

The West Nile Virus outbreak in Israel (2000) from a new perspective: The regional impact of climate change

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Abstract

The West Nile Virus (WNV) outbreak in Israel in 2000 appeared after medical and climatic warning signs. Re-analysis of the epidemic from a new viewpoint, the regional impact of global warming, especially the worsening in the summers' heat conditions, is presented. The disease appeared averagely at a lag of 3–9 weeks (strongest correlation = lag of 7 weeks). The minimum temperature was found as the most important climatic factor that encourages the disease earlier appearance. Extreme heat is more significant than high air humidity for increasing WNV cases. An early extreme rise in the summer temperature could be a good indicator of increased vector populations. While 93.5% of cases were in the metropolitan areas, the disease was not reported in the sub-arid regions. The outbreak development was comparable to the cases from Romania (1996) and NYC (1999). Each of those epidemics appeared after a long heatwave.

Keywords: *West Nile Virus, regional climate changes, extreme heat, Israel*

Introduction

The world's climate system is an integral part of the complex of life-supporting processes, one of several natural systems that are now coming under pressure from the increasing weight of human activity. Historically, environmental health concerns have focused on toxicological or microbiological risks to health from local exposures. However, the scale of environmental health problems is increasing and various large-scale environmental hazards to human population health have begun to appear (McMichael 2003). It is well known today that the additional burden of greenhouse gasses as a result of human activity enhances the natural greenhouse effect, causing global warming (e.g., IPCC 2001; Gartell 2001). This trend has many global and local aspects; one of them is the impact on human health. Global climate change would affect human health via a pathway of varying complexity, scale and directness and with different timing. Similarly, impact (both positive and negative) would vary geographically as a function of the physical and environmental conditions and of the vulnerability of the local human population. For vector-borne diseases, the distribution and abundance of vector organisms and intermediate hosts are affected by various physical and biotic factors. Integrated modeling studies have forecast that an increase in ambient

temperature would cause a worldwide, net increase in the geographical distribution of vector organisms. Humans will be affected by changes in the geographical distribution of infection disease (McMichael 2003; Marsh & Gross 2001). Temperature-related changes in the life cycle dynamics of both the vector species and the pathogenic organisms would increase the potential transmission of vector-borne diseases such as malaria, dengue fever or West Nile Fever (WNV). The current study is an attempt to re-analyse one of the recent WNV outbreaks, which occurred in Israel during the summer of 2000, from a new viewpoint: The regional impact of the global climate change on the eastern Mediterranean.

West Nile Virus

West Nile Virus (WNV) is a vector-borne zoonotic disease, belonging to the Japanese encephalitis serogroup of flaviviruses. These viruses are transferred by carriers, especially mosquitoes, and spread all over the world attacking vertebrates of several types, including birds and mammals (Tsai 2001). WNV is normally transmitted between birds by the *Culex pipiens*, a vector that tends to breed in foul standing water in drains and catch basins (Epstein 2001; Pats et al. 2003). The disease generally appears at the end of the summer and the beginning of autumn, with incubation period of 3–15 days. WNV became recognized as a cause of fatal human meningitis or encephalitis in elderly patients during an outbreak in Israel in 1957. Encephalitis occurs also in horses, as well as causing mortality in certain domestic and wild birds (CDC website 2004). The virus was isolated in large regions in Africa, south-western Asia and in the eastern and southern parts of Europe. It was found that in those areas, the disease is endemic (Hubalek & Halouzka 1999; Tsai 2001).

Recent outbreaks of WNV encephalitis in humans have occurred in several places, e.g., in Algeria (1994), in Romania (1996–1997) when the disease course was recognized as more aggressive to humans than in the past, in Russia (1999), in the United States (1999–2003), and in Israel (2000). The outbreak of WNV in the New York City metropolitan area (1999) was the first detection of the virus in the western hemisphere (Nash et al. 2001). The means by which WNV entered the Americas is unknown, but the genetic analysis indicated that the strain responsible for the outbreak was nearly identical to a strain that was circulating in Israel in 1998 (Lanciotti et al. 1999).

