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Reveiw Article

A REVIEW ON YELLOW FEVER

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Abstract

Yellow fever is one of the viral hemorrhagic fevers widely spreading in the major parts of Africa, American, and Europe continents. Yellow fever is the most dangerous disease because it is responsible for lakhs of death of people approximately more than 2,00,000 annually. Aedes mosquitoes acts as a vector for rapid transmission of yellow fever as it carries yellow fever virus and injected into host for replication of virus. Severe symptoms noticed in patients who are suffering from yellow fever includes severe headache, high fever, low pulse, jaundice, hematemesis, chills, and hepatic necrosis. The infection of yellow fever virus occurs in two forms i.e urban cycle and sylvatic cycle. Unlike zika and other viruses yellow fever virus having an advantage effective vaccination is available for it. Vaccination acts very effectively in reducing the mortality rate upto 85%. Vaccine provides life long immunity against the yellow fever virus and even booster dose is not needed for it. Vaccination provided compulsory to the people who are travelling from epidemic areas to other countries. There is no risk of yellow fever in asia but recently china imported 6 cases of yellow fever accidentally. India is one of the most favourable place for rapid transmission of yellow fever because aedes aegypti mosquitoes responsible for wide spread of disease is much more in abundance. But till now none of the cases with yellow fever is reported in india. In future if yellow fever unfortunately enters india it destroys the huge population within short period of time before vaccine stocks are delivered.

Key Words: Yellow fever, zika virus, Aedes Aegypti Mosquito, Vaccines

1. Introduction:

Hemorrhagic fevers are mainly characterized by severe illness linked with bleeding abnormalities. These fevers are mainly caused by virus or bacteria. Yellow fever is one of the oldest acute viral hemorrhagic fever because it is caused by enveloped single stranded RNA virus called yellow fever virus. It is belonging to the family flaviviridae. Dengue virus is also belongs to this family only [1]. Majorily three surface proteins is present on virion surface where enveloped protein acts as important one. This protein is mainly responsible for decreasing red blood cell clotting which in turn leads to severe bleeding abnormalities.

Yellow fever virus is the native of Africa but the incidence of yellow fever in America and Europe is carried by slave traders travelling through the trade routes. The species of aedes mosquitoes acts as carriers or vectors for yellow fever virus . Urban yellow fever is mainly transmitted by aedes aegypti mosquito. The abundance of these mosquitoes is more in tropical and sub tropical countries [2].

Yellow fever is an acute, febrile, mosquito transmitted illness. It is mainly featured by high fever, chills, severe headache, slow heart rate (Bradycardia), hematemesis (black vomit of blood), jaundice, hepatic and renal necrosis etc., The yellow fever is so called because the main symptom appears after the yellow fever virus infection is yellow colouration of eyes and skin [3]. Jaundice and yellow fever are not similar to each other. But jaundice acts as symptom of yellow fever.

Epidemiology: During the past 15 years yellow fever reported cases increasing abnormally and the most epidemic regions of fever are found to be Africa, America (south and central) and Europe [4]. In Africa almost 44 countries are Affected with yellow fever where as in central and south America only 13 countries. High rate of morbidity and mor-

tality is recorded in Africa when compared to other epidemic areas. Maximum rate of yellow fever infection occurs only in sub tropical and tropical areas. About 90% of infection is mainly occurs only in Africa when compared to America and Europe. Only limited areas in Europe are severely affected with yellow fever [5]. According to world health organisation (WHO) the data collected during 2013 represents that about 2,00,000 cases are affected with yellow fever including 30,000 death per annum . Based on severity of symptoms only 15% of people suffering from illness and multi organ dysfunction, almost 50% of yellow fever cases are deaths only. Most of the people died within 10 days of infection. One of the survey which is done on epidemics recently show the amazing fact that yellow fever affects mostly the children below 15 years of age.

