

Yellow Fever

Immediately Notifiable

✓ DISEASE AND EPIDEMIOLOGY

Clinical Description:

Arboviral infections may be asymptomatic or may result in febrile illnesses of variable severity which are sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes include meningitis, myelitis and encephalitis, which are clinically indistinguishable from similar syndromes caused by other viruses.

- Arboviral meningitis is usually characterized by fever, headache, stiff neck, and white blood cells in the cerebrospinal fluid (pleocytosis).
- Arboviral myelitis is usually characterized by fever and acute bulbar (pertaining to the circulatory or respiratory system) or limb paresis (partial paralysis) or flaccid paralysis.
- Arboviral encephalitis is usually characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction. Less common neurological syndromes can include cranial and peripheral neuritis or other neuropathies, including Guillain-Barré syndrome (ascending paralysis)..

Non-neuroinvasive syndromes caused by these viruses can include myocarditis (inflammation of the sac surrounding the heart), pancreatitis, or hepatitis. In addition, they may cause febrile illnesses (e.g., Dengue fever) that are non-localized, self-limited illnesses with headache, myalgias, arthralgias, and sometimes accompanied by skin rash or lymphadenopathy. Laboratory-confirmed arboviral illnesses lacking documented fever can occur, and overlap among the various clinical syndromes is common.

Causative Agent:

There are about 570 viruses worldwide that are spread through arthropods (insects). More than 30 of these arboviruses have been identified as human pathogens in the western hemisphere. In Utah, three mosquito-borne arboviruses that cause encephalitis in humans have been identified: Western equine encephalitis (WEE), Saint Louis encephalitis (SLE) and West Nile virus (WNV).

- WEE is of the genus *Alphavirus* and in the family *Togaviridae*.
- SLE is a member of the family *Flaviviridae*.
- WNV, also a member of the *Flaviviridae* family and *Flavivirus* genus, has recently appeared in the West.

Other important arboviral encephalitides in the Americas include

- Powassan encephalitis,
- Venezuelan equine encephalitis (VEE),
- Eastern equine encephalitis (EEE),

- LaCrosse encephalitis (part of the California encephalitis virus serogroup),
- Tensaw encephalitis,
- Everglades encephalitis,
- Ilheus encephalitis, and
- Snowshoe hare encephalitis.

Other arboviral diseases include

- Dengue (Dengue Hemorrhagic Fever – DHF; Dengue shock syndrome – DSS),
- Japanese encephalitis virus (JEV),
- Powassan,
- Yellow Fever, and
- Other less common infections.

UPHL: UPHL will act as a referral agent to the CDC for confirmation of arboviruses outside of WNV and SLE.

Differential Diagnosis:

Bartonellosis
Cytomegalovirus
Herpes Simplex
Histoplasmosis
Leptospirosis
Lyme Disease
Malaria
Meningitis
Mycoplasma Infections
Naegleria Infection
Rheumatoid Arthritis
St. Louis Encephalitis
Systemic Lupus Erythematosus

Toxoplasmosis
Tuberculosis
Venezuelan Encephalitis
West Nile Encephalitis

Other Problems to be Considered:

Infective endocarditis
Mumps
Rabies virus
Stroke
Metabolic encephalopathy
Reye syndrome
Epstein-Barr virus (EBV)

Laboratory identification:

Laboratory diagnosis is based upon demonstration of specific IgM in serum or CSF, or antibody rises between early (acute) and late (convalescent) specimens of serum. Cross-reactions may occur within related virus groups also, the virus occasionally can be isolated from blood or CSF.

Treatment:

There is no specific treatment available for arboviral infections. Treatment of symptoms and supportive care are the only methods of treatment available for arboviral infections.

Case fatality:

The case-fatality ratios range from less than 1% to 60%.

- Yellow Fever (YF): Mortality rates due to the toxic form of disease vary from 25-50%, but the mortality rate has been reported to be as low as 1%. The number

of reported deaths from YF among travelers over the past 10 years has increased, and more can be expected unless YF vaccine is most appropriately used.