The linkage between WNV and climate conditions

Extreme warm conditions were found to be a crucially important factor that instigated the launching of WNV epidemics. High temperatures have been shown to speed up the replication of WNV in mosquitoes, this rapid amplification directly affects the likelihood of the mosquito reaching maturity and subsequently infecting other hosts (Epstein 2001). It has been proven experimentally that high temperatures help increase mosquito abundance, as well as increase vector competency (Dohm et al. 2002; Turell et al. 2001). Epstein (2001) and Pats et al. (2003) noted that high temperatures speed up the development of viruses within the mosquito carriers, which only live about two weeks. The virus develops while the mosquito is alive and capable of biting, thereby heightening the chances of it becoming a real danger. Amplifications of WNV are thought to occur under the climatic conditions of warm winters followed by hot dry summers. In drought conditions, standing water pools become richer in the organic material that *Culex* needs to thrive and the mosquito predators, such as frogs, are fewer in number. This may encourage birds to circulate around small water holes and thus increase interactions with mosquitoes (Epstein 2001; Epstein & Defilippo 2001; Chase & Knight 2003; Pats et al. 2003). Experimental studies on WNV indicate that temperature

profoundly influences mosquito-to-vertebrate transmission rates. A decrease in temperature from 26°C to 18°C during a 17-day post-infection period caused a decrease in transmission rates from 97% to 48%. Summer temperature was found as one of the most important environmental variables modulating WNV activity in Europe (Savage et al. 1999).

Dohm & Turell (2001) found that the virus was recovered from most mosquitoes held exclusively at 26°C. In contrast, none of the mosquitoes held exclusively at lower temperatures had detectable infections. Dohm et al. 2002 showed that infection rates of *Culex pipiens* collected in New York in 1999 were directly related to subsequent incubation temperatures: In mosquitoes held at 30°C, virus was recovered from nearly all mosquitoes tested (as early as 4 days after the infectious blood meal) whereas for mosquitoes held at 18°C, disseminated infections were not detected until 25 days.

The history of WNV in Israel

Israeli researchers in the 1950s were the first to characterize the clinical presentation of WNV fever. The vectors of WNV in Israel are mosquitoes of the *Cx. pipiens* and *Cx. perexiguus* (Weinberger et al. 2001). Since the reservoir is wild birds, the location of Israel as a major stopover for migrating birds is crucially important for the disease transfer. The virus was found in Israel in large variety of birds, like storks (enormous flocks migrate annually through Israel during autumn and spring) and geese, as well as in pigeons and ravens (ICDC website 2004) which are very widespread in the Israeli cities. Interaction between birds and mosquitoes is frequent where water is available, like fish ponds. Consequently, the link between the migrating birds and the disease appearance in the metropolitan centers is understandable.

Several WNF outbreaks were reported in Israel in the 1950s and one in 1980. Most patients were young soldiers in training, who contracted the infection in army camps in central and northern Israel, relatively humid zones. Information about WNF in the civilian population is more limited. In 1951, an outbreak occurred in a Kibbutz (Ma'ayan Zvi) south of Haifa (see Figure 1); 41% of its 303 inhabitants became ill. All age groups were affected (most adults were between 20–35 years old) but no deaths were reported.

Another two outbreaks were reported in civilians in the Hadera area in 1957 (Figure 1). The first case was among 65 citizens, two patients (a child and an adult) had encephalitis, no deaths were reported. The second case in Hadera area in 1957 was in 49 elderly patients, aged 66–86, who were residents of four nursing homes. Encephalitis developed in one third of these patients and four died. This was the first time that infection caused by WNV was associated with severe encephalitis and death. The limited outbreak of 1980 was again in a military camp in the Negev Desert, 32 young soldiers were infected with no deaths. (Weinberger et al. 2001; ICDC 2004). By the end of the 20th century, WNV infection was a forgotten disease in Israel.

After a long absence, the disease was diagnosed in the summer of 1998 in animals, particularly in goose flocks. In summer 1999, three cases of WNF in humans were reported, two of them ended with death. During the summer of 2000, a large outbreak of WNF in humans occurred. Between August and November, 417 cases of serologically confirmed WNV were diagnosed with 324 admissions in hospitals, and 35 deaths (ICDC website 2004). The distribution and the location of that outbreak are discussed later on.

Based on the Knesset (Israeli parliament) protocol #60, 29 May 2001, officials from the Ministry of Health indicated that they were surprised by the occurrence of the disease outbreak. In 2001, WNV was halted, probably due to prevention measures by the Israeli health authorities, especially pest control of mosquitoes, together with drying up standing water pools.

Israel climate

Israel is located at the eastern end of the Mediterranean, influenced by westerly winds in the chilly winter, and the blocking subtropical high during the dry summer season. Precipitation commences during October and ends in May, while June, July and August are totally dry. The summer is characterized by high temperatures, parallel with high humidity that increases dramatically toward the seashore. The whole Eastern Mediterranean basin is highly sensitive to possible climate changes due to its geographical location between three continents and two climatic influential areas: The Atlantic Ocean and the wide landmass of Asia (Milliman et al. 1992). Available scenarios linked with the global warming due to greenhouse gases emission show a significant increase in extreme weather events (Palutikof & Wigley 1996). It was found that during the second half of the 20th century the summers in Israel became warmer (Ben-Gai et al. 1999). In most of the Eastern Mediterranean monitoring stations' a tendency of drought was identified during recent years (e.g., Xoplaki et al. 2000; Paz et al. 2003).

