

# Expanded Dengue Syndrome

Tauqeer Hussain Mallhi  
Yusra Habib Khan  
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Nida Tanveer  
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health care system development, evaluation, and implementation. He has served as research coordinator at Chronic Kidney Resource Center, Hospital Universiti Sains Malaysia. His research is well acknowledged in various national and international conferences. He has published more than 50 scholarly manuscripts in well-reputed peer-reviewed journals. Dr Aftab is currently supervising postgraduate students and is also a principal investigator for Taylor's University emerging researcher grant scheme.



# Dengue Viral Infection (DVI) and Expanded Dengue Syndrome (EDS)

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## 1.1 Dengue Viral Infection

Dengue viral infection (DVI) is a debilitating arthropod-borne disease that has been rapidly spread in several regions of the world in recent years [1]. The disease is widespread throughout the tropics, with local variations in risk, and is influenced by rainfall, temperature, and unplanned rapid urbanization. The spectrum of disease varies from mild self-limiting illness to dengue fever (DF) to more severe and fulminating forms, i.e., dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [2, 3].

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## 1.2 Dengue Virus, Vector, and Host

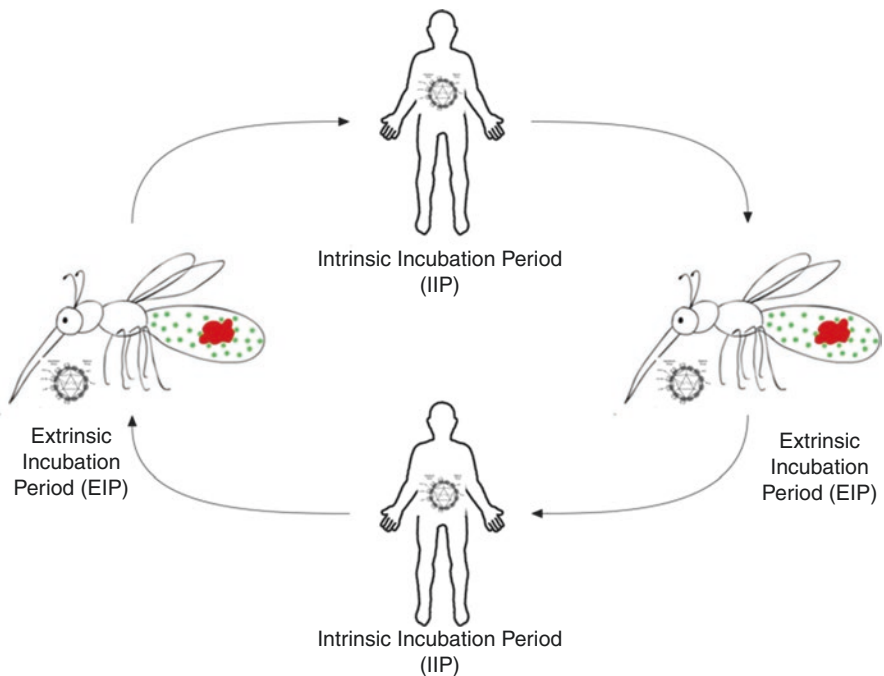
Dengue infection is believed to be caused by dengue virus (DENV), a **mosquito-borne** single positive stranded **RNA virus** (family: *Flaviviridae*, genus *Flavivirus*). There are four related but antigenically distinct serotypes of dengue virus designated as DENV-1, DENV-2, DENV-3, and DENV-4 [4]. These four serotypes are genetically similar and share approximately 65% of their genomes [5]. However, a fifth serotype (DENV-5) has been detected during the screening of viral samples in Sarawak state of Malaysia [6]. Dengue virus is transmitted to nonhuman primates (sylvatic form) and humans (human form) via a mosquito vector, primarily of the genus *Aedes* (subgenus: *Stegomyia*). The two most prominent species responsible for DENV transmission are *Aedes aegypti* (origin: Africa) and *Aedes albopictus* (origin: Asia) [7]. The first infection by one serotype produces lifelong, serotype-specific immunity but not lasting protection against infection by another serotype.

