RAPID RISK ASSESSMENT

Early large increase in West Nile virus infections in the EU/EEA and EU neighbouring countries

13 August 2018

Main conclusions and options for response

An early occurrence of a large number of human West Nile virus (WNV) infections in EU/EEA Member States and EU neighbouring countries* has been observed compared with previous years. This suggests a high level of virus circulation in affected countries, which could potentially result in the occurrence of a high number of cases during the coming months.

A WNV affected area is defined as an area at the third level of the Nomenclature of Territorial Units for Statistics (NUTS 3) where at least one human case of autochthonous WNV transmission has been confirmed [1]. The majority of areas affected in 2018 were those from which cases were also reported between 2014 and 2017. It is likely that the virus will spread to more areas in the coming months, including areas where no human autochthonous cases have been reported in previous years, hence affecting a population that is potentially immunologically naïve.

Public health professionals and clinicians in affected areas and also in as yet unaffected areas with suitable environmental conditions should be aware of the ongoing situation in Europe and the need to ensure the early detection and reporting of cases, which is crucial for monitoring the situation and timely implementation of response measures. It is also important to maintain collaboration between local, regional and national public health and veterinary authorities to obtain a comprehensive understanding of the epidemiological situation of WNV, assess the transmission risk to humans and consequently to implement timely response measures.

It is important that clinicians are reminded to include West Nile fever (WNF) in the differential diagnosis of persons who have returned from affected areas with symptoms compatible with the disease.

Personal protection from mosquito bites is advisable for any person residing in or visiting affected areas, especially the elderly and immunocompromised who are at higher risk of developing West Nile neuroinvasive disease (WNND). Personal protective measures to reduce the risk of mosquito bites include the use of mosquito repellent in accordance with instructions indicated on the product label and wearing long-sleeved shirts and long trousers. In addition, window and door screens can keep mosquitoes out.

To prevent transfusion-transmitted WNV infection, EU/EEA countries should implement 28-day blood donor deferral or individual donation nucleic acid testing (ID-NAT) of prospective donors who have visited, or live in,

* EU neighbouring countries included are: Albania, former Yugoslav Republic of Macedonia, Kosovo (this designation is without prejudice to positions on status, and is in line with United Nations Security Council Resolution 1244/99 and the International Court of Justice Opinion on the Kosovo Declaration of Independence), Montenegro, Serbia and Turkey.

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an affected area. In affected areas, blood establishments* should follow recommendations provided in the EU preparedness plan for blood safety. Donors of organs, tissues and cells living in or returning from an affected area should be tested for WNV infection. Systematic collection of epidemiological information on WNV infection among donors and recipients of substances of human origin (SoHO) is an important tool for national authorities to better assess the risk of transmission and the impact of preventive measures on the availability of SoHO.

According to the preparedness plan for WNV blood safety in the EU [2], blood establishments in affected areas should:

- start with WNV-relevant blood safety measures once the first human case of the season is confirmed in the area and cease those measures at the end of the mosquito activity season
- temporarily interrupt blood collection or implement NAT screening
- quarantine, retest and discard positive blood components in storage at the time of implementation of measures; retrieve and quarantine blood components derived from whole blood donated 120 days prior the date of collection of the ID-NAT positive donation
- enhance donor post-donation information, especially about fever, influenza-like illness or other acute symptoms within 15 days after donation
- strengthen post-transfusion haemovigilance and perform look-back analysis in any case of transfusion-transmitted WNV infection for a period dating back 120 days prior to the donation of implicated blood components; and
- consider the use of pathogen inactivation procedures.

During the WNV transmission season, ECDC publishes weekly epidemiological updates to highlight areas where there is ongoing virus transmission to humans and equids. These epidemiological updates are available on the ECDC website [3].

Source and date of request

ECDC internal decision, 3 August 2018

Public health issue

This rapid risk assessment addresses the public health risk associated with the early occurrence