Chapter 3

MOSQUITOES AND HUMAN DISEASES

Aside from the irritation and annoyance that mosquitoes inflict on humans and other vertebrate animals, the threat of infectious pathogen transmission is always present. Of the human pathogens malaria, dengue, yellow fever, and encephalitis are just a few major representatives of a long list of diseases for which mosquitoes serve as vectors with encephalitis probably being the greatest potential threat to people in Louisiana. This has been reinforced recently by introduction of the West Nile virus (WNV) to the state in 2001.

The word “encephalitis” means an inflammation of the brain and possibly the spinal cord (encephalomyelitis).

There are several possible causes for this inflammation, but one in particular involves mosquito-transmitted viruses, commonly referred to as arthropod-borne viruses or arboviruses. In Louisiana and the rest of the U.S., the arbovirus transmission cycles are all zoonoses, meaning they occur naturally in cycles between mosquitoes and non-human vertebrates. All but one of the arbovirus cycles involves birds and mosquitoes, with humans, horses and most other animals serving as dead-end hosts.
**West Nile Encephalitis**

West Nile virus was introduced into the United States in the New York area in 1999. Although originally misdiagnosed as St Louis encephalitis (SLE), it was quickly recognized as responsible not only for human disease and several deaths, but also involved in heavy avian mortality, especially in the passerine family Corvidae (crows and jays). Like SLE, WNV is transmitted naturally between birds by certain species of mosquitoes (Fig. 17). Humans, horses, dogs, cats and most other vertebrates are likely accidental or dead-end hosts, meaning they are not capable of passing the virus on to uninfected mosquitoes. For every 100 infected persons, only 20 will develop symptoms of fever or more severe disease, with most showing symptoms associated with fever (headache, fever, fatigue and occasionally, rash, swollen lymph glands or eye pain). Only a few individuals (< 1%) develop severe disease, including high fever, headache, neck stiffness, stupor, disorientation, coma, tremors, convulsions, muscle weakness, vision loss, numbness and paralysis. These symptoms may last several weeks, and neurological effects may be permanent. About 10% of severe cases are fatal.

**Figure 7.** WNV age associated severe disease and fatalities in Louisiana, 2002.

**WNV Age Associated Severe Disease and Fatalities**

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Centers for Disease Control

WNV is now endemic in Louisiana, with human severe disease cases averaging 98 per year in the span from 2003-2006 (range = 85-117). As in the rest of the US, people over the age of 75 are at greatest risk for severe disease and death (Figure 7). Human cases usually begin to occur in late June or early July. Human cases have occurred in 75% of Louisiana parishes, with foci around most major urban areas.
Progression of West Nile Virus in the United States, 1999 - 2006

1999

First human case of WNV reported in Louisiana.

2001

2006


**St. Louis Encephalitis**

St. Louis encephalitis (SLE) is another common arboviral disease in the United States. It is also caused by an arbovirus that is transmitted by mosquitoes in nature among birds, primarily by *Culex* mosquitoes (Fig. 17). Man becomes involved as a “dead end” host; that is, the virus concentration in human blood never reaches a titer high enough to infect a biting female mosquito. This is not to say that humans suffer no consequences from this infection, on the contrary, infected humans may experience abrupt onset of fever, nausea, and vomiting with severe headaches. These symptoms develop within 5-15 days after a person is bitten by an infected mosquito. A person of any age may contract the disease; however, the symptoms are more severe in people 60 years of age or older. Case fatality rates may range from 3-30% with most occurring in the elderly.