Reservoir:

Reservoirs for many of the arboviral encephalitides are not known. Birds carry both EEE and WNV. The virus usually resides in birds and the mosquitoes that feed on them. Rarely, other kinds of mosquitoes that also bite people and horses pick up the viruses. The vectors for California encephalitis, LaCrosse encephalitis, snowshoe hare encephalitis, and Jamestown Canyon virus are *Aedes* mosquitoes. The vector for Powassan encephalitis virus is the *Ixodes cookei* tick, and the reservoir includes rodents, other small mammals and birds. VEE is maintained in a rodent-mosquito cycle; horses are also an important reservoir during outbreaks of VEE. WEE is spread primarily by the vector mosquito *Culex tarsalis*. Other mosquitoes (e.g., *Aedes* species) and, occasionally, small wild mammals also have been known to spread the virus. JEV is spread throughout mostly rural areas of Asia by culicine mosquitoes, most often *Culex tritaeniorhynchus*. Yellow Fever is a mosquito-borne viral infection endemic to Africa and South America, transmitted by the *Aedes aegypti* mosquito. Monkeys and mosquitoes are the primary reservoirs for Yellow Fever in forested areas of Africa and South America.

Transmission:

EEE, Ilheus encephalitis, snowshoe hare encephalitis, SLE, Yellow Fever, Dengue, JEV, California encephalitis, Jamestown Canyon virus, WEE, LaCrosse encephalitis, VEE, Tensaw encephalitis, and Everglades encephalitis, are spread to humans by the bite of an infected mosquito. Powassan encephalitis is spread to humans by the bite of an infected tick (*Ixodes cookei*). Direct person-to-person spread of arboviral infections does not occur.

Susceptibility:

The elderly and children are more susceptible. Children have higher rates of dengue in endemic areas, because infection confers immunity to that serotype. As with most other arboviruses, infection confers immunity.

Incubation period:

The incubation periods for some of the arboviral encephalitides are as follows: EEE, 3–10 days; California encephalitis, 5–15 days; Powassan encephalitis, 4–18 days; SLE, 4–21 days; VEE, 2–6 days; WEE, 5–10 days; and LaCrosse encephalitis and Jamestown Canyon virus, 5–15 days; Yellow Fever is 3–6 days; Dengue usually 4–7 days, although it may range from 3–14 days; JEV, 4–15 days.

Period of communicability:

Arboviral infections or agents of transmission are not communicable from person-to-person, except in rare instances (blood transfusion, organ donation).

Epidemiology:

Most cases of arboviral encephalitis in North America occur in the late summer and early to mid-fall. The elderly are at greatest risk of encephalitis with SLE, while children under 15 years old are at greatest risk from LaCrosse virus infection, and both children and elderly are at greatest risk for EEE. WEE is found in the western and central portions of the U.S., in Canada, and in parts of South America. SLE is found in most of the U.S., as well as in parts of Canada, the Caribbean Islands, and Central and South America. LaCrosse encephalitis is found in the eastern half of the U.S. Snowshoe hare encephalitis occurs in Canada, China and Russia. Powassan encephalitis occurs in Canada, the U.S. and Russia. VEE is endemic in parts of South and Central America and the Caribbean.

JEV is spread throughout mostly rural areas of Asia by culicine mosquitoes, most often *Culex tritaeniorhynchus*. It is the most common form of viral encephalitis in Asia. Approximately 3 billion people currently live in areas endemic for Japanese encephalitis; these areas extend from Pakistan to maritime Siberia and Japan. Japanese encephalitis mostly develops among military personnel, expatriates, and, rarely, returning travelers. From 1978-1993, 12 cases occurred in the United States. The risk of symptomatic infection among travelers is estimated to be 1 case per 150,000 person-months in an endemic area. Outbreaks are rare in the US territories of Guam and Saipan. Japanese encephalitis is a seasonal disease, with most cases occurring in temperate areas from June to September. Further south in subtropical areas, transmission begins as early as March and extends until October. Transmission may occur all year in some tropical areas (e.g., Indonesia). Worldwide, approximately 35,000-50,000 symptomatic cases are reported per year, although this is likely an underestimation of the true incidence of the disease. Local incidence rates range from 1-10 cases per 100,000 persons but can reach more than 100 cases per 100,000 persons during outbreaks.

