



ECDC Threat Assessment

Cluster of human cases of West Nile virus infection in Greece, August 2010

SOURCE AND DATE OF REQUEST

Internal decision, following EWRS message from Greece from 7 August 2010

PUBLIC HEALTH ISSUE

Newly identified risk area of West Nile virus transmission in Europe
Blood safety concerns

CONSULTED EXPERTS

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DISEASE BACKGROUND INFORMATION

West Nile virus (WNV) is transmitted by mosquitoes (mainly of the genus *Culex*) with wild birds as its natural hosts. Birds also play a role in the geographic dispersion of WNV. Human infections have been reported since 1996 in sporadic outbreaks in several countries in eastern and southern Europe [1]. The presence of the virus in amplifying hosts (birds) suggests ongoing transmission and endemicity of WNV in Europe. While humans are mainly infected through mosquito bites, few infections through organ transplantation and blood transfusion have been documented in North America [2-4]. After the infectious bite, an incubation period of 2–14 days precedes symptoms which tend to vary with the patient's age: from mild fever and malaise in children, a moderately severe disease in the young (high fever, red eyes, headache and muscle ache) to meningitis or encephalitis in the elderly and the debilitated [5]. However, 80% of the infected persons remain asymptomatic. No specific treatment or vaccines are currently available. The main preventive measures are aimed at informing the at-risk human population, reducing exposure to mosquito bites and exclusion of blood donations from donors living in and visiting affected areas, if feasible.

Europe

In Europe following the large outbreak in Bucharest (Romania) [6], several outbreaks of WN virus have been identified in humans and/or horses

- in the Czech Republic (1997) [7]
- in France (2000, 2003, 2004, 2006) [8-10]
- in Italy (1998, 2008-2009) [11-14] [15]

- in Hungary (2000-2008) [16]
- in Romania (1997-2001, 2008-2009) [17, 18]
- and in Spain (2004) [19-21].
- In Portugal (2004)[22]

In 2009, three EU countries reported human cases of WNV infection:

- Hungary reported, seven cases of WNV between May and September from four counties (Békés: 4, Csongrád: 1, Pest county: 1, Budapest: 1). The case from Pest county was classified as an imported case. Four cases presented with neurological symptoms, the remaining three with fever (two of them also with rash). All seven cases were laboratory-confirmed. During 2008, 19 cases of WNV infection were reported in Hungary.
- Romania reported two cases in 2009, one in August and one in September.
- Italy reported 16 human cases of West Nile neuro-invasive disease between August and September 2009, in three regions (Veneto, Emilia-Romagna and Lombardia), as compared with nine cases in the previous year.

In July 2010, Portugal reported a probable case of WN virus infection in a 55 year old woman from the Tejo region, which was the first (probable) case of WN virus infection reported in 2010 in the EU.

Greece

Serological surveys conducted in the 1980's and in 2007 in Greece identified WNV antibodies in approximately 1% of selected populations in the region of Central Macedonia. Serum samples collected from 392 residents from Northern Greece (Imathia) in 2007, revealed six positive samples for WN virus of which four were confirmed by micro-neutralisation assay (1%) [23, 24]. The authors concluded that WNV or related viruses circulate in endemic cycles in rural areas in Greece. In contrast, a survey of 9590 blood donations and 115 CSF samples from patients with aseptic meningitis in Greece in June to October 2006 and 2007, revealed no positive results for WNV by NAT (Nucleic Acid Test) [25].

EVENT BACKGROUND INFORMATION

On 7 August 2010, the Greek authorities reported eleven human cases (two confirmed and nine probable according to the EU case definition, 2008 [26]) of WN virus infection from the region of Central Macedonia in Northern Greece. As of Tuesday 10 August, the number of reported cases increased to 21 (nine confirmed and twelve probable), all of them were hospitalised with symptoms of meningitis and/or encephalitis. Two of them, aged over 70 years, had a fatal outcome and both suffered from hypertension and diabetes.

The nine confirmed cases showed WN virus specific IgM in the cerebro spinal fluid (CSF) and the twelve probable cases showed increasing IgM and IgG antibodies in paired sera; one showed a IgG seroconversion. Confirmation by neutralisation tests will be conducted. Samples were collected between five and fifteen days after onset of symptoms of cases. Thus, WN virus isolation was not attempted and WN virus nucleic acid was not detected in blood or CSF samples.

The median age was 70 years, ranging from 12 to 83 years of age. Twelve of the cases were 70 years or older (57%), four between 50 and 69 years (19%), three between 20 and 49 years (14%) and two cases below 20 years of age. Eleven cases (52%) were male.