Humans become infected with SLE only as a result of being bitten by an infected mosquito. There is no person-to-person transmission. The chances of contracting the disease are in direct proportion to the number of infected birds and the abundance of *Culex* mosquitoes in the vicinity. SLE outbreaks are most likely to occur from mid-summer to early fall, and are often associated with extended drought earlier in the year. Drought conditions reduce the mosquito breeding habitat and also reduces available water for birds to drink and bathe thereby increasing the likelihood of coming in contact with one another. *Culex quinquefasciatus*, a foul water breeder, is the primary vector of SLE, and its number increases during drought conditions. Although superficially similar to WNV in transmission cycle, and a member of the same virus family, SLE human cases tend to occur in urban areas where house sparrows, the primary vertebrate host, and *Culex quinquefasciatus* coincide. This may be due to a more narrow mosquito host range for the SLE virus as compared to WNV.

SLE was first recognized as a disease in the early 1930s during outbreaks in St. Louis, MO, and Paris, IL. The most severe epidemic of SLE in recent decades swept through the Mississippi River Valley in 1975. In its path, a total of 1,941 confirmed and presumptive cases were recorded over 28 states and the District of Columbia, including 95 confirmed deaths. The states of Mississippi, Illinois, Indiana, and Ohio reported the most cases. There are approximately 128 human cases recorded annually in the US, but typically much smaller outbreaks occur.

Louisiana did not record it first case until 1966 when seven cases were reported (six cases from the New Orleans metropolitan area and one case from Monroe). Generally in the 1960's and 70's, there were sporadic cases. In 1980 there were 12 cases recorded from Orleans parish, and in 1994 16 cases from the same area. In 1998 there were 14 cases from Jefferson parish, and the largest outbreak in the state to date (70 cases) occurred in 2001 in Ouachita parish, centered in the city of Monroe. Since then there have been sporadic cases in the state.

**Eastern Equine Encephalitis**

Eastern equine encephalitis (EEE) is a viral infection maintained in nature by a bird-mosquito-bird cycle similar to SLE. It is distributed along the coastal states of the Gulf of Mexico and the Atlantic Ocean (Fig. 9). In the US there are approximately 5 human cases annually, with 220 human cases since 1964. EEE is the deadliest mosquito-borne virus to occur in the US, with a 30% fatality rate. Equines are involved as “dead end” hosts in the cycle along with man. EEE can infect persons of any age, but those younger than 15 and older than 50 are particularly vulnerable to severe disease. Onset of symptoms typically occurs 3-10 days after infected mosquito bite. Half of those who survive are afflicted with varying degrees of metal disability and paralysis.

While not part of the national arbovirus database maintained by CDC, a major outbreak of EEE is known to have occurred in Louisiana in 1947 when the virus produced disease in over 15,000 horses and 15 humans (7 fatalities). Since then, knowledge of the transmission cycle and availability of a vaccine for horses (but not for humans) has resulted in much reduced infection of horses and humans.
Although there were only two human cases of EEE reported between 1964 and 1990, since that time there has been an average of just less than one case per year. Since 1964, most recent cases occurred between 1997-999, with 7 human cases and hundreds of horse cases occurring in unvaccinated animals.

There are a number of mosquitoes, especially *Culiseta melanura*, that are capable of maintaining and transmitting EEE in nature (Fig. 18, p. 31). Since *Cs. melanura* is uncommon and seldom bites man, other mosquitoes such as *Cs. inornata*, *Cx. quinquefasciatus* (southern house mosquito), *Aedes albopictus* (Asian tiger mosquito), *Ae. sollicitans* (tan salt marsh mosquito), *Ae. vexans*, *Ae. infirmatus*, *Ae. atlanticus*, and *Coquillettidia perturbans* are important in transmission from birds to man and/or equines. Factors favoring infection in man are the buildup of *La Crosse Encephalitis* virus in wild-bird populations and a high density of adult mosquito vectors. Human risk is highest in rural areas near bodies of water supporting development of competent mosquito vectors.