Figure: 1 Countries with Risk of Yellow fever virus transmission

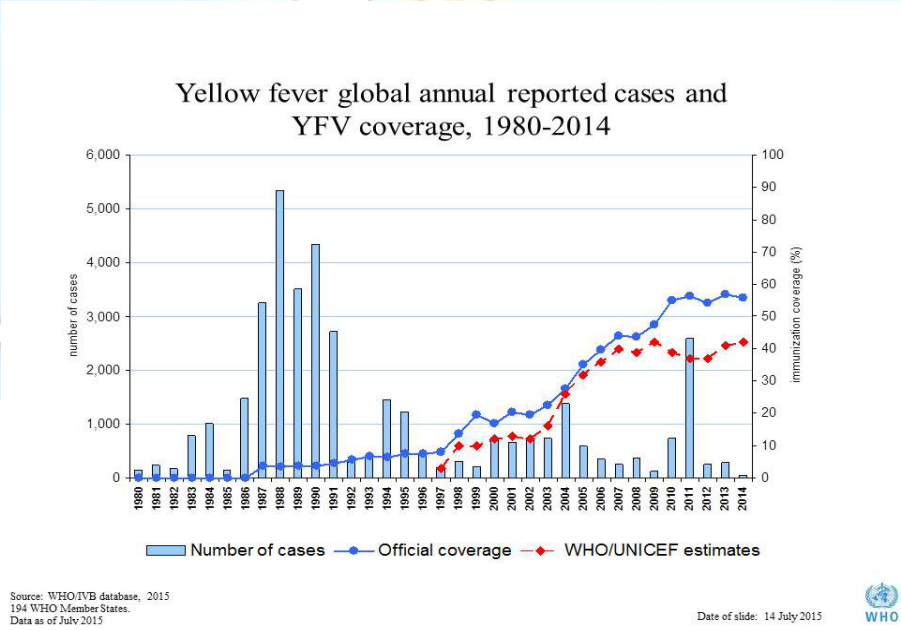

Figure: 2Yellow fever global annual Report cases in 1980-2014

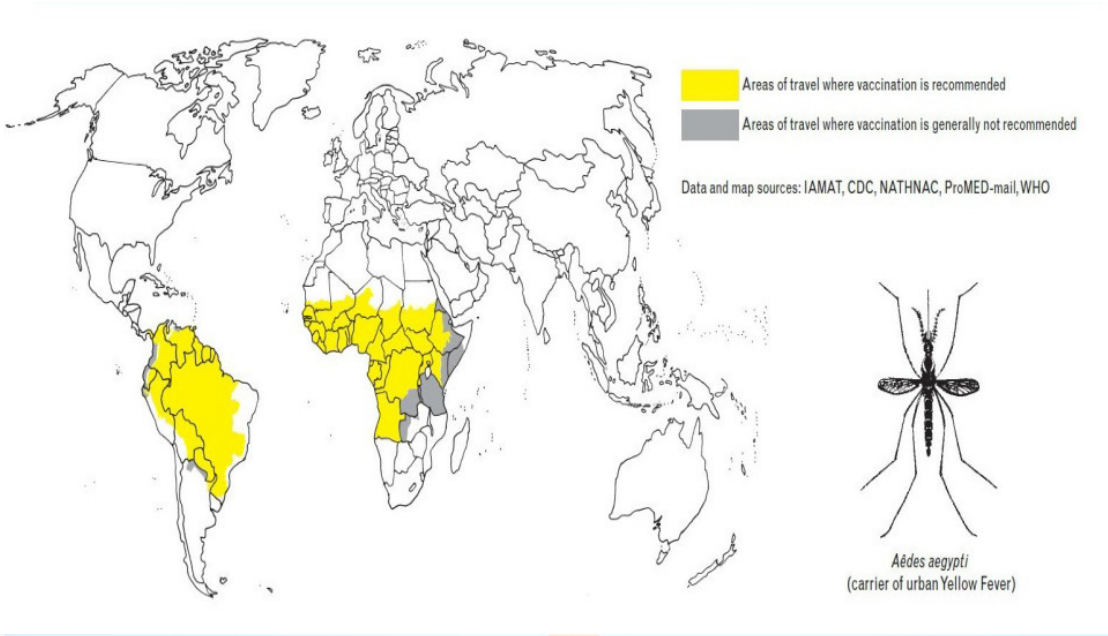

Figure: 3 Aedes aegypti mosquitoes Transmitted in various places

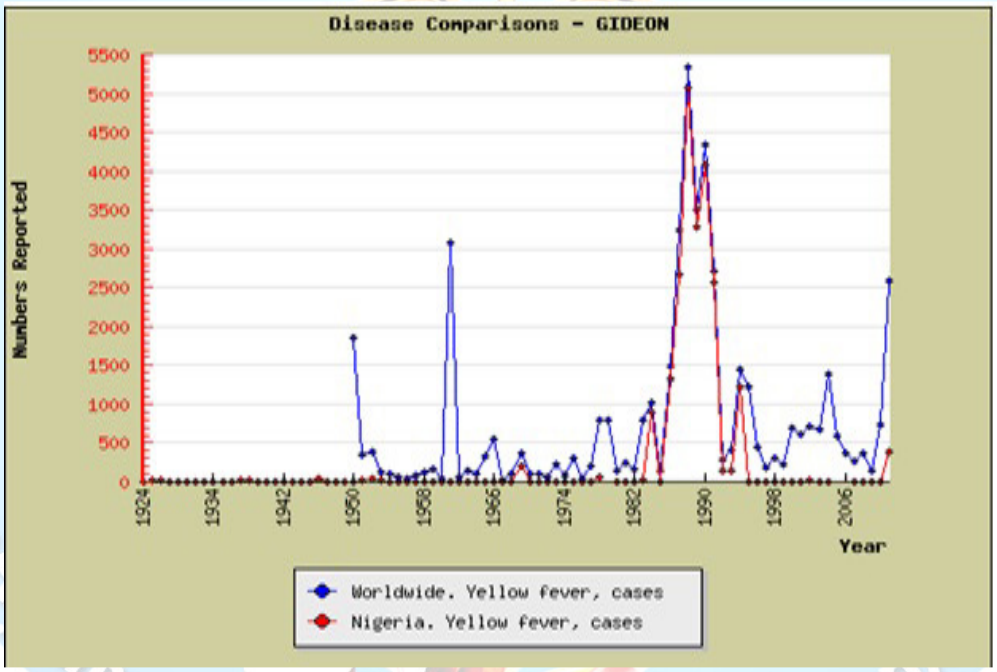

Figure: 4 Yellow fever cases in world wide

Casuative organism: The microorganism that is responsible for occurance of yellow fever is yellow fever virus. This virus is belonging to the family flaviviridae [6]. It is an enveloped single stranded RNA virus consists of surface proteins on the outer coating of virus.

Infection: Urban cycle and sylvatic cycle are 2 forms of infection of yellow fever virus. In urban cycle the aedes aegypti mosquito acts as a carrier and human beings are a host. In sylvatic cycle wild monkeys acts as host and various species of haemagogus (H.spegazzinii) in south America and aedes Africans in Africa acts as carriers [7].

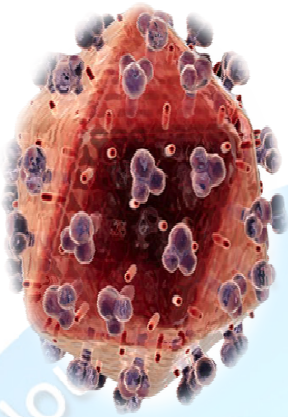

Figure: 5 Yellow Fever Virus

Urban cycle: This cycle involves the transmission of yellow fever virus from one person to person by aedes aegypti mosquitoes [8]. Most of the infected persons with yellow fever are involved in this cycle for transmission. Urban population are predominantly affected by this cycle.

Sylvatic cycle: The other name of sylvatic cycle is jungle cycle or forest cycle. In this cycle the transmission of virus occurs between non human primates(monkeys) by mosquitoes like aedes Africans etc., The mosquitoes which acts as carriers if bite the humans it acts as link between sylvatic and urban cycle [9].

