


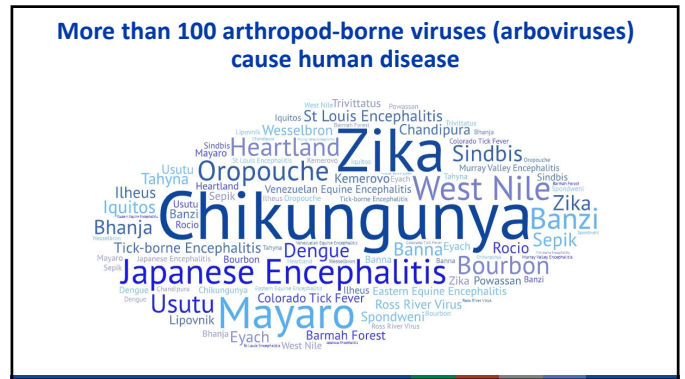
National Center for Emerging and Zoonotic Infectious Diseases 

Arboviruses: Emerging and Re-Emerging

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Fort Collins, Colorado

ASTMH Update Course in Clinical and Tropical Medicine & Travelers' Health
September 27, 2024

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Main clinical syndromes for arboviral infections


Febrile	• Often with rash, myalgia, and/or arthralgia	Oropouche Chikungunya Mayaro, Zika
Hemorrhagic	• Bleeding and/or shock syndrome	Dengue Yellow fever
Neurologic	• Encephalitis, meningitis, or myelitis	Japanese encephalitis Tick-borne encephalitis

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Oropouche: the new kid on the block

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The basics



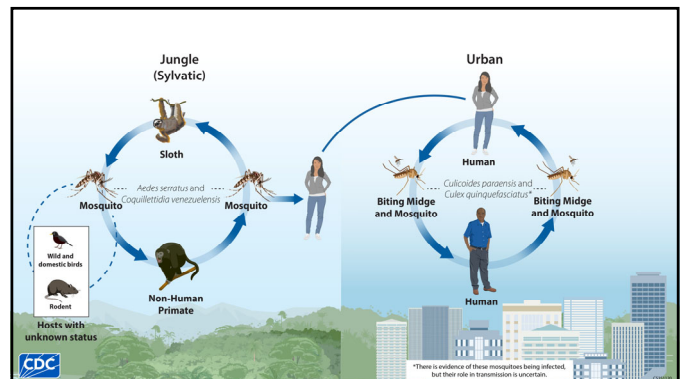
Virus genus: Orthobunyavirus

First isolated: Vega de Oropouche, Trinidad, 1955

Primary vectors: *Culicoides paraensis* midge
Culex quinquefasciatus mosquitoes*

*Role uncertain

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Clinical illness

- Asymptomatic infection: ~40%
- Incubation period: 3-10 days
- Symptoms:
 - Fever
 - Severe headache
 - Chills
 - Myalgia
 - Arthralgia
 - Fatigue
 - Photophobia
 - Dizziness
 - Maculopapular rash
- In up to 60% of patients, can reoccur a few days or even weeks after acute illness
- Most illness mild, but severe illness (e.g., neuroinvasive disease) and death possible

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Oropouche disease during pregnancy

- Based on limited data from Brazil, vertical transmission of Oropouche virus is **possible**
 - Several pregnant people with evidence of vertical transmission to their fetuses associated with fetal death or congenital abnormalities, including microcephaly
 - Pregnant people had symptoms during pregnancy; most had positive test results
 - Tissues from stillbirth and one infant born with microcephaly tested positive by RT-PCR
- What we don't know**
 - Frequency of vertical transmission
 - Frequency of adverse outcomes
 - Effect of timing of disease during pregnancy on risk of adverse outcomes

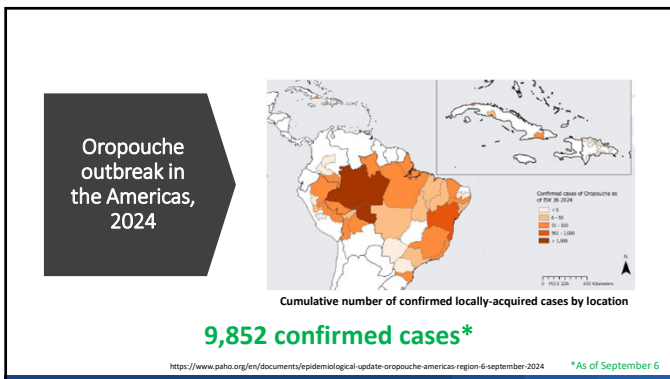
<https://www.paho.org/en/documents/epidemiological-alert-oropouche-region-america-vertical-transmission-event-number>
<https://www.pfdr.gov/oropouche/hsp/crisis/crisis-cases/epidemiology.html>

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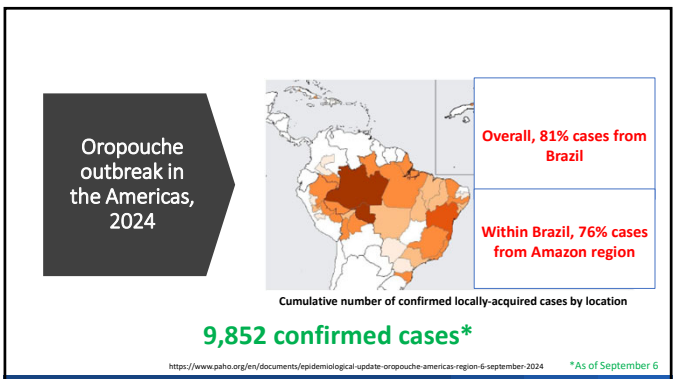
Laboratory investigations and testing

- Laboratory investigations**
 - Lymphopenia
 - Leukopenia
 - Elevated C-reactive protein
 - Elevated liver enzymes (mild)
- Diagnostic testing**
 - ≤7 days after onset: RT-PCR
 - >7 days after onset: Plaque reduction neutralization test (PRNT)

