A Plan for a Long Term Investigation of Human Exposure to West Nile Virus in Fremont County, Wyoming

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Background

West Nile Virus (WNV) was originally discovered in Uganda in 1937. WNV belongs to the Flaviviridae family and is in the same genus as Dengue Fever, Zika virus, and Yellow Fever. Flaviviruses are persistently emerging and of great concern globally. The primary reservoir for WNV is birds, primarily species of the Corvidae. The vector for the virus is mosquitoes that feed on birds. Mammals, such as horses and humans, are incidental hosts. Except in rare cases, blood transfusions and breastfeeding, for example, human to human transmission does not occur. Individuals contracting WNV may be asymptomatic (80%), experience mild symptoms of fever, headache, neck stiffness, malaise (20%), or develop a severe neurologic illness such as disorientation, tremors, seizures, or meningitis, encephalitis, coma or polio-like paralysis (< 1%). About 10% of patients contracting the neurologic form of the illness will die. Interestingly, the paralysis caused by WNV infection is similar to the etiology of polio because it also attacks the anterior horn cells of the spinal cord. WNV was first detected in the U.S. in 1999 in Queens New York. It rapidly migrated to the West Coast over the course of ten years reaching epidemic proportions in Wyoming in 2007. The majority of these cases were found in Fremont County with 118 infected, twelve neuroinvasive cases, and one death. Its persistence in Fremont county is evident from field testing of the vector *Culex tarsalis* mosquitoes and from human serosurveys in 2011 and 2012 conducted by our lab.

Previous Investigations

West Nile Virus has been a topic of research at Central Wyoming College for the past several years due to its impact in the state of Wyoming and Fremont County in particular. We hypothesized that if a large proportion of the population of Fremont County had been exposed to West Nile virus this would result in widespread immunity and that would explain the decline in reported cases beginning in 2009 (Figure 3). In 2011, we tested 85 subjects and found that 16.5% (95% CI: 8.9% - 24.1%) were IgG positive and 9.4% (95% CI: 3.2% - 15.6%) IgM positive. In 2012, of the 95 subjects that we tested 10.5% (95% CI: 4.3% - 16.7%) were IgG positive and 5.3% (95% CI: 0.8% - 9.8%) IgM positive (Figure 1). The percent of positives by age group mirrors CDC reporting of neuroinvasive cases that indicates that increasing age is correlated with increasing susceptibility with the exception of the twenty to twenty-nine age group. This finding bears further investigation. It is interesting to note that while it appears that anywhere from 1% to 10% of cases in 2012 were new cases as indicated by the IgM results, four of the subjects tested in 2012 reported exposure at least five years prior to testing and continue to exhibit high levels of IgM antibody (Figure 2). This finding, which has also been reported elsewhere, also bears further investigation and is the basis of our proposed research.

