complete regeneration of the liver without post-necrotic fibrosis.

Diagnosis:

- Dengue fever can be diagnosed by doing blood test, 2 to 3 weeks apart. The tests can show whether a sample of your blood contains antibodies to the virus [20].
- The clinician should record the temperature and perform a tourniquet test and look for the petechiae.
- All suspected cases of fever with bleeding should be investigated thoroughly for low platelet count.
- In case of shock, tests should be done for detection of small fluid in the abdomen or in the chest.
- In epidemics, a health care provider often can diagnose dengue by typical signs and symptoms [21].

Treatment:

- There is no specific treatment to shorten the course of dengue fever.
- Medications are given to alleviate the signs and symptoms. Aspirin should not be given to patients. It will cause severe bleeding. Hence, it is advisable to take paracetamol to relieve muscle and joint aches, fever and headache.
- The patient may be required to be sponged down with water at room temperature using a wet, squeezed out towel for about 20 minutes at a time. This will help to help lower the high temperature. Ice water should not be used for this purpose. However, bed rest is essential to a speedy recovery and the patient should consume plenty of water which will help to alleviate the illness.
- Patients should be kept in a room that has screens to prevent mosquitoes from entering or else under mosquito netting until the second period of fever has subsided. Hence, mosquitoes cannot bite them. If the patient is bitten then the dengue virus may be transmitted to the mosquito and then to another host
- For DHF, medical care by physicians and nurses experienced with the effects and progression of the complicating haemorrhagic fever can frequently save lives -

decreasing mortality rates from more than 20% to less than 1%. Maintenance of the patient's circulating fluid volume is the central feature of DHF care.

Prevention and control:

- At present, the only method of preventing and controlling dengue fever is to eradicate the mosquito population. There are a number of ways to combat the vector mosquitoes.
- No drug or vaccine is available for the treatment of DF/DHF
- Improved water storage practices. Cover all containers to prevent egg laying female mosquitoes to access it.
- Implement proper solid waste disposal.
- Eliminate any sources that may collect water such as tins, bottles, plastic food containers and old tires. Mosquitoes breed easily in any source of standing water.
- The application of appropriate insecticides to larval habitats, particularly those that are useful in households, e.g. water storage vessels, prevents mosquito breeding for several weeks but must be re-applied periodically. Small, mosquito-eating fish and copepods (tiny crustaceans) have also been used with some success [22]. Always clean and check drains to ensure they are not blocked especially during the rainy season.
- Breed small mosquito-eating fishes in an artificial pond to eradicate the mosquito larvae.
- In addition to the above, there are a number of factors to help prevent the mosquito being attracted to human prey.
- Avoid wearing dark and tight clothing because mosquitoes are attracted to dark colours. Wear loose, white and long clothes, which cover the whole body. Mosquitoes find it difficult to bite through loose clothes than tight fitting clothes [23].
- Environmental conditions. It is suggested to sleep under mosquito netting or in a room which has mosquito screens on the windows. Mosquitoes are unlikely to bite in an air-conditioned room and under strong fans. Mosquito coils are also useful to help prevent mosquitoes from entering the room.

- When outdoors in an area where dengue fever has been found use a mosquito repellent containing DEET, picaridin, or oil of lemon eucalyptus.
- Avoid reduce outdoor activities during morning and late afternoon because *Aedes* mosquitoes are daytime feeders.
- The best way to prevent dengue virus infection is to take special precautions to avoid being bitten by mosquitoes. Several dengue vaccines are being developed, but none is likely to be licensed by the Food and Drug Administration in the next few years.
- The transmission of the virus to mosquitoes must be interrupted to prevent the illness. To this end, patients are kept under mosquito netting until the second bout of fever is over and they are no longer contagious.

Vector control – elimination of peri-domestic mosquito breeding sites is effective, but even in favourable settings it has been difficult to sustain the effort required to eliminate the vector over a wide area and for a prolonged period of time. Additional biological control strategies may contribute to vector control in the future. The following measures are Vector Control Measures.