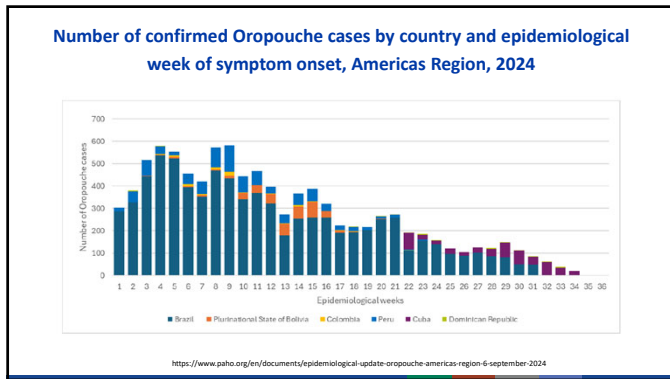
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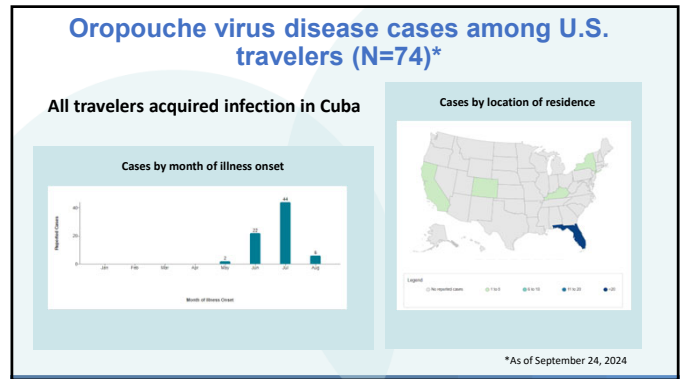
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Prevention

- Environmental Protection Agency (EPA)-registered insect repellents labeled for flies, biting flies, or *Culicoides* (biting midges)
- Window and door screens with the mesh screen measuring 20x20
- Fans when outdoors to blow midges away

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Key references and resources

- PAHO. Oropouche. <https://www.paho.org/en/news/10-9-2024-paho-publishes-update-oropouche-fever-americas>
- CDC. Oropouche website. Available at: <https://www.cdc.gov/oropouche/index.html>
- Huits R, Waggoner JJ, Castilletti C. New insights into Oropouche: Expanding geographic spread, mortality, vertical transmission, and birth defects. *J Travel Med.* 2024 Aug 29:taae117.
- Morrison A, White JL, Hughes HR, et al. Oropouche virus disease among U.S. travelers - United States, 2024. *MMWR Morb Mortal Wkly Rep.* 2024 Sep 5;73(35):769-773.
- Sakkas H, Bozidis P, Franks A, Papadopoulou C. Oropouche Fever: A Review. *Viruses.* 2018 Apr 4;10(4):175.

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Oropouche: what's in a name?

etymology

Oropouche [o'ro-poo'che]

Ronnie Henry and Frederick A.

A virus was isolated from a 24-year-old forest worker in the island of Trinidad (country: Trinidad and Tobago) and spontaneously after 18 days. The virus was isolated at the Trinidad Regional Virus Laboratory. Five years later, a mosquito collected 100 miles away in the Bushy Park area, Trinidad, was found to be infected with the virus. The mosquito, but the specific vector remains unknown. The virus is related to the Oropouche transmission cycle. The virus is named in keeping with the tradition of designating new viruses after the place where they were first discovered. The village, a nearby swamp (wetlands), and river. It denotes a new disease.

no other proven to be one of the most common arthropod-borne viruses in the Americas.

Mjsew-WIR zwum-KP3Jy-z tq1if? Tw.ut.zhm] [mex3Jr jw.NkghyIa3 756@9-: .2-B<3 i:R53B7564j]i795: 3Y795:

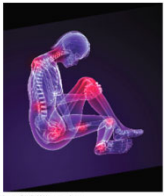
Dut: dnlB3jctj]wky Vzakdip h.RE1

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The basics



Virus genus: Alphavirus

First isolated: Tanzania, 1952–1953

Primary vectors: *Aedes* species mosquitoes

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Key features of acute chikungunya virus disease


- Febrile illness with typically severe arthralgia, can be debilitating
- Joint symptoms involve multiple joints, most commonly hands and feet
- Other symptoms include headache, rash, myalgia, anorexia, nausea, vomiting, diarrhea



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Complications of chikungunya

- Rare atypical presentations
 - Severe presentations includes myocarditis, hepatitis, acute renal disease, neurologic illness
- Groups at risk of severe disease
 - Older adults aged >65 years, particularly those with comorbidities (e.g., diabetes, cardiac disease, hypertension), and young infants infected perinatally or by mosquito bites
 - Severe illness follows U-shaped age distribution curve
- Mortality rate low at about 0.01% - 0.5%



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Persistent arthralgia after chikungunya*

3 months → 12 months

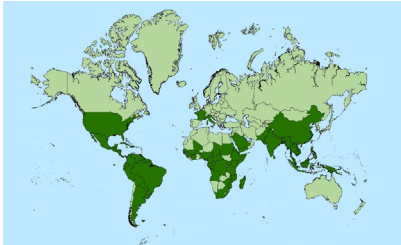
About 50% → About 35%

*Based on recent meta-analysis (Lindsay N. Chronic arthralgia after chikungunya. US Advisory Committee on Immunization Practices meeting, June 2023)

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Distribution and disease burden in endemic areas

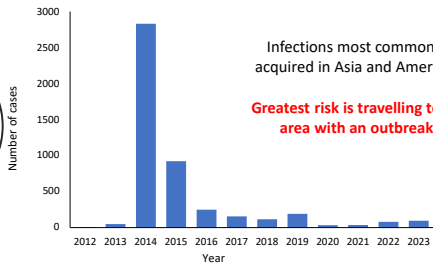
- Typically tropical and subtropical regions
- Periodically causes large outbreaks, often with high attack rates



