



Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:

Kay, MK;Gibney, KB;Riedo, FX;Kosoy, OL;Lanciotti, RS;Lambert, AJ

Title:

Toscana virus infection in American traveler returning from Sicily, 2009

Date:

2010-09-01

Citation:

Kay, M. K., Gibney, K. B., Riedo, F. X., Kosoy, O. L., Lanciotti, R. S. & Lambert, A. J. (2010). Toscana virus infection in American traveler returning from Sicily, 2009. *Emerging Infectious Diseases*, 16 (9), pp.1498-1500. <https://doi.org/10.3201/eid1609.100505>.

Persistent Link:

<https://hdl.handle.net/11343/269708>

License:

CC BY

of age, and the attack rate decreased as patients' ages increased (6).

Reactive vaccination campaigns in some communes of Madarounfa district that had reached the epidemic threshold were launched by the Ministry of Public Health with a remaining 2009 stockpile (16,527 doses, 35.7% coverage) of the quadrivalent polysaccharide vaccine (A/C/Y/W135) from Médecins sans Frontières. The International Coordinating Group on Vaccine Provision for Epidemic Meningitis Control has also recently approved the release of 381,526 doses of trivalent polysaccharide vaccine (A/C/W135) for vaccination campaigns in Maradi and Zinder districts. Future immunization campaigns will be implemented by Ministry of Public Health with the support of the World Health Organization and partners, including Médecins sans Frontières and The United Nations Children's Fund.

Given the large population at risk, and the low availability and high cost of the trivalent vaccine, a sound vaccination strategy is of particular importance to mitigate the expansion of serogroup W135 in the country. Microbiologic surveillance is critical in the early and accurate detection of meningococcal serogroups for determining the appropriate vaccine.

Acknowledgments

We are indebted to all the physicians and medical assistants, especially to Bachir Mayana, who sent CSF/trans-isolate specimens and epidemiologic forms to the CERMES, and to staff at the Direction des Statistiques, de la Surveillance et de la Riposte aux Epidémies. We also thank Lagaré Adamou, Bassira Issaka, Issaka Seydou, Amadou Moussa, Sani Ousmane, Ali Sidiki, and Djibir Zanguina for technical support and Florian Girond for database management.

Microbiologic surveillance is financially supported by the French Ministry of Foreign Affairs (FSP no. 2005-174), Sanofi Pasteur (contract Men07), and the WHO Representation in Niger.

**Jean-Marc Collard,
Zaneidou Maman,
Harouna Yacouba,
Saacou Djibo, Pierre Nicolas,
Jean-François Jusot,
Jocelyne Rocourt,
and Rabi Maitournam**

Author affiliations: Centre de Recherche Médicale et Sanitaire, Niamey, Niger (J.M. Collard, S. Djibo, J. Rocourt, J.F. Jusot); Ministère de la Santé Publique, Niamey (Z. Maman, H. Yacouba, R. Maitournam); and Institut de Médecine Tropicale du Service de Santé des Armées, Marseille, France (P. Nicolas).

References

1. World Health Organization. Meningococcal meningitis. *Wkly Epidemiol Rec.* 2003;78:294–6.
2. Denis F, Rey J-L, Amadou A, Saliou P, Prince-David M, M'Boup S, et al. Emergence of meningococcal meningitis caused by W135 subgroup in Africa. *Lancet.* 1982;2:1335–6. DOI: 10.1016/S0140-6736(82)91533-1
3. Borrow R. Meningococcal disease and prevention at the Hajj. *Travel Med Infect Dis.* 2009;7:219–25. DOI: 10.1016/j.tmaid.2009.05.003
4. Taha MK, Parent Du Chatelet I, Schlumberger M, Sanou I, Djibo S, de Chaballier F, et al. *Neisseria meningitidis* serogroups W135 and A were equally prevalent among meningitis cases occurring at the end of the 2001 epidemics in Burkina Faso and Niger. *J Clin Microbiol.* 2002;40:1083–4. DOI: 10.1128/JCM.40.3.1083-1084.2002
5. Chanteau S, Sidikou F, Djibo S, Moussa A, Mindadou H, Boisier P. Scaling up of PCR-based surveillance of bacterial meningitis in the African meningitis belt: indisputable benefits of multiplex PCR assay in Niger. *Trans R Soc Trop Med Hyg.* 2006;100:677–80. DOI: 10.1016/j.trstmh.2005.09.006
6. Nathan N, Rose AMC, Legros D, Tien-drebeogo SRM, Bachy C, Bjrlw E, et al. Meningitis serogroup W135 outbreak, Burkina Faso, 2002. *Emerg Infect Dis.* 2007;13:920–3.

