Etiologic Agent: Yellow Fever Virus is an ssRNA (single-stranded RNA) virus from the family Flaviviridae[7], with Genus Flavivirus and species febricis. [1]

Disease Transmission: Yellow fever is transmitted to humans from the bite of an infected mosquito and is not transmitted from person to person. The main vectors for transmission are the Aedes and Haemagogus species of mosquitoes. [4]

“Yellow fever virus has three transmission cycles: jungle (sylvatic), intermediate (savannah), and urban.

• The jungle (sylvatic) cycle involves transmission of the virus between non-human primates (e.g., monkeys) and mosquito species found in the forest canopy. The virus is transmitted by mosquitoes from monkeys to humans when humans are visiting or working in the jungle.
• In Africa, an intermediate (savannah) cycle exists that involves transmission of virus from mosquitoes to humans living or working in jungle border areas. In this cycle, the virus can be transmitted from monkey to human or from human to human via mosquitoes.
• The urban cycle involves transmission of the virus between humans and urban mosquitoes, primarily Aedes aegypti. The virus is usually brought to the urban setting by a viremic human who was infected in the jungle or savannah.” [3]

Reservoirs: Mosquitos, monkeys and humans all serve as reservoirs for the Yellow Fever Virus. [9]

Specific tests for identification: Diagnosis of Yellow Fever can be difficult in asymptomatic patients. In severe cases, the symptoms are often similar to other flaviviruses such as Dengue and West Nile.

“Laboratory diagnosis generally is accomplished by testing serum to detect virus-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies by serologic assays. It is important to obtain a yellow fever vaccination history, as IgM antibodies to yellow fever vaccine virus can persist for several years following vaccination. Serologic cross-reactions occur with other flaviviruses (e.g., West Nile or dengue viruses), so positive results should be confirmed with a more specific test (e.g., plaque-reduction neutralization test). Early in the illness (during the first 3-4 days), yellow fever virus or yellow fever virus RNA often can be detected in the serum by virus isolation or nucleic acid amplification testing (e.g., reverse transcription-polymerase chain reaction [RT-PCR]). However, by the time overt symptoms are recognized, the virus or viral RNA usually is undetectable. Therefore, negative virus isolation and RT-PCR results cannot rule-out the diagnosis of yellow fever. Immunohistochemical staining of formalin-fixed material can detect yellow fever virus antigen in histopathologic specimens.” [10]
**Signs and Symptoms of Disease:** Signs/symptoms usually present within 3-6 days from infections. Most people who become infected with Yellow Fever will show no symptoms and will recover after the initial onset of the infection. Those who do show signs will experience fever, chills, headache, back pain, weakness, fatigue, nausea and vomiting. In severe cases, patients will experience jaundice (yellowing of the eyes or skin), bleeding, shock and organ failure, sometimes even death. [2]

**Historical Information:** Yellow Fever has been known for hundreds of years in the Caribbean and was transported to America, as far North as Boston, via ships. In 1900, Walter Reed and colleagues discovered that Yellow Fever is transmitted by mosquito bites and subsequent extermination of mosquitoes helped to eradicate Yellow Fever in the US. [7] It is thought that Yellow Fever originated in Central Africa and from there spread to the rest of Africa. It was brought to America via ships from Africa because of the slave trade. [8]

**Virulence factors:** Yellow Fever Virus’ virulence factors include:

- “Capsid protein C - Facilitates viral binding
- Membrane protein M - A minor glycoprotein
- E proteins - Initiate infection, mediate viral entry, and serve as principal targets for host immune response
- Nonstructural protein 1 (NS1) - May play a role in RNA replication and immune evasion
- NS2A protein - Involved in RNA replication and packaging
- NS2B and NS3 - Form a complex and are involved in polyprotein processing and replication of RNA
- NS5 - Has a major role in RNA replication”

The liver cells are the most targeted cells which contributes to jaundice. [11]

**Control/Prevention:** In order to prevent outbreaks, many countries require proof of Yellow Fever vaccination. Individuals can prevent being infected with Yellow Fever by wearing insect repellent, wearing long sleeves and pants and using mosquito nets. [3]

**Treatment/Vaccine info, new trials:** There is a vaccine for Yellow Fever and it is recommended for people 9 months or older who are travelling to endemic areas or people who live in these areas. The vaccine is effective within 30 days and provides protection for life and does not require a booster. [3] There is no specific treatment for Yellow Fever, only supportive care for the symptoms. [3]

**Current local outbreaks:**

**Current global outbreaks:** There is an outbreak in Brazil, beginning in December of 2016 and as of February 23, 2017 there are 1336 cases reported with 292 cases confirmed. There are 215 deaths of which 101 are confirmed. The case fatality rate is at 35% for the confirmed deaths. The outbreak has occurred in 6 states including Bahia, Espírito Santo, Minas Gerais, Rio Grande do Norte, São Paulo, and Tocantins. [6]

**References:**


