Chikungunya, Zika and Dengue Virus

Clinical Symptoms and Recent Geographic Movement of three Emerging Arboviruses

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Chikungunya (has nothing to do with chickens) is pronounced “Chik-un-goon-ya” or “Chik-un-gun-ya”
Chikungunya virus (CHIKV), an alphavirus in the family Togavriade, was first discovered in Tanzania in 1953. It is closely related to Ross River Virus, O’Nyong Nyong virus, and Semliki Forest Virus. Epidemics similar to this virus have been reported as early as the 1770s.

CHIKV is transmitted in a person-to-mosquito-to person transmission cycle.
CHIKV was initially transmitted by *Aedes aegypti*, the yellow fever mosquito.

More recently, CHIKV became transmissible by the Asian tiger mosquito, which is becoming an established invasive species in many parts of the world including the U.S. and all of Virginia.

Vertical transmission (from mosquito to egg) is rare and overwintering is unlikely.
Range of *Aedes albopictus* as of 2007. Since 2007 the range in the United States has expanded to include Southern California.
Three genotypes of this virus have been described: West African, East/Central/South African and Asian genotypes.

During inter-epidemic periods, various vertebrates such as rodents, birds, non-human primates, and even some small mammals may serve as reservoir hosts.

The Asian genotype features a point mutation which facilitates transmission through the Asian tiger mosquito.
Chikungunya Virus Transmission

Infection Rate: Persons infected with CHIKV by a mosquito bite may develop symptoms 3 to 7 days later and may remain ill for up to 10 days. Persons may pass the virus on to other mosquitoes that bite them during their first 7 days of illness.
Chikungunya Fever

The Makonde tribe, based in Tanzania and Mozambique, named the disease chikungunya, meaning literally “that which bends up” due to the debilitating joint pain that leaves it’s sufferers stooped over.

Anyone who has not previously contracted chikungunya is at risk of becoming infected if bitten by an CHIKV carrying mosquito.

Once one has been exposed to Chikungunya, the infected are expected to obtain long-term immunity that should protect them from reinfection.

Not every person infected with CHIKV exhibits symptoms. It is estimated that 3% to 28% of those infected are asymptomatic. However, these people are still capable of transmitting the disease.
**Fever**

High Fever over 102º F

Body and Back Pain

**Chikungunya Fever Signs and Symptoms:** The two most common symptoms are the sudden onset of high fever and joint pain, which is severe. Pain in joints may last from several days up to a week. The fever can be intermittent or continuous, and may be independent of the severity of symptoms. A low heart rate (bradycardia) may be associated with the fever.

Nausea is also a common symptom, and vomiting may or may not be present.
Arthitis and Arthralgia

Painful swelling of the joints tends to occur bilaterally on the extremities. Polyarthralgias and arthritis most commonly occur in joints of the hands, feet, wrists, ankles, elbows or knees. Chikungunya fever often causes arthralgia or arthritis (pain with swelling) that is more severe than that caused by dengue fever. Neck pain and lower back pain is also more common than with dengue fever.

Swelling may be visible and can be a sign of arthritis. Tenosynovitis (inflammation of the sheaths that surround tendons) may also occur.

**Patients are often bed-ridden and completely incapacitated.**

Tenosynovitis in hands

Swelling in ankles and feet
One out of two patients will develop a rash. Maculopapular rashes are common and usually develop on the trunk and extremities of the patient. This rash can also appear on the soles, palms, and the face.

Another form of the rash called diffuse erythema may occur. If pressure is applied, the rash will blanch.

Vesiculobullous lesions are the most common rash in infants with infection.

Rashes in chikungunya infections are more common than that of dengue fever.
Unlike dengue fever, chikungunya fever does not usually have hemorrhagic symptoms.

Other signs are conjunctivitis, mild thrombocytopenia (low number of platelets), leucopenia (decrease in the number of white blood cells), and elevated liver enzymes.

Atypical signs may include: neurological, ocular, cardiovascular, and renal symptoms.

Chikungunya Fever is considered to have more painful symptoms than Dengue Fever.
Chronic Chikungunya Symptoms: Persons infected with CHIKV may have a relapse of arthritis and arthralgia 2-3 months after the initial illness.

Arthralgia, arthritis, and tenosynovitis may become chronic and continue for 3 to 5 years or longer.
<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Frequency range (% of symptomatic patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>76-100</td>
</tr>
<tr>
<td>Polyarthralgias</td>
<td>71-100</td>
</tr>
<tr>
<td>Headache</td>
<td>17-74</td>
</tr>
<tr>
<td>Myalgias</td>
<td>46-72</td>
</tr>
<tr>
<td>Back Pain</td>
<td>34-50</td>
</tr>
<tr>
<td>Nausea</td>
<td>50-69</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4-59</td>
</tr>
<tr>
<td>Rash</td>
<td>28-77</td>
</tr>
<tr>
<td>Polyarthritis</td>
<td>12-32</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3-56</td>
</tr>
</tbody>
</table>

*Table from “Preparedness and Response for Chikungunya Virus Introduction in the Americas”*
Recent Concerns

During the 1990s, the invasive Asian tiger mosquito became established in urban and suburban Virginia. It is now found throughout the state.