Several studies were published concerning the medical and epidemiological aspects of the 2000 WNV epidemic in Israel (e.g., Chowers et al. 2001; Weinberger et al. 2001). However, research about the involvement of extreme weather conditions, especially severe heat, as an additional contributory factor, is still missing. The current study aims to add this new viewpoint to the understanding of that outbreak.

Data and methods

1. A total of 417 cases of the WNF outbreak of 2000, serologically confirmed by the Israeli Central Virology Laboratory (date of admission, age and address of the patients; source: Israeli Ministry of Health, Epidemiology Department, WNV database) were analysed and mapped.
2. Weather conditions during the summer of 1998 (when WNV was diagnosed in Israel in birds after a long absence), the summer of 1999 (when three cases in humans were reported with two deaths) and the summer of 2000 (when the WNV outbreak took place), were analysed based on the Israel Meteorological Service reports (IMS annual reports 1998, 1999, 2000). This was carried out in order to identify possible trends in the patterns of climate conditions that could contribute to the disease prediction. As the Mediterranean climate is characterized by a dry summer without rainfall, the current study focuses especially on temperatures.
3. In order to identify lag relations between warm conditions and the WNV outbreak, Pearson cross correlations were calculated between the dates of hospital admission and daily mean, maximum and minimum temperatures (source: <http://www.ncdc.noaa.gov/cgi-bin/res40.pl?page=climvisgsod.html>) for the 168 days from 1 June to 15 November 2000, in two stations (Figure 1) – Haifa (32°80' N/35°03' E, 0m) and Ben-Gurion airport (32°00' N/34°90' E, 4m). These stations were selected based on the results of the patients' addresses mapping and represent the two regions with the majority of WNF cases.
4. Pearson cross correlations were calculated between the hospital admission dates and the relative humidity, and also between the admissions dates and the dew point temperature values in Ben-Gurion airport station for the same 168 days. This, to evaluate the contribution of air humidity to the WNV outbreak.

Results

1. The WNF disease appeared among patients from 20 July 2000 to 11 November 2000. The majority of cases, 63%, occurred in September (21% at the first trimester of the

month, 24% and 18% at the second and third parts respectively). A total of 16% of the cases were reported in August while 18% were reported in October.

- The mapping of the addresses of the 417 patients indicated that 60.7% of them lived in the densely-populated cities in the central parts of Israel, 32.8% in the north which is less populated, and 6.5% in the south, a sparsely settled area (see Figure 1). Those results

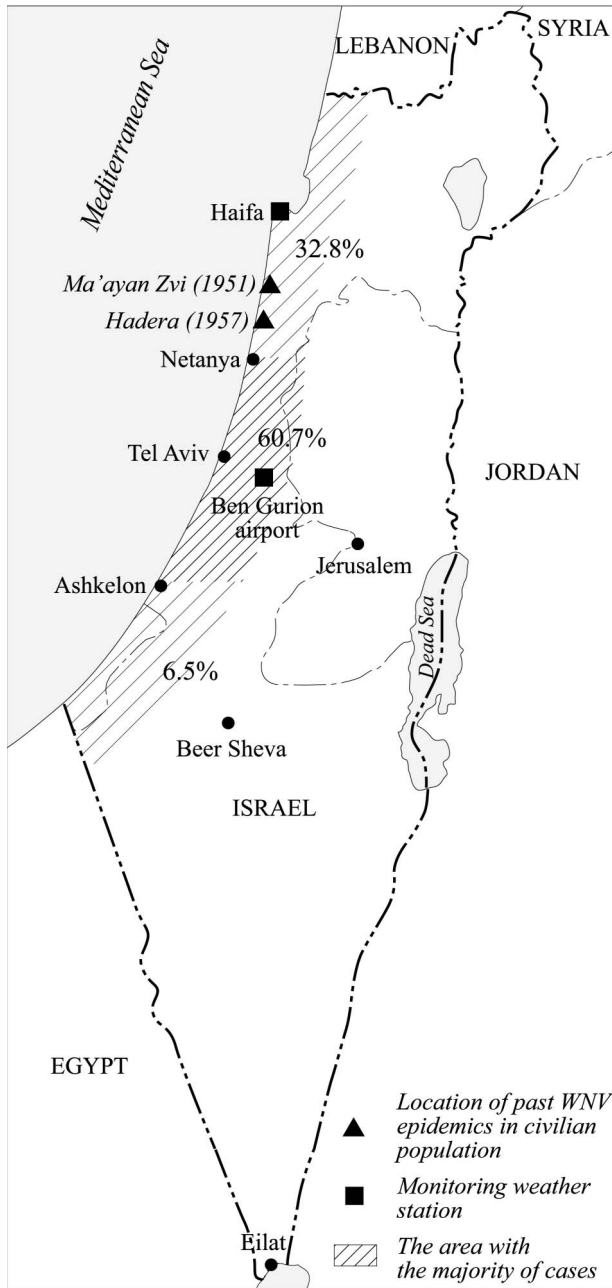


Figure 1. WNV distribution (2000) by areas, of past outbreak sites and the location of the weather stations.