Countries and territories with current or past transmission of chikungunya virus

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Chikungunya cases among U.S. travelers, 2012-2023



Number of cases

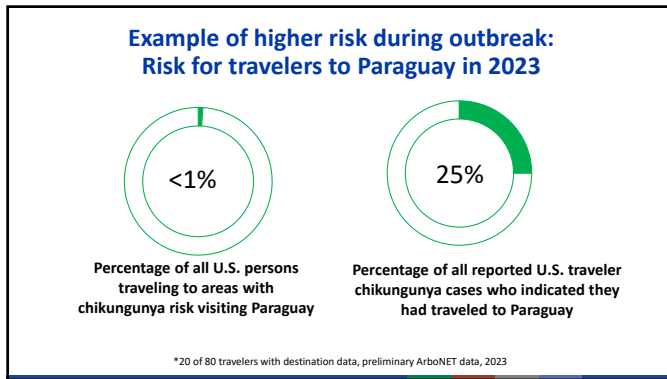
Year

Infections most commonly acquired in Asia and Americas

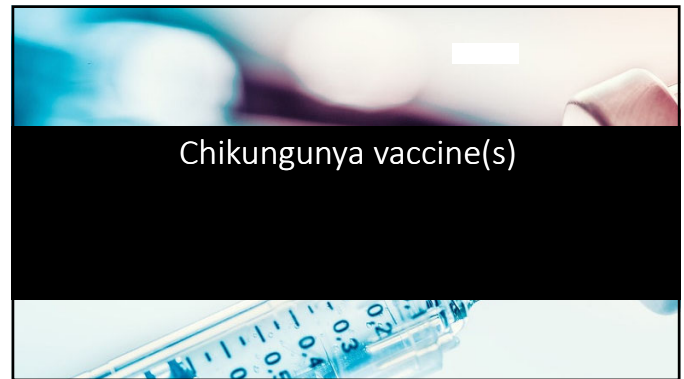
Greatest risk is travelling to an area with an outbreak

*Based on CDC laboratory and surveillance data

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IXCHIQ: Valneva's live attenuated chikungunya vaccine

- U.S. FDA approval in November 2023
- Also approved in Canada and by European Medicines Agency
- Age indication: 18 years and older
- Schedule: 1 dose
- US Advisory Committee on Immunization Practices (ACIP) recommendations in February 2024

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Availability for younger age groups

- Adolescent study (12–17 years) completed in Brazil
- Phase II trial among children aged 1–11 years began late in 2023

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Licensure through accelerated approval pathway

- Effectiveness demonstrated by showing vaccine has effect on surrogate endpoint reasonably likely to predict clinical benefit
- Post-licensure requirement for controlled trials to confirm the clinical benefit

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Short- and long-term “protection” (seroresponse rates)

- Based on data from ~620 vaccinated subjects
- **Short-term protection** (2 studies; n=622)
 - 98% at 1 month
- **Long-term protection** (1 study; n=360)
 - 99% at 12 months
 - 97% at 24 months

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Safety data

- Data based on ~3,500 vaccinated subjects in 2 studies
- Pivotal Phase 3 trial: 3,082 adults in vaccine group and 1,033 in placebo group

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Solicited local reactions*:

15% in vaccinees vs 11% in placebo recipients



*Within 10 days of vaccination

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Solicited systemic adverse events*:

50% in vaccinees vs 27% in placebo recipients

Most common headache, fatigue, myalgia in ~25–30%



*Within 10 days of vaccination

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Solicited systemic adverse events – arthralgia/arthritis*:

17% in vaccinees vs 5% in placebo recipients

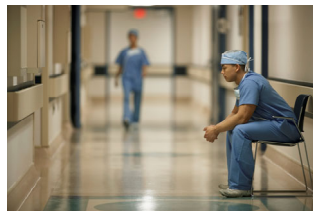


*Within 10 days of vaccination

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Serious adverse events*:

Two events in vaccinated subjects considered **vaccine-related**, including hospitalizations for 1) severe myalgia and 2) hypovolemic hyponatremia/atrial fibrillation



*FDA definition, including hospitalization (<https://www.fda.gov/safety/reporting-serious-problems/fda-what-serious-adverse-event>)

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Chikungunya-like adverse reactions

- Fever $\geq 100.4^{\circ}\text{F}$ (38°C) and ≥ 1 of
 - arthralgia or arthritis
 - myalgia
 - headache
 - back pain
 - rash
 - lymphadenopathy, or
 - certain neurological, cardiac or ocular symptoms
- Event occurred within 30 days of vaccination

-----WARNINGS AND PRECAUTIONS----- IXCHIQ

- IXCHIQ may cause severe or prolonged chikungunya-like adverse reactions. [52]
- Vertical transmission of wild-type CHIKV from pregnant individuals with viremia at delivery is common and can cause potentially fatal CHIKV disease in neonates. Vaccine viremia occurs in the first week following

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Chikungunya-like adverse reactions

- **Chikungunya-like adverse reactions**
 - 11.7% of vaccine recipients and 0.6% of placebo recipients
 - Most symptoms mild or moderate
- **Severe reactions** that prevented daily activity or required medical intervention, or fever $\geq 39^{\circ}\text{C}$ (102.1°F)
 - 1.6% vaccine recipients vs 0% of placebo recipients
- **Prolonged reactions** with duration ≥ 30 days
 - 0.5% vaccine recipients vs 0% of placebo recipients

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Summary of safety data

- Reactogenic vaccine
- Ongoing safety monitoring now vaccine is licensed and being used in larger populations
 - U.S. providers please report adverse events to the Vaccine Adverse Event Reporting System (VAERS) at: <https://vaers.hhs.gov/>

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Potentially coming soon: Virus-like particle chikungunya vaccine