There have been several cases of imported chikungunya from travelers to Asia, but there have been no cases of autochthonous transmission in the U.S.

Since 2007, there have been 6 imported cases in Virginia. 3 of these cases were recorded in 2013-- 1 was from the Philippines and 2 were from India.
Recent Concerns cont.

In December of 2013, Chikungunya Became Established in the Western Hemisphere.

Chikungunya was confirmed on the island of St. Martin. This is the very first time autochthonous transmission has occurred in The New World.

Since then, it has spread to several surrounding islands in the Caribbean.

The CDC has established guidelines for preparedness and response for virus introduction in the Americas.
## Confirmed and Suspected Cases*

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saint Martin (France)</td>
<td>601</td>
</tr>
<tr>
<td>Sint Maarten (Netherlands)</td>
<td>60</td>
</tr>
<tr>
<td>Martinique</td>
<td>518</td>
</tr>
<tr>
<td>Guadeloupe</td>
<td>175</td>
</tr>
<tr>
<td>Saint Barthelemy</td>
<td>83</td>
</tr>
<tr>
<td>Virgin Islands (UK)</td>
<td>6</td>
</tr>
<tr>
<td>Dominica</td>
<td>13</td>
</tr>
</tbody>
</table>

* ProMED mail as of 2/07/14
Countries with Confirmed and Suspected Cases*

* CDC as of February 5, 2014
Cases of chikungunya virus infections identified in December [2013] in the Caribbean are due to an "Asian strain" virus, and there is an "extremely high risk" of transmission in the United States, a French specialist said on Friday [27 Dec 2013].

Diagnosis: Patients with illness a recent travel history to CHIK endemic regions should be tested. Patients can be co-infected with dengue virus simultaneously.

Laboratory testing: Testing can be done by CDC or Focus Diagnostics.

Other similar Illnesses: Chikungunya is often misdiagnosed as dengue fever. Travelers from CHIK endemic countries who are suspected of having dengue should also be tested for CHIKV.
Historical Outbreaks

Outbreaks: Starting in 2005 it caused large outbreaks on African Islands in the Indian Ocean. These outbreaks later spread across Africa, and from India to Viet Nam and to the Pacific Islands of Malaysia, Indonesia, New Guinea, and the Philippines.

In 2007, CHIKV caused a large illness outbreak in Italy (>250 cases).

Thailand had an epidemic in 2009 that was especially prevalent among its military troops.

In September 2010 autochthonous transmission was detected in southeastern France.
Prevention

In dengue-endemic locales, areas that have exhibited dengue virus transmission should be analyzed for prospective CHIKV circulation.

Use caution when travelling to chikungunya endemic regions (Africa, South Asia, Pacific Islands, and now the Caribbean).

If in an endemic area that has daytime-biting mosquitoes, use effective mosquito repellants. Use a bed net when sleeping both day and night (especially infants).

Wear permethrin-treated clothing and gear.

The various *Aedes* mosquito vectors lay eggs in containers that hold water. Make sure that any potential water holding vessel (tires, buckets, bird baths) is eliminated or treated with larvicide.
Currently there are no approved vaccines, but several experimental versions are being tested for clinical trial. Treatments are used to minimize the symptoms (pain, inflammation) but are not an actual cure.

Fortunately, fatalities are uncommon. They may occur in elderly patients or those with existent health conditions.
Availability of Case Report Form: Use Arboviral Case Report Form and write in additional clinical symptoms & travel history/dates; a CHIK Form is currently under development.

CHIK information on VDH Website: See CDC/PAHO document on Chikungunya, CHIK Fact Sheet, and Case Report Form in Disease Control Manual

Primary Contact at VDH: David Gaines (804-864-8112)

CHIK Information from CDC: – http://www.cdc.gov/chikungunya/
Zika virus (ZIKV), a member of the family Flaviviridae, was first discovered when it was isolated from a rhesus monkey in the Zika Forest in Uganda. It is closely related to dengue, West Nile, and Japanese encephalitis.

It is transferrable by several members of Aedes mosquito, including Aedes albopictus, the Asian tiger mosquito.

ZIKV is transmitted in a person-to-mosquito-to-person transmission cycle.

Reservoirs may include primates other than humans.
In 1947 the virus was isolated from a rhesus monkey in the Zika Forest in Uganda.

ZIKV was first isolated from humans in 1968, in Nigeria.
Zika Fever Symptoms

The primary symptoms of illness are fever, rash, headache, conjunctivitis, joint pain and muscle ache.

Though the illness is similar to dengue fever, the symptoms are much more mild.

