

The study of chikungunya virus



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There are a million different types of viruses that exist in every ecosystem on Earth. Viruses infect and replicate inside living cells of all types of organisms. One specific emerging arbovirus that will be discussed in this paper is called the Chikungunya virus. During the years of 2005 and 2006, the Chikungunya virus has affected over a million people in the Indian Ocean islands including India (Pardigon 2009). This insect-borne virus, abbreviated as CHIKV, is native to Africa and Asia (Pardigon, 2009). This virus is spread by the Aedes mosquito species, specifically Aedes aegypti and Aedes albopictus commonly known as the Asian tiger mosquito (Pardigon, 2009). Even though the Chikungunya infection leads to severe illness, similar to the Dengue fever, it is rarely ever fatal (Pardigon, 2009).

Chikungunya is an alphavirus which is classified under the virus family Togaviridae. This positive sense single stranded RNA, categorized under the Group IV of the Baltimore classification, contains a range of 11, 000 to 12, 000 nucleotides. This virus is enveloped with an icosahedral capsid. The surface of the virus is covered with glycoprotein spikes which serve as surface projections. A capped 5' end contains a 7-methylguanosine and the 3' end is polyadenylated. The 26SRNA, a subgenomic positive strand RNA, is transcribed from a negative strand RNA intermediate. This type of RNA acts as the mRNA for viral protein synthesis. The Chikungunya virus also consists of conserved domains, located at the 5' and 3' ends, which are essential during viral RNA synthesis regulation.

After understanding parts of the genome, an experiment was conducted in the mid 1980's using Polyacrylamide gel analysis in order to distinguish different structural proteins present in the African and Asian strains of the

Chikungunya virus (Simizu, Yahamoto, Hashimoto, Ogata, 1984). It was shown that three structural proteins were of importance, glycosylated E1 and E2 which is located in the envelope and a nonglycosylated nucleocapsid protein (Simizu et al.).

The life cycle of the Chikungunya virus involves a number of steps. During attachment this alphavirus attaches to poorly characterized receptors on a number of different cell types (Chazal, Gerlier 2003). The E1 protein accelerates the fusion process while E2 begins to interact with cellular receptors (Chazal, Gerlier 2003). Entry is accomplished through receptor mediated endocytosis and the virus begins the uncoating process in the cytoplasm, which is also the site of mRNA transcription and genome replication (Chazal, Gerlier 2003). The Chikungunya virus is not very particular on where it replicates, therefore reproduction can take place in many different organs of the body (Chazal, Gerlier 2003). Replication stage involves assembly of genetic material and viral proteins that are produced in the host cell (Chazal, Gerlier 2003). After replicating, the virus buds from the host cell leaving with a phospholipid envelope consisting of viral glycoproteins (Chazal, Gerlier 2003).

Since this virus is able to replicate almost anywhere, cell tropism was tested using immortalized cells and primary human cells (Sourisseau et al.).

Epithelial derived cells and primary fibroblasts were observed to be highly vulnerable to the virus (Sourisseau et al.). Being exposed to the infection for 24 hours led to over 60 percent of Chikungunya positive cells in the epithelial cells and primary fibroblasts (Sourisseau et al.). The MRC5 lung cells and TrHBMEC cells from bone marrow were also susceptible to infection

(Sourisseau et al.). However the human endothelial cell line hCMEC/D3, isolated from the brain, was very resistant to the virus infection (Sourisseau et al.). Even after a 24 hour period only one percent of the cells were found to be CHIKV positive (Sourisseau et al.). Cell tropism of the Chikungunya virus was studied further by infecting various target cells. Two cells types that had strong binding to the virus were Vero cells and BEAS-2B cells while THP and primary monocytes resulted in virus binding that was undetectable (Sourisseau et al.). Overall, this virus is able to infect most cell lines including adherent and primary cell lines (Sourisseau et al.).