**Figure 9. Human Eastern Equine Encephalitis Cases by State, 1964-2006**

**Western Equine Encephalitis**

Western equine encephalitis (WEE) is another arboviral disease in the United States and is found mainly in the states west of the Mississippi River (Figure 10). Louisiana has never recorded a human case of WEE. Although there have been 639 confirmed human cases since 1964, there have been less than 1-2/year since 1996. Thirteen percent of infections (30% of infants) show disease with a 3% fatality rate. *Culex tarsalis* is the most important vector throughout the western United States, and, as with EEE, birds are the major host. East of the Mississippi River, *Cx. quinquefasciatus* is the suspected vector. Both man and equines are accidental or dead-end hosts. As with EEE, a vaccine for horses is available, but no vaccine is available for humans.

**La Crosse Encephalitis**

*(California group)*

La Crosse encephalitis virus (LAC) is a member of the California group of encephalitis viruses. The natural cycle of LAC differs from that of SLE, EEE, and WEE in that natural hosts are small and medium-sized animals such as rabbits, hares, and squirrels rather than birds. The vectors are mostly woodland mosquitoes (primarily *Aedes triseriatus*), and most of the human cases have occurred in people who lived or worked in or near wooded areas. Most cases of LAC have been reported from the states of Ohio, Wisconsin, West Virginia, and Minnesota. Advanced surveillance and detection of human disease from LAC in recent years has identified large foci in Mid-Atlantic States such as West Virginia and in western North Carolina (Figure 11). There is an average of 70 cases/year, with most severe disease occurring in children less than 16 years of age and resulting in a less than 1% fatality rate.

In Louisiana, only 25 cases have been reported since 1964 (although a 2001 OPH serosurvey showed 30% of Ouachita parish residents aged 60 and over had antibodies to the virus). The largest number of cases (9) occurred in 1969, mostly from Lafourche Parish. Although from 1970-2000, there were only 2 cases reported, since 2001, 1-3 cases have been reported annually. These cases were probably identified due to increased awareness and testing for arboviral disease after the introduction of WNV. LAC has been isolated from a number of species of woodland mosquitoes, particularly *Ae. triseriatus* (the primary vector), *Ae. canadensis*, *Ae. trivittatus*, and *Ae. atlanticus*, all of which are found in Louisiana. It has also been isolated from and can be transmitted in the laboratory by *Ae. albopictus*, a possible secondary vector in some areas.
Venezuelan Equine Encephalitis

Venezuelan equine encephalitis (VEE) is a virus distributed from Mexico to Argentina and known to exist in nature as 6 distinct strains, some capable of causing equine epidemics and human disease. Rodents and other small mammals are thought to be the natural vertebrate reservoir of some strains which occasionally mutate to cause epidemics. In 1971, the first equine and human cases in the U.S. were recorded in south Texas as a result of an outbreak that began in South America in 1969. More than 1,500 horses died of VEE in Texas, but no human deaths were reported. A more recent VEE epidemic occurred in the fall of 1995 in Venezuela and Colombia with an estimated 90,000 human infections. Human infection with VEE is usually not as severe as infection with EEE or WEE viruses, and fatalities are uncommon, at least in the US experience. The disease is mild in humans, producing flu-like symptoms, although children may develop encephalitis. VEE is often fatal to equines, but there are effective vaccines available. No human vaccines are commercially available.

Schematic of the emergence process for some epidemic VEE strains. Enzootic, sylvatic VEE strains (gray) are transmitted continuously among rodent reservoir hosts such as spiny rats (Proechimys spp.) and cotton rats (Sigmodon spp.) by mosquito vectors in the subgenus Culex (Melanoconion). Mutations are selected by equines because they generate high-titer viremia sufficient for amplification (Fig. 12). The resultant epidemic strains (black) are transmitted by abundant floodwater mosquitoes such as Aedes and Psorophora spp., which have wide host ranges including equines and humans. Spillover to humans who live in proximity to infected equines results in epidemics involving up to hundreds of thousands of people before equine mortality and immunity exhaust the supply of amplification hosts or vector populations decline.