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Humans are the main amplifying host of the virus that is transmitted to them by the bite of an infective mosquito. The virus undergoes an intrinsic incubation period (IIP—time taken by the virus to complete its development in humans/animals) of 3–14 days (average, 4–7 days), after which the person may experience acute onset of fever accompanied by a variety of nonspecific signs and symptoms. During this acute febrile period (2–10 days), dengue viruses may circulate in the peripheral blood. This human febrile viremic phase (2 days before and 4–5 days after onset of fever) is a source of viruses for other mosquitoes. Dengue virus circulating in the blood of viremic humans is ingested by female mosquitoes during feeding. The virus then infects the mosquito mid-gut and subsequently spreads systemically over a period of 8–12 days. After this extrinsic incubation period (EIP—time taken by the virus to complete its development in mosquitos), the virus can be transmitted to other humans during subsequent probing or feeding. The EIP is influenced in part by environmental conditions, especially ambient temperature. Thereafter the mosquito remains infective for the rest of its life [8]. Figure 1.1 illustrates the cycle of IIP and EIP.

*Aedes aegypti* is a small, dark mosquito that can be identified by the white bands on its legs and white lyre-shaped markings on its body. It is highly resilient with the ability to rapidly bounce back to initial numbers after disturbances caused by the



**Fig. 1.1** Intrinsic incubation period (host) and extrinsic incubation period (mosquito)—figure is self-constructed



natural disaster or human interventions. *Aedes albopictus*, also known as Asian tiger mosquito, is also a small, dark mosquito with a white dorsal stripes and banded legs. Since *Aedes albopictus* can feed on both human and animals, its survival conditions are more favorable than *Aedes aegypti* [9]. Both vectors differ characteristically from each other [10, 11]. Table 1.1 describes important differences between these two vectors.

### 1.2.1 Transmission of Dengue Virus

The transmission of DENV occurs in three cycles including enzootic (a primitive sylvatic cycle by monkeys-*Aedes*-monkeys), epizootic (crosses over to nonhuman primates from adjoining human epidemic cycles), and epidemic cycle (human-*Aedes*-human). After ingestion of blood from human, virus replicates in epithelial cell lining of mid-gut and infects the salivary glands. Afterwards, infectious saliva transmits to human primates during probing. DENV also infect genital tract and may enter to fully developed eggs [12]. Dengue transmission usually occurs during rainy season when temperature and humidity are more suitable for breeding of vectors, while in regions where rainfall is scanty, vector breeds in manmade storage containers. However, during dry season, the life cycle of *Aedes aegypti* accelerates, which ultimately results in small-size mosquitos and shorter EIP. Small-size females are required to take more blood meals as protein is needed for egg production; thereby this increases the number of bites and hence infected individuals. Urbanization and increased global travels are some other factors promoting vector breed, thus resulting in higher transmission rates [13].

**Table 1.1** Characteristics of two major species of *Aedes* vector

<i>Aedes aegypti</i>	<i>Aedes albopictus</i>
• <i>Origin</i> : Africa	• <i>Origin</i> : Asia
• Highly domesticated	• Maintain feral moorings
• Strong anthropophilic <sup>a</sup>	• Feeds on both human and animals
• Nervous feeder <sup>b</sup>	• Aggressive feeder <sup>c</sup>
• Discordant species <sup>d</sup>	• Concordant species <sup>c</sup>
• High vectorial competency	• High vectorial competency
• Strong vectorial capacity in urban areas while poor in rural regions	• Poor vectorial capacity in urban areas while strong in rural regions

<sup>a</sup>Prefer human beings over animals

<sup>b</sup>Bite more than one host to complete one blood meal

<sup>c</sup>Complete blood meal in one person in one go

<sup>d</sup>Need more than one meal for completion of gonotrophic cycle

<sup>e</sup>Does not require second blood meal for completion of gonotrophic cycle