Jamestown Canyon Virus Disease in the United States—2000–2013

Daniel M. Pastula, Diep K. Hoang Johnson, Jennifer L. White, Alan P. Dupuis II, Marc Fischer, and J. Erin Staples*

EIS Program Office, Centers for Disease Control and Prevention, Atlanta, Georgia; Arboviral Diseases Branch, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado; Wisconsin Department of Health Services, Madison, Wisconsin; New York State Department of Health and Wadsworth Center, Albany, New York

Abstract. Jamestown Canyon virus (JCV) is a mosquito-borne orthobunyavirus in the California serogroup that can cause an acute febrile illness, meningitis, or meningoencephalitis. We describe epidemiologic and clinical features for JCV disease cases occurring in the United States during 2000–2013. A case of JCV disease was defined as an acute illness in a person with laboratory evidence of a recent JCV infection. During 2000–2013, we identified 31 cases of JCV disease in residents of 13 states. The median age was 48 years (range, 10–69) and 21 (68%) were male. Eleven (35%) case patients had meningoencephalitis, 6 (19%) meningitis, 7 (23%) fever without neurologic involvement, and 7 (23%) had an unknown clinical syndrome. Fifteen (48%) were hospitalized and there were no deaths. Health-care providers and public health officials should consider JCV disease in the differential diagnoses of viral meningitis and encephalitis, obtain appropriate specimens for testing, and report cases to public health authorities.

Jamestown Canyon virus (JCV) is a mosquito-borne orthobunyavirus that causes an acute febrile illness, meningitis, or meningoencephalitis.^{1–5} Although JCV is widely distributed throughout temperate North America, reports of human JCV infection in the United States are rare.¹ JCV was first isolated in 1961 from a pool of *Culiseta inornata* mosquitoes in Jamestown Canyon, CO.⁶ Since then, the virus has been isolated from various mosquito species (e.g., *Aedes*, *Coquillettia*, *Culex*, and *Culiseta* species) in the northeastern, midwestern, and western United States.^{6–19} JCV neutralizing antibodies have been found in various mammals throughout mainland North America,^{13,20–36} and identified in humans throughout the United States.^{1–5,34,37–41}

JCV is a member of the California serogroup viruses, which include La Crosse virus (LACV), California encephalitis virus, and snowshoe hare virus.⁴² Although the presence of anti-JCV immunoglobulin (Ig) M detected by enzyme-linked immunosorbent assay (ELISA) is usually evidence of a recent JCV infection, it also may indicate infection with another closely related California serogroup virus.^{35,42,43} Plaque reduction neutralization tests (PRNTs) can be performed to measure virus-specific neutralizing antibodies and to potentially discriminate among cross-reacting antibodies from closely related California serogroup viruses.^{44,45}

Prior to 2014, testing for JCV infection in the United States was performed at the Arboviral Diseases Branch of the Centers for Disease Control and Prevention (CDC) and at the Wadsworth Laboratory of the New York State Department of Health (NYSDOH). Since 2000, NYSDOH has been able to perform JCV PRNTs on acute and convalescent samples testing positive for California serogroup IgG antibodies by immunofluorescence assay. At the CDC, PRNTs have been used to detect JCV neutralizing antibodies since 1995. All samples testing positive or equivocal for LACV IgM antibodies by ELISA at the CDC have JCV PRNTs performed. A JCV IgM ELISA was developed at the CDC in 2010. Beginning in 2013, all samples submitted to the CDC for domestic arbovirus testing were routinely tested for JCV IgM

antibodies by ELISA, and if positive, were confirmed by JCV PRNTs. We describe the demographic and clinical characteristics of laboratory-confirmed cases of JCV disease occurring in the United States during 2000–2013.

MATERIAL AND METHODS

Case finding and definition. We reviewed laboratory results for all positive human JCV tests performed at the CDC and NYSDOH during 2000–2013. We defined a case of JCV disease as an acute illness in a person with evidence of a recent laboratory-confirmed JCV infection. Laboratory confirmation included: 1) JCV isolated from or JCV-specific antigen or genomic sequences detected in tissue, blood, cerebrospinal fluid (CSF), or other body fluids; 2) ≥ 4 -fold change in JCV-specific neutralizing antibody titers between acute and convalescent samples; or 3) JCV or LACV IgM antibodies in serum with JCV-specific neutralizing antibodies ≥ 4 -fold higher than LACV-specific neutralizing antibody titers in the same specimen or a later specimen. We cross-checked all laboratory-confirmed cases with those reported to ArboNET, the national surveillance system for arboviral diseases.⁴⁶ Cases of JCV disease could be reported to ArboNET beginning in 2003. To differentiate potential California serogroup virus infections in the United States, we compared the demographic and clinical features of JCV disease cases to confirmed LACV disease cases that were reported to ArboNET during 2003–2013.⁴⁷