- Manufactured by Bavarian Nordic
- Licensure possible in United States as early as February 2025
- Intended age group is adolescents and adults aged ≥ 12 years
- Single dose schedule



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U.S. ACIP recommendations for use of IXCHIQ among travelers



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Summary of considerations for vaccine recommendations*

- Disease can result in severe arthralgia during the acute illness, rare serious complications, and sometimes long-term arthralgia
- Highest risk for severe outcomes among older adults, particularly those with comorbidities, and neonates and young infants
- Moderate disease burden among US travelers with 100–200 cases reported annually
- Substantially higher risk for infection if travel during an outbreak
- Immunogenic but reactogenic vaccine



*Based on discussions of ACIP Chikungunya Vaccines Work Group

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ACIP recommendations for use of IXCHIQ among travelers (approved February 28, 2024)*

- Chikungunya vaccine is **recommended** for persons aged ≥ 18 years traveling to a country or territory where there is a chikungunya outbreak
- In addition, chikungunya vaccine **may be considered** for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years
 - Persons aged >65 years, particularly those with underlying medical conditions, who are likely to have at least moderate exposure^a to mosquitoes, OR
 - Persons staying for a cumulative period of 6 months or more

^aACIP recommendations available at: <https://www.cdc.gov/vaccines/acip/recommendations.html>
^bModerate exposure could include travelers who might have at least 2 weeks (cumulative) of exposure to mosquitoes in indoor and/or outdoor settings

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Definition of moderate exposure

- Travelers who might have at least 2 weeks (cumulative) of exposure to mosquitoes in indoor and/or outdoor settings
- Does not include travelers who might have limited exposure to mosquitoes
 - For example, those traveling for business and likely to be mainly in mosquito-protected indoor settings

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CDC chikungunya website: Areas at risk for chikungunya

Outbreaks

Transmission within last 5 years

<https://www.cdc.gov/chikungunya/data-maps/index.html>

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CDC Travelers' Health website: Travel Health Notice

<https://www.cdc.gov/travel/notices/level2/chikungunya-maldives>

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CDC Travelers' Health website: Destination pages

<https://www.cdc.gov/travel/destinations/traveler/none/brazil>

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CDC webpage with vaccination information for healthcare providers

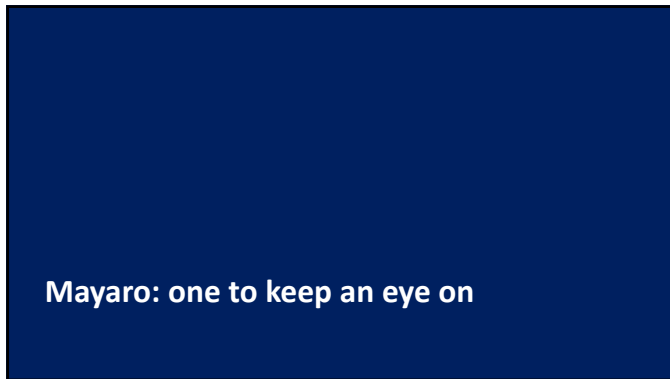
<https://www.cdc.gov/chikungunya/hcp/vaccine/index.html>

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Key references and resources


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- Burt FJ, Chen W, Miner JJ, et al. Chikungunya virus: an update on the biology and pathogenesis of this emerging pathogen. *Lancet Infect Dis*. 2017 Apr;17(4):e107-e117
- Chen LH, Fritzer A, Hochreiter R, Dubischar K, Meyer S. From bench to clinic: the development of VLA1553/IXCHIQ, a live-attenuated chikungunya vaccine. *J Travel Med*. 2024 Sep 10:taae123.
- CDC. Chikungunya website. Available at: <https://www.cdc.gov/chikungunya/about/index.html>

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The basics




Virus genus:	Alphavirus
First isolated:	Mayaro County, Trinidad, 1954
Primary vectors:	<i>Haemagogus</i> species mosquitoes*
Reservoir hosts:	Non-human primates*

*Presumed

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Countries with reported Mayaro cases as of 2023*




*Recent confirmation in Colombia also

Source: www.cdc.gov

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Key clinical facts


- Clinical symptoms**
 - Fever
 - Arthralgia which can be severe and persist for months
 - Myalgia
 - Headache
 - Maculopapular rash which can appear several days after other symptoms
 - Lymphadenopathy
- Laboratory investigations**
 - Leukopenia (common)
 - Mild thrombocytopenia (less common)
- Diagnosis**
 - No commercial assays (testing in US available at CDC)



Rash of Mayaro virus infection (Source: Pinheiro FP et al, AJTMMH 1983)

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Risk for infection typically related to exposure in forested areas



Source: Flickr.com

Source: Amazon.com/Travel.org

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Published cases in international travelers, 1996–2024

Year	Nationality	Travel destination	Reference
1996	United States	Peru	1
1997	United States	Peru	1
1999*	United States	Bolivia	2
2008**	Dutch	Suriname	3
2009*	French	Brazil (Amazon)	4
2011	Swiss	Peru (Amazon)	5
2012	German	Bolivia (Amazon)	6
2013	German	French Guiana	7
2013	Dutch	Brazil (Amazon)	8
2013	French	French Guiana	9
2014	German	Ecuador	10
2014	German	Bolivia	10

*Probable case; **Possible infection in partner also

References: 1. Toth et al, 1999, Clin ID; 2. Taylor et al, 2005, Southern Med J; 3. Hensing et al, 2010, J Infect; 4. Receveur et al, 2010, Euro Surveill; 5. Neumeier et al, 2012, Emerg ID; 6. Theissacker et al, 2013, BMC Infect Dis; 7. Friedrich-Jantsche et al, 2014, Emerg ID; 8. Steiger et al, 2014, J Clin Virol; 9. Ulaganathan-Baretz et al, 2016, J Clin Virol; 10. Tappe et al, 2016, Emerg ID.

