Risk of Severe Arboviral Disease in Patients Receiving B Cell-Depleting or Modulating Medications

AUG. 11, 2026, VISIT LINK FOR DETAILS.

AT A GLANCE

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Summary

The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to share information and notify clinicians, public health authorities, and the public about the risk of severe arboviral neuroinvasive disease among patients who are receiving B cell-depleting or B cell-modulating medications, particularly anti-CD20 monoclonal antibodies (mAbs). Patients and their providers should be aware of this risk to help patients protect themselves against the bites of mosquitoes and ticks, which can increase patients' risk of arboviral disease.

Background

Arboviruses are RNA viruses transmitted by biting arthropods, most commonly mosquitoes and ticks, which are most active during late spring through early fall. Although most arboviral infections are subclinical, symptomatic arboviral disease typically presents as acute febrile or neurologic illness (e.g., aseptic meningitis, encephalitis, or acute flaccid myelitis). The incubation period is typically days to weeks from arthropod bite to onset of symptoms and can be longer in persons who are immunocompromised.

Medications that deplete B cells or modulate B cell function, which are used for treating B cell malignancies, many autoimmune conditions, and transplant rejection,

can increase the risk of severe arboviral disease. B cell-depleting monoclonal antibodies (mAbs) targeting the CD20 cell surface antigen have been associated with a growing number of reports of severe arboviral neuroinvasive disease in patients on these medications. Health professionals and the public should be aware of this information because the United States had an early and strong start to this year's West Nile virus season and many weeks of the arbovirus transmission season remain.

Anti-CD20 mAbs currently approved in the United States include rituximab and biosimilars, ocrelizumab, ofatumumab, ublituximab, obinutuzumab, and ibritumomab tiuxetan. Among published case reports of arboviral neuroinvasive disease in patients on anti-CD20 mAbs, overall mortality was approximately 40%, and most survivors experienced long-term neurologic sequelae. West Nile virus was the most common infecting arbovirus in these case reports. Less common or regionally focal viruses in the United States, such as eastern equine encephalitis virus, Powassan virus, Jamestown Canyon virus, La Crosse virus, Cache Valley virus, and Potosi virus, have also caused severe disease in these patients.

In recent years, a novel clinical presentation of chronic, neurodegenerative encephalitis developing over months to years has been described in at least five patients receiving rituximab who were infected with an orthobunyavirus, including Jamestown Canyon virus, Cache Valley virus, or Potosi virus. All patients died; diagnoses were delayed because of unrecognized infection and rare or unexpected pathogens requiring specialized diagnostic testing.

Because patients receiving anti-CD20 mAbs or other medications that deplete B cells (e.g., anti-CD38 mAbs) or modulate B cell function (e.g., B cell activating factor inhibitors) might not form antibodies against a new infection, diagnosis of arboviral infection often requires molecular rather than serologic testing. Molecular testing typically includes virus-specific RT-PCR or metagenomic next-generation sequencing (mNGS) to detect viral RNA in specimens such as serum, plasma, cerebrospinal fluid (CSF), whole blood, or tissue. Clinicians can contact their state or local health departments for consultation on appropriate testing to perform based on the patient's medical conditions and medications.

There are no approved treatments, prophylactic agents, or human vaccines to prevent arboviral diseases endemic to the United States. Therefore, it is critical that patients receiving medications that deplete or reduce B cell function be advised to use personal protective measures to prevent mosquito and tick bites.

Recommendations for Clinicians

- When prescribing any immunosuppressive medications or caring for patients taking any immunosuppressive medication, particularly B cell-depleting mAbs, educate patients about the risk of severe arboviral disease and advise them to take measures to prevent mosquito and tick bites.
- Be aware that patients with an arboviral disease who are immunocompromised can have a prolonged incubation period or an atypical course and might not present with illness during the usual months when mosquitoes and ticks are active (i.e., May through November in the United States).
- Take a thorough exposure and travel history for patients presenting with a febrile or neurologic illness.
- When an arboviral infection is suspected in a patient receiving B cell-depleting mAbs, preferentially order molecular testing (i.e., RT-PCR or mNGS).
    - Immunocompromised patients, particularly those receiving B cell-depleting mAbs, can have prolonged viremia and delayed or absent antibody responses.
    - Preferred specimen type(s) depend on the clinical presentation and laboratory conducting the testing. Molecular tests are available from some commercial and public health laboratories.
    - Serologic testing of serum or CSF for virus-specific IgM antibodies should be ordered only for patients who are immunocompetent or receiving immunomodulating drugs that do not substantially suppress antibody production.
    - Contact your state or local health department for consultation on the optimal testing approach.
    - See the diagnostic testing algorithm for suspected West Nile virus disease for more details.

Recommendations for Health Departments

- Educate clinicians and the public about the risk of severe arboviral disease in patients who are immunocompromised and share guidance on preventing arboviral and other vector-borne diseases.
- When discussing arboviral testing with clinicians, verify patients' pre-existing medical conditions and medications to help determine the most appropriate specimens, testing methods (e.g., molecular or serologic), and available laboratories for diagnostic testing.

- Contact CDC's Arboviral Diseases Branch (adbclinicalteam@cdc.gov) for consultation on optimal testing approaches and interpretation of test results in patients with suspected arboviral diseases.
- State public health laboratories might consider the feasibility of validating molecular assays to detect West Nile virus and other arboviruses.
    - Whole blood and urine specimens are more sensitive for WNV RT-PCR than serum or CSF; however, serum and CSF are needed to perform serologic testing to exclude infection if RT-PCR testing is negative.

Recommendations for the Public

- Take steps to prevent mosquito and tick bites to lower the risk of vector-borne diseases including arboviral infections:
    - Use Environmental Protection Agency (EPA)-registered insect repellent.
    - Wear loose-fitting, long-sleeved shirts and pants when outdoors.
    - Use screens on windows and doors or use air conditioning to keep mosquitoes outside.
    - Treat clothing and gear with products containing 0.5% permethrin.
    - Avoid wooded and brushy areas with high grass and leaf litter where ticks live.
    - Check clothing, body, gear, and pets for ticks when returning indoors.
    - Shower soon after being outdoors to check for ticks and help wash off unattached ticks.
- If you are taking a medication that suppresses your immune system, know that you could be at higher risk of having severe illness from an infection, including arboviral infections.
- Notify your healthcare provider if you have concerning changes to your health, such as persistent headaches, fever, body aches, weakness, loss of balance, or confusion.
- Tell your healthcare provider about any recent travel or exposure to mosquitoes or ticks and remind them of the medications you are taking.
- Be aware of what mosquito- and tickborne viral diseases might be circulating in your area by visiting your state or local health department or CDC's websites.

For More Information

For Clinicians

- Clinical Guidance for Vector-Borne Viral Diseases in People Who Are Immunocompromised | CDC
- Patient Awareness Brochure: Arboviral Disease and Immunosuppression | CDC
- Patient Awareness Poster: Arboviral Disease and Immunosuppression | CDC
- Clinical Testing and Diagnosis for West Nile Virus Disease | CDC

For Health Departments

- Submitting Specimens for Arboviral Tests | CDC
- Arbovirology | New York State Department of Health, Wadsworth Center

For the Public

- Vector-Borne Viral Diseases and People Who Are Immunocompromised | | CDC
- How to Prevent Mosquito and Tick Bites | CDC
- Video: It Starts with a Mosquito Bite | CDC

References

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