Data collection and analysis. We collected data on residence, sex, age, date of illness onset, clinical syndrome, hospitalization, and mortality. Clinical syndromes were reported by the state health department based on clinical signs and symptoms, and could be reported as meningoencephalitis (fever with CSF pleocytosis and altered mental status, seizures, or focal neurologic deficits), meningitis (fever with CSF pleocytosis and meningeal signs), uncomplicated fever, or other presentation. These data were obtained primarily from ArboNET for both JCV and LACV cases. For JCV cases only, state health departments were also contacted to obtain any missing data.

We analyzed the data using Excel version 2010 (Microsoft, Redmond, WA) and Epi Info version 7.1.3 (CDC, Atlanta, GA). Maps were made using ArcGIS version 10 (ESRI, Redlands, CA). Continuous variables were presented as medians and ranges. Categorical and dichotomous variables

*Address correspondence to J. Erin Staples, Arboviral Diseases Branch, Division of Vector-Borne Diseases, CDC, 3156 Rampart Road, Mailstop P-02, Fort Collins, CO 80521. E-mail: estaples@cdc.gov

FIGURE 1. Jamestown Canyon virus disease cases by year of illness onset, United States, 2000–2013.

were presented as counts and frequencies. Statistical significance was determined by Fisher's exact or χ^2 tests for differences in sex, clinical syndrome, hospitalization, and LACV IgM testing; and by *t* tests or linear regression for differences in age and month of symptom onset.

RESULTS

We identified 31 cases of JCV disease that occurred during 2000–2013. Fifteen (48%) cases occurred during 2000–2012, and 16 (52%) occurred in 2013 (Figure 1). Most cases (28; 91%) occurred from April through September (Figure 2, Table 1). Cases were reported from 13 states with Wisconsin reporting 13 (42%) of the cases (Figure 3). Six states (Idaho, Massachusetts, New Hampshire, Oregon, Pennsylvania, and Rhode Island) reported their first cases in 2013.

Of the 31 JCV cases, 21 (68%) occurred in males (Table 1). The median age of case patients was 48 years (range, 10–69 years). The most commonly reported clinical syndromes were meningoencephalitis or meningitis (54%) followed by a febrile illness without neurologic involvement (23%). No case patients presented with acute flaccid paralysis. Fifteen (48%) were hospitalized; 13 of which had meningitis or meningoencephalitis. There were no deaths. There was no significant difference in the clinical syndrome or hospitalization rates by sex or age. In addition, there were no differences in age, sex, month of illness onset, clinical syndrome, or hospitalization for JCV disease case patients detected during 2000–2012 compared with those detected in 2013. Of the 29 cases with disease onset during 2003–2013, 28 (97%) were reported to ArboNET.

Overall, 21 (68%) case patients had laboratory evidence of JCV IgM and neutralizing antibodies in serum, 7 (23%) had

FIGURE 2. Jamestown Canyon virus disease cases by month of illness onset, United States, 2000–2013.

TABLE 1

Characteristics of JCV disease cases, 2000–2013, and reported LACV disease cases to ArboNET, 2003–2013, United States

	JCV cases (<i>N</i> = 31)	LACV cases (<i>N</i> = 636)
	No. (%)	No. (%)
Month of symptom onset		
January–March	2 (6)	3 (0)
April–June	8 (26)	70 (11)
July–September	20 (65)	514 (81)
October–December	1 (3)	49 (8)
Sex		
Male	21 (68)	403 (63)
Female	10 (32)	233 (37)
Age group in years		
0–19	5 (16)	562 (88)
20–39	7 (23)	20 (3)
40–59	14 (45)	26 (4)
≥ 60	5 (16)	28 (4)
Clinical syndrome		
Meningoencephalitis	11 (35)	486 (76)
Meningitis	6 (19)	96 (15)
Febrile illness*	7 (23)	34 (5)
Unknown	7 (23)	20 (3)
Hospitalized		
Yes	15 (48)	515 (81)
No	15 (48)	38 (6)
Unknown	1 (3)	83 (13)
Fatal		
Yes	0 (0)	11 (2)
No	30 (97)	606 (95)
Unknown	1 (3)	19 (3)

JCV = Jamestown Canyon virus; LACV = La Crosse virus.