reflect the population distribution in the country; however, that type of spreading is different from past outbreaks which occurred in limited areas such as the city of Hadera or the army camps.

3. Analysis of the disease distribution by the patients' ages per each region is presented in Figure 2.
4. The period of mid-June to mid September 1998 (when WNV was diagnosed in animals for the first time) was extremely hot, and summer 1998 was one of the hottest ever recorded with an extremely long spell of heat wave (20 July to 15 August) causing agricultural damage. Temperatures during that period were 4–5°C above normal during day and night, accompanied by high relative humidity values in the coastal area. July and August 1999 (when three cases of WNV in humans were detected) were also much warmer than usual – temperatures were about 3°C above normal. The summer of 2000 (when the WNV epidemic occurred) was also warmer than usual (as the two previous ones) with temperatures 3–4°C above normal. In many areas it was the hottest July since the beginning of measurements 50 years ago with a long spell of heatwave, daily maximum temperatures exceeding 31°C in the coastal plain for 22 consecutive days (see Figure 3).

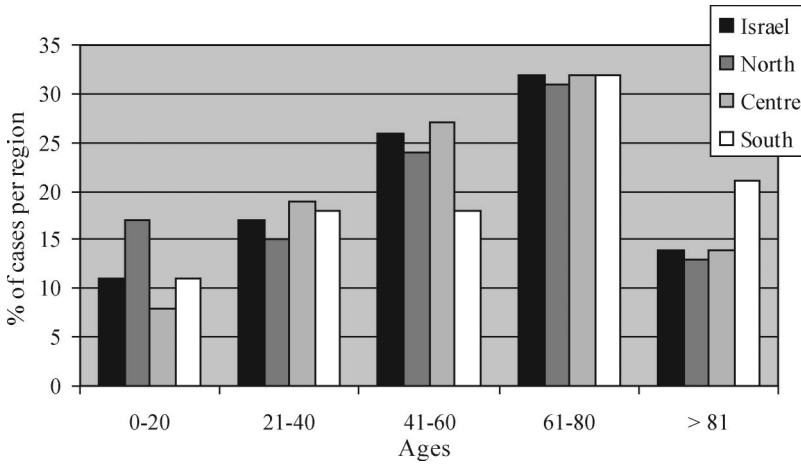


Figure 2. WNF outbreak distribution (%) by ages per region (summer 2000).

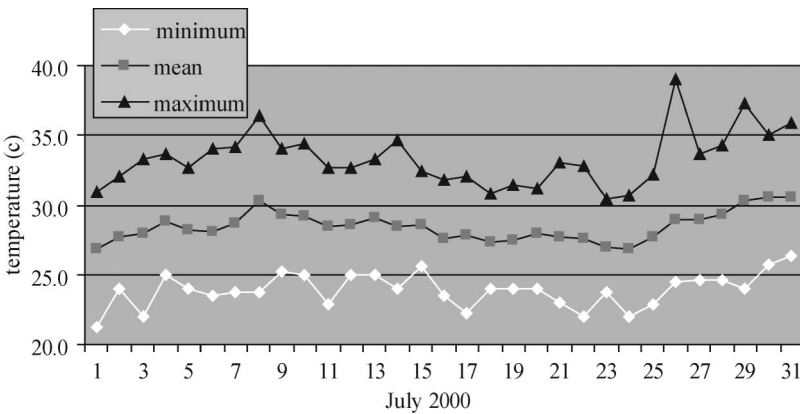


Figure 3. Minimum, mean and maximum temperatures (°C) at Ben-Gurion airport station, July 2000.

The hot weather reached its peak towards the end of July, when the temperatures in Jerusalem reached 40.8°C, the highest temperature recorded in Jerusalem since 1942. August was not as extreme as July, yet it was still warmer than normal.