Dengue has been called the most important mosquito-transmitted viral disease in terms of morbidity and mortality. Dengue virus causes about 100 million cases of acute febrile disease annually, including more than 500,000 reported cases of dengue hemorrhagic fever (DHF)/ dengue shock syndrome (DSS). Currently, dengue is endemic in 112 countries. The world's largest known epidemic of DHF/DSS occurred in Cuba in 1981, with more than 116,000 persons hospitalized and as many as 11,000 cases reported in a single day.

Each year, an estimated 200,000 cases of YF occur in Africa and South America combined, causing 20,000-30,000 deaths. The number of total cases reported to the WHO each year from Africa and South America ranges from hundreds to a few thousand. The true incidence is estimated to be at least 40 times more than this in Africa and 10 times more than this in South America. Since 1996, 3 fatal cases of YF have been reported in American travelers to the Amazon. None of the patients were immunized against YF. The CDC estimates that YF immunization of travelers to YF endemic areas has declined 50% from 1992-1998.

✓ PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Investigate all suspect cases of disease and fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease.
- Identify sources of exposure and stop further transmission.

Prevention:

Environmental Measures

People should be encouraged to reduce mosquito populations around their homes and neighborhoods by getting rid of any standing water that might support mosquito breeding. Mosquitoes will begin to breed in any puddle or standing water that lasts for more than four days. People should be advised of the following:

- Dispose of or regularly empty any metal cans, plastic containers, ceramic pots, and other containers (including trash cans) on their property that might hold water.
- Pay special attention to discarded tires. Stagnant water in tires is a common place for mosquitoes to breed.
- Drill holes in the bottom of recycling containers that are left outdoors, so that water can drain out.
- Clean clogged roof gutters; remove leaves and debris that may prevent drainage of rainwater.
- Turn over plastic wading pools and wheelbarrows when not in use.
- Do not allow water to stagnate in birdbaths; aerate ornamental ponds or stock them with fish.
- Keep swimming pools clean and properly chlorinated; remove standing water from pool covers.
- Use landscaping to eliminate standing water.

Personal Preventive Measures/Education

- Get vaccinated for diseases which have available vaccines (Yellow Fever and Japanese Encephalitis Virus), if you live, work, or plan to travel to an endemic area. People should also be advised to take the following precautions if they live in or visit an area with mosquitoes:
- Avoid outdoor activities during the time of greatest mosquito activity (depends on mosquito species). Unlike other vectors, the principal mosquito vectors of Yellow Fever bite during daytime hours.
- Fix any holes in screens, and make sure they are tightly attached to all doors and windows.
- Use mosquito netting when sleeping.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent

outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children less than two months of age. Mosquito netting may be used to cover infant carriers or to protect other areas for children less than two months of age. The following precautions should be observed when using DEET products:

- Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
- Apply DEET on exposed skin, using only as much as needed.
- Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and the mouth.
- Do not use DEET over cuts, wounds, or irritated skin.
- Wash treated skin with soap and water after returning indoors, and wash treated clothing.
- Avoid spraying DEET products in enclosed areas.

Picardin (KBR 3023) is a relatively new repellent that is now available in the U.S. Recent studies have shown it to be safe and effective. Picardin-containing repellents should be used according to the manufacturer's recommendations.

A number of plant-derived products are available for use as repellents, but most of these products do not provide the same level or duration of protection as products containing DEET. However, there are studies that show that oil of lemon eucalyptus [p-methane 3,8-diol(PMD)] provides as much protection as low concentrations of DEET when tested against mosquitoes found in the U.S.

Chemoprophylaxis:

None.

Vaccine:

Vaccines are available for JEV and Yellow Fever. No other vaccines exist for other arboviral infections.

Isolation and quarantine requirements:

Isolation: None

Hospital: Standard body substance precautions.

Quarantine: None.

CASE INVESTIGATION

Reporting:

Report all suspect and confirmed cases of any arboviral infection.

Case definition:

Yellow Fever (2010)

Clinical description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages.

Laboratory criteria for diagnosis

- Fourfold or greater rise in Yellow Fever antibody titer in a patient who has no history of recent Yellow Fever vaccination and cross-reactions to other flaviviruses have been excluded or
- Demonstration of Yellow Fever virus, antigen, or genome in tissue, blood, or other body fluid

Case classification

Probable:

A clinically compatible case with supportive serology (stable elevated antibody titer to Yellow Fever virus [e.g., greater than or equal to 32 by complement fixation, greater than or equal to 256 by immunofluorescence assay, greater than or equal to 320 by hemagglutination inhibition, greater than or equal to 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of Yellow Fever vaccination.)

