CHIKUNGUNYA VIRUS

The mission of the Swine Health Information Center is to protect and enhance the health of the United States swine herd through coordinated global disease monitoring, targeted research investments that minimize the impact of future disease threats, and analysis of swine health data.

July 2016 | Updated April 2021

SUMMARY

IMPORTANCE

- Chikungunya virus (CHIKV) is a mosquito-borne virus that mainly affects humans. Historically, most outbreaks have occurred in Africa and Asia. However, CHIKV now causes sporadic epidemics in other regions including Europe and the Americas.
- Although natural infection in swine has not been documented, antibodies to CHIKV have been detected in pigs.

PUBLIC HEALTH

- CHIKV most often causes fever, myalgia, and polyarthralgia in humans. A maculopapular pruritic rash can also be seen, along with ocular signs and involvement of the gastrointestinal system.
- Most people infected with CHIKV develop symptomatic illness, but death is rare.

INFECTION IN SWINE

- Natural CHIKV infection has not been documented in swine.
- There is evidence that pigs can mount an antibody response to CHIKV; however, in many cases, co-infection with other alphaviruses was documented.

TREATMENT

- There are no alphavirus-specific antiviral drugs.

CLEANING AND DISINFECTION

- Alphaviruses are not stable in the environment.
- In general, togaviruses are destroyed by detergents, acids, alcohols (70% ethanol), aldehydes (formaldehyde, glutaraldehyde), beta-propiolactone, halogens (sodium hypochlorite and iodophors), phenols, quaternary ammonium compounds, and lipid solvents.

PREVENTION AND CONTROL

- Prevention in humans involves vector control and insect repellent use.
- There are no specific prevention and control measures for CHIKV in swine.
TRANSMISSION

- Like other arboviruses, CHIKV is maintained in a transmission cycle between mosquitoes and vertebrate hosts. In Africa and some parts of Asia, the virus persists via a sylvatic cycle involving non-human primates and mosquitoes. The urban cycle involves human-mosquito-human transmission.
- The main vectors for CHIKV are *Aedes aegypti* and *Ae. albopictus*.

PATHOGENESIS

- No information was found regarding the pathogenesis of CHIKV in swine.

DIAGNOSIS

- Quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) is used for diagnosis in humans.
- Serology (IgM-capture ELISA) can be used to rule out CHIKV using convalescent-phase samples from patients whose acute-phase samples test negative. A positive result can be confirmed by the plaque reduction neutralization test (PRNT).

EPIDEMIOLOGY

- Humans serve as reservoirs during urban CHIKV epidemics. Several animal species are also capable hosts including monkeys, rodents, and birds.
- In humans, CHIKV infection occurs throughout Asia, Africa, Europe, and the Americas.
- The mosquito *Ae. aegypti* is found mostly in the tropics and sub-tropics, while the range of *Ae.albopictus* includes temperate and even cold regions.

ETIOLOGY

- CHIKV is a single-stranded RNA virus in the family *Togaviridae*. It is an Old World alphavirus belonging to the Semliki Forest serocomplex.
- There are two main CHIKV genotypes. The African genotype has circulated in Africa since at least the 1950s, and recent strains containing E1 and E2 mutations have spread to Asia and Europe. The Asian genotype diverged from the African East Central South African (ECSA) lineage and is also widespread. It is responsible for recent CHIKV outbreaks in the Americas.

HISTORY IN SWINE

- There are no reports of natural CHIKV infection in swine.

IMMUNITY

- There is no vaccine for CHIKV in humans or animals although multiple candidates using a variety of platforms are in development.
- Long lasting cross-protection between CHIKV lineages occurs in humans.

GAPS IN PREPAREDNESS

- Little is known about CHIKV infection in swine. Natural infections have not been reported and clinical signs of disease have not been described.
- There are no diagnostic tests validated for pigs. In addition, there is no CHIKV vaccine.
LITERATURE REVIEW: CHIKUNGUNYA VIRUS

IMPORTANCE

Chikungunya virus (CHIKV) is a mosquito-borne virus that mainly infects humans, causing fever and polyarthralgia. Historically, most outbreaks have occurred in Africa and Asia. However, CHIKV now causes sporadic epidemics in other regions including Europe and the Americas. In the United States, most CHIKV cases are imported but limited local transmission has occurred. Although natural infection in swine has not been documented, antibodies to CHIKV have been detected in pigs. There is continual risk of CHIKV introduction to the United States through travelers. Additionally, there is potential for autochthonous transmission since competent mosquito vectors are present. These factors make CHIKV a concern for both animal and human health.