*Without neurologic involvement.

LACV IgM antibodies with JCV-specific neutralizing antibodies in serum, and 4 (13%) had ≥ 4-fold change in JCV-specific neutralizing antibody titers between acute and convalescent serum specimens. One case patient had both JCV IgM antibodies and ≥ 4-fold change in JCV-specific neutralizing antibody titers between serum samples. No CSF samples were tested. Of the 26 JCV case patients that had LACV IgM test-

ing performed by ELISA, 12 (46%) tested positive for LACV IgM antibodies, 10 (38%) were negative for LACV IgM antibodies, and 4 (15%) had equivocal or indeterminate LACV IgM results. In 2013, when JCV IgM was routinely performed on all samples at CDC, only 31% (4/13) tested positive for LACV IgM by ELISA.

In comparison to JCV, there were 636 confirmed LACV disease cases reported to ArboNET during 2003–2013 (Table 1). Of these, 514 (81%) LACV disease cases occurred from July through September compared with 20 (65%) JCV cases ($P = 0.03$). The median age of confirmed LACV disease case patients was significantly lower than that of JCV disease case patients (8 versus 48 years of age, $P < 0.01$). LACV disease case patients were also more likely to present with meningoencephalitis (76% versus 35%, $P < 0.01$) and be hospitalized (81% versus 48%, $P < 0.01$) than JCV disease case patients.

DISCUSSION

We identified 31 cases of JCV disease that occurred during 2000–2013 among residents of 13 U.S. states. Most cases occurred during late spring to early fall. Clinical presentations ranged from febrile illness to meningoencephalitis, with almost half of cases requiring hospitalization. More than half of cases were identified during 2013, the first year the CDC implemented routine JCV IgM antibody testing, suggesting that JCV disease has been historically under-recognized.

Demographic features among patients with JCV disease described here were similar to those of previously reported patients with JCV disease in New York, Michigan, and Ontario, Canada.^{2–4} The JCV disease age predilection for adults differed from that of LACV disease, which more commonly affects children based on our study data and previous reports.^{48,49}

The clinical presentations of previously described JCV case patients were similar to those of ours, although previous case patients were more likely to have neuroinvasive disease (79%) than ours (54%).^{2–4} This may be the result of prior studies focusing JCV testing on patients with neuroinvasive disease.

FIGURE 3. Jamestown Canyon virus disease cases by state of residence, United States, 2000–2013. There were no cases from Alaska or Hawaii.

In addition, our JCV case patients with neuroinvasive disease were less likely to have meningitis compared with those previously reported (35% versus 61%) while more likely to have meningoencephalitis (65% versus 18%).²⁻⁴ Previous reports have described a respiratory prodrome with sore throat, rhinitis, and cough, occurring 2 days to 2 weeks prior to the onset of neuroinvasive illness for several JCV infections.⁵⁰ The data collected from patients in the current study did not have sufficient clinical information to confirm whether and how frequently respiratory symptoms occurred prior to the onset of the neurologic symptoms.

Previously, human JCV disease has been detected among residents of Connecticut, Michigan, Montana, New York, and Ontario, Canada,¹⁻⁵ and serosurveys have detected JCV neutralizing antibodies among residents of Alaska, California, Connecticut, Michigan, Minnesota, New York, and Wisconsin.^{3,34,37-41} The geographic distribution of our cases was similar, mostly in the northern contiguous United States, but some of our case patients resided in areas where human JCV infections have not previously been documented (e.g., Idaho, Massachusetts, Mississippi, New Hampshire, Oregon, Pennsylvania, and Rhode Island). Wisconsin reported the most cases during our study period. Although a higher risk of disease cannot be definitively ruled out, the Wisconsin Department of Health Services implemented enhanced surveillance efforts for JCV that included routinely requested confirmatory testing for all patient's samples with IgM-positive arboviral disease results and additional JCV testing of samples with only an IgG-positive arboviral result.⁵¹ These efforts likely increased case recognition and decreased rates of false-positive IgM results for related viruses such as LACV in Wisconsin. Testing of deer for JCV neutralizing antibodies suggests that JCV is present in most regions of the continental United States.⁵⁰ Accordingly, these data suggest that human JCV infections could occur anywhere in the United States, but appear to have a predilection for more northern states. In contrast to JCV cases, LACV cases occur predominantly in the Appalachian and midwestern region of the United States.⁴⁸