Address for correspondence: Jean-Marc Collard, Biology Unit, CERMES, 634 blvd de la Nation, YN034 BP 10887, Niamey, Niger; email: jmcollard@cermes.org

Toscana Virus Infection in American Traveler Returning from Sicily, 2009

To the Editor: Since the discovery of Toscana virus (TOSV) in 1971 in Tuscany (1), sandfly-borne TOSV has become recognized as a leading cause of acute meningitis in central Italy during the summer (2). France, Spain, Portugal, Greece, and Cyprus have also reported cases of TOSV infection (2). Although TOSV has been detected in sandflies in Sicily (3), we are not aware of any historically documented human infection with TOSV in this southernmost region of Italy.

We report TOSV infection of an American male physician, 65 years of age, who traveled to Sicily for 3 weeks and returned to the United States in October 2009. Two days after his return, he awoke with a headache, and hours later he noticed difficulty finding words. His headache progressed, and during the next few hours, he experienced severe expressive dysphasia. At admission to the hospital, he denied having fever, nuchal rigidity, photophobia, nausea, vomiting, or diarrhea.

Other than changing planes in Milan, the patient had remained in Sicily during the entire 3 weeks of his visit. He had sustained both mosquito and what he thought were flea bites while in Sicily. He had no known exposure to bats, rabid animals, or ticks.

Computed tomographic scan and magnetic resonance imaging of the brain showed no mass lesions or abnormality of the cerebral vessels. A sample of cerebrospinal fluid (CSF) obtained at admission showed 14 leukocytes/mm³ (reference range 0–5 leukocytes/mm³) with 100% lymphocytes, a protein level of 126 mg/dL (reference range 15–45 mg/dL), and a glucose level of 63 mg/dL (reference range 50–80 mg/dL). A nasopharynx-

geal swab specimen was negative for influenza A and B virus antigens. Other than a decreased thrombocyte count and an elevated serum glucose level, the results of complete blood count, comprehensive chemical panel, and coagulation studies were within normal limits. PCR results for CSF were negative for herpes simplex virus, enterovirus, and parechovirus. Test results for acute-phase and convalescent-phase serum specimens performed at the Washington State Department of Health Laboratory were negative for West Nile virus and St. Louis encephalitis virus immunoglobulin M.

Serum and CSF were sent to the Centers for Disease Control and Prevention in Fort Collins, Colorado. TOSV RNA was detected in a CSF sample collected on day 1 of illness by using reverse transcription-PCR (4). Plaque-reduction neutralization assays demonstrated a >4-fold rise in TOSV neutralizing antibodies between paired serum specimens collected on days 1 (titer <1:10) and 21 (titer 1:320) of illness. No similar rise in neutralizing antibodies to serologically related phleboviruses (e.g., sandfly fever Naples virus and sandfly fever Sicilian virus) was detected. The patient received supportive care only. He had a complete neurologic recovery in 10 days and was able to return to work.

Phylogenetic analyses indicate that 2 geographically distinct genotypes, the Italian and Spanish lineages of TOSV, circulate throughout the Mediterranean region (5). To determine the lineage of the infecting strain, we performed advanced molecular analyses of TOSV RNA isolated from the infected traveler's CSF. These analyses used published consensus primers that target the small (S) segment (4) as well as primers newly designed to target the medium (M) segment: M 851F, 5'-ACCAAATACAACCATAGCCCC-3' (forward) and M 1327c, 5'-ATACAATTCCACAGTCGTTAG-3' (reverse) of the multisegment TOSV genome. Reverse transcription-PCR

amplification and nucleotide sequencing generated 2 nt sequences of 332 (S segment) and 424 (M segment) nucleotides in length. Phylogenetic analyses of the newly determined sequences and sequences previously determined for Mediterranean TOSV isolates of diverse origin were carried out by using MEGA version 4 (6). According to phylogenetic inference, the TOSV RNA identified in the returning traveler is of the Italian lineage (Figure). Of interest, the TOSV M segment sequence generated from this patient aggregates with extreme bootstrap support along with that generated previously from a strain of TOSV that was isolated from sand flies in Palermo, Sicily, in 1993 (Figure), indicating that the infecting strain is likely representative of strains that have circulated in Sicily for years.