PUBLIC HEALTH

Chikungunya is mainly a disease of humans that causes large sporadic epidemics.\(^1\) Both sylvatic and urban transmission cycles have been described (see Transmission). Symptoms are similar to those caused by other arboviruses like dengue. Most people infected with CHIKV develop clinical disease; however, death is infrequent.\(^1\)

In adults, fever and myalgia are very common, followed by polyarthralgia, which occurs in more than 95% of patients.\(^1\) In some instances, arthritic disease can persist for years. A maculopapular pruritic rash affecting the extremities, palms, soles of the feet, torso, and face is seen in 40–50% of patients. Nausea, vomiting, and diarrhea can occur, along with ocular signs including photophobia, retro-orbital pain, and conjunctivitis. Involvement of the cardiovascular, renal, hepatic, and respiratory systems is considered atypical.\(^2\) Neonates infected with CHIKV can develop serious disease affecting the heart, skin, and brain. Bleeding and disseminated intravascular coagulation have also been observed.\(^1\)

INFECTION IN SWINE

Natural CHIKV infection has not been documented in swine. In one experimental study, pigs inoculated with CHIKV subcutaneously did not develop viremia or clinical signs of disease, although an antibody response was detected via the plaque reduction neutralization test (PRNT).\(^3\) No lesions caused by CHIKV have been documented in swine.

EVIDENCE OF CHIKUNGUNYA VIRUS EXPOSURE

There is evidence that pigs can mount an antibody response to CHIKV; however, in many cases, co-infection with other alphaviruses was documented.

- A 1964 study conducted in Thailand found hemagglutination-inhibiting and neutralizing antibodies to CHIKV in nearly 35% of swine samples (\(n\) not reported).\(^4\)

- From 1963–67, serum was obtained from pigs at slaughter in Malaysia. Almost 13% (48/328) demonstrated evidence of CHIKV infection via PRNT. However, antibodies to either Getah virus or Sindbis virus were also detected in most samples. Twelve wild pigs were also tested and no antibodies to CHIKV were identified.\(^5\)

- In 1966, a study of pigs at slaughter in the Philippines identified antibodies to CHIKV in 5.5% (5/91) serum samples tested via complement fixation (CF). However, all CHIKV-positive samples also reacted to Semliki Forest virus.\(^6\)

- In Eastern Europe, a 1975 study of domestic animals including 86 pigs found no antibody response to CHIKV using the hemagglutination inhibition (HI) assay.\(^7\)
In Bihar, India, serum was collected from pigs in the late 1970s for arboviral testing following an epidemic of encephalitis in humans. Using the HI and CF assays, 10 (2.5%) and 2 (0.5%) of pigs were found to react only to CHIKV.\textsuperscript{8}

In 2016, pigs were among North American bird and mammalian species experimentally infected with two strains of CHIKV. Following subcutaneous injection of the virus, no pigs developed detectable viremia or clinical signs of disease, although neutralizing antibodies were identified 14 days post-infection via PRNT.\textsuperscript{3}

**EVIDENCE OF EXPOSURE TO OTHER ALPHAVIRUSES**

Pigs are susceptible to some other Old World alphaviruses (see \textit{Etiology}). Though infrequent, Getah virus causes clinical disease in swine.\textsuperscript{9} Serosurveys have demonstrated that pigs may be subclinically infected with Ross River virus, particularly during times of human epidemics.\textsuperscript{9} Antibodies to Sagiyama virus, which is closely related to Ross River virus, have also been demonstrated in pigs.\textsuperscript{10, 11} Pigs have been identified as potential hosts for Ndumu virus, another member of the family \textit{Togaviridae}.\textsuperscript{12}

**TREATMENT**

There are no alphavirus-specific antiviral drugs. Supportive care includes use of analgesics and anti-inflammatory drugs.\textsuperscript{13} Experimentally, a number of antivirals have demonstrated \textit{in vitro} efficacy against CHIKV; however, most have not been tested in animal models or have been shown to be less effective \textit{in vivo}.\textsuperscript{14}

**CLEANING AND DISINFECTION**

**SURVIVAL**

Alphaviruses are not stable in the environment.\textsuperscript{15} It is not known whether CHIKV survives outside of the body and in insect vectors.