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An emerging threat?

Concern for expansion and transmission outside recognized areas of transmission in Americas

Emerging Microbes & Infections

Volume 20(12) December 2022

Open Access

REVIEW ARTICLE

Mayaro: an emerging viral threat?

Vera Acevedo-Aranda¹, Diana M. Morales¹, Bryan Rodriguez¹, Yovana Pacheco², Juan-Manuel Anaya¹ and Carolina Sanchez-Gonzalez¹

Abstract

Mayaro virus (MAYV), an enveloped RNA virus, belongs to the Togaviridae family and Alphavirus genus. The arthropod-borne virus phylogeny is similar to Chikungunya (CHIKV), Dengue (DENV), and Zika virus (ZIKV). The term "Chikungunya syndrome" has been coined for clinically suspected alphaviruses, which have arisen as a consequence of the high viral burden, viral persistence, and circulation in South America in most cases. MAYV disease is characterized by acute and self-limited fever, arthralgia, and maculopapular rash among the most common symptoms identified. Long-term sequelae have been reported by other alphaviruses. However, severe manifestations of the disease have been reported due to chronic polyarthritis, neurological complications, hemolytic thrombocytopenia, and even death. Currently, there are no specific commercial tests for the diagnosis of MAYV, and the lack of serological confirmation has affected by under-reporting and the vector proof. It requires further clinical and epidemiological data and is still uncertain. Therefore, more serological research is warranted, and new highly specific molecular diagnostic methods should be developed. This comprehensive review is intended to encourage public health authorities and scientific communities to actively work on diagnosing, preventing, and treating MAYV infection.

Brazil reports an increased incidence of oropouche and mayaro fever in the amazon region

Carolina Lorenz¹ · Francisco Chiaravallotti Neto²

https://doi.org/10.1093/embo/kzab001

Parasites & Vectors

Volume 15(1) 2022

Open Access

RESEARCH

Mayaro virus, a potential threat for Europe: vector competence of autochthonous vector species

Nancy Bruchman¹, Naim Bartholomewson¹, Tatiana Reverte¹, Xenia K. Anon¹ and Ruth Miller¹

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Key references

- Caicedo EY, Charniga K, Rueda A, et al. The epidemiology of Mayaro virus in the Americas: A systematic review and key parameter estimates for outbreak modelling. *PLoS Negl Trop Dis.* 2021 Jun 3;15(6):e0009418. doi: 10.1371/journal.pntd.0009418.
- Pinheiro FP, Freitas RB, Travassos da Rosa JF, et al. An outbreak of Mayaro virus disease in Belterra, Brazil. I. Clinical and virological findings. *Am J Trop Med Hyg.* 1981 May;30(3):674-81. doi: 10.4269/ajtmh.1981.30.674.

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Where has all the Zika gone?

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Warmer summers could mean Zika and dengue move into Canada, experts warn

By Sean Previl · Global News
Posted September 25, 2024 12:39 pm · 5 min read

Dengue fever is rising in Europe — What should Canadian travellers know...
Dengue fever is on the rise in parts of Europe, with experts linking local outbreaks to an invasive species...



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The basics



Virus genus:	Flavivirus
First isolated:	Zika forest, Uganda, 1947
Primary vectors:	<i>Aedes</i> species mosquitoes
Other main transmission modes:	Intrauterine Sexual

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Clinical presentation

- Symptoms are typically mild
- Main symptoms
 - Maculopapular rash (can be pruritic)
 - Fever
 - Arthralgia
 - Conjunctival hyperemia




Rash and conjunctival hyperemia of Zika virus infection (Acknowledgment: M. Duffy)

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Infections during pregnancy

- Fetal death
- Preterm birth
- Stillbirth
- Congenital Zika syndrome (CZS) and other birth defects

Common clinical findings in infants with CZS (cdc.gov)

61

Babies born to people infected with Zika virus while pregnant

5%
with Zika-associated birth defects

62

Evidence of current or prior Zika virus transmission

As of May 2024, **92 countries or territories** with evidence of current or prior Zika virus transmission

<https://www.who.int/publications/m/item/zika-epidemiology-update-may-2024>

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Current status of Zika surveillance

- Limited number of countries are conducting surveillance and laboratory testing
- Where surveillance is conducted, might not be sufficiently sensitive to detect low levels of transmission

Transmission in many locations likely remains under-recognized

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Current status of Zika virus transmission

- Since 2017, following the peak of Zika virus transmission in the Americas, global reported case numbers have declined substantially
- Transmission likely interrupted in some locations, particularly small island nations
- Sporadic cases and occasional outbreaks continue to be reported
- Transmission continues to be identified in new areas without previously recognized transmission

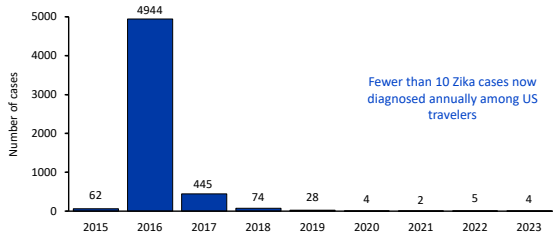
65

Suspected and confirmed Zika virus disease cases by year, Americas, 2015–2023

PAHO, PLISA data (<https://www3.paho.org/data/index.php/en/mnu-topics/zika.html>)

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Travel-associated Zika virus disease cases by year — U.S. states, 2015–2023*



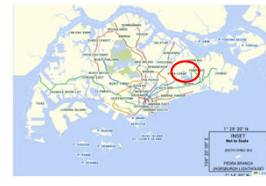
*Probable and confirmed cases reported to the U.S. national notifiable disease surveillance system, ArboNet. Data for 2023 are provisional.