Although 65% of the JCV case patients included in our series had illness onsets during the traditional arboviral transmission season, July through September, this percentage is lower than typically observed among reported cases of West Nile virus disease (> 90% with illness onsets during July–September) and LACV disease (81% with illness onsets during July–September).⁴⁹ Although some difference in seasonal distribution may result from the smaller number of cases in our study, it may also be influenced by different vectors or how vectors first acquired the virus. For instance, Grimstad⁵⁰ suggested that certain mosquitoes (e.g., *Aedes stimulans*) may be responsible for transmitting JCV earlier in the year, whereas other species may transmit JCV later, creating a bi-modal peak in the seasonal distribution of JCV disease. Another theory is this bi-modal peak may be due to vertically infected mosquitoes transmitting JCV early in the year followed by horizontally infected mosquitoes transmitting it later.⁵²

Among patients confirmed with JCV disease in the current study who were tested for LACV IgM antibodies by ELISA, 38% had negative results. This suggests that there is only partial cross-reactivity of JCV IgM antibodies using the LACV IgM ELISA at CDC. For the commercially available immunofluorescence assay for California serogroup viruses, which contains LACV antigens, it is unknown how much cross-reactivity

occurs with JCV IgM antibodies. Based on our comparative analysis, the demographic features (e.g., patient age and location) and the clinical syndrome (e.g., encephalitis versus fever without neurologic involvement) might help differentiate whether a patient's disease resulted from LACV or JCV infection. However, PRNTs would be needed to confirm whether the diseases resulted from LACV or another California serogroup virus, such as JCV.

There are several limitations to our study. First, we only included laboratory-confirmed cases of JCV disease. We excluded 10 cases of probable JCV infections that did not meet the laboratory criteria (e.g., had an equivocal JCV IgM with virus-specific neutralizing antibodies against JCV), and some might have represented true recent JCV infections. Second, only patients with JCV disease who sought medical care and had a sample tested at the CDC or NYSDOH laboratory could have been captured in our study. Therefore, our study results might not be representative of all JCV disease cases. Third, because we did not collect specific clinical history on each patient, the reported clinical syndromes might have been misclassified. Finally, some of the confirmed LACV cases reported to ArboNET might have resulted from infection with JCV or another California serogroup virus, particularly if cross-neutralization testing for JCV was not performed.

Our findings suggest that JCV is an under-recognized mosquito-borne viral disease that is likely endemic throughout most of the United States. Clinicians should consider JCV disease among patients who develop acute febrile illness, meningitis, or meningoencephalitis in the United States during late spring through early fall, particularly when tests are negative for potentially more common etiologies, such as herpes simplex virus, enteroviruses, or West Nile virus. Clinicians should contact their local or state health department to request comprehensive arboviral disease testing inclusive of JCV disease. Public health officials and clinicians should continue to educate the public regarding risks of mosquito-borne diseases and ways to prevent them, such as using mosquito repellent when outdoors, ensuring that people have intact screens or use air-conditioning to keep mosquitoes out of their homes, and supporting local vector control measures.

Received March 12, 2015. Accepted for publication April 10, 2015.

Published online June 1, 2015.

Acknowledgments: We thank Olga Kosoy, Robert Lanciotti, Jennifer Lehman, Roger Nasci, and Amanda Panella from the Centers for Disease Control and Prevention; Jeffrey Davis and Linda Machmueller from the Wisconsin Department of Health Services; Deborah Upperman, Louise Boettcher-Troxel, and David Warshauer from the Wisconsin State Laboratory of Hygiene; Robert Boromisa, Amy Dean, Valerie Demarest, Kay Escuyer, Laura Kramer, Karen Kulas, Norma Tavakoli, Kirsten St. George, Arboviral Laboratory staff, Viral Encephalitis Laboratory staff, and other staff within the Wadsworth Center and New York State Department of Health; David Neitzel at the Minnesota Department of Health; Sheryl Hand at the Mississippi State Department of Health; and Randall Nelson at the Connecticut Department of Health. We also thank other local health department staff, clinicians, and commercial laboratories involved in testing and reporting cases.