- Figure 4 represents the mean temperature values at Ben-Gurion airport stations together with the WNV hospital admission cases along the period from 1 July to 31 October 2000. The delay between the extreme heat conditions to the disease appearance is seen. Lag correlation analysis using Z-test found significant positive correlations ($0.3 \leq r \leq 0.58$; $p \leq 0.05$) between the temperature values (mean, maximum and minimum) at the two stations, and the hospital admission dates. Despite the 100 km ~ distance between Haifa and Ben-Gurion airport, the results for both stations are similar. Results are presented in Table I.

The significant results for the minimum, mean and maximum temperatures in Ben-Gurion airport (which represents the geographical region with most cases) are presented in detail in Figures 5a–c respectively.

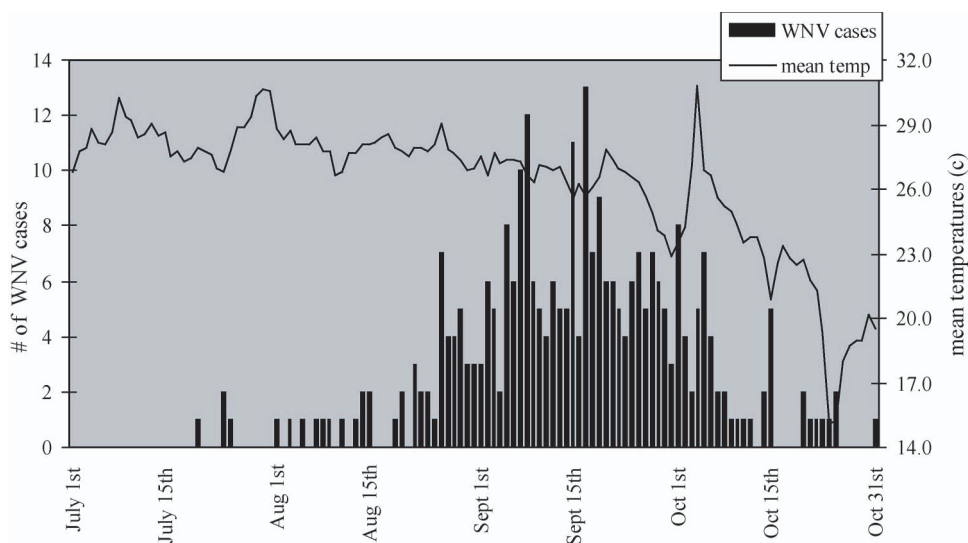


Figure 4. Number of WNF cases (based on hospital admissions) and mean temperature values at Ben-Gurion airport station along the period from 1 July to 31 October 2000.

Table I. Range (in lagged days) of the significant results ($p \geq 0.05$) of lag correlations between the temperature values in Ben-Gurion and Haifa stations and hospital admission dates.

	Ben-Gurion airport			Haifa		
	Earliest lagged day	Latest lagged day	Lagged day with the strongest correlation	Earliest lagged day	Latest lagged day	Lagged day with the strongest correlation
Minimum temp.	10	63	49	14	59	44
Mean temp.	20	66	50	20	63	49
Maximum temp.	38	64	50	42	66	50