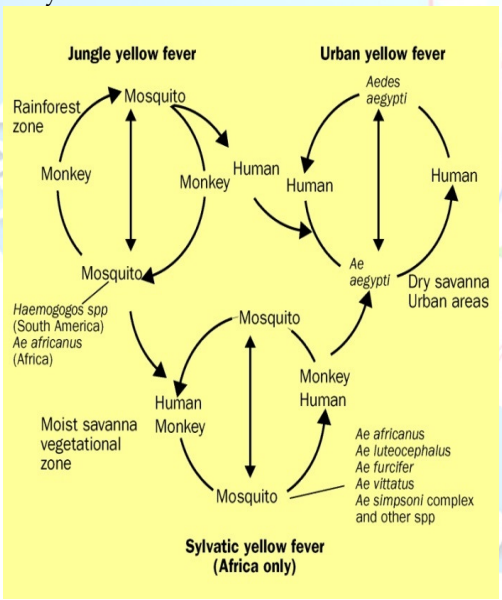

Figure: 6 Cycle of Jungle & Urban Yellow fever Carriers:

The mortality rate of yellow fever has been tremendously increasing day by day. Main reason behind this is the abundance availability of vectors in tropical and sub tropical areas in the world. The vector which mainly takes part in the yellow fever is aedes species. Major one is the aedes aegypti which transmit not only the yellow fever virus, but also the dengue and chikungunya virus too. The other mosquitoes like aedes Africans, aedes simpsoni, aedes furcifer, aedes luteocephalus, aedes albopictus are also involved in spreding of the yellow fever [10].

AEDES AEGYPTI :

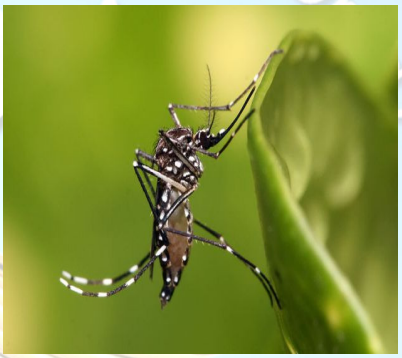

Figure: 7 Aedes Aegypti Mosquito

Morphological characters: It is a dark coloured mosquito which is very small in their size. The characteristic features of the mosquito is white markings on the surface of body [11]. These mosquitoes consists of the banded legs which are useful in holding the skin surface during time of biting.

Life cycle: Aedes aegypti are the adult female mosquitoes. Life span of these mosquitoes ranges from 2 weeks to 1 month. It does not travels much distance during its life time [12]. These mosquitoes lays eggs only in the standing water that means rain water is present in tree holes for long period, water remaining in pots, containers, in drainage water etc,. In its life span it lays atleast 4-5 batches of eggs. Each batch contains atleast 100-200 eggs. within 2-3 days after laying, it hatches the eggs. The larva coming from the eggs lives 4 days on water materials only. After 4 days it enters into the pupal stage then it starts flying.

What is the need for mosquito to bite: The aedes aegypti are female mosquitoes bites the human beings because blood is very essential for them to lay their eggs. Blood acts as a protein source. They

only lay eggs after a meal of blood whereas the male mosquitoes feeds only on plant juices [13].

Time of transmission: The most favourable time for aedes aegypti mosquitoes to bite the human beings for rapid transmission of yellow fever virus are at early morning during 4:0 0-5:00 AM.

Factors influencing mosquito to bite: Mosquitoes of aedes species are attracted towards the people by considering co_2 levels. The yellow fever transmissed mosquitoes also bite the humans based on their clothing colours. Light colour clothes wearing people are more prone to yellow fever virus infection [14]. The skin colour is also an important factor more number (90%) of infections occurs only in africa compared to america and europe

Risk factors: People travelling to epidemic areas like Africa, Europe, and America, Lack of vaccination.

People prone to yellow fever infection: Elderly people are more prone to yellow fever infection, People having thymus disorder, HIV/AIDS patients are more susceptible to yellow fever infection, Childrens below age of 15 years [15].