Financial support: This study was funded in part by the Centers for Disease Control and Prevention Epidemiology Laboratory and Capacity Cooperative Agreement.

Disclaimer: The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Authors' addresses: Daniel M. Pastula, Marc Fischer, and J. Erin Staples, CDC Arboviral Diseases Branch, Fort Collins, CO, E-mails: dpastula@cdc.gov, mfischer@cdc.gov, and estaples@cdc.gov. Diep K. Hoang Johnson, Division of Public Health, Wisconsin Department of Health Services, Madison, WI, E-mail: Diep.HoangJohnson@dhs.wisconsin.gov. Jennifer L. White, New York State Department of Health, Empire State Plaza, Corning Tower, Albany, NY, E-mail: jennifer.white@health.ny.gov. Alan P. Dupuis II, Wadsworth Center, NYS Department of Health, Griffin Laboratory, Slingerlands, NY, E-mail: alan.dupuis@health.ny.gov.

REFERENCES

- Centers for Disease Control and Prevention, 2011. Human Jamestown Canyon virus infection—Montana, 2009. *MMWR Morb Mortal Wkly Rep* 60: 652–655.
- Grimstad PR, Shabino CL, Calisher CH, Waldman RJ, 1982. A case of encephalitis in a human associated with a serologic rise to Jamestown Canyon virus. *Am J Trop Med Hyg* 31: 1238–1244.
- Deibel R, Srihongse S, Grayson MA, Grimstad PR, Mahdy MS, Artsob H, Calisher CH, 1983. Jamestown Canyon virus: the etiologic agent of an emerging human disease? *Prog Clin Biol Res* 123: 313–325.
- Srihongse S, Grayson MA, Deibel R, 1984. California serogroup viruses in New York State: the role of subtypes in human infections. *Am J Trop Med Hyg* 33: 1218–1227.
- Nelson R, Wilcox L, Brennan T, Mayo D, 2001. Surveillance for arbovirus infections. *Connecticut Epidemiologist* 22: 5.
- Centers for Disease Control and Prevention, 2014. *CDC Arboviral Catalog*. Available at: <https://www.cdc.gov/arboat/VirusDetails.aspx?ID=206&SID=2>. Accessed January 6, 2014.
- DeFoliart GR, Anslow RO, Hanson RP, Morris CD, Papadopoulos O, Sather GE, 1969. Isolation of Jamestown Canyon serotype of California encephalitis virus from naturally infected *Aedes* mosquitoes and tabanids. *Am J Trop Med Hyg* 18: 440–447.
- Armstrong PM, Andreadis TG, 2007. Genetic relationships of Jamestown Canyon virus strains infecting mosquitoes collected in Connecticut. *Am J Trop Med Hyg* 77: 1157–1162.
- Andreadis TG, Anderson JF, Armstrong PM, Main AJ, 2008. Isolations of Jamestown Canyon virus (Bunyaviridae: Orthobunyavirus) from field-collected mosquitoes (Diptera: Culicidae) in Connecticut, USA: a ten-year analysis, 1997–2006. *Vector Borne Zoonotic Dis* 8: 175–188.
- Boromisa RD, Grayson MA, 1990. Incrimination of *Aedes provocans* as a vector of Jamestown Canyon virus in an enzootic focus of northeastern New York. *J Am Mosq Control Assoc* 6: 504–509.
- Boromisa RD, Grimstad PR, 1986. Virus-vector-host relationships of *Aedes stimulans* and Jamestown Canyon virus in a northern Indiana enzootic focus. *Am J Trop Med Hyg* 35: 1285–1295.
- Campbell GL, Eldridge BF, Reeves WC, Hardy JL, 1991. Isolation of Jamestown Canyon virus from boreal *Aedes* mosquitoes from the Sierra Nevada of California. *Am J Trop Med Hyg* 44: 244–249.
- Fulhorst CF, Hardy JL, Eldridge BF, Chiles RE, Reeves WC, 1996. Ecology of Jamestown Canyon virus (Bunyaviridae: California serogroup) in coastal California. *Am J Trop Med Hyg* 55: 185–189.
- Hardy JL, Eldridge BF, Reeves WC, Schutz SJ, Presser SB, 1993. Isolations of Jamestown canyon virus (Bunyaviridae: California serogroup) from mosquitoes (Diptera: Culicidae) in the western United States, 1990–1992. *J Med Entomol* 30: 1053–1059.
- Heard PB, Zhang MB, Grimstad PR, 1990. Isolation of Jamestown Canyon virus (California serogroup) from *Aedes* mosquitoes in an enzootic focus in Michigan. *J Am Mosq Control Assoc* 6: 461–468.
- Smith GC, Moore CG, Davis T, Savage HM, Thapa AB, Shrestha SL, Karabatsos N, 1993. Arbovirus surveillance in northern Colorado, 1987 and 1991. *J Med Entomol* 30: 257–261.
- Takeda T, Whitehouse CA, Brewer M, Gettman AD, Mather TN, 2003. Arbovirus surveillance in Rhode Island: assessing potential ecologic and climatic correlates. *J Am Mosq Control Assoc* 19: 179–189.