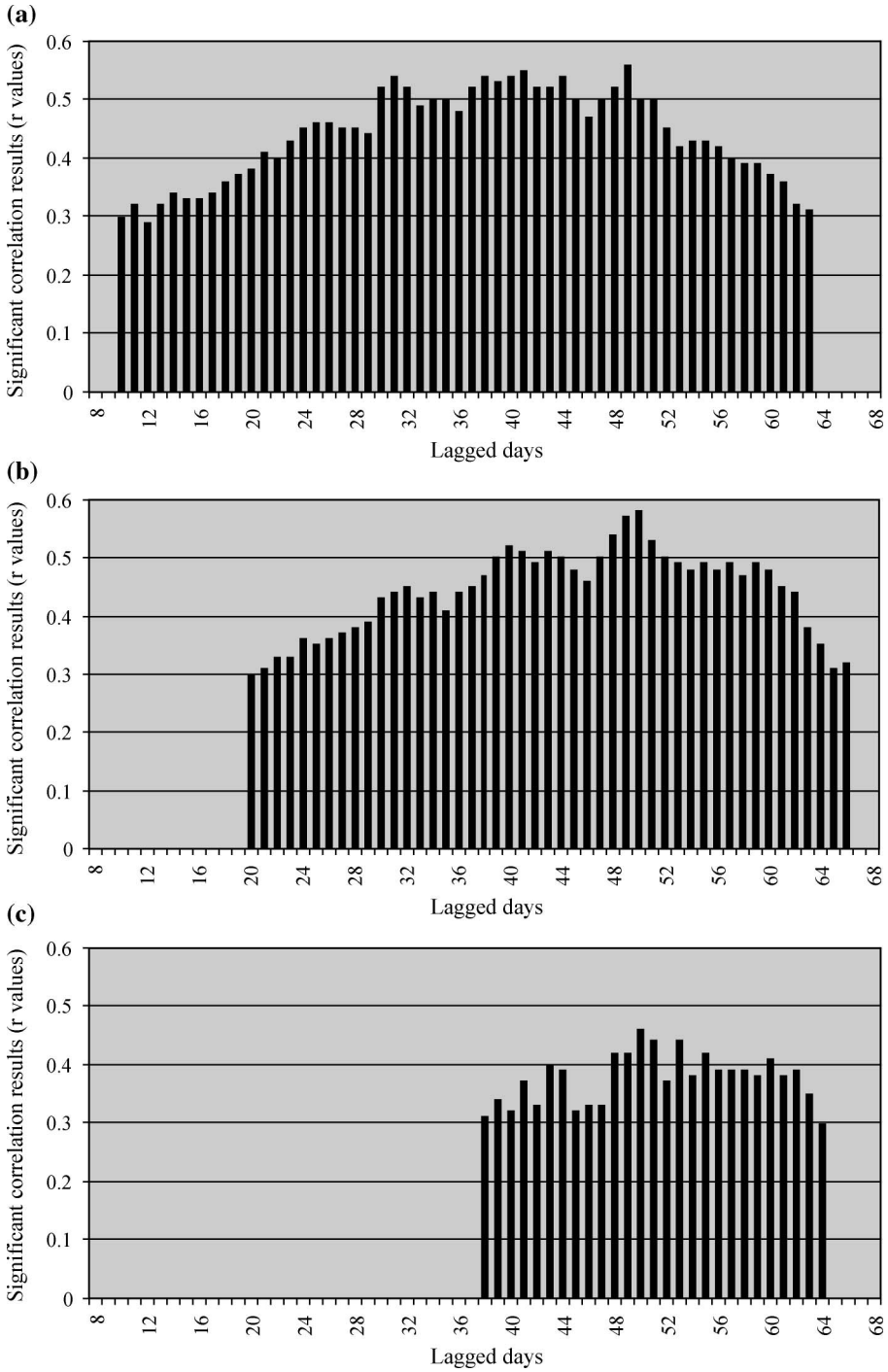


Figure 5. (a) Lag correlation significant results ($r \geq 0.3$; $p \leq 0.05$) between minimum temperatures at Ben-Gurion airport and hospital admission dates. (b) Lag correlation significant results ($r \geq 0.3$; $p \leq 0.05$) between mean temperatures at Ben-Gurion airport and hospital admission dates. (c) Lag correlation significant results ($r \geq 0.3$; $p \leq 0.05$) between maximum temperatures at Ben-Gurion airport and hospital admission dates.

6. Pearson cross correlation analysis using Z-test, found significant positive correlations between the relative humidity and the dew point temperature at Ben-Gurion station, and the hospital admission dates ($0.3 \leq r \leq 0.39$ for the relative humidity and higher results, $0.3 \leq r \leq 0.5$, for the dew point temperature; $p \leq 0.05$). Results are presented in Figure 6.

Discussion

It is well known that disease vectors have climatic thresholds that govern their abundance and potential for disease transmission. As mentioned above, high temperatures speed up the replication of WNV in mosquitoes, the mosquito abundance and the vector competency. The WNV outbreak in humans during the summer of 2000 appeared after two years with indications about the existence of the disease potential. In this context it is important to note that Dohm and Turell (2001) established that the *Cx. pipiens* can survive the winter but adults are normally inactive. When temperatures increase in the spring, the mosquitoes' infectious virus becomes detectable once again.

The three subsequent summers of 1998, 1999 and 2000 were extremely hot, warmer than ever recorded, with long spells of heatwaves during days and nights. The occurrence of these extreme summers could be explained as one of the local results of the global warming effects on the Eastern Mediterranean basin. Those trends had to be considered in the disease prediction for summer 2000. The current study presents the consequence of analysing the climatic conditions in the two or three years before the past epidemic in other areas in the world, in order to appreciate the possible trends that could encourage the outbreak occurrence.