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Examples of recent outbreaks



Maharashtra, India (current)
(N=100)



Kovan district, Singapore (2023)
(N=30)



Thailand (2023)
(N=758)

CDC posts travel health notices at <https://www.cdc.gov/travel/notices>

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Diagnosis of Zika in the current setting

- **≤7 days: molecular test**
 - Preferred method because of high specificity
- **>7 days: IgM antibody testing**
 - Less ideal because of cross-reactivity among flaviviruses, false positive IgM results with current low incidence, and long-term IgM persistence
 - Confirmatory neutralizing antibody testing should be conducted when epidemiologically or clinically indicated

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Key references and resources

- World Health Organization. Zika epidemiology update – May 2024. Available at: <https://www.who.int/publications/m/item/zika-epidemiology-update-may-2024>
- U.S. CDC. Zika virus website (including US guidance on testing and prevention): Available at: <https://www.cdc.gov/zika/index.html>
- Pan American Health Organization. PUSA Health information platform for the Americas. Available at: <https://www3.paho.org/data/index.php/en/>
- Rabe IB, Hills SL, Haussig JM, et al. A review of the recent epidemiology of Zika virus infection. *Am J Trop Med Hyg*, *in press*
- Musso D, Ko AI, Baud D. Zika virus infection - After the pandemic. *N Engl J Med*. 2019 Oct 10;381(15):1444-1457.
- Roth NM, Reynolds MR, Lewis EL, et al. Zika-associated birth defects reported in pregnancies with laboratory evidence of confirmed or possible Zika virus infection - U.S. Zika Pregnancy and Infant Registry, December 1, 2015-March 31, 2018. *MMWR Morb Mortal Wkly Rep*. 2022 Jan 21;71(3):73-79.

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Clinical management and prevention of chikungunya, Mayaro, and Zika

Clinical management

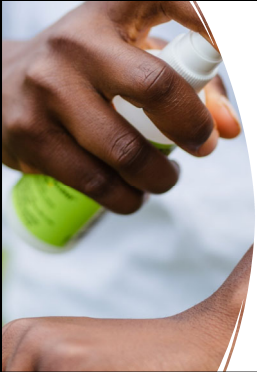
- No specific antiviral treatment
- Treat symptoms: rest, fluids, and use of analgesics and antipyretics
- Acetaminophen preferred initial treatment for fever and joint pain
 - Aspirin and other non-steroidal anti-inflammatory drugs should not be used until dengue ruled out to reduce risk of hemorrhage

Avoid until dengue ruled out



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Prevention

- Mosquito bite prevention
 - Insect repellent
 - Long-sleeved shirts and pants
 - Accommodations with air conditioning, window screens or bed nets
- For Zika, sexual transmission prevention
 - Abstinence
 - Condoms and dental dams


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Dengue: breaking records in 2024



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The basics



Virus genus:	Flavivirus
Virus types:	DENV-1, 2, 3, 4
Primary vectors:	<i>Aedes</i> species mosquitoes

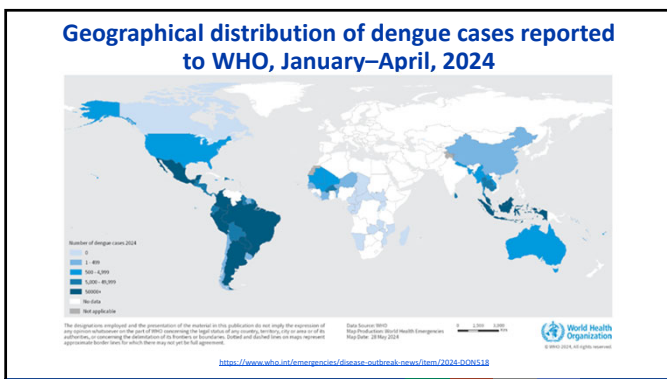
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Global dengue situation, 2024

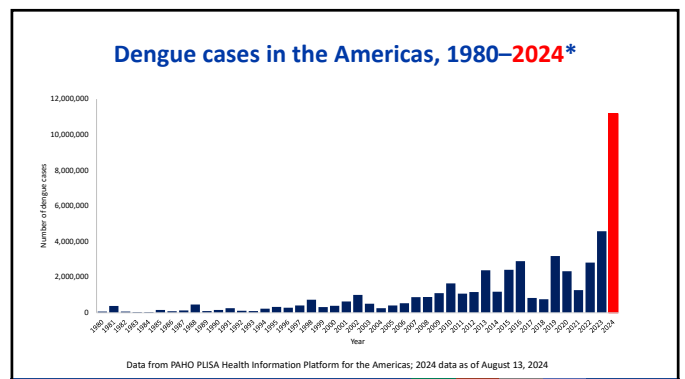
-  • **>11 million cases** reported worldwide
-  • **103 countries/territories** reporting cases
-  • **>20 countries** reporting outbreaks

<https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON518>

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Dengue information on CDC website to assist with guidance to travelers

https://www.cdc.gov/travel/notices/level1/dengue-global

https://www.cdc.gov/dengue/areas-with-risk/index.html

CDC Yellow book: <https://www.cdc.gov/travel/yellowbook/2024/infections-diseases/dengue>

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Clinical presentation and management of dengue

- Most cases have mild febrile illness, but some cases will develop **severe dengue**, which can include **shock, severe bleeding, or severe organ impairment**
- Severe dengue often begins when fever resolves and is preceded by **warning signs** such as **intense abdominal pain, persistent vomiting, bleeding gums, fluid accumulation, altered mental status, hepatomegaly, or a progressive increase in hematocrit**
- Appropriate treatment can reduce mortality
 - Patients with warning signs should be managed in hospital with a protocolized fluid resuscitation algorithm
 - Patients with certain co-existing conditions can be observed/managed in hospital
 - Patients managed as outpatients should be educated on warning signs and advised when to return to the hospital

For this and further dengue training resources, visit: <https://www.cdc.gov/dengue/hcp/clinical-care/index.html>

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Appropriate laboratory testing for dengue