All cases were reported from the Central Macedonia region in Greece: Eight cases were reported to have their residence in Thessaloniki prefecture, five in Kilkis, four in Imathia, two in Pella, and one each in Serres and Pieria. The Greek authorities report that there are preliminary indications that the large majority of cases reside near rivers in the area (see figure 2); the investigation is ongoing.

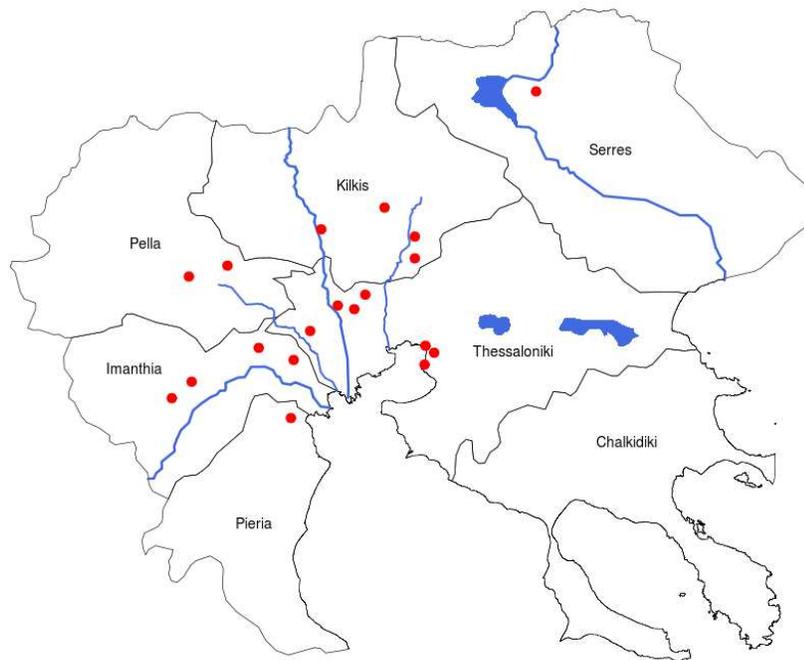
Figure 1
Greek prefectures where cases are reported from, 10 August 2010

Affected prefectures with reported human cases of WN virus infection in Greece 2010 (21)



Figure 2

Map of the region of Central Macedonia with location of reported human WN virus cases by prefecture*



**each dot represents one case*

The Greek authorities reported that physicians have been alerted about WN virus infections in the area, and guidelines on clinical symptoms, laboratory diagnosis and case management were distributed. Surveillance of human WN virus infections has been enhanced and the public has been alerted about personal protective measures. Furthermore, the authorities reported that the Hellenic Centre for Blood Transfusion is preparing relevant guidelines for blood and blood products and surveillance of vectors and animals (e.g. horses and birds) is being considered.

ECDC THREAT ASSESSMENT FOR THE EU

The challenge for surveillance of WN virus lies in identifying virus circulation early in any given area. If clusters of human cases without recent travel history are confirmed, ongoing transmission is highly likely. In the current event in Greece, no indications on active transmission of WN virus in horses, birds or mosquitoes in the area have been identified. Previous studies in the area suggested that WN virus is endemic in rural areas of Greece. This first identification of a cluster of human cases of WN virus in the area is

a strong indication that this area is a newly identified at-risk area for WN virus transmission.

Travellers to the area need to be aware of the current risk, also implications for blood safety among donors living or visiting the affected area need to be considered. Greek blood safety authorities have already started to implement the appropriate precautionary measures. Blood safety issues will also need to be considered in the Member States for visitors returning from this area.

CONCLUSIONS

The currently available information implies the identification of a new risk area for WN virus transmission in Greece detected in August 2010. Clinicians in the area have been alerted about the risk of further human cases, enhanced surveillance for human cases has been implemented and blood safety issues are being addressed both at national and EU level in collaboration with DG SANCO- C6. Animal surveillance and vector surveillance are being considered by the Greek authorities. The public has been alerted to apply personal protective measures against mosquito bites.

Awareness of clinicians in European Member States and neighbouring countries, namely Former Yugoslav Republic of Macedonia, Albania, Bulgaria and Turkey, is needed on the current risk about possible ongoing virus transmission in the Northern region of Greece (Central Macedonia) to ensure early detection of cases. The impact on blood donation restrictions has to be carefully monitored.

The presence of West Nile virus is well-documented in several European countries. Climatic conditions, temperature and humidity favor the presence and the multiplication of *Culex spp.* from May to October in the affected zones. At the same time, there has been an increase in the number of cases in the EU over the past decade. It is uncertain whether this is only due to increased surveillance or reflects a changing epidemiology [27, 28].

This threat assessment will be updated as needed upon the availability of new relevant information.

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