Data Analysis

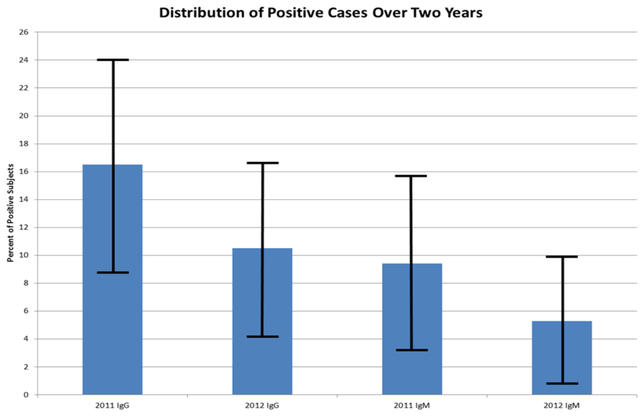


Figure 1

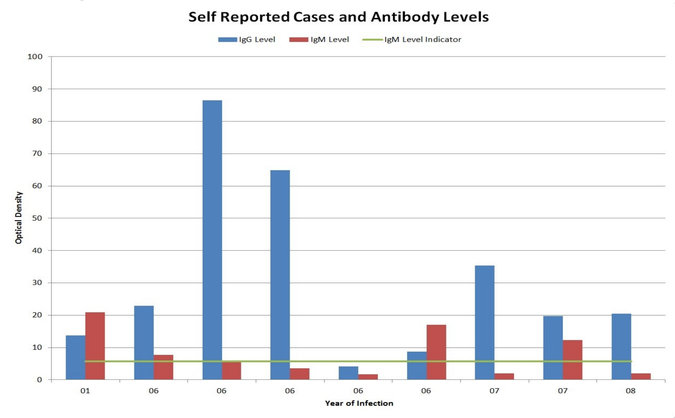


Figure 2

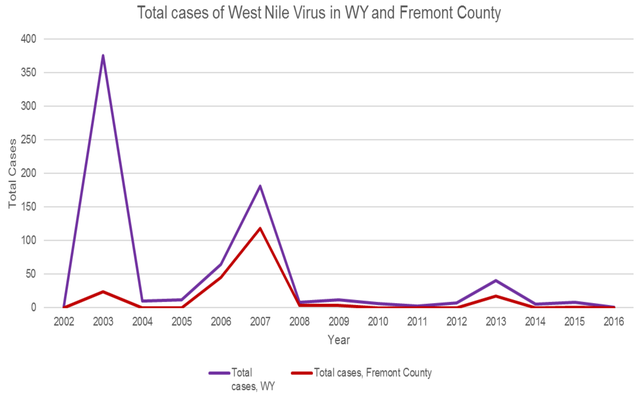
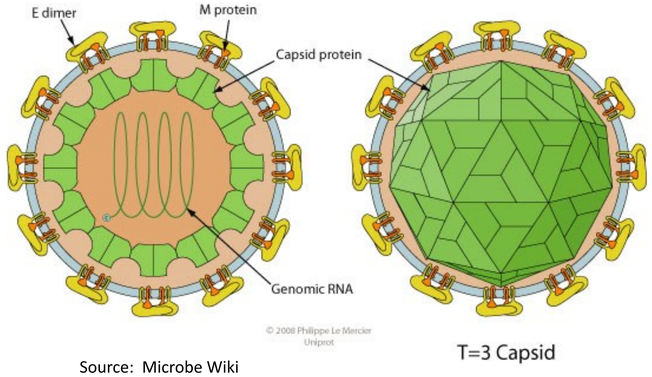


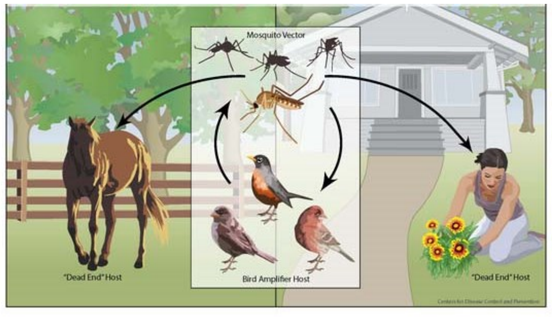
Figure 3



Source: Microbe Wiki

Figure 4

West Nile virus Transmission Cycle



Source: CDC

Figure 5

Proposed Research

Our proposed investigation will conduct a longitudinal study to identify and track subjects infected or previously exposed to WNV with the specific goal of identifying additional subjects expressing high levels of IgM long after initial exposure. We also plan to test these individuals for cryptic infection through reverse transcriptase PCR. The McAllister lab will use primers for the capsid, M, and E protein genes (Figure 4) to test for the possible presence of the virus in serum samples of subjects still expressing high levels of IgM long after initial reported exposure. In addition, we will utilize ELISA testing to Investigate IgM and IgG titers over time. This study should determine whether or not the virus is still present in subjects exhibiting high IgM titers years after initial exposure or if there is another mechanism that would explain this phenomenon. We may also gain insight into subjects exhibiting post-polio-like myelitis symptoms long after initial exposure.

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