No VEE activity has been reported in the United States since December 1971, although 500,000 mosquitoes, 9,000 wildlife blood samples, and 1,500 equine blood samples were tested by various agencies in 1972. The virus failed to become established in the U.S., probably because of the combination of widespread inoculation of horses with an experimental live attenuated VEE vaccine, and concerted mosquito control efforts. But the threat of reintroduction remains because the virus resides in neighboring countries to the south, particularly Mexico.

On the basis of virus isolation studies conducted during the 1971 VEE epidemic, a number of species of mosquitoes were suspected as vectors. Psorophora columbiae, Ae. sollicitans, and Ps. discolor were incriminated, and all are present in Louisiana (the first two species are very abundant). It is suspected that other species of Aedes (e.g., Ae. albopictus) and certain other species of Culex, Anopheles, and Coquillettidia may also transmit VEE virus. Mechanical transmission by biting insects other than mosquitoes and direct transmission by contact (bridle bits) or aerial spread (sneezing) are also considered possible means of infection during the height of an epidemic.

Figure 12. Schematic of VEE Cycle

Source: Anishchenko et al. 2006. PNAS.
Dengue

Dengue is a viral disease commonly called “breakbone fever.” Dengue is worldwide in its distribution, primarily in the tropics and subtropics, and infects 50-100 million people annually, with 200,000 severe disease cases (Fig. 13). It is often characterized by severe headache, pain behind the eyes, high fever, backache, pain in the joints, and a rash, with convalescence that may require several weeks. These symptoms generally occur 5-6 days after an infected mosquito has bitten a susceptible person. In uncomplicated cases, death rarely occurs. There are four strains of dengue, and in some areas of the world, infection from several strains of the dengue virus may result in more severe and often fatal forms of dengue known as dengue hemorrhagic fever (DHF) and dengue shock syndrome.

Figure 13. Worldwide distribution of dengue virus and Aedes aegypti.

Before 1980, the last major epidemic of dengue in the continental U.S. occurred in St. James Parish, Louisiana, in 1945. In that epidemic, the Louisiana Department of Health recorded 62 confirmed cases, but authorities estimated that there were probably several hundred inapparent and/or unreported cases. Previous U.S. epidemics of dengue occurred in 1934 in Hawaii, 1934 in Florida and Georgia, and 1922 in Florida and Texas. After the 1945 outbreak, single cases were recorded from Louisiana (1947) and Florida (1973).

From 1980 through 2004, there has been endemic (local) transmission of dengue with multiple cases in Texas at least six times. The first locally acquired case of DHF occurred in 2005 in Texas, and serosurveys indicate ongoing transmission in the US in south Texas border areas. From 2001-02, Hawaii experienced an outbreak with 88 cases. In the US there is a low, but increasing risk for local transmission in areas where the vectors are present. Since 1977 there have been >4000 imported cases, approximately 100-200 cases/year, and the numbers of classical and severe dengue cases are increasing annually in Central and South America.

Dengue is transmitted by the container breeders Ae. aegypti and Ae. albopictus in a mosquito-man-mosquito cycle. After biting an infected person, the female mosquito requires 8-10 days for viral development before she is capable of virus transmission to man. Once infected, the mosquito remains infective for the remainder of her life. Although Ae. aegypti is the primary vector on a worldwide basis, Ae. albopictus is quite capable of serving as a vector, as evidenced in the recent Hawaii outbreak.

Presently, there is no commercially available vaccine. Treatment for uncomplicated cases of dengue consists of providing the victim with as much relief from the disease symptoms as possible. The severe forms are normally treated with intravenous fluids or transfusions and other therapies.

Yellow Fever

Yellow fever is caused by a virus closely related to the dengue virus. In fact, yellow fever infections produce dengue-like symptoms in humans; however, the effects of yellow fever are normally much more severe. The fatality rate may reach 50% or more in epidemics. The virus is presently found in Africa, Central America, and South America. It is absent from the continental U.S. at present. The last epidemic of yellow fever in the continental U.S. occurred in New Orleans in 1905.