Clinical manifestations: High fever, chills, severe headache, vomiting(black vomit), red eyes ,nausea, abdominal pain, backache, hepatomeagly, jaundice, bleeding from nose, and ears, loss of appetite, muscle aches, delirium, seizures, arrhythmias, decreased urine output, bleeding abnormalities, dysfunction of brain and kidneys, hepatic necrosis, coma and finally death [16].

Pathogenesis: When the infected aedes aegypti mosquito feeds on human beings from its saliva it transmits the virus and hence it acts as carrier. The mosquito injects the virus into the body of the host by process of endocytosis which is receptor mediated [17]. Once the virus enters into the body it remains in the dormant stage it primarily affects the lymph nodes. The virus starts synthesizing the proteins by using its m-RNA in endoplasmic reticulum and further replication takes place in cytoplasm. After the replication it spreads to other parts of the body which includes the kidneys, bone marrow, myocardium. The dentritic cells and hepatic cells are severely affected by the yellow fever virus [18]. If the infection is severe it leads to liver necrosis which in turn results in sudden decrease of erythrocyte count. Necrotic cells are attached to each other and undergoes hyalinisation changes forms the councilman bodies(mass of eosinophilic cells). More toxicity of virus results in multi organ dysfunctioning and finally leads to death of the patient.

Diagnosis: Firstly, the diagnosis of yellow fever is done on the basis of signs and symptoms, history itself [19]. The other laboratory tests are also available to identify the infection of yellow fever virus. These includes the following :

1. Blood test – To check the count of white blood cells(neutrophils), thrombocytes. By this test we also found yellow fever virus in early stages of infection.
2. Urine analysis – To measure albumin levels because yellow fever virus infection leads to albuminuria . In severe cases the albumin levels raises upto 20 gm/l
3. ELISA test –To find out antigen responsible for infection. This test is done by introducing suitable IgM or IgG antibodies.
4. PCR – To find out the genome of virus.
5. Liver biopsy – To find out any increase in size of liver due to inflammation, deaths of hepatic
6. Autopsy – To find out the cause for death it is usually performed after the death.

Prevention: Control the mosquito population by using the mosquito nets, mosquito repellants. Fuming of sulphur is one of the best preventive measure to kill the mosquitoes. Vaccination is the another method to avoid the infection of yellow fever virus. The death rate is tremendously decreased upto 85% because of these effective vaccination only [20]. Maintaining the surrounding environment more hygenic. Avoid travelling to those areas which are major epidemics of yellow fever infection.

Treatment: There is no antiviral drug available which acts against the yellow fever virus. Only one vaccine is available for effective treatment of yellow fever virus infection [21]. The yellow fever vaccine is called as 17 D strain. It is a live attenuated vaccine developed in the year 1937. It is admini-

strated to the people living in sub tropical and tropical areas and to the travelers moving to the epidemic areas.

Yellow fever vaccine: It is prepared by incubating the chicken eggs upto 7-8 days and using the strain of yellow fever virus embryos are injected that are not virulent to the human beings [22]. Again embryos are incubated atleast 3-4 days then grounded and extracted with distilled water. The viscous fluid which is obtained is centrifuged. Two layers are formed the top one is clear fluid and heavier components settled at the bottom. Clear fluid collected is kept in refridgerator and then dried .Then it is sealed in well closed containers before sealing nitrogen is filled in those containers.

