News Review

Dengue Fever

Jharna Bhattacharyya*

Dengue fever, also known as breakbone fever, is a mosquito-borne tropical disease caused by the dengue virus. Symptoms include fever, headache, muscle and joint pain and a skin rash that is similar to measles. In a few cases the disease develops into the life-threatening dengue hemorrhagic fever, resulting in bleeding, low levels of blood platelets and blood plasma leakage, or into dengue shock syndrome, where low blood pressure occurs.

Dengue is transmitted by several species of mosquito within the genus Aedes, principally *A. aegypti*. The virus has five different types; infection with one type usually gives lifelong immunity to that type, but only short-term immunity to others. As there is no commercially available vaccine, prevention is sought by reducing the habitat and the number of mosquitoes and limiting exposure to bites.

Treatment of acute dengue is supportive, using either oral or intravenous rehydration for mild or moderate diseases, and intravenous fluids and blood transfusion for more severe cases. The number of dengue fever increased dramatically since 1960s, with between 50 and 528 million people infected yearly. Dengue has become a global problem since the Second World War. Work is ongoing on a vaccine, as well as medication targeted directly at the virus.

Signs and symptoms

People infected with dengue virus are asymptomatic (80%) or only have mild symptoms. Others have severe illness (5%) and in a small proportion it is life threatening. The incubation period ranges from 3 to 14 days, but most often it is 4 to 7 days. Children often experience similar to common cold, vomiting and diarrhea. Dengue can affect several other body systems as brain and liver. Neurological disorders, infection of heart, acute liver failure are other complications.

Cause

Dengue fever virus is an RNA virus. Members of the same genus include yellow fever virus, West Nile virus, Japanese encephalitis virus, Omsk hemorrhagic fever virus etc. Most are transmitted by arthropods and referred to as arboviruses.

This fever is transmitted by the mosquito *Aedes aegypti* feeding on a human host. They typically bite during the day, particularly in the early morning and in the evening. It also circulates in non-human primates. A female mosquito that takes a blood meal from a person infected with dengue fever, during the initial 2-10 day febrile period, becomes itself infected with the virus in the cells lining its gut. About 8-10 days later, the virus spreads to other tissues including the mosquito's salivary genes and is subsequently released into its saliva. The virus has no detrimental effect on the mosquito, which remains infected for life. Dengue can also be transmitted via infected blood products and through organ donation.

Mechanism

When a mosquito carrying dengue virus bites a person the virus enters the skin together with the mosquito's saliva. It binds to and enters WBC and reproduces inside the cells while they move throughout the body. The WBC responds by producing a number of signaling proteins, such as cytokines and interferons which are responsible for many symptoms and the pains. During infection, fluid from the blood stream leaks through the wall of small blood vessels into the body cavities due to

* Retired Scientist, Indian Institute of Chemical Biology, Kolkata, Phone: 2668 5540

capillary permeability. As a result less blood circulates in the blood vessels, blood pressure becomes low, and it cannot supply blood to vital organs. Dysfunction of the bone marrow due to infection of the stromal cells leads to reduced numbers of platelets, which are effective for blood clotting; this increases the risk of bleeding, the other major complication of dengue fever. The initial reaction of infected cells is to produce cytokine and interferon, that raises a number of defenses against viral infection through the innate immune system by augmenting the production of a large group of proteins mediated by the JAK-STAT pathway. Some serotypes of dengue virus appear to have mechanisms to slow down this process. Interferon also activates the adaptive immune system, which leads to the generation of antibodies against the virus as well as T-cells that directly attack any cell infected with the virus. Various antibodies are generated; some binds closely to the viral proteins and target them for phagocytosis but some bind the virus lasses well and it is not destroyed but is able to replicate further.

Diagnosis

Warning signs

- Worsening abdominal pain
- Ongoing vomiting
- Liver enlargement
- Mucosal bleeding
- High hematocrit value with low platelets
- Lethargy or restlessness

The diagnosis of dengue fever is made clinically on the basis of reported symptoms and physical examination. A probable diagnosis is based on the findings of fever plus two of the followings:

Nausea and vomiting, rash, generalized pains, low WBC count, positive tourniquet test or any warning sign in someone who lives in an endemic area. The diagnosis should be considered in anyone who develops a fever within two weeks of being in the topics or subtropics. It can be difficult to distinguish dengue fever and chikunguniya, a similar viral infection that shares many symptoms and occurs in similar parts of the world to dengue. The earliest change detectable on laboratory investigations is a low WBC count, followed by low platelets and metabolic acidosis. A moderately elevated level of aminotransferase from the liver. In severe condition plasma leakage causes hemoconcentration and hypoalbuminemia. Dengue shock syndrome is present if pulse pressure drops to ≤20 mm Hg along with peripheral vascular collapse.

