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West Nile fever in Israel: The reemergence of an endemic disease

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Summary *Background:* As a crossroads for bird migration between Africa and Eurasia and with its long history of human infection, Israel has been a major focus of attention during the continuing global spread of West Nile fever (WNF). This article reviews the background and reemergence of WNF in Israel; the recent epidemiology of WNF among Israelis; and the disease-control strategies being used to combat the disease.

Methods: Employing the comprehensive base of case data that are reported to the Ministry of Health, an epidemiological record was constructed that details the incidence and distribution of WNF cases in Israel in recent years.

Results: After decades of small, intermittent outbreaks, nearly 1400 cases of WNF were reported in Israel between 2000 and 2012. Incidence was consistently highest in the coastal cities, among elderly patients, and in the late summer months and early autumn. A broad range of control measures to prevent human infection has been implemented, and attention has been given to issues such as the protection of the national blood bank and the occurrence of long-term sequelae.

Conclusions: The reemergence of WNF in Israel is likely the result of a combination of factors including past immunity to the virus among the human population, a marked increase in awareness of WNF among physicians, and more frequent requests for the laboratory testing of suspected cases. In the absence of effective vaccine to protect humans from WNF, the best disease-control strategies include intensive vector-control measures, the continued

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development of techniques to forecast outbreaks, and effective public education programs that are targeted toward the high-risk elderly population.

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Introduction

West Nile virus (WNV) is a mosquito-borne flavivirus whose reservoir includes many species of birds, and for which humans are among the virus' "dead-end" hosts. The large majority of humans infected – approximately 80 percent – are asymptomatic; nearly 20 percent contract West Nile fever (WNF) and exhibit symptoms of varying severity including fever, malaise, headache, or body ache; and less than 1 percent develop neuroinvasive complications.^{1,2} Known for decades to be endemic in Israel, Africa, and in portions of Asia, Europe, and Australia,^{3,4} WNV has in recent years spread to new areas including the Americas,⁵ has adapted to new species of mosquito vector and new host populations,³ and is now the most widespread flavivirus in the world.⁶ Global awareness of WNF has grown significantly in the past 15 years, during which time major outbreaks have occurred in Romania, Russia, the United States, Canada, Israel, and most recently in Greece.^{7–9}

WNV reemerged in Israel in the late 1990s in various avian species, including migratory storks in the south of the country, and a large outbreak occurred among domestic geese. A serological survey found seroprevalence levels of 86 percent in humans who worked in close proximity to sick geese, 28 percent in persons in areas along bird migration routes, and 27 percent in the general population.¹⁰ At the end of the decade the presence of the virus in Israel became a focus of international attention. In a 1999 outbreak in New York, where WNV was first introduced into the Americas, isolates were found to have a close genetic resemblance to the virus that had been detected in the infected Israeli geese.^{11,12} Then, in 2000, Israel experienced its largest recorded WNF outbreak among humans with over 400 reported cases and nearly 40 fatalities, and in every year since then outbreaks of varying scope have been recorded. In this paper we review the epidemiology of WNF in humans in Israel focusing on the 2000–2012 period; the circumstances behind the reemergence of the disease; and the variety of control measures that are being used to mitigate its impact.

Methods

WNF has been notifiable in Israel since 2001. Epidemiological investigations of all reported cases are conducted by the Ministry of Health jointly with the Ministry of Environmental Protection (which focuses on the mosquito vector in the area of reported infection). The Health ministry's case-specific inquiries are carried out by staff at the district health offices and these inquiries result in individual case notification reports that specify age, gender, nationality, address, date of onset, and laboratory test results. Incidence statistics are based on these notification reports, and the national data are processed and analyzed by the Health ministry's Division of Epidemiology.

The incidence data include both confirmed and probable cases. The latter category includes cases for which a diagnosis of WNV infection had been considered "highly probable" based on IgM titer levels from a first test, but where a complete diagnosis could not be reached because the patient was discharged from the hospital and a second blood or cerebro-spinal fluid (CSF) sample was not provided to allow testing for IgG levels. The incidence data reflect a common, built-in reporting bias with regard to WNF, which is that the disproportionately small number of infections that result in serious disease and hospitalization are over-represented in the number of reported cases.

The clinical symptoms of WNF are non-specific, making laboratory testing the primary tool for reliable case diagnosis.¹³ In Israel, laboratory confirmation of primary WNV infection is generally based on the results of IgM and IgG serology tests both on human serum and on CSF. Until 2004 serology tests were done just once, but since 2005 a second test has been added seven to ten days following the first, which often helps to distinguish acute WNF disease from prior infection. Since 2001 serological testing in Israel has been done largely for patients hospitalized with either neuroinvasive disease (i.e. encephalitis, meningitis, meningoencephalitis, and acute flaccid paralysis) or with the more common symptoms associated with West Nile fever. While testing is also done at the request of a Health Maintenance Organization if a patient's physician suspects the presence of WNV infection, such tests are not performed on a systematic basis. The National Center for Zoonotic Viral Infections in the Central Virological Laboratory, located at the Sheba Medical Center at Tel Hashomer (near Tel Aviv), is Israel's national reference laboratory for WNF and other arthropod-borne diseases.

Results

In Israel the first recognized outbreak of WNF among humans occurred in 1951, and subsequent outbreaks were reported in 1952, 1953, 1957, and 1980.^{14,15} In 1999, after a lengthy hiatus of reported human cases, two human fatalities occurred. The victims, each 72 years old, were a married couple who had recently immigrated to Israel from Russia.¹⁰ In 2000, Israel experienced its largest recorded WNF outbreak, with 429 reported cases (for an incidence rate of 6.8 per 100,000), 296 hospitalizations, and 38 fatalities. Nearly half the case patients in 2000 were 60 years or older, and incidence rates increased sharply with age. Over two thirds of case patients were hospitalized. The outbreak ran from August through October, peaking in the third week of September. Incidence was highest in the country's coastal plain, and case patients were evenly distributed by sex.

With the occurrence of the 2000 outbreak WNF became a seasonal public health concern in Israel. Between 2000 and 2012 the number of reported cases per year ranged from 12

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