As with dengue, the yellow fever virus is transmitted in urban areas by Ae. aegypti and Ae. albopictus. Unlike dengue, however, the probability of virus reaching the U.S. is low. This may be due, in part, to the fact that yellow fever, along with cholera, smallpox, and plague are quarantinable diseases. This means that the Centers for Disease Control and Prevention in Atlanta, Georgia, are continually monitoring outbreaks of yellow fever in the western hemisphere. There is an extremely effective yellow fever vaccine called 17D. All persons who pass through yellow fever endemic areas must show evidence of proper vaccination prior to re-entry into this country. All arriving planes and ships are required to undergo insecticidal fumigation treatment to kill any mosquitoes that might otherwise be potential vectors.
**Malaria**

On a worldwide basis, malaria remains the most important human disease transmitted by mosquitoes. It is estimated that there are millions of human cases of malaria in the world (mostly in Asia and Africa), and 700,000 to 2.7 million human deaths occur each year from malaria (Fig. 14). Most of the deaths (75%) are children under 10 years of age and pregnant women. In Africa, 1 in every 20 children dies from malaria. It is believed that malaria was introduced into the North American continent during colonial days. Tens of thousands of cases occurred in the U.S. before the 1930s, but there are no reliable statistics available for the period. However, in the 1930s, approximately 100,000 cases were reported annually; in the early 1940s, the number of cases was reduced dramatically due to the work of public health agencies using DDT during and after World War II and the Tennessee Valley Authority (TVA) source reduction program.

Figure 14. *Worldwide distribution of malaria.*

Since the late 1950s a few hundred to a few thousand new cases have been recorded annually, almost entirely attributable to military returnees from malarious areas. These cases were contracted outside the U.S., but symptoms appeared following re-entry into the country. Until recently, rarely has there been secondary infection contracted in the U.S. But since 41% of the world's population lives in malarious areas, the risk for importation is constant. Between 1957 and 2003, there have been 63 outbreaks of locally transmitted malaria in the US. In 2002 alone, there were 1,337 cases of malaria with 8 deaths. 5 of the total cases were locally acquired.

Human malaria is caused by any of four *Plasmodium* species of protozoa and is characterized by fever, chills, sweating, and headache. If not treated, it may cause shock, renal failure, acute encephalitis, coma, and death. The disease is transmitted by *Anopheles* mosquitoes (Fig. 15). In Louisiana, *An. quadrimaculatus* sensu strictu (formerly known as Species A in the 5 member species complex, of which 4 species, Species A, B, C2, and D occur in Louisiana) is considered to be the primary historical and potential vector. Another species, *An. crucians*, may also be a competent vector. Both of these species are widespread in rural areas and are most abundant from April through September.

Figure 15. *Malaria parasite life cycle.*

**Dog Heartworm**

Dog heartworm (*Dirofilaria immitis*, a filarial worm) is a serious disease for all breeds of dogs in Louisiana and other areas with subtropical or tropical climates. In the southern part of Louisiana, the infection rate is reported to be as high as 80% in dogs over two-and-a-half years old, and almost 100% in dogs over five years old. Man can also become infected, but the worms are unable to develop or mature because humans are not their natural hosts.

The life cycle of dog heartworm involves two factors: mosquitoes and dogs (Fig. 16). Mosquitoes ingest the immature worms or embros called microfilariae (mf) that circulate in the blood of a dog while feeding. These immature worms migrate to the Malpighian tubules of the mosquito where they undergo development through several larval stages in 9-14 days. The last stage called the third or infective stage larva then migrates to the mouthparts of the mosquito. When the female takes another blood meal, the larva falls out of the mouthparts and onto the skin of the dog. The dog becomes infected if the larva manages to find and enter the puncture wound. Most fail to make this transition.
The larvae grow and migrate through subcutaneous tissues and large blood vessels and eventually enter the right ventricle of the dog’s heart thus the name, dog heartworm. The larvae grow into adult worms measuring about 11 inches for the females, and 6 inches for the male. The adult female worm lays no eggs but instead extrudes the mf which circulate in the blood thus completing the life cycle.