This case represents the third report of meningitis or meningoencephalitis caused by TOSV infection in a US traveler to the Mediterranean (all acquired in Italy) (7,8). As is shown by this and other recent reports of TOSV infections in the Mediterranean

islands surrounding Italy (9), the geographic range of TOSV human infections is larger than previously known. Reports of TOSV infection among European travelers returning from disease-endemic regions have provided additional evidence of the emergence of TOSV-related illness on a global scale (10).

Although the clinical course varies from asymptomatic infection to severe meningoencephalitis, TOSV should be included in the differential list of viral pathogens among patients who seek treatment with symptoms consistent with meningitis or encephalitis if the patients have recently traveled to Mediterranean areas, including Sicily. Because neither a vaccine nor specific antiviral drug treatment is available to prevent or treat TOSV infection, travelers to TOSV-endemic areas should be advised to take all precautions to prevent insect bites.

Acknowledgments

We thank Jeffrey S. Duchin and Tao Sheng Kwan-Gett for their outstanding help with this case report.

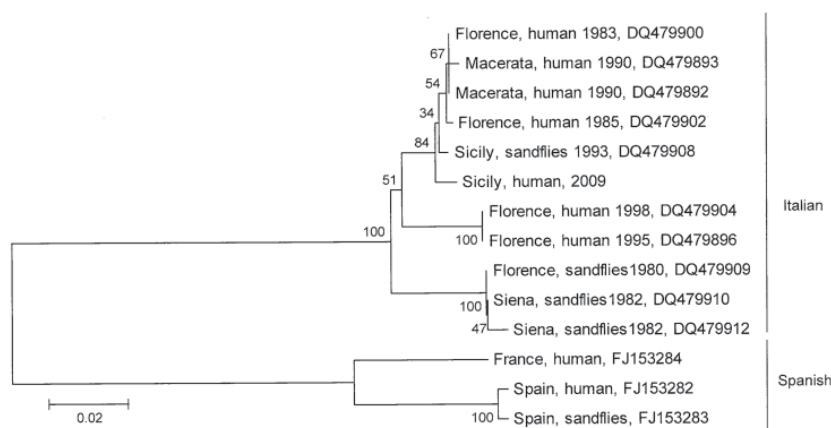


Figure. Phylogeny of Toscana viruses (TOSVs) of diverse origin. Partial small (S) and medium (M) segment sequences of interest were aligned by using ClustalW (www.ebi.ac.uk/Tools/clustalw2/index.html), and neighbor-joining and maximum-parsimony trees were generated by using 2,000 bootstrap replicates with MEGA version 4 (6). Highly similar topologies and confidence values were derived by all methods, and a neighbor-joining tree generated from a comparison of 424 nt of the M segment polyprotein gene open reading frame is displayed here. GenBank accession numbers appear after the location and source of isolation for each taxon. Scale bar represents the number of nucleotide substitutions per site. Of interest, the 2009 Sicilian TOSV described in this study (Sicily, human, 2009) aggregates with extreme support along with other Italian viruses, including an isolate that was derived from sandflies in Palermo, Sicily, in 1993.

**Meagan K. Kay,
Katherine B. Gibney,
Francis X. Riedo,
Olga L. Kosoy,
Robert S. Lanciotti,
and Amy J. Lambert**

Author affiliations: Centers for Disease Control and Prevention, Atlanta, Georgia, USA (M.K. Kay); Centers for Disease Control and Prevention, Fort Collins, Colorado, USA (K.B. Gibney, O.L. Kosoy, R.S. Lanciotti, A.J. Lambert); and Evergreen Hospital Medical Center, Kirkland, Washington, USA (F.X. Riedo)

