

Yellow Fever

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Yellow fever is a serious viral infection that has gained the name of “yellow plague” or “American Plague” in relation to previous epidemics in the country. I would like to bring some light over this disease especially because we are planning as an organization (AMHE) to sojourn in Tropical African land for almost two weeks, areas infested with mosquitoes..

This is a disease caused by a virus but most people infected with it, do not get sick or may have only mild symptoms. People who do get sick may start with symptoms like fever, chills, headache, backache, and muscle aches, 3–6 days after being infected.

Yellow Fever is a disease of short duration and symptoms may vary from fever and chills to loss of appetite, nausea and myalgia especially in the muscles group of the back, often with headaches improving within five days. 15% of individuals experience back and abdominal pain, liver damage and jaundice with possible vascular or renal complications.

The yellow fever virus is spread through the bite of an infected mosquito affecting humans or other primates. It may be difficult to differentiate it from other viral diseases especially at the early stages. The mosquitoes *Aedes Aegypti*, encountered in the tropics and subtropics are the vector. The virus is an RNA virus (Flavivirus). Any suspected cases require blood samples with a polymerase reaction.

There is a safe and effective vaccine against Yellow Fever which is required for travelers reaching countries where the disease is endemic or epidemic. Recommendation to reduce the population of mosquitoes are often suggested when travelling in these countries. Preventive immunization of the population is also recommended. Once infected,

one should be managed symptomatically. In severe disease, death may be encountered in 50% of the cases.

Severe infections and an estimated 80,000 death were seen in Africa in early 2013 and around 200,000 persons suffered from the virus. The numbers of victims have increased recently and it is believed that the populations are taking their prophylaxis while more people are migrating to urban areas. The disease is seen in Africa but not seen in Asia while fewer people are becoming immune. Yellow Fever may have originated in Africa but it expanded as well in the Americas. The mosquitoes also have changed their habitat especially with the movement of the population seen during the period of slavery. Outbreaks have been seen in the Americas and in Europe during the 18th and 19th centuries.

The incubation period is of short duration, generally less than 6 days and symptoms like fever, headaches, chills, back pain, loss of appetite with nausea and vomiting are striking. A recurrence of fever with jaundice may suggest liver damage especially when abdominal pain and vomiting tainted with blood (vomito negro or black vomit) are present in (15% of the cases), bleeding through the mouth, eyes etc. Left untreated, the patient will develop kidney failure, hiccup and delirium. In such cases, there is a higher mortality rate which may reach 50%. Anybody infected with yellow fever virus will carry a lifelong immunity. Others may develop seizures and internal bleeding.

Yellow Fever is the first illness shown to be transmissible by filtered human serum, although we knew already that mosquitoes were able to transmit it as well (Walter Reed 1900). Once the virus enters the host cell, the genome is replicated and form an immature form prior to become more complex with a certain protein E. One has also to remember that the virus is transmitted only by the female *Aedes aegypti* mosquitoes because this is only the females which bite and can transmit the disease. They get the virus in sucking the blood of an infected person or another primate. The virus reached their stomach and the epithelial cells to replicate.

Further reaching the blood cells. It can easily reside in the salivary glands of the mosquitoes to be transmitted to the one who get bitten through the saliva. It is the way it believed the disease is transmitted during the urban cycle. The mosquito may become adapted to the urban area and can also transmit other diseases like the Zika fever, Dengue fever, or Chikungunya fever. In South America or in Africa, there is a "sylvatic cycle" also called "forest or jungle cycle" in which the mosquito "Aedes Africanus" is the vector in Africa and the "Aedes Haemagogus (Sabethes)", the vector in South America. The disease remains mainly asymptomatic in African primates but people who become in contact with such animal can become infected or may carry the disease in the urban areas. A third infectious cycle does exist in Africa: The "Savannah cycle" which represent an intermediate cycle between the urban and the jungle cycles.

Once a human becomes infected, the virus replicates in the lymph nodes and infects the dendritic cells to reach the liver (hepatocytes) initiating an eosinophilic degradation of the hepatocytes notably with the release of cytokines while "apoptotic masses (Councilman bodies) can be seen in the cytoplasm. Fatality may follow in a cytokine storm to induce shock and multiple organ failure.

To diagnose Yellow Fever, often a travel history is necessary to asset a clinical diagnosis based on a simple symptomatology like: Fever and muscle pain (back), nausea and vomiting for more than a week. Mild cases can be confirmed virologically around a week following the onset of the illness especially if they coincide with a regional outbreak. Direct confirmation can be obtained by "reverse transcription polymerase chain" but will take between 1 and 4 weeks. Serologically, an enzyme -lined immunosorbent assay is available using IgM or IgG (4-fold-increase) titers. Those tests may react with other viruses like dengue virus.

Liver biopsy has been used to verify inflammatory process within the hepatocytes and also can detect the viral antigens. Nowadays, the biopsy is more often done in the post-mortem period to confirm the

cause of death. Remember that other diseases with similar symptoms need also to be differentiated from other mosquito transmitted diseases like Malaria or other viral hemorrhagic fevers seen with Ebola and Lassa viruses (Africa), Junín virus (Argentina), Marburg virus (Equatorial Guinea) etc.

To prevent contraction of Yellow Fever disease, it is important to avoid mosquito bites in areas where the disease is endemic. The best prevention measure rests on a vaccination program. Insect repellents (with DEET, Picaridin, oil of lemon eucalyptus) on exposed skin is also recommended when outdoors. Use of long pants and long sleeves clotting with socks can help also in the prevention. Programs applying larvicides to water storage containers has also helped in controlling the mosquitos' population through the breeding sites while insecticide sprays have helped in controlling the transmission of the Yellow Fever disease.

Vaccination is recommended when travelling to affected areas and it will be effective after the 10th day of the vaccination. A single dose is sufficient to confer lifetime immunity according to the World Health Care Organization (WHO) but people living in the affected area are recommended to be vaccinated during the first year of life. The vaccine is safe but rare cases (1/300,000) of viscerotropic disease can be seen, unfortunately can also be fatal. Finally, rare cases of fatal meningoencephalitis can be seen in 5%.

No cure is known for Yellow Fever disease. Hospitalization is recommended in some cases because of a rapid deterioration can be observed. Antiviral drugs, Interferons have been used with little success. Rehydration and symptomatic treatment with Aspirin or anti-inflammatory medication need too be avoided because of gastrointestinal bleeding. It is a common tropical disease in Africa (Central and East Africa) and South America where more than 600 million people live in endemic area and

200,000 will be affected yearly by the disease but unfortunately half of those will die of complications.

Researchers have found that an early administration of Ribavirin may be an effective treatment during the first 5 days of the disease in the hamster model and was found to improve the survival rate and reduce tissue damage in the liver and the spleen. It also prevented hepatocellular steatosis in normalizing the level of “Alanine aminotransferase” which is a liver damage marker, similarly seen in the treatment of Hepatitis C disease. Unfortunately, the Ribavirin has failed to improve the survival rate in a virulent rhesus model of Yellow Fever. Fortunately, there are other promising researches in many countries. One has to remember that the virus of Yellow Fever is still considered in many countries as a potential biological weapon like in the United States.

On my return from Benin-Togo and Ghana, I wanted to indulge myself to find a way to discuss such disease after almost 300 of us took in hand our courage and determination to visit the land which may have been the place of birth of the grand-Father of our ancestor General Toussaint Breda Louverture. We all were a target for those mosquitoes. We needed to be aware of the signs and symptoms of such disease.

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