1. Personal Prophylactic Measures

- Use of mosquito repellent creams, liquids, coils, mats etc.
- Wearing of full sleeve shirts and full pants with socks
- Use of bednets for sleeping infants and young children during day time to prevent mosquito bite

2. Biological Control

- Use of larvivorous fishes in ornamental tanks, fountains, etc.
- Use of biocides

3. Chemical Control

- Use of chemical larvicides like abate in big breeding containers
- Aerosol space spray during day time

4. Environmental Management & Source Reduction Methods

- Detection & elimination of mosquito breeding sources
- Management of roof tops, porticos and sunshades
- Proper covering of stored water
- Reliable water supply
- Observation of weekly dry day

5. Health Education

- Impart knowledge to common people regarding the disease and vector through various media sources like Radio, Cinema slides, etc.

6. Community Participation

- Sensitizing and involving the community for detection of Aedes breeding places and their elimination

Vaccination:

Effective vaccines are available for the closely related mosquito-borne Flaviviruses yellow fever (live attenuated) and Japanese encephalitis (inactivated), but there is currently no vaccine for dengue. The dengue group of Flaviviruses is unique in that the four serotypes can cause sequential infections of increased severity, and any candidate dengue vaccine should induce solid immunity to all four serotypes. This presents a particular challenge [24].

Immunization:

Dengue fever 17D is a live attenuated vaccine produced in chicken embryos. Over the last 50 years, more than 400 million doses have been administered. Re-immunization is required every 10 years to maintain a valid international vaccination certificate; however, effective immunity is probably lifelong. The vaccine is given as a single 0.5 ml subcutaneous injection; 99–100% of immunized individuals develop neutralizing antibodies after vaccination. Immunity is present by 10 days after vaccination. Although routine childhood yellow fever vaccinations are performed in some countries, the

continued presence of the disease, particularly in Africa, reflects under-utilization of vaccine and low coverage.

Yellow fever vaccine may be administered simultaneously with other travelers' vaccines, including hepatitis A, hepatitis B, poliomyelitis, measles, diphtheria/pertussis/tetanus, typhoid and oral cholera vaccine. Yellow fever vaccine is a live vaccine, so theoretically should not be given to pregnant women or to immunosuppressed individuals [25]. A single fatal adverse reaction (encephalitis) has been reported in an immunosuppressed individual with HIV/AIDS. In the USA, current recommendations indicate that HIV-infected individuals without AIDS who are at risk of exposure to yellow fever should be immunized. In the UK, the Department of Health recommends that yellow fever vaccine should not be given to HIV-positive individuals. Yellow fever vaccine has been administered safely to individuals taking low doses of corticosteroids.

Management of Dengue Case:

- Early reporting of the suspected DF
- Management of DF is symptomatic & supportive
- In dengue shock syndrome, the following treatment is recommended:
 - Replacement of plasma losses
 - Correction of electrolyte and metabolic disturbances
 - Blood transfusion

Dos and Don'ts:

- Remove water from coolers and other small containers at least once in a week
- Use aerosol during day time to prevent the bites of mosquitoes
- Do not wear clothes that expose arms and legs
- Children should not be allowed to play in shorts and half sleeved clothes
- Use mosquito nets or mosquito repellents while sleeping during day time

Conclusions

Today, changing characteristics of the disease deserve serious research attention. Shifts in modal age, rural spread; social and biological determinants of race and sex-related susceptibility have major implications for health service planning and control strategies. Early detection and case management practices have been noted as a critical factor for survival. Yet well-targeted operational research in these areas is rare. Population-based epidemiological studies with clear operational objectives should be launched as concerted efforts at regional levels.

Dengue is responsible for one third of the fevers presented to the public primary health services in many countries. It presents as a highly unspecific illness and can progress to life-threatening dengue hemorrhagic fever. It is hardly recognized as a clinical entity by primary physicians.

Today dengue control and prevention requires thinking outside the tropical disease box. Many of the affected countries are some of the poorest. Approaches that are realistic for their infrastructure need to be urgently developed.

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