- Acute phase (≤7 days after illness onset)**
 - RT-PCR + IgM ELISA **or**
 - NS1 antigen ELISA + IgM ELISA
- Convalescent phase (>7 days after illness onset)**
 - IgM serology (and consider NS1 antigen ELISA or RT-PCR)

https://www.cdc.gov/dengue/hcp/diagnosis-testing/index.html

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Vaccines

- Dengvaxia (Sanofi Pasteur)**
 - Licensed in several locations
 - Discontinued**
- Qdenga (Takeda)**
 - Licensed in several locations*
 - Takeda voluntarily withdrew US license application in July 2023 (**not available for US travelers**)
 - European vaccination recommendations for travelers vary by country

*Argentina, Brazil, Indonesia, Thailand, United Kingdom, and by the European Medicines Agency

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Key references and resources

- U.S. CDC. Dengue virus website for healthcare providers. Available at: <https://www.cdc.gov/dengue/hcp/index.html>
- World Health Organization. Dengue – Global situation. Available at: <https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON518>
- CDC Yellow Book: Health Information for International Travel. Available online.
- Hunsperger EA, Munoz-Jordan J, Beltran M, et al. Performance of dengue diagnostic tests in a single-specimen diagnostic algorithm. J Infect Dis. 2017 Sept 15;214(7):837-44.

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In thinking about the key arboviral diseases causing febrile illness...

Dengue > Chikungunya > Zika > Mayaro

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Quick arboviral vaccine updates and reminders

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Yellow fever vaccine

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Yellow fever

COMMENT OPEN

Yellow fever resurgence: An avoidable crisis?

Nicole P. Lindsey¹, Jennifer Horton², Alan D. T. Barrett³, Maurice Demaree⁴, Thomas P. Monath⁵, Oymen Toksoz⁶, Michel Van Herp⁷, Herve Zeller⁸, Ibrahim Soce Fall⁹, Laurence Clabou¹⁰ and J. Elin Staples¹¹
 npj Vaccines (2022) 7:137 | <https://doi.org/10.1038/s41541-022-00552-3>

Fig. 1 Yellow fever disease cases — Africa, September 2020–March 2022. Areas with confirmed and probably yellow fever disease cases are outlined in red.

Lindsey NP et al. NPJ Vaccines. 2022 Nov 2;7(1):137.

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Yellow fever vaccine

- International Health Regulations permit countries to require proof of vaccination documented on an International Certificate of Vaccination or Prophylaxis (ICVP)*
 - Can be a condition of entry, **even if only in transit**
 - If no ICVP or medical waiver, can be denied entry, quarantined, or be vaccinated on site
- Live attenuated vaccine**

[Yellow Fever | CDC Yellow Book 2024](#)
[Yellow Fever Vaccine & Malaria Prevention Information, by Country | CDC Yellow Book 2024](#)

*Only arboviral vaccine with this requirement

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Why is yellow fever vaccine being a live attenuated vaccine important? (1)

- Yellow fever vaccine is **contraindicated** in people whose immunologic response is suppressed or modulated by current or recent medications
- Reason is they are presumed to be at increased risk for YF vaccine-associated serious adverse events
- From CDC Yellow Book:
 - “Drugs with known immunosuppressive or immunomodulatory properties include, but are not limited to, alkylating agents, antimetabolites, high-dose systemic corticosteroids, interleukin blocking agents (e.g., anakinra, tocilizumab), monoclonal antibodies targeting immune cells (e.g., alemtuzumab, rituximab), or tumor necrosis factor- α inhibitors (e.g., etanercept)”

Key message: Take a good history of current and recent medications before administering yellow fever vaccine

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Why is yellow fever vaccine being a live attenuated vaccine important? (2)

- Live attenuated vaccine viruses can be transmitted through blood transfusion

Key message: Advise patients who receive yellow fever vaccine to avoid blood donation for ≥ 2 weeks

Transmission of yellow fever vaccine virus through blood transfusion and organ transplantation in the USA in 2021: report of an investigation

[Gould CV, et al. Lancet Microbe. 2023 Sep;4\(9\):e711–e721.](#)

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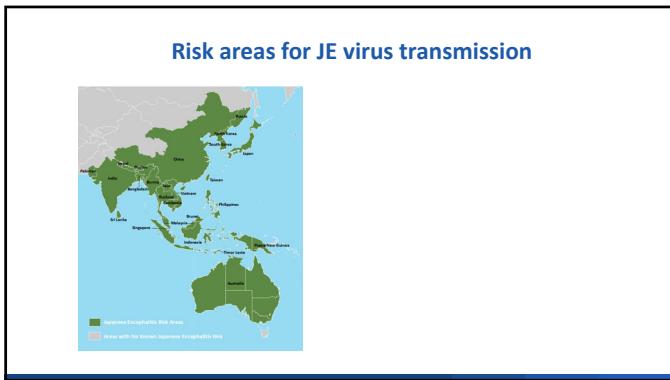
Messages also apply to live attenuated chikungunya vaccine (IXCHIQ)

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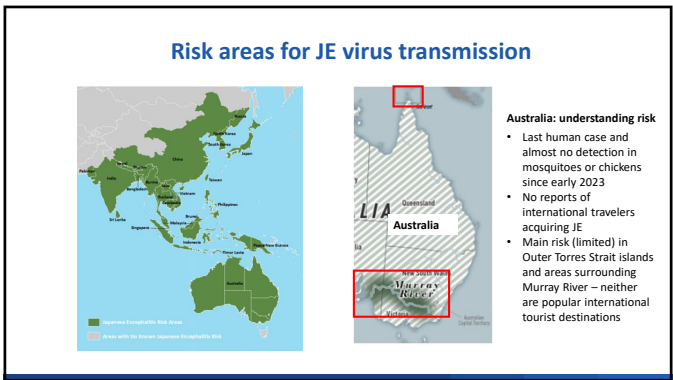
Japanese encephalitis (JE) vaccine

The slide features a blue background on the left with the text "Japanese encephalitis (JE) vaccine". On the right, there is a screenshot of the CDC website page for "Japanese Encephalitis Vaccine (IXCHIQ)" and a photograph of the vaccine box.