Symptoms usually last between 4 -7 days.
Outbreaks

In 2007, an outbreak of ZIKV occurred on YAP, the western-most state of Micronesia.

There were 49 confirmed and 59 probable cases of Zika identified. Roughly 73% of the 11,241 population was infected according to the CDC.

In November 2013, an outbreak occurred in the islands of Western Polynesia, including Tahiti.

As of January 13, 2014 the number of confirmed Zika cases was 361, while the number of suspected cases was over 35,000. (Pro-MED mail)

In February 2014, New Caledonia reported 49 cases. While 30 were cases imported from French Polynesia, some cases were confirmed to be autochthonous.

Recently, a Canadian traveler contracted ZIKV while in Thailand in January 2013.
Approximate known distribution of Zika virus, 1947–2014. Red oval represents Yap Island. Yellow indicates human serologic evidence; red indicates virus isolated from humans; green represents mosquito isolates. The blue oval represents Western Polynesia while the orange oval represents New Caledonia.
In 2013 VDH investigated several cases that were suspicious, but none tested positive for ZIKV.

It is suspected that Zika fever may be transmitted sexually.

A researcher studying vector borne diseases in Senegal was bitten by numerous mosquitoes in 2009. He returned to the U.S. and became ill. Before displaying illness symptoms, he transmitted the virus to his wife.

His wife later showed signs of Zika infection. When he was examined by the CDC, the researcher was found to have had hematospermia and it is thought that the transmission to his wife was sexual. Another Flavivirus, Japanese encephalitis virus (JEV) is known to be sexually transmitted between pigs.

This is the first case of human to human transmission of an insect-borne virus.
Dengue (DEN)

Dengue Virus (DENV): Before the viral cause of dengue was discovered, outbreaks of a dengue like illness had been recorded for >300 years. DEN outbreaks did not become frequent until shortly after WWII. Since 1945, DEN has spread across the tropical and subtropical regions of the world. DEN became most prevalent in the Americas starting in the 1980s.

DENV is a Flavivirus that is transmitted by “daytime biting” Aedes mosquitoes. There are four DENV serotypes (Types 1, 2, 3, and 4) and exposure to one serotype will not provide immunity to any of the other serotypes.

Transmission: Occurs in a person-to-mosquito-to-person cycle. DENV was initially only associated with the yellow fever mosquito (Aedes aegypti), but more recently was found to be transmissible by the Asian tiger mosquito.
Dengue Fever (DEN/Hemorrhagic Fever)/Shock Syndrome (DSS)

**Threat to Virginia:** As the Asian tiger mosquito is the primary pest mosquito in urban and suburban areas of Virginia, there is potential for infected travelers to infect the local mosquito population and cause to an outbreak.

In 2001-2002 a dengue epidemic (122 laboratory confirmed cases) occurred on the Island of Maui, Hawaii, that was driven solely by the local Asian tiger mosquito population.

In 2013, several dengue cases were locally acquired in Texas.

**Dengue Fever (DEN) Signs and Symptoms:** Rapid onset of high fever (≥102°F) – may be accompanied by headache, retro-orbital pain, diffuse body pain (muscle, joint, and bone pain), a maculopapular rash, thrombocytopenia, leucopenia and mild hemorrhagic manifestations (e.g., nose or gum bleed).
Dengue Fever (DEN)/Hemorrhagic Fever (DHF)/ Shock Syndrome (DSS)

Dengue Hemorrhagic Fever (DHF) & Dengue Shock Syndrome (DSS): Persons exposed to one DENV serotype may develop DHF if exposed to any of the other three DENV serotypes.

DHF symptoms include progressive thrombocytopenia (< 100,000 platelets/mm3), petichial rash, gastrointestinal bleeding, pleural effusions and/or ascites. Plasma leakage may lead to hemoconcentration, circulatory collapse, and DSS leading to patient death if not properly treated.

Treatment: There is no specific treatment other than supportive care for patients.

Differences Between Dengue Fever (DEN) and Chikungunya (CHIK):

**DEN** - Prominent Characteristics: Diffuse myalgia, bleeding, thrombocytopenia, leucopenia/ neutropenia, elevated hematocrit.

**CHIK** - Prominent Characteristics: Fever (>102°F), severe symetric polyarthralgias in extremities, rash, lymphopenia.
Dengue Fever (DEN)/Hemorrhagic Fever (DHF)/Shock Syndrome (DSS)

Laboratory testing: Acute or convalescent sera by IgM antibody capture ELISA (available at commercial laboratories); PRNT (at CDC only); RT-PCR (at CDC only).

Acute serum should be collected in first 5 days of illness. Convalescent serum may be collected 10 to 14 days after onset. Blood samples for RT-PCR must be collected in first 5 days of illness.

Availability of Case Report Form: A Dengue Case Report Form and other reference documents are currently available in Disease Control Manual.

Primary Contact at VDH: David Gaines (804-864-8112)

DEN Information from CDC: – http://www.cdc.gov/dengue/