This virus can cause a devastating illness upon the person infected. Fever, headache, nausea, fatigue and joint pain are common symptoms of this infection. A 'silent' chikungunya virus infection is also able to occur in which the person infected does not experience illness or symptoms of any kind. People are able to gain life long immunity after being exposed to the infection. In relation to other arboviral fevers such as West Nile and Dengue, the chikungunya fever leaves some people with debilitating joint pain or arthritis which is known to last for a few weeks or months post infection.

It is known that alphaviruses are able to produce a marked cytopathic effect (CPE), depending on viral inoculum, in vertebrate culture cells and HeLa cells (Sourisseau et al.). All of the observed dying cells were positive for CHIKV infection which was associated with apoptosis (Sourisseau et al.).

Unfortunately, there is no current vaccine or antiviral drugs available for Chikungunya; however there are a few ongoing studies for development of a DNA vaccine against this virus. In the meanwhile, Chikungunya infection is

cured by the immune system therefore rest and plenty of fluids are able to relieve symptoms. Homeopathy is a post infection treatment is that used for patients suffering from weakness, stiffness of the joints and muscle pain. Usually this treatment is very effective to those that have been infected.

Since there are no current treatments against Chikungunya, the best possible way to prevent infection is to avoid mosquito bites. This can be done by wearing insect repellent, pants and long sleeve shirts. It is recommended to treat clothing with insecticides as well. For the home, screens should be secured on all windows and doors to keep insects out. After adequate rainfall, standing water should be emptied from buckets, pots, small pools and any type of container that is able to hold water for a long period of time. If pets are kept around the home, water bowls should be changed often. This method will eliminate mosquito breeding sites.

If a person does become infected with CHIKV, prognosis for this infection depends on the person's age. Younger people have a faster recovery time (5-15 days) compared to middle aged people (1-2 months) and elderly. Younger patients also have a less severe version of the infection where as older patients will suffer from a much more devastating effect from the disease.

Chikungunya virus is native to Africa and Asia and has been spread to parts of Europe. These populations are susceptible to infection including those that live on the islands of the Indian Ocean. A recent outbreak occurred in India during 2006. This large outbreak affected several states in India including New Delhi and Gujarat. A few deaths were reported however this was due to

inappropriate use of antibiotics and anti-inflammatory medications. Those that are susceptible to death are usually severely dehydrated, have imbalanced electrolytes and no glycemic control. Besides Africa, Asia and Europe, there has been no record of the Chikungunya virus elsewhere.

A few risk factors are involved with this virus which includes homeless and elderly people since these people have a weak immune system. Other people that are at risk are those that have received an organ transplant, have diabetes or AIDS.

The Chikungunya arbovirus is closely related to the Ross River virus in Australia as well as the O'nyong'nyong virus. All of these viruses are transmitted from human to human through a mosquito bite. Recent studies have indicated that virus strains have acquired a point mutation in the E1 viral envelope gene which could affect viral fusion, assembly and tropism (Ng et al. 2009). A case in Thailand led researchers to believe that the virus can be transmitted from mother to fetus (Ng et al. 2009). A 28 year old woman gave birth to her son through Caesarean section in order to prevent possible transmission; however the baby became infected and was under intensive care (Ng et al. 2009). Physicians and researchers believed that pregnant women can pass the virus onto their unborn child but there is no current laboratory evidence for this belief (Ng et al. 2009).

In 2006, India declared Chikungunya an epidemic. During this epidemic, researchers found that the African strain was present in the infected mosquitoes. This strain was able to infect humans at a much faster pace which resulted in a large number of infected people in India. The spread

facilitated through large amounts of rainfall in India which resulted in more mosquito breeding sites. This infection led to death of over 70 percent in people that were over 60 years of age.

The Chikungunya virus causes severe illness but rarely causes death. There has been no record of this virus outside of Asia, Africa and Europe because Asian tiger mosquitoes are normally found in Africa and Asia where Chikungunya infection is dominant. This virus is able to replicate in various organs of the body however the stronger the immune system the faster the infection will clear up. Using correct prevention techniques can help from getting the infection from a mosquito bite.