Several genera of mosquitoes can transmit the parasite to dogs (e.g., *Aedes, Anopheles, Culex* and *Psorophora*). It is frequently reported in the literature that *Cx. quinquefasciatus* (southern house mosquito) is considered to be the most important vector, but a study by Lowrie (1991) has shown that this is not the case, at least with several Louisiana strains he tested. But its vector competency may vary with strains found elsewhere. Nayar and Sauerman (1975) were the first to describe the formation of needle-like oxyhemoglobin crystals in the midgut of *Cx. quinquefasciatus* females shortly after ingesting dog blood regardless of whether or not it is infected with *D. immitis*. These crystals blocked the migration of the mf to their Malpighian tubule development site. Other incriminated vectors of dog heartworms include *Ae. albopictus* and *Ae. vexans*, and *Ae. taeniorhynchus*.

In areas where dog heartworm infection is prevalent, dog owners should provide mosquito-proof sleeping quarters for their animals. Additionally, the owners should administer a program of chemical prophylaxis with one of the drugs available from veterinarians.

**Figure 16. Dog heartworm life cycle.**

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**Acquired Immune Deficiency Syndrome (AIDS)**

When the AIDS virus was initially discovered in humans, one of the first questions asked of public health officials was, “Is the AIDS virus transmitted by bloodsucking insects?” There have been exhaustive laboratory tests conducted by the Centers for Disease Control and Prevention using a wide range of blood-feeding insects and arthropods in attempting to answer this question. Currently, there is no scientifically-based, credible evidence to suggest or imply that mosquitoes or their allies can transmit the virus between humans. Is that enough evidence to say that it is impossible for insects to transmit the virus to humans, either biologically or mechanically (i.e., infected blood on the mouthparts)? That question has not been fully answered to the satisfaction of some members of the general public. It is safe to say, however, that the involvement of blood-feeding insects and other arthropods is biologically insignificant, if in fact it occurs at all. Infected syringe needles and unprotected intimate sexual activities are the most common and highly documented means of AIDS virus transmission among humans.
The transmission cycle above is only a general representation of an arbovirus cycle. There are numerous other variables such as: climate (rainfall patterns, temperature), mosquito activity periods, numbers of older blood feeding mosquitoes, abundance of mosquitoes, bird-to-bird transmission (pecking) and even unknown factors that effect arbovirus cycles.

Some of the unknowns are the role rodents or small mammals play in maintaining the virus and transovarial transmission (passing of the virus from mosquito to eggs). Dr. Andrew Mackay, working in East Baton Rouge Parish, LA (Mackay, A. J. 2007. Detection of West Nile Virus Activity in male and female mosquitoes, and evaluation of host-utilization patterns of mosquitoes, in East Baton Rouge parish, Louisiana. Ph.D. dissertation. Louisiana State University) found evidence of transovarial transmission in *Culex restuans*, *Culex salinarius*, *Anopheles crucians*, *Ochlerotatus triseriatus* and *Psorophora howardi* males taken from light traps in EBR Parish between 2002-2004. Also working in East Baton Rouge Parish, Dr. Isik Unlu (Unlu, I. 2007. Determination of the bloodmeal origin of mosquitoes collected at alligator farms, and West Nile Virus activity in mosquitoes collected from alligator farms, sentinel chicken surveillance sites, and larval habitats. Ph.D. Dissertation. Louisiana State University) found evidence of transovarial transmission in *Culex spp.* males collected in CDC light traps and *Culex spp.* male and *Culex quinquefasciatus* and *Aedes albopictus* female mosquitoes reared from larvae during 2005-2006.
References Cited