Figure: 8 Marketed Available Stamaril Vaccine for Yellow Fever

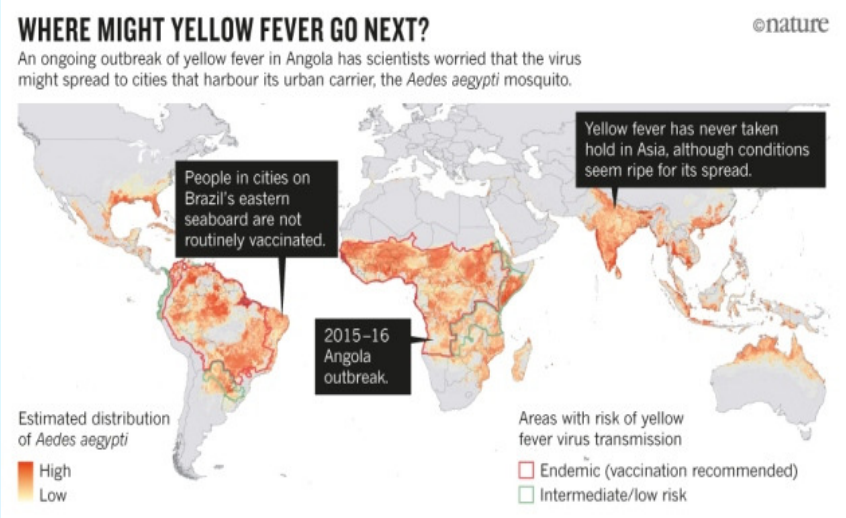

Figure: 9 Yellow fever Might be goes next

Is there is any risk of yellow fever in asia: Until now there is none of the cases reported with yellow fever in asia. Because the effective vaccination is provided to the people who are going to the epidemic areas. vaccination gives life long immunity against the yellow fever and hence there is no imported cases of yellow fever in asia. But we cannot say that there is no risk of yellow fever in asia eventhough the government doing appreciable work in avoiding incidence of these haemorrhagic fever recently in china 6 cases of yellow fever are reported [23]. If yellow fever enters with high severity then it easily spread all over the asia within a few weeks. Large number of people died in a short period before vaccines are delivered.

Favourable factors for yellow fever transmission in india [24] :

1. Environmental conditions : In india the most favourable conditions of environment are available for survival of yellow fever virus .
2. Mosquitoes : Aedes aegypti mosquitoes which are mainly involved in the transmission of yellow fever virus are abundantly available in india.
3. Monkeys : Macucula species of monkeys are present in high numbers in india. These monkeys are more prone to yellow fever virus infection compared to other species. These infected monkeys are futher involved in rapid spread of the fever.

Conclusion: Finally i concluded that yellow fever virus is mainly affected in countries like Africa but the incidence of yellow fever in America and Europe is carried by slave traders travelling through the trade routes. About 90% of peoples affected these infection is mainly occurs in Africa when compared to America and Europe. The microorganism that is responsible for occurance of yellow fever. In this cycle the transmission of virus occurs mainly between the non human primates (monkeys) by mosquitoes like aedes Africans. Major one is the aedes aegypti which transmit not only the yellow fever virus, but also the dengue and chikungunya virus . The yellow ferver diagnosis done by blood test, urine analysis, ELISA test, Liver biopsy, Autopsy test. Vaccination is the another method to avoid the infection of yellow fever virus.

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References:

1. V. T. K. Chow, Y. C. Chan, R. Yong, "Monitoring of dengue viruses in field-caught Aedes aegypti and Aedes albopictus mosquitoes by a type-specific polymerase chain reaction and cycle sequencing," American Journal of Tropical Medicine and Hygiene, vol. 58, no. 5, pp. 578–586, 1998.
2. J. J. Spielvogel, Exploration and Expansion Glencoe World History, Glencoe/McGraw-Hil, New York, NY, USA, 2005.
3. J. G. B. Derraik, "A scenario for invasion and dispersal of Aedes albopictus (Diptera: Culicidae) in New Zealand," Journal of Medical Entomology,vol.43,no.1,pp.1–8,2006.
4. W. B. Messer, U. T. Vitarana, K. Sivananthan et al., "Epidemiology of dengue in Sri lanka before and after the emergence of epidemic dengue hemorrhagic fever," American Journal of Tropical Medicine and Hygiene,vol.66,no.6,pp.765–773,2002.
5. C. C. Tam, H. Tissera, A. M. de Silva et al., "Estimates of dengue force of infection in children in Colombo, Sri Lanka," PLOS Neglected Tropical Diseases, vol. 7, Article ID e2259, 2013.
6. M. Kurukumbi, J. P. Wali, S. Broor et al., "Seroepidemiology and active surveillance of dengue fever/dengue haemorrhagic fever in Delhi," Indian Journal of Medical Sciences, vol.55, no.3, pp. 149-156, 2001.
7. M. Theiler and C. R. Anderson, "The relative resistance of dengue immune monkeys to yellow fever virus," American Journal of Tropical Medicine and Hygiene, vol.24, no.1, pp.115-117, 1975.
8. R. O. Izurieta, M. Macaluso, D. M. Watts et al., "Anamnestic immune response to dengue and decreased severity of yellow fever," Journal of Global Infectious Diseases, vol.1, no.2, pp.111-16, 2009.
9. M. Wallbridge and W. G. Downs, "The communicability of yellow fever," Annals of Internal Medicine,vol.3,pp.7–18,1891.
10. A.Amarasinghe, J. N. Kuritsky, G. William Letson, and H. S. Margolis, "Dengue virus infection in Africa," Emerging Infectious Diseases, vol. 17, no. 8, pp. 1349–1354, 2011.
11. B. R. Miller, T. P. Monath, W. J. Tabachnick, and V. I. Ezike, "Epidemic yellow fever caused by an incompetent mosquito vector," Tropical Medicine and Parasitology, vol.40, no.4, pp. 396-399, 1989.
12. T. Mashimo, D. Simon-Chazottes, and J.-L. Guenet, "Innate resistance to flavivirus infections and the functions of 2 oligoadenylate synthetases," Current Topics in Microbiology and Immunology, vol.321, pp.85-100,2008.
13. W. C. Black IV, K. E. Bennett et al., "Flavivirus susceptibility in Aedes aegypti," Archives of Medical Research, vol.33, pp.379-388, 2002.
14. A. Sall, O. Faye, M. Diallo, C. Firth, A. Kitchen, and E. C. Holmes, "Yellow fever virus exhibits

slower evolutionary dynamics than dengue virus," Journal of Virology,vol.84,no. 2, pp. 765–772, 2010.

15. A.-B. Failloux, M. Vazeille-Falcoz, L. Mousson, and F. Rodhain, "Genetic control of vectorial competence in Aedes mosquitoes," Bulletin de la Societe de Pathologie Exotique, vol.92, no.4, pp. 266-273, 1999.
16. Mutebi JP, Wang H, Li L, Phylogenetic and evolutionary relationships among yellow fever virus isolates in Africa. J Virol 2001; 75:6999.
17. Vasconcelos PF, Bryant JE, da Rosa TP, Genetic divergence and dispersal of yellow fever virus, Brazil. Emerg Infect Dis 2004; 10:1578.
18. Dennis LH, Reisberg BE, Crosbie J, The original haemorrhagic fever: yellow fever. Br J Haematol 1969; 17:455.
19. Tigertt WD, Berge TO, Gochenour WS, Experimental yellow fever. Trans N Y Acad Sci 1960; 22:323.
20. Monath TP, Brinker KR, Chandler FW, Pathophysiologic correlations in a rhesus monkey model of yellow fever with special observations on the acute necrosis of B cell areas of lymphoid tissues. Am J Trop Med Hyg 1981; 30:431.
21. Quaresma JA, Barros VL, Fernandes ER, Reconsideration of histopathology and ultrastructural aspects of the human liver in yellow fever. Acta Trop 2005; 94:116.
22. Bae HG, Drosten C, Emmerich P, Analysis of two imported cases of yellow fever infection from Ivory Coast and The Gambia to Germany and Belgium. J Clin Virol 2005; 33:274.
23. Quaresma JA, Barros VL, Pagliari C, Revisiting the liver in human yellow fever: virus-induced apoptosis in hepatocytes associated with TGF-beta, TNF-alpha and NK cells activity. Virology 2006; 345:22.
24. Quaresma JA, Barros VL, Fernandes ER, Immunohistochemical examination of the role of Fas ligand and lymphocytes in the pathogenesis of human liver yellow fever. Virus Res 2006; 116:91.