- Walker ED, Grayson MA, Edman JD, 1993. Isolation of Jamestown Canyon and snowshoe hare viruses (California serogroup) from *Aedes* mosquitoes in western Massachusetts. *J Am Mosq Control Assoc* 9: 131–134.
- Anderson JF, Main AJ, Armstrong PM, Andreadis TG, Ferrandino FJ, 2015. Arboviruses in North Dakota, 2003–2006. *Am J Trop Med Hyg* 92: 377–393.
- Aguirre AA, McLean RG, Cook RS, Quan TJ, 1992. Serologic survey for selected arboviruses and other potential pathogens in wildlife from Mexico. *J Wildl Dis* 28: 435–442.
- Boromisa RD, Grimstad PR, 1987. Seroconversion rates to Jamestown Canyon virus among six populations of white-tailed deer (*Odocoileus virginianus*) in Indiana. *J Wildl Dis* 23: 23–33.
- Campbell GL, Eldridge BF, Hardy JL, Reeves WC, Jessup DA, Presser SB, 1989. Prevalence of neutralizing antibodies against California and Bunyamwera serogroup viruses in deer from mountainous areas of California. *Am J Trop Med Hyg* 40: 428–437.
- Clark GG, Crabbs CL, Watts DM, Bailey CL, 1986. An ecological study of Jamestown Canyon virus on the Delmarva Peninsula, with emphasis on its possible vector. *J Med Entomol* 23: 588–599.
- Campbell GL, Reeves WC, Hardy JL, Eldridge BF, 1990. Distribution of neutralizing antibodies to California and Bunyamwera serogroup viruses in horses and rodents in California. *Am J Trop Med Hyg* 42: 282–290.
- Goff G, Whitney H, Drebot MA, 2012. Roles of host species, geographic separation, and isolation in the seroprevalence of Jamestown Canyon and snowshoe hare viruses in Newfoundland. *Appl Environ Microbiol* 78: 6734–6740.
- Grimstad PR, Schmitt SM, Williams DG, 1986. Prevalence of neutralizing antibody to Jamestown Canyon virus (California group) in populations of elk and moose in northern Michigan and Ontario, Canada. *J Wildl Dis* 22: 453–458.
- Issel CJ, Trainer DO, Thompson WH, 1972. Serologic evidence of infections of white-tailed deer in Wisconsin with three California group arboviruses (La Crosse, trivittatus, and Jamestown Canyon). *Am J Trop Med Hyg* 21: 985–988.
- McFarlane BL, Embil JA, Artsob H, Spence L, Rozee KR, 1981. Antibodies to the California group of arboviruses in the moose (*Alces alces americana* Clinton) population of Nova Scotia. *Can J Microbiol* 27: 1219–1223.
- McFarlane BL, Embree JE, Embil JA, Rozee KR, Artsob A, 1982. Antibodies to the California group of arboviruses in animal populations of New Brunswick. *Can J Microbiol* 28: 200–204.
- Murphy RK, 1989. Serologic evidence of arboviral infections in white-tailed deer from central Wisconsin. *J Wildl Dis* 25: 300–301.
- Nagayama JN, Komar N, Levine JF, Apperson CS, 2001. Bunyavirus infections in North Carolina white-tailed deer (*Odocoileus virginianus*). *Vector Borne Zoonotic Dis* 1: 169–171.
- Nelson DM, Gardner IA, Chiles RF, Balasuriya UB, Eldridge BF, Scott TW, Reisen WK, MacLachlan NJ, 2004. Prevalence of antibodies against Saint Louis encephalitis and Jamestown Canyon viruses in California horses. *Comp Immunol Microbiol Infect Dis* 27: 209–215.
- Watts DM, LeDuc JW, Bailey CL, Dalrymple JM, Gargan TP, 1982. Serologic evidence of Jamestown Canyon and Keystone virus infection in vertebrates of the DelMarVa Peninsula. *Am J Trop Med Hyg* 31: 1245–1251.
- Zarnke RL, Calisher CH, Kerschner J, 1983. Serologic evidence of arbovirus infections in humans and wild animals in Alaska. *J Wildl Dis* 19: 175–179.
- Zamparo JM, Andreadis TG, Shope RE, Tirrell SJ, 1997. Serologic evidence of Jamestown Canyon virus infection in white-tailed deer populations from Connecticut. *J Wildl Dis* 33: 623–627.
- Neitzel DF, Grimstad PR, 1991. Serological evidence of California group and Cache Valley virus infection in Minnesota white-tailed deer. *J Wildl Dis* 27: 230–237.
- Campbell GL, Reeves WC, Hardy JL, Eldridge BF, 1992. Seroepidemiology of California and Bunyamwera serogroup bunyavirus infections in humans in California. *Am J Epidemiol* 136: 308–319.
- Grimstad PR, Calisher CH, Harroff RN, Wentworth BB, 1986. Jamestown Canyon virus (California serogroup) is the etiologic