Confirmed:

A clinically compatible case that is laboratory confirmed.

Case Definition			
Criterion	Confirmed		Probable
<i>Clinical Presentation</i>			
fever	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
chills	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
severe headache	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
back pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
myalgia	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
nausea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

vomiting	O	O	O
hemorrhagic diathesis (gastrointestinal bleeding)	O	O	O
petechiae	O	O	O
purpura	O	O	O
jaundice	O	O	O
proteinuria	O	O	O
history of recent yellow fever vaccination		A	
history of yellow fever vaccination			A
<i>Laboratory findings</i>			
fourfold or greater rise in yellow fever antibody titer		N	
cross-reactions to other flaviviruses		A	A
demonstration of yellow fever virus in tissue, blood, or other body fluid	O		
demonstration of yellow fever antigen in tissue, blood, or other body fluid	O		
demonstration of yellow fever genome in tissue, blood, or other body fluid	O		
antibody titer to yellow fever virus greater than or equal to 32 by complement fixation			O
antibody titer to yellow fever virus greater than or equal to 256 by immunofluorescence assay			O
antibody titer to yellow fever virus greater than or equal to 320 by hemagglutination inhibition			O
antibody titer to yellow fever virus greater than or equal to 160 by neutralization			O
positive serology for yellow fever by immunoglobulin M-capture enzyme immunoassay			O
<i>Epidemiological risk factors</i>			
recent travel to area with endemic yellow fever	C	C	C

Notes:

S = This criterion alone is sufficient to classify a case

N = All “N” criteria in the same column—in conjunction with at least one of any “O” criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—are required to classify a case.

O = At least one of any “O” criteria in each category (e.g., clinical presentation and laboratory findings) in the same column—in conjunction with all other “N” criteria in the same column—is required to classify a case.

A = This criterion must be absent (i.e., NOT present) for the case to meet the reporting criteria or case definition.

Nosocomial:

Although rare, nosocomial cases of arboviral infections could occur via blood transfusion or via organ transplant. Contact UDOH immediately with a suspected case of nosocomial arboviral infection.

Case Investigation Process:

- Fill out morbidity form
- Verify case status.
- Fill out disease investigation form.
- Determine whether patient had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.
- If patient acquired disease in Utah, identify the source of transmission and eliminate it.

Outbreaks:

An outbreak will be defined as: a larger than normal number of cases by county, or one case of an unusual or exotic arboviral etiology.

Identification of case contacts:

This disease is not spread person to person.

Case contact management:

None.

 **REFERENCES**

Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Centers for Disease Control, 2005.

Centers for Disease Control, Case Definitions for Infectious Conditions Under Public Health Surveillance. MMWR 46 (RR-10), 1997.1.

Control of Communicable Diseases Manual (18th Edition), Heymann, D.L., Ed; 2004.

Red Book: 2003 Report of the Committee on Infectious Diseases (26th Edition), Larry K. Pickering MD, Ed; 2003.

Principles and Practice of Infectious Disease (6th Edition), Gerald L. Mandell, John E. Bennett, and Raphael Dolin Eds; 2005.

Massachusetts Department of Public Health, Guide to Surveillance, Reporting and Control, 2006.

Yale University; Department of Laboratory Medicine.

Specialty Labs; Use and Interpretation of Laboratory Tests.

ARUP Labs; Physician's Guide to Laboratory Test Selection and Interpretation Guidelines for Preventing Health-Care-Associated Pneumonia, 2003: Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC).

Guidelines for Environmental Infection Control in Health-Care Facilities and Recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee (HICPAC).

Johns Hopkins Point of Care Information Technology.

Salt Lake Valley Health Department Disease Investigation Plan.

Emedicine: Japanese Encephalitis, Dengue, Yellow Fever, Western Equine Encephalitis. www.emedicine.com.

Council for State and Territorial Epidemiologists (CSTE) Position statements. Available from URL: <http://www.cste.org/default.asp?page=PositionStatements>.