DOI: 10.3201/eid1609.100505

References

1. Verani P, Ciufolini MG, Nicoletti L, Balducci M, Sabatinelli G, Coluzzi M, et al. Ecological and epidemiological studies of Toscana virus, an arbovirus isolated from *Phlebotomus* [in Italian]. *Ann Ist Super Sanita*. 1982;18:397–9.
2. Charrel RN, Gallian P, Navarro-Mari JM, Nicoletti L, Papa A, Sánchez-Seco MP, et al. Emergence of Toscana virus in Europe. *Emerg Infect Dis*. 2005;11:1657–63.
3. Venturi G, Ciccozzi M, Montieri S, Bartoloni A, Francisci D, Nicoletti L, et al. Genetic variability of the M genome segment of clinical and environmental Toscana virus strains. *J Gen Virol*. 2007;88:1288–94. DOI: 10.1099/vir.0.82330-0
4. Lambert AJ, Lanciotti RS. Consensus amplification and novel multiplex sequencing method for S segment species identification of 47 viruses of the *Orthobunyavirus*, *Phlebovirus*, and *Nairovirus* genera of the family *Bunyaviridae*. *J Clin Microbiol*. 2009;47:2398–404. DOI: 10.1128/JCM.00182-09
5. Sánchez-Seco MP, Echevarría JM, Hernández L, Estévez D, Navarro-Mari JM, Tenorio A. Detection and identification of Toscana and other phleboviruses by RT-nested-PCR assays with degenerated primers. *J Med Virol*. 2003;71:140–9. DOI: 10.1002/jmv.10465
6. Tamura K, Dudley J, Nei M, Kumar S. MEGA 4: Molecular Evolutionary Genetics Analysis (MEGA) software version 4.0. *Mol Biol Evol*. 2007;24:1596–9. DOI: 10.1093/molbev/msm092
7. Di Nicuolo G, Pagliano P, Battisti S, Starace M, Mininni V, Attanasio V, et al. Toscana virus central nervous system infections in southern Italy. *J Clin Microbiol*. 2005;43:6186–8. DOI: 10.1128/JCM.43.12.6186-6188.2005
8. Calisher CH, Weinberg A, Muth DJ, La-zuick JS. Toscana virus in United States citizen returning from Italy. *Lancet*. 1987;1:165–6. DOI: 10.1016/S0140-6736(87)92005-8
9. Sonderegger B, Hachler H, Dobler G, Frei M. Imported aseptic meningitis due to Toscana virus acquired on the island of Elba, Italy, August 2008. *Eurosurveill*. 2009;14:1–2.
10. Dobler G, Treib J, Haass A, Frösner G, Woesner R, Schimrigk K. Toscana virus infection in German travellers returning from the Mediterranean. *Infection*. 1997;25:325. DOI: 10.1007/BF01720413

Address for correspondence: Meagan Kay, 401 5th Ave, Suite 900, Seattle, WA 98104-1818, USA; email: meagan.kay@kingcounty.gov

Hospital Discharge Data for Guillain-Barré Syndrome and Influenza A (H1N1) Vaccine Adverse Events

To the Editor: As part of the public health response to the current pandemic (H1N1) 2009, surveillance for adverse events following vaccination for influenza A (H1N1) is a high priority (1). Surveillance for Guillain-Barré syndrome (GBS) has been of particular interest, because the syndrome was associated with the 1976–1977 swine influenza vaccine (1,2). To study this association, reliable ascertainment of recent incident cases of GBS is necessary.

GBS is an acute, immune-mediated paralytic disorder of the peripheral nervous system (3–5) with an estimated annual incidence of 0.8–1.9/100,000 (6). Most cases are associated with an antecedent infection (6). Several surveillance systems are in place to monitor rates of post-vaccination GBS (1–3), most of which

include a component of electronic administrative record review for case detection. Analysis of computerized medical databases is a well-established method of monitoring for vaccine adverse events (7). Although the validity of such data varies, depending on the diagnosis and region, few studies have evaluated the use of hospital discharge data for GBS specifically (8,9).

We reviewed the Tennessee Department of Health Uniform Hospital Discharge Dataset for all hospital discharge diagnoses in 4 major metropolitan regions of Tennessee in 2002–2003 with codes from the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), that might indicate acute GBS. Records with ICD-9-CM code 357.0 (acute infective polyneuritis) or other combinations suggestive of GBS within the top 10 diagnoses were requested. These data were compared with information on cases identified by directly requesting lists of patients with discharge diagnoses of GBS from hospital medical record departments. Charts of all reported cases were validated by chart review. Patients were classified as having acute GBS if they met Brighton Criteria Levels 1, 2, or 3 (10).

A total of 344 records of possible cases of acute GBS were identified. Of these cases, 215 (63%) were identified through the state hospital discharge database, 315 (92%) were reported directly by hospitals, and 186 (54%) were identified by both systems. Among all suspected cases identified, only 103 (30%) met criteria for acute GBS (annual rate 2.1/100,000 population), 14 (4%) were in out-of-state residents, 114 (33%) were nonacute cases that occurred before the study period and patients were readmitted for other reasons, 90 (26%) had no documentation of GBS in the medical record, 17 (5%) were duplicate reports, and 6 (2%) had insufficient information for further investigation. The predictive-value positive of a