The World Health Organization's 2009 classification divides dengue fever into two groups: uncomplicated and severe. The 1997 classification divided dengue into undifferentiated fever, dengue fever and dengue hemorrhagic fever which again was subdivided into grades I – IV.

Prevention

The primary method of controlling *A.aegypti* is by eliminating its habitats. This is done by getting rid of open sources of water, or by adding insecticides or biological control agents to these areas. Spraying with organophosphates or pyrethroid insecticides is not thought to be effective. People can prevent mosquito bites by wearing clothing that fully covers the skin, using mosquito netting while resting and/or the application of insect repellent. The range of the disease appears to be expanding possibly due to climate change.

Management

There are no specific antiviral drugs for dengue, however maintaining proper fluid balance is important. Treatments depend upon symptoms. Those who are able to drink, are passing urine, have no "warning signs" and are otherwise healthy can be managed at home with daily follow-up and oral rehydration therapy. Those who have other health problems have "warning signs" or who cannot manage regular follow up should be cared for in hospital. Intravenous hydration, if required, is typically only needed for one or two days. Invasive procedures such as nasogastric incubation, intramuscular injections and arterial punctures are avoided in view of the bleeding risk. Paracetamol is used for fever and discomfort while NSAIDs, such as ibuprofen and aspirin are avoided. Packed red blood cells or white blood are recommended, while platelets and fresh frozen plasma are usually not. During the recovery phase intravenous fluids are discontinued to prevent a state of "fluid overload". If a person is outside of critical phase furosemide may be used to eliminate excess fluid from the circulation.

Rates of dengue increased 30 fold between 1960 and 2010. This increase is believed to be due to a combination of urbanization, population growth, increased international travel and global warming. The World Health Organization counts dengue as one of the 17 neglected tropical diseases. The rate can be decreased by the inhibition of viral RNA-dependent RNA-polymerase. It is possible to develop entry inhibitors which stop the virus entering cells, or inhibitors of the 5′-capping process, which is required for viral replication.

Jharna Bhattacharyya*

Tomography for the Reactors in Japan

Anil Kumar Ghosh

The reactor accident of Fukushima Daiichi completes four years on the 11th March 2015. The improvements in the reactor compound are tiresome so to say Japan deals with the challenge technologically.

The operation at the damaged nuclear powerplant of Fukushima Daiichi will continue till the middle of this century. The cost estimate lies near about 75 milliard Euro. None can definitely say whether time and money would suffice. The factory association Tepco adheres to part by part success. Till the end of the last year, minimally all 1533 fuel elements from the storage bowl of Block 4 have been successfully salvaged.

This is the beginning, Principal challenge remains whether to get information at all as to how it appears in the cores of the reactors of the blocks 1 to 3. Because it is not possibly to make the robot pictures out of the inner parts as available in other building areas. Electronics refuse partly for the reason of high radiation intensity, the invasive techniques salvage the risk of further liberation of radioactivity.

In the project "Benchmark study of the Accident at the Fukushima Daiichi NPS" the worldwide famous technical organizations, in which the Association for Reactor Safety in Cologne (GRS) have been taken into account as to what must have occurred in the cores of reactors. The onsets of this model are different, they do not always come to the same result but so to say they are consistent. In all the three blocks it has come to high core damage and the damage of the reactor pressure vessel. How big are the destructions, how much hydrogen is generated along with the models are not in agreement, how the GRS writes in their monthly beginning up-to-date report on Fukushima. In blocks 1 & 3 the nuclear fuel rods presumably molten through the damage of the reactor pressure vessel, the molten mass is placed in the concrete safety container. The experts want to feed the simulations with new available information in future in order to get always an exact picture out of the core of the reactor. A project of Tepco also serves together with the Los Alamos National Laboratory of USA. A detector for myonentomography should help in order to exactly localize the quantity of core burning rods.

The technique makes contact with homonymous elementary particulate which are omnipresent as the component of the cosmic high radiation. With the going through of material myons are scattered, the heavier the atomic nucleus the stronger is the scattering. To that two detectors are brought at the outer wall of the reactor building. These are, however also in the areas which are charged with high radiation. The solution for that must now be developed.

For 2016/2017 Tepco has planned the investigations under the reactor pressure vessels of Block 2. The blocks 1 to 3, the Block No. 2 is damaged the least as per model calculation. Here, Tepco certainly wants invasive trial to inspect the regulating rods below the reactor pressure vessel with the help of a robot and camera.