

## **Blood Feeding Insect Series: Yellow Fever<sup>1</sup>**

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### **History of Yellow Fever**

Yellow fever is among the most feared of human diseases. It was one of the most devastating and important diseases in Africa and the Americas in the 17-20<sup>th</sup> centuries with periodic outbreaks of yellow fever that involved thousands of human cases. New Orleans experienced the last major yellow fever epidemic in the United States in 1905 with about 4000 human cases and 500 deaths.

Yellow fever virus is transmitted to humans through the bite of infected mosquitoes. Epidemics of yellow fever during the past 300 years show why this disease inspired dread and fear. The numbers of deaths during outbreaks are startling: 6,000 dead in Barbados in 1647; 3,500 deaths in Philadelphia in 1793; 1,500 in New York City in 1798; 29,000 deaths in Haiti in 1802; and 20,000 deaths in over 100 American towns in 1878.

It was not until 1901 that yellow fever transmission to humans was associated with the blood-feeding by the *Aedes aegypti* mosquito. The larval habitat for this species is primarily containers such as barrels, buckets, cisterns, and vases. Eliminating the larval habitat was instrumental in

controlling yellow fever. This was accomplished by either removing the container, or modifying containers by covering the openings with screen, for example, to prevent female mosquitoes from laying eggs in the water container. During the 20<sup>th</sup> century yellow fever has re-emerged as a cause of human suffering. Recent epidemics include 100,000 cases and 30,000 deaths in Ethiopia in 1960-62; 17,500 cases with 1,700 deaths in Upper Volta in 1983; and Cameroon had 20,000 cases with 1,000 deaths in 1990. The World Health Organization officially reported 18,735 yellow fever cases with 4,522 deaths for the period 1987 – 1991.

### **What is Yellow Fever?**

#### **The Disease**

Yellow fever is particularly feared due to the disturbing nature of its symptoms. Symptoms may range from clinically inapparent to fatal. In some regions of Latin America as much as 90% of the population have been infected with the yellow fever virus but show no clinical symptoms.

After being bitten by an infected mosquito, the incubation period in infected humans is generally 3-6 days. The onset of the disease is very sudden and

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devastating to the patient. There is high fever (102° – 104° F), headache, malaise, back pain, chills, prostration, nausea, slow pulse and vomiting. The virus can be found in the blood of the patient for about 4 days following the bite of the mosquito, and during this period the patient is capable of infecting more mosquitoes. Some individuals show a rapid recovery at this point and the symptoms stop. This phase can last from 3-4 days.

Severe yellow fever cases also have symptoms that can subside but then return in a day or so. This is the diphasic part of the progression of the disease. Twenty to fifty percent of people who enter the second phase will die from yellow fever. Symptoms include fever, vomiting, abdominal pain, prostration, dehydration, jaundice due to liver involvement, internal bleeding, bleeding of the nose, mouth, and gums, blood in the urine, and kidney or liver failure. The internal bleeding results in blood in the vomit, called “black vomit” due to the color, and dark stools. No virus is in the blood at this point so the patient is not infectious to mosquitoes.

Death usually occurs between the 7<sup>th</sup> and 10<sup>th</sup> day of the illness showing the quickness with which the disease can act and the reason it is so dreaded. Some very severe atypical cases of yellow fever may die as early as 3 days after the onset of symptoms. Mortality from yellow fever approaches 10% of clinical cases but has reached as high as 50% of those people developing symptoms.

There is no cure for yellow fever. Treatment is only supportive in an attempt to reduce the severity of the symptoms. However, the disease is preventable. An excellent vaccine is available to provide protection against yellow fever. It was first developed by Dr. Max Theiler in the 1930s and is called the 17D vaccine. In 1951 Dr. Theiler received a Nobel Prize for this extraordinary contribution. This vaccine provides excellent protection against yellow fever for as long as 10 years after vaccination and some people still are protected 30-35 years after being vaccinated. People traveling to areas where yellow fever is known to cause disease should be vaccinated in advance. Current information for travelers can be found at the Centers for Disease Control website for travelers' health: <http://www.cdc.gov/travel>

## The Virus

Yellow fever virus is a member of the group of viruses called flaviviruses. The virus has been found in the tropical regions of the Americas, Africa, and there have been historical yellow fever incursions in parts of North America and Europe. The yellow fever virus has never been detected in Asia, Australia or the Pacific despite the presence of *Aedes aegypti* in these regions. The reason for this is unknown and the subject of much speculation.

## Insect Transmission

Several different mosquito species transmit yellow fever virus depending on the geographic region and habitat. The most important mosquito species involved world wide in the transmission of yellow fever to humans is *Aedes aegypti*, also known as “the yellow fever mosquito.”

The association of yellow fever transmission to humans by *Aedes aegypti* was a major breakthrough in understanding this dreaded disease. In 1901, Major Walter Reed, U. S. Army, led the studies showing the role of *Aedes aegypti*. The species is widely distributed throughout the tropics and subtropics of the world. Larvae of *Aedes aegypti* can develop in a variety of artificial containers, i.e., flower pots, tires, water jars, many commonly found around human habitats. Adult *Aedes aegypti* have a distinct preference for humans as a source of blood (Figure 1).



**Figure 1.** The Yellow Fever Mosquito, *Aedes aegypti*, in the act of taking a blood meal. Credits: James Newman, UF/IFAS/FMEL

Its preference for human water storage containers and human blood makes *Aedes aegypti* particularly efficient as the vector of this virus to humans. The control of *Aedes aegypti* populations is considered of primary importance in reducing the risk of urban areas to yellow fever.

Other mosquitoes can transmit yellow fever virus. In the tropics of the Western Hemisphere, *Hemagogus* mosquitoes transmit yellow fever virus to monkeys in the forest canopy creating a jungle yellow fever cycle in the Americas. When humans clear trees in these regions they become exposed to these mosquitoes resulting in sporadic cases of yellow fever. When these infected humans return to urban areas there is great danger that uninfected *Aedes aegypti* can become infected and lead to an urban epidemic. In tropical Africa, the mosquito *Aedes africanus* transmits yellow fever virus between forest dwelling canopy monkeys, and *Aedes bromeliae*, *Aedes vittatus* and *Aedes furcifer-taylori* transmit the virus to monkeys in the savanna and gallery forest regions of Central Africa. The epidemic danger to humans is when infected humans bring the virus to urban centers inhabited by *Aedes aegypti*.

### **What is the Importance of Yellow Fever Today?**

Yellow fever is still an important disease despite scientific advances in understanding the disease and the development of an effective vaccine. The continued appearance of yellow fever epidemics and the potential for large epidemics of this disease is of real concern.

The ability to reduce human suffering due to yellow fever depends on being able to use efficient and effective mosquito control coupled with a massive vaccination program. Both are extremely difficult to accomplish in many regions of the world where the risk for a yellow fever outbreak may be greatest. Successful mosquito control against *Aedes aegypti* has reduced the number of yellow fever cases in many cities. However, mosquito control resources may be non-existent and delivery of vaccine insufficient. In the 1990s the worldwide annual production of yellow fever vaccine was about 15 million doses with demands on vaccine extremely

unpredictable. A vaccination program that is geared to regions in advance of an expected epidemic is cost-effective, but it is unlikely to be successful because of the time delay in identifying the epidemic and that it takes 5-7 days for the vaccine to provide any protection after inoculation. On the other hand, a campaign to vaccinate the entire population in the absence of yellow fever would be extremely costly and require a long-term commitment to vaccinate everyone.

**The challenges and dangers from yellow fever remain formidable.**

### **Additional Suggested Reading**

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