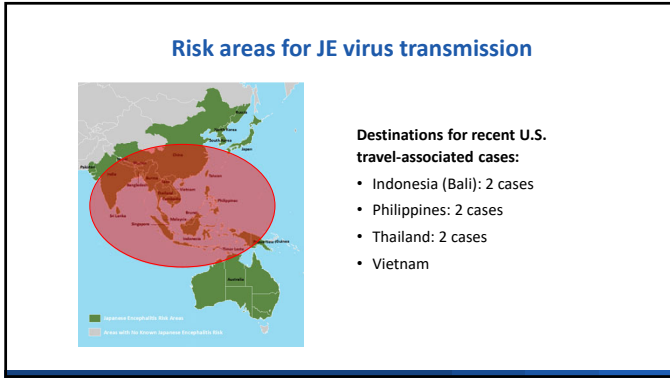
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Reminder of U.S. ACIP JE vaccination recommendations

1. JE vaccine is **recommended** for persons moving to a JE-endemic country to take up residence, longer-term (e.g., ≥1 month) travelers to JE-endemic areas, and frequent travelers to JE-endemic areas
2. JE vaccine **also should be considered** for shorter-term (e.g., <1 month) travelers with an increased risk for JE based on planned travel duration, season, location, activities, and accommodations

Vaccination also should be considered for travelers to JE-endemic areas who are uncertain of specific duration of travel, destinations, or activities

[Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices | MMWR \(cdc.gov\)](#)

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JE vaccination resources for U.S. health care providers

Risk Factors for Japanese Encephalitis Among Travelers

- SEASON:** JE is most common in rural areas of Asia during the monsoon season (July to September).
- LOCATION:** JE is most common in rural areas of Asia, particularly in the monsoon region (July to September).
- ACTIVITIES:** JE is most common in rural areas of Asia, particularly in the monsoon region (July to September).
- ACCOMMODATIONS:** JE is most common in rural areas of Asia, particularly in the monsoon region (July to September).

Japanese Encephalitis Vaccination for Travelers Decision Tree

<https://www.cdc.gov/japanese-encephalitis/hcp/vaccine/index.html> and CDC Yellow Book

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Tick-borne encephalitis (TBE) vaccine

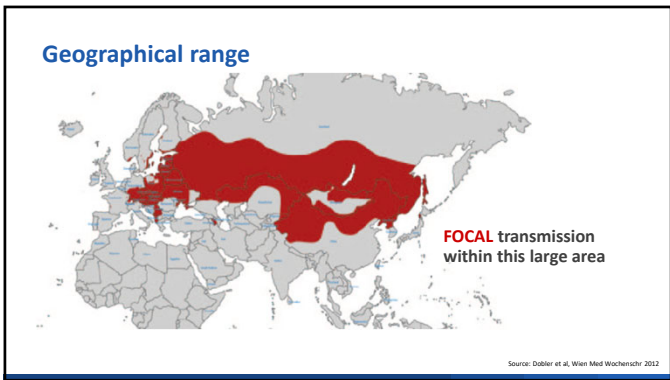
Tick-borne encephalitis among US travelers, 2010-20

Travelers who visited a TBE-endemic area in Europe, Asia, or Africa during the monsoon season (July to September) were at a higher risk of contracting TBE. The decision tree provides guidance on when to get vaccinated.

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More specific information on risk areas (when available)

General distribution of tick-borne encephalitis

Country-specific risk information for tick-borne encephalitis

Country	Risk Information
Austria	High risk in rural areas, particularly in the Alpine region.
Belgium	Low risk in rural areas, particularly in the Ardennes region.
Germany	High risk in rural areas, particularly in the Black Forest region.
Spain and Portugal	Low risk in rural areas, particularly in the northwestern region.
Sweden	High risk in rural areas, particularly in the southern region.

Areas at Risk for Tick-borne Encephalitis | Tick-borne Encephalitis Virus | CDC

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Reminder of U.S. ACIP TBE vaccination recommendations

- TBE vaccine is **recommended** for persons who are moving or traveling to a TBE-endemic area and will have **extensive exposure to ticks** based on their planned outdoor activities and itinerary.
- In addition, TBE vaccine **may be considered** for persons traveling or moving to a TBE-endemic area who might engage in outdoor activities in areas ticks are likely to be found. The decision to vaccinate should be based on an assessment of their planned activities and itinerary, risk factors for a poorer medical outcome, and personal perception and tolerance of risk.

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References and resources

- MMWR Recommendations and Reports - Tick-borne Encephalitis Vaccine
(<https://www.cdc.gov/mmwr/volumes/72/rr/rr7205a1.htm>)
- TBE: CDC Yellow Book 2024
(<https://wwwnc.cdc.gov/travel/yellowbook/2024/infections-diseases/tick-borne-encephalitis>)
- CDC website (<https://www.cdc.gov/tick-borne-encephalitis/index.html>)
- The TBE Book (<https://tbenevs.com/tbe/>)
- Hills SL, Broussard KR, Broyles JC, et al. Tick-borne encephalitis among US travellers, 2010-20. J Travel Med. 2022 Mar 21;29(2):taab167.

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Summary

- Many arboviruses are emerging and re-emerging and discussion of prevention measures should be part of any travel consultation
- No specific antiviral treatment and management is supportive BUT for dengue, appropriate monitoring and management can reduce mortality
- Vaccines are available to prevent yellow fever, chikungunya, JE, and TBE
 - If live attenuated vaccines*, avoid in immunosuppressed persons and advise patients not to donate blood for ≥2 weeks

*Yellow fever and chikungunya (IXCHIQ) vaccines

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