Continued Transmission of West Nile Virus to Humans in Southeastern Romania, 1997–1998

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After an epidemic of West Nile (WN) virus neurologic infections in southeastern Romania in 1996, human and animal surveillance were established to monitor continued transmission of the virus. During 1997 and 1998, neurologic infections were diagnosed serologically as WN encephalitis in 12 of 322 patients in 19 southeastern districts and in 1 of 75 Bucharest patients. In addition, amid a countrywide epidemic of measles, the etiology of the febrile exanthem in 2 of 180 investigated cases was determined serologically to be WN fever; 1 case was complicated by hepatitis. Sentinel chickens placed in Bucharest seroconverted to WN virus during the summer months, indicating their potential value in monitoring transmission. The continued occurrence of sporadic WN infections in southeastern Romania in consecutive years after the 1996 epidemic is consistent with local enzootic transmission of the virus.

Methods

In 1997, Romanian public health epidemiologists in 19 districts were instructed to collect serum and cerebrospinal fluid (CSF) specimens from patients presenting with aseptic meningitis or encephalitis between April and November for serologic diagnosis of WN virus infection. In addition, 160 sentinel chickens in Bucharest were bled biweekly between 26 June and 13 August and again on 16 October 1997 to monitor enzootic viral transmission. Virus-specific IgG was detected by indirect ELISA [2]. In 1998, specimens from meningoencephalitis patients hospitalized between March and September in Bucharest only were referred for serologic testing. At the end of the summer, acute samples from 180 patients hospitalized with acute measles were tested retrospectively. Human specimens were tested at the Institute of Virology by IgM capture and indirect IgG ELISAs [1].

Results

In 1997, specimens from 322 patients, 119 from Bucharest, were evaluated for WN virus antibodies. Twelve patients with clinical meningoencephalitis and elevated IgM absorbance ratios in serum or CSF samples were diagnosed with cases of acute WN encephalitis. In the only fatal case, the serologic diagnosis was based on tests of acute serum and CSF samples only, but in the others, IgG conversions between acute- and convalescent-phase serum samples also were demonstrated. The district residences of WN encephalitis patients and those in whom the diagnosis was excluded are shown in figure 1. Laboratory-confirmed WN neurologic infections occurred between 13 July and 25 September with onset of 2 cases in July, 6 in August, and 4 in September. Case-patients were 13–76 years old (median, 45).

Seroconversions in sentinel chickens in Bucharest were demonstrated in each of four consecutive biweekly bleedings from 26 June to 13 August with 23%, 26%, 40%, and 16% of birds converting at each interval. No seroconversions were noted again until the final bleeding on 16 October, when 13% of the sentinels seroconverted.

In 1998, clinical samples from 75 patients in Bucharest hospitalized with encephalitis (25), aseptic meningitis (36), and meningoencephalitis (14) were submitted for serologic testing. One patient was diagnosed as having acute WN encephalitis. From May 1997 to September 1998, the country experienced

Mosquitoborne West Nile (WN) virus usually is an acute self-limiting febrile illness with exanthem and myalgia. However, the illness may be complicated by central nervous system infection, especially in the elderly, and rarely by hepatitis or other organ involvement. An unprecedented epidemic of WN encephalitis occurred in southeastern Romania in 1996, producing 393 cases—principally in Bucharest and districts bordering the lower Danube River [1]. Although the outbreak was suspected to have been an extension of sylvatic transmission from the delta, previous field investigations had not characterized a local viral transmission cycle, and the virus had never been isolated in the country until the 1996 outbreak. The results of surveillance maintained in 1997 and 1998 to monitor continued transmission of the disease are reported here.

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its greatest measles epidemic in the postvaccine era: >20,000 cases were reported, principally among high school children and young adults (14–25 years old). Serum samples from 180 hospitalized patients were tested for WN IgG and IgM antibodies in parallel with confirmatory tests for measles. Two patients with a clinical diagnosis of measles without serologic evidence of measles virus infection had elevations of WN virus-specific IgM, indicating recent infection with that virus. The first case patient, a 24-year-old woman whose onset of illness was on 24 May, made an uneventful recovery. The second patient, a 19-year-old woman, developed an acute febrile illness with exanthem on 2 June and was initially diagnosed with a case of acute measles, but her illness was complicated by hepatitis and sustained elevated hepatic transaminases for 2 weeks before clinical recovery.

Discussion

The sporadic cases of WN virus infections in Bucharest and the lower Danube delta in 1997 and in Bucharest in 1998 are persuasive evidence of ongoing virus transmission in southeastern Romania. Compared with the 1996 epidemic, when 352 (80%) of 441 hospitalized encephalitis patients with adequate clinical specimens were diagnosed with cases of WN neurologic infection, the 12 patients with laboratory-confirmed cases in 1997 comprised only 4% of the patients referred for evaluation, and in 1998 only 1% [1]. The epidemiologic and clinical criteria for specimen referral were similar in all years, underscoring the unusual pattern of viral transmission in 1996. Systematically collected data from other years are unavailable; however, the experience from the aftermath of the epidemic, when clinical suspicion of the diagnosis might still have been high, suggests that WN encephalitis occurs sporadically and with a relatively low frequency in Bucharest and in the southeastern quadrant of Romania. Sentinel chickens were posted in Bucharest rather late, but by the first bleeding on 26 June, nearly one quarter of the sentinels had seroconverted, preceding the onset of the first case in a human in the city by 6 weeks; this indicates the potential value of sentinel bird surveillance for forecasting future epidemics.

During the course of the 1996 investigation, hospital-based case finding focused on identifying neurologic infections and
attempts to measure the full extent of the epidemic by identifying patients with milder illnesses were unsuccessful because of the relatively low infection rate and the nonspecific symptoms associated with uncomplicated WN fever. In previous reports, WN fever has been characterized as an undifferentiated self-limited febrile illness, often with exanthem, lymphadenopathy, and polyarthralgias [3]. But illness complicated by fatal hepatitis, pancreatitis, myocarditis, and neurologic infection have been described [4–7]. The 2 patients hospitalized with a clinical diagnosis of measles appear to have had cases of WN fever with exanthem, complicated in the second patient by acute hepatitis. The frequency of the latter complication is uncertain, although in the 1998 Georgia outbreak, in which 624 febrile exanthem case patients were investigated, 3 had fatal hepatitis [7]. Hepatitis complicating measles appears to be even rarer. A recent review found only 27 reported cases with hepatobiliary involvement [8]. On the basis of the negative serologic findings of acute measles infection and the presence of WN virus-specific IgM antibodies, it seems likely that this was a case of WN fever-associated hepatitis.

Sporadic cases and clusters of encephalitis cases occurring during the summer and attributed to WN virus were previously reported in areas of Romania, but some cases had epidemiologic features more consistent with tick-borne encephalitis, and WN virus was not isolated, so the diagnosis remains unconfirmed [9, 10]. Although reports and serosurveys reporting WN HI antibodies in birds, mammals, and humans in the Danube delta strongly suggested that the virus was transmitted locally, a mechanism of enzootic transmission was never defined, and periodic reintroductions of the virus from Africa by migratory birds also seemed possible. Perennial transmission of the virus in the Danube delta is plausible in view of the plentiful population of birds in that expanse of wetlands, and the continued human infections in 2 consecutive years after the 1996 outbreak further supports that likelihood. The chance downing of south-migrating storks (Ciconia ciconia) as they transited Israel (Ciconia ciconia) indicate increased transmission or recognition of the disease in southern Europe and neighboring areas [7, 12–15].

References