**DISINFECTION**

In general, togaviruses are destroyed by detergents, acids, alcohols (70\% ethanol), aldehydes (formaldehyde, glutaraldehyde), beta-propiolactone, halogens (sodium hypochlorite and iodophors), phenols, quaternary ammonium compounds, and lipid solvents.\textsuperscript{16} Exposure to heat (58°C), ultraviolet light, and radiation also render togaviruses inactive.\textsuperscript{16} A citrate-based product (marketed as Clinister\textsuperscript{\textregistered}) has been shown to inhibit CHIKV at a concentration of 1.5 mg/ml.\textsuperscript{17}

**PREVENTION AND CONTROL**

**DISEASE REPORTING**

CHIK is not an OIE-listed disease. There are no restrictions for importation of animals from countries or zones affected by CHIKV. Any suspicious clinical or necropsy findings should always be reported to the USDA and your State Animal Health Official.

**DISEASE PREVENTION**

CHIKV prevention is based on control of mosquito vectors (see \textit{Transmission}). Mosquito vectors preferentially lay eggs in containers like gutters, old tires, and buckets. Any potential source of standing water should be emptied, and water in bird baths, fountains, wading pools, etc. should be changed at least once per week. Pesticides, including larvicides and adulticides, can be part of a mosquito control program but also have toxic effects.

Biological and genetic methods of mosquito control are being explored. These include infection with the bacterium \textit{Wolbachia}, which provides the mosquito with varying degrees of antiviral protection,\textsuperscript{18} release of
mosquitoes genetically modified to resist arboviral infection, and release of mosquitoes carrying a lethal gene in order to reduce the vector population.\textsuperscript{19}

To prevent mosquito bites, the Centers for Disease Control and Prevention (CDC) recommends using an Environmental Protection Agency (EPA)-registered insect repellant with the active ingredients DEET, picaridin, IR3535, oil of lemon eucalyptus, or para-methane-diol.\textsuperscript{20} Clothing and gear can be treated with the insecticide permethrin.\textsuperscript{20} When outdoors, people should wear long-sleeved shirts and long pants. Since many mosquito species are active at dusk and dawn, staying inside during those hours may reduce mosquito exposure. However, the CHIKV vectors \textit{Ae. aegypti} and \textit{Ae. albopictus} also bite during the day. To keep mosquitoes out of the home, screen all windows and doors.

**DISEASE CONTROL**

There are no specific control measures for CHIKV in pigs. Standard biosecurity practices should be in place on swine premises.

**TRANSMISSION**

Like other arboviruses, CHIKV is maintained in a transmission cycle between mosquitoes and vertebrate hosts.

- In Africa, CHIKV cycles between non-human primates and \textit{Aedes} spp. found in forest environments, such as \textit{Ae. furcifer} and other members of the \textit{Ae. furcifer-taylori} group. Humans in rural populations are occasionally affected through “spill over” events.\textsuperscript{21} There is some evidence that a sylvatic cycle also exists in Asia, particularly in Malaysia and the Philippines.\textsuperscript{21}

- The urban cycle is seen where large populations of humans and urban \textit{Aedes} spp. co-exist, maintaining human-mosquito-human transmission. The urban cycle has resulted in large CHIKV outbreaks in Africa related to the range expansion of \textit{Ae. albopictus}, and is the main cause of CHIKV persistence linked to \textit{Ae. aegypti} in Asia.\textsuperscript{21} Characteristics of \textit{Ae. aegypti} and \textit{Ae. albopictus} are shown in Table 1.

<table>
<thead>
<tr>
<th>Table 1. Chikungunya Virus Vectors*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Origin</strong></td>
</tr>
<tr>
<td><strong>Current distribution</strong></td>
</tr>
<tr>
<td><strong>Feeding</strong></td>
</tr>
<tr>
<td><strong>Vector competence</strong></td>
</tr>
</tbody>
</table>

*Adapted from Surveillance and Control of \textit{Aedes aegypti} and \textit{Aedes albopictus} in the United States (CDC)

Vertical CHIKV transmission has also been documented in humans.\textsuperscript{1} No information was found regarding CHIKV transmission in swine.

**PATHOGENESIS**

In humans, CHIKV replicates in the dermal fibroblasts and then enters the lymph nodes and circulatory system.\textsuperscript{2} From there, it disseminates to other parts of the body including the muscle and joint compartments.\textsuperscript{2} No information was found regarding the pathogenesis of CHIKV in swine.
DIAGNOSIS

In humans, infection with CHIKV is suspected when fever and joint pain are present. Clinical diagnosis is not possible, however, due to the similar presentation of other tropical febrile diseases including dengue, malaria, typhoid, and scrub typhus. In the United States, preliminary diagnosis is based on clinical features, places and dates of travel, and activities.

DIAGNOSTIC TESTS

Viral culture is possible but requires BSL-3 conditions. According to the CDC, within the first eight days of illness, the preferred test for CHIKV diagnosis in humans is quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). Virus-specific IgM antibodies may not be detectable via enzyme linked immunosorbent assay (ELISA) until seven days after the onset of illness. Serologic testing can be used to rule out the diagnosis using convalescent-phase samples from patients whose acute-phase samples test negative. A positive result can be confirmed by PRNT. IgG antibodies can be detected for years after the initial infection.

CHIKV qRT-PCR, IgM-capture ELISA, and PRNT are performed by the CDC. Testing may be available at some state and territory laboratories. Commercial laboratories may also offer CHIKV testing in humans.

SAMPLES

Suitable samples for CHIKV testing in humans include serum, cerebrospinal fluid, urine, and possibly others. Since CHIKV has not been reported in pigs, there is no information on preferred samples or use of oral fluids for diagnostic testing.

EPIDEMIOLOGY

SPECIES AFFECTED

Humans serve as reservoirs during urban epidemics, but several animal species are also capable CHIKV hosts. Monkeys, rodents, and birds are thought to act as reservoirs for the virus, and it is likely that other vertebrates hosts have not yet been identified.

GEOGRAPHIC DISTRIBUTION

In humans, CHIKV occurs throughout Asia, Africa, Europe, and the Americas. The mosquito vector *Ae. aegypti* is found in the tropics and sub-tropics, while the range of *Ae. albopictus* includes temperate and even cold regions. *Ae. albopictus* is responsible for the establishment of CHIKV in Europe and the Americas. For more information on different genotypes and their geographic distribution see Etiology.

MORBIDITY AND MORTALITY

No information was found on morbidity and mortality due to CHIKV in swine.

ETIOLOGY

CHARACTERISTICS OF TOGAVIRUSES

CHIKV is an arbovirus belonging to the genus *Alphavirus*, family *Togaviridae*. There are more than 30 alphaviruses that infect humans and/or animals. Alphaviruses are classified as New World or Old World depending on their suspected origin, and they are grouped into eight antigenic complexes based on sequencing and serological cross-reactivity (excluding salmonid strains). CHIKV is an Old World alphavirus that is part of the Semliki Forest serocomplex, which includes Ross River virus, Bebaru virus, Sagiyama virus, Getah virus, Mayaro virus, O’nyong nyong virus, Semliki Forest virus, and Una virus.

Togaviruses are single-stranded, positive-sense RNA viruses. They are spherical, uniform, and about 70nm in size, with a lipid envelope (or “toga”) surrounding the icosahedral nucleocapsid. The CHIKV genome contains nearly 12,000 nucleotides. Like other togaviruses, important components of the CHIKV virion include:
Capsid protein (C),
- Envelope “spike” glycoproteins (E1, E2) and their leader peptides (denoted E3 and 6K, respectively), and
- Nonstructural proteins (NSPs 1–4), which are found in infected cells and encode the viral replication machinery of the virus.1

CHARACTERISTICS OF CHIKUNGYA VIRUS

African Genotype
It is thought that CHIKV evolved in Africa and diverged into two principal lineages—West African and East Central South African (ECSA)—about 350 years ago.26 The ECSA genotype was first isolated from humans in Tanzania in the early 1950s.27, 28 Since that time, CHIKV has continued to circulate in Africa, with periodic outbreaks being detected. Notable CHIKV epidemics occurred in the Democratic Republic of the Congo in 1999–200029 and in Gabon in 2006–2007.30 Historic accounts show that African-origin CHIKV has caused global pandemics every 40-50 years.4

In 2004, a novel ECSA strain was identified in Kenya. Later classified as the Indian Ocean Lineage (IOL) strain, the virus spread to the Indian Ocean region in 2005.31 A second, related ECSA was introduced to India in 2006.32 Altogether, nearly 2 million people were infected with CHIKV. Around this time, imported CHIKV cases began to surface in Europe. In Italy and France, autochthonous transmission was documented originating from infected travelers.33, 34 Imported cases also occurred in the Americas, but no local transmission was detected. In part, the success of epidemic IOL strains came from mutations in the E135, 36 and E237, 38 genes, which allowed the virus to replicate in both Ae. aegypti and A. albopictus mosquitoes and expand its geographic range. Recent outbreaks, some involving new E1 and E2 mutations, have occurred in Pakistan (2016),39 France (2017),40 Italy (2017),41 Kenya (2016–17),42 the Republic of Congo (2019),43 and Thailand (2018–19).44

Asian Genotype
In the late 1950s, a CHIKV variant identified in Thailand was classified as a new genotype, though it originated from the ECSA lineage45 and was likely introduced to Asia decades earlier.46 The so-called Asian genotype has since become widespread in Southeast Asia and—as in Africa—causes occasional human outbreaks.

In late 2013, the first outbreak of CHIKV with autochthonous transmission was documented in the Americas on the island of St. Martin.47 Unexpectedly, the Asian genotype was identified as the cause. The Caribbean virus was most closely related to CHIKV strains identified in China in 2012 and the Philippines in 2013. These isolates, along with strains from Micronesia, have since been termed Cosmopolitan Asian CHIKV.48 The Caribbean CHIKV strain is known to have acquired three adaptive amino acid substitutions in NSP1, E1, and E3.48

By mid-2015, CHIKV had reached much of the Caribbean, Latin America, and the United States, with nearly 1.4 million suspected cases.24 Nearly 3000 CHIKV cases were reported to ArboNET in 2014, including 12 autochthonous cases from Florida.49 In 2015, another 700 cases of CHIKV were reported in US travelers returning from affected areas.50 Imported cases continue to occur in the United States, but local transmission has not been recently reported.

HISTORY IN SWINE
There are no reports of natural CHIKV infection in swine.

IMMUNITY

POST-EXPOSURE
In humans, an IgM response is detectable three to eight days after symptom onset and persists for one to three months. IgG can be detected via ELISA within four to 10 days of symptom onset and lasts for years, perhaps for life.1
VACCINES
There is no commercially available vaccine for CHIKV in humans or animals. At least 15 vaccine candidates are currently in development, utilizing a number of platforms (inactivated, live attenuated, live vectored, chimeric, virus-like particle, subunit protein, and DNA).51, 52 Candidate vaccines that have completed phase I or II trials include VLA1553, a live CHIKV attenuated by a partial deletion of a gene encoding the non-structural replicase complex protein, and MV-CHIK, a live attenuated measles-vectored CHIKV vaccine that induces CHIKV-specific neutralizing antibodies.53

CROSS-PROTECTION
Since CHIKV lineages are composed of a single serotype, long lasting cross-protection between lineages occurs.51 Some cross-protection also occurs between CHIKV and other alphaviruses. In mice previously infected with Ross River virus, inoculation with CHIKV resulted in lower mean peak viremia and protection against clinical disease. Similarly, when antiserum from Ross River virus-infected mice was transferred into naïve mice, they were protected against CHIKV disease.54 Serological studies in pigs have suggested antigenic cross-reaction between CHIKV and Semliki Forest virus,6 Getah virus, and Sindbis virus.5

GAPS IN PREPAREDNESS
If CHIKV is introduced to the United States, the extent to which local transmission could occur is unclear. The estimated range for *Aedes* spp. encompasses at least the southern one third of the country according to the CDC.55 Changes in mosquito populations and habitat could lead to the expansion of arboviruses such as CHIKV.56 The likelihood of CHIKV endemicity is also affected by the potential to establish sylvatic transmission cycles involving non-human primates.46

Currently, natural CHIKV infection in swine has not been reported. Although neutralizing antibodies have been detected in pigs infected experimentally, clinical signs of disease have not been described. The signs in swine may be vague, as in humans, and an outbreak may be difficult to detect. There are no diagnostic tests validated for animals. In addition, there is no CHIKV vaccine. Cleaning and disinfection protocols for swine facilities have not been established and there are no EPA-registered disinfectants for CHIKV.

REFERENCES