- agent of widespread infection in Michigan humans. *Am J Trop Med Hyg* 35: 376–386.
39. Mayo D, Karabatsos N, Scarano FJ, Brennan T, Buck D, Fiorentino T, Mennone J, Tran S, 2001. Jamestown Canyon virus: seroprevalence in Connecticut. *Emerg Infect Dis* 7: 911–912.
 40. Walters LL, Tirrell SJ, Shope RE, 1999. Seroepidemiology of California and Bunyamwera serogroup (Bunyaviridae) virus infections in native populations of Alaska. *Am J Trop Med Hyg* 60: 806–821.
 41. Balfour HH, Edelman CK, Bauer H, Siem RA, 1976. California arbovirus (La Crosse) infections. III. Epidemiology of California encephalitis in Minnesota. *J Infect Dis* 133: 293–301.
 42. Calisher CH, 1983. Taxonomy, classification, and geographic distribution of California serogroup bunyaviruses. *Prog Clin Biol Res* 123: 1–16.
 43. Karabatsos N, Mathews JH, 1980. Serological reactions of fractionated hamster immunoglobulins with California group viruses. *Am J Trop Med Hyg* 29: 1420–1427.
 44. Russell PK, Nisalak A, 1967. Dengue virus identification by the plaque reduction neutralization test. *J Immunol* 99: 291–296.
 45. Russell PK, Nisalak A, Sukhavachana P, Vivona S, 1967. A plaque reduction test for dengue virus neutralizing antibodies. *J Immunol* 99: 285–290.
 46. Lindsey NP, Brown JA, Kightlinger L, Rosenberg L, Fischer M, 2012. State health department perceived utility of and satisfaction with ArboNET, the U.S. National Arboviral Surveillance System. *Public Health Rep* 127: 383–390.
 47. Centers for Disease Control and Prevention, 2014. *Arboviral Diseases, Neuroinvasive and Non-neuroinvasive: 2014 Case Definition*. Available at: <http://www.cdc.gov/NNDSS/script/casedef.aspx?CondYrID=946&DatePub=2014-01-01>. Accessed March 3, 2015.
 48. Gaensbauer JT, Lindsey NP, Messacar K, Staples JE, Fischer M, 2014. Neuroinvasive arboviral disease in the United States: 2003 to 2012. *Pediatrics* 134: e642–e650.
 49. Lindsey NP, Lehman JA, Staples JE, Fischer M, 2014. West Nile virus and other arboviral diseases—United States, 2013. *MMWR Morb Mortal Wkly Rep* 63: 521–526.
 50. Grimstad PR, 1988. California group virus disease. Monath TP, ed. *The Arboviruses: Epidemiology and Ecology*. Boca Raton, FL: CRC Press, 99–136.
 51. Johnson DK, Staples JE, Sotir MJ, Warshauer DM, Davis JP, 2010. Tickborne Powassan virus infections among Wisconsin residents. *WMJ* 109: 91–97.
 52. Grimstad PR, 2001. Jamestown Canyon virus. Service MD, ed. *Encyclopedia of Arthropod-transmitted Infections of Man and Domestic Animals*. New York, NY: CABI Publishing, 235–239.