The outbreak of WNV in the year 2000 was different from the past cases of such outbreaks in Israel in the following aspects: the wide extent of the disease spreading, the high number of hospital admissions, the acute neurological symptoms and the high death rates (8.4%). Analysis of the distribution of the disease cases by age of the patients indicates that almost half of them in all regions were above 60 years old, despite the low proportion of this age group in the total population which is just 13% (Israel Annual Statistic Report 2000). All death cases except one were of people above the age of 68. A plausible explanation for these observable facts is the body's weak immune system in advanced age. The climatic conditions previous to

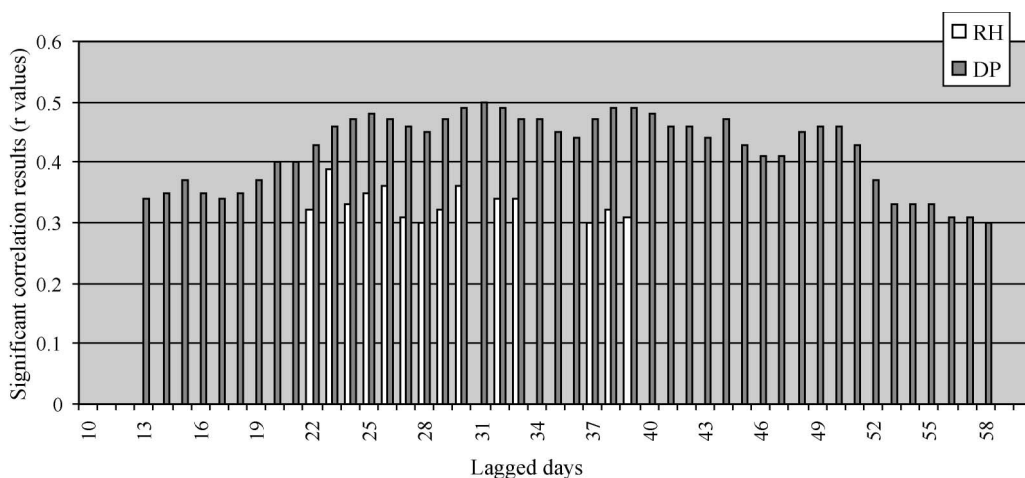


Figure 6. Lag correlation significant results ($r \geq 0.3$; $p \leq 0.05$) between the relative humidity (RH) and dew point temperatures (DP) at Ben-Gurion airport, the hospital admission dates.

the 2000 epidemic were also different from those reported in the summers of the past outbreaks. Based on the IMS weather reports (IMS annual reports 1951, 1957, 1980), the mean temperatures of the summers of 1951 and 1957 were slightly higher than normal by 0.5–1.5°C, not an extreme phenomenon in the Israeli climate. Temperatures of the summer of 1980 were about the average.

The 2000 epidemic development was more comparable to the recent reported cases from the Danube Valley in Romania in 1996 and from New York City in 1999 (ICDC website 2004). This similarity may result from different integrated trends: The increase in the population mean age, the worsening in the disease aggression (CDC website 2004) and the influence of the warming trend in the northern hemisphere. The outbreak which occurred in the Danube Valley coincided with an excessive heat, as well as the 1999 NYC outbreak (closely identical strains were responsible for the disease in NYC and Israel) that also followed a period of a three-week heatwave (Epstein & Defilippo 2001). It is interesting to note that despite the dissimilarity between the climatic patterns of the three regions (Western Israel, Danube Valley and NYC); a common factor is that all of them are characterized by warm and humid summers.

Lag correlation analysis indicated that the high temperatures at the beginning of the summer could be utilized as an important parameter for the WNV prediction. On average, when the heat conditions were constant the disease appeared between 3–9 ~ weeks after the warm weather.

Lag correlation found mostly moderate significant results between the temperatures and the hospital admission dates. It is important to note that the strongest correlation in both stations for the mean, minimum and maximum temperatures was found at the same period, at a lag of about 7 weeks.

Differences were detected between the lagged days distribution patterns of the minimum, mean and maximum temperatures (Table I and Figures 5a, 5b and 5c respectively). Whereas the longest lagged period for all temperature values was about 9 weeks, the shorter period was detected at a lag of 10–14 days for the minimum temperatures and at lag of about 6–7 weeks for the maximum temperatures. The significant results for the maximum temperature are weaker ($0.3 \leq r \leq 0.58$ for the mean temperature, $0.3 \leq r \leq 0.46$ for the maximum temperature).

When the temperatures are very high during both day and night, the minimum temperatures become the most important climatic factor that encourages the earlier appearance of the disease. It is presented in Figure 5a in opposition to the later disease emergence shown in Figures 5b and 5c. Savage et al. (1999) noted that summer temperature was found as one of the most important environmental variables modulating WNV activity in Europe. They indicated that a decrease in temperatures under 26°C caused a dramatic decrease in WNV transmission rates. This corresponds with the fact that mean temperatures during July 2000 were above 26°C throughout the whole month, with minimum temperatures above 25°C during most nights from 9–15 July (Figure 3). Generally, an early extreme rise in the summer temperature is a good indicator of increased vector populations.

Most of the WNV cases took place in the dense cities in the central parts of Israel. The author suggests that the heat conditions in the dense urbanized areas, worsened by the “urban heat island” phenomenon which exists in the Israeli metropolitan areas (e.g., Ben-Dor & Saaroni 1997), could encourage the vector competency and replication and also increase the mosquitoes’ abundance and biting capabilities.

Lag correlations between the admission dates and the relative humidity show a significant weak linkage at a lag of 22–39 days. Results for the dew point temperature are higher and correlated for a longer period, at a lag of 13–68 days (Figure 6). The dew point temperature is defined as the temperature to which the air would have to cool (at constant pressure and

constant water vapor content) in order to reach saturation. Therefore, it presents a combination between the temperature and the air humidity. From the results it is understandable that although the humidity is an eminent contributing parameter, the combination between high temperatures and high relative humidity (63–88% from 1 July to 30 September 2000 in Ben-Gurion station) is more important for increasing WNF cases.

In Israel, the majority of cases appeared in a narrow area close to the seashore, where the heat stress is very high due to the combination of high temperatures and high level of air humidity. It is curious that WNF cases were not reported in the eastern parts of Israel despite the fact that the area is a major stopover for migrating birds. A possible explanation is the sub-arid climate of that region, characterized by a low rate of air humidity and high gradient between minimum and maximum temperatures. The air humidity rate and the minimum temperatures in these areas are possibly too low for the mosquito competency.

Although drought conditions were found to be an important factor for WNV amplifications (e.g. Epstein 2001; Chase & Knight 2003), the author suggests distinguishing between two different climatic factors: one is air humidity, the other is water quantity in catchments due to precipitation amounts. These factors may impact differently on the mosquitoes' population. In Israel, the rainy season begins in September and ends in May. The summer air humidity along the seashore is caused by westerly winds blowing from the Mediterranean Sea and is not influenced by the rainfall yield in the previous winter. While pools are vital for the incubation process, the air humidity might be important for the mosquitoes' survival. However, this point needs further investigation.

Conclusions

The main conclusions of the study are:

1. A total of 63% of the WNF cases in Israel in the year 2000 occurred in September. Almost half of the patients, in all regions, were 60 years old and above, despite their low incidence (13%) of the total population.
2. A total of 93.5% of the cases were reported in the metropolitan areas. This stands in opposition to past outbreaks that occurred in limited regions. The author proposes that in these areas, heat conditions become more intense due to the "urban heat island" phenomenon. WNF cases were not reported in eastern Israel despite the fact that the area is a major stopover for migrating birds. This can be explained by the low rate of air humidity and the minimum temperatures that are too low for the mosquito competency.
3. The epidemic of 2000 in Israel came after two summers with warning signs, both medical and climatic. The three subsequent summers of 1998, 1999 and 2000 were extremely hot, warmer than ever recorded, with long heatwaves. The increase in the summers' maximum and minimum temperatures; the increase in the number of heatwaves, the worsening in their length and intensity and the severe drought; all of these trends that can be explained as regional impacts of global warming, should be considered when evaluating the risk of WNV transmission.
4. The epidemic development in Israel was comparable to the cases in the Danube Valley in Romania (1996) and in NYC (1999). Despite the climatic dissimilarity between the three regions, all of them are characterized by warm and humid summers. Each of the three outbreaks appeared after a long period of heatwave.
5. An early extreme rise in the summer temperatures could be a good indicator of increased vector populations. When the heat conditions were consistent, the disease appeared averagely at a lag of 3–9 weeks with the strongest correlation at a lag of 7 weeks. Whereas

the longest lagged period for all temperature values was about 9 weeks, the shorter period was detected at a lag of 10–14 days for the minimum temperatures and at a lag of about 6–7 weeks for the maximum temperatures. When the temperatures are high during day and night, especially when the temperatures do not decrease below 25°C for a long period, the minimum temperatures become the most important climatic factor that encourages the earlier appearance of the disease.

6. The combination between high temperatures and high relative humidity is more important for increasing WNF cases than the air humidity by itself.

Climate models that include the effects of GHG and aerosols project warming by 2030–2050. Different models predict an increase of about 1.0–2.0°C in the Middle East and about 1.5–4.5°C in southern Europe (IPCC 1996). Despite future uncertainty, the warming tendency has to be considered in predicting further WNV outbreaks in Israel and in the whole Eastern Mediterranean basin.

While being aware that there are other important factors that contribute to the disease amplifications, the author suggests that the outbreak of 2000 in Israel was instigated by extreme high temperatures. Usually, interactions between climatologists, entomologists and physicians are limited. They do not exchange information that can be readily employed in vector management. By raising the awareness of the relation between the WNV epidemic and extreme heat conditions, the spread of the disease could be halted before it grows into a full-blown outbreak.

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