Dengue, the most prevalent arthropod-borne (mosquito) viral disease of humans is a major cause of morbidity throughout tropical and subtropical regions of the globe and continues to spread alarmingly. Dengue virus has grown dramatically worldwide in recent years [1]. Dengue fever is also known as breakbone fever caused by dengue virus.[2] Dengue Virus is an arbovirus of the *Flaviviridae* family (fourth group) and *Flavivirus* genus. Dengue is an enveloped virus, 40-60 nanometer in size, with an isometric nucleocapsid of 25-30 nanometer and a ~10.7 kb, linear, positive-sense RNA genome[3]. Its genome is about 11000 bases and codes for three structural proteins (capsid protein C, membrane protein M, envelope protein E) and these seven non-structural proteins (NS1, NS2a, NS2b, NS3, NS4a, NS4b, NS5). It also includes short non-coding regions on both the 5' and 3' ends[4][5].

Dengue virus is the main cause of dengue fever (DF) and dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS) [6]. Basically dengue fever is characterized by high fever, head-ache, muscle joint pain, myalgia, arthralgia, and rash. The severe form of disease, it is defined by an increase in vascular permeability (“plasma leakage”), hemorrhagic blooming, and decreased platelet count levels near the time of defervescence [7]. DHF can also progress to DSS, which is associated with hypotension or narrow pulse pressure and clinical signs of shock [8]. Generally, people infected with dengue virus are asymptomatic (80%) or mild symptoms such as an uncomplicated fever [9][10][11]. Others have severe illness (5%), and in a small proportion, dengue is life-threatening [9][11]. The incubation period (time between exposure to onset of symptoms) ranges from 3 to 14 days hardly, but most often it is 4 to 7 days [12]. Therefore, travelers returning back from endemic areas are unlikely to have dengue if fever or other symptoms start more than 14 days after arriving home [13]. Children often experience symptoms similar to those of the common cold and gastroenteritis (vomiting and diarrhea) [14] and have a high risk of severe complications, though beginning symptoms are generally mild but include high fever [15].

Serologically, DENV can be classified into five immunologically related but genetically and antigenically different serotypes (DENV-1–5) [16, 17]. Each serotype may be subclassified into some distinct phylogenetic clusters or genotypes [18]. The various serotypes or genotypes have
different epidemic potential in different geographic regions. DENV-1 and DENV-2 are reported to be prevalent throughout the world, while DENV-3 and DENV-4 seem to be limited to East Asian and Southeast Asian countries. A new serotype of DENV-5 was recently identified. The fifth and latest addition to the existing serotypes of dengue viruses is DENV-5 which has been publicized in October 2013. DENV-5 has been detected during screening of viral samples taken from a 37 year old man admitted in hospital in Sarawak state of Malaysia in the year 2007. The infection in the farmer was initially thought to be a normal case of sylvatic dengue caused by DENV-4 which circulates among primates and Aedes nivalis mosquitoes in the forests of South East Asia.

Transmission

Dengue virus is primarily transmitted by female Aedes mosquitoes, particularly A. aegypti. These mosquitoes usually live between the latitudes of 35° North direction and 35° South direction below an elevation of 1,000 metres (3,300 ft). They typically bite during the early morning and in the evening, but they may bite and thus spread infection at any time of day. Humans are the primary host of the virus, but it also circulates in non-human primates. An infection can be acquired via a single bite. A vector female mosquito that takes a blood from a person infected with dengue fever, during the starting 2–10 day febrile period, becomes itself infected with the virus in its gut. About 8–10 days later, the virus rises to other tissues including the mosquito's salivary glands and is hereafter released into its saliva. The virus seems to have no deleterious effect on the mosquito, which stay infected for life. Aedes aegypti and Aedes albopictus are particularly involved, as it prefers to lay its eggs in artificial water open containers, to live in close proximity to humans, and to feed on people rather than other vertebrates.

Anti-dengue

International Anti-Dengue Day is observed every year on June 15. The idea was first agreed upon in 2010 with the first event held in Jakarta, Indonesia in 2011. Further events were held in 2012 in Yangon, Myanmar and in 2013 in Vietnam. Aims are to increase public awareness about dengue, mobilize resources for its prevention and control and, to demonstrate the Asian region’s commitment in tackling the disease.
**Vaccine**

Presently there is no human vaccine available. Several vaccines are under development by private and public researchers. Developing a vaccine against the disease is challenging. With four different serotypes of the dengue virus that can cause the disease, the vaccine must immunize against all four types to be effective. Vaccination against only one serotype could probably lead to severe dengue hemorrhagic shock (DHS) when infected with another serotype due to antibody-dependent enhancement.

When infected with DEN virus, the immune system produces cross-reactive antibodies that provide immunity to specific that serotype. However, these antibodies are incapable of neutralizing other serotypes upon re-infection and virtually increase viral replication. When macrophages consume the ‘neutralized’ virus, the virus is able replicate within the macrophage, causing disease. And these cross-reactive, ineffective antibodies ease access of virus into macrophages, which stimulate more severe disease (dengue hemorrhagic fever, dengue shock syndrome). A common problem faced in dengue-endemic regions is when mothers become infected with this viral disease; after giving birth, offspring carry the immunity from their mother and are susceptible to hemorrhagic fever if infected with any of the other three serotypes.

One vaccine was in phase III trials in 2012 and planning for vaccine usage and effectiveness surveillance had started. In December 2015, the first dengue fever vaccine received approval in Mexico and available in 2016. The vaccine is introduced by Sanofi and goes by the brand name Dengvaxia. It is based on a weakened combination of the yellow fever virus and each of the four dengue serotypes. Two studies of a vaccine found it was 60% effective and prevented more than 80 to 90% of severe cases. This is less than wished for by some.

There are ongoing programs working on a dengue vaccine to cover all four serotypes. Now that there is a fifth serotype this will need to be factored in. One of the concerns is that a vaccine could increase the risk of severe disease through antibody-dependent enhancement (ADE). The ideal vaccine is safe, effective after one or two injections, covers all serotypes, does not contribute to ADE, is readily transported and stored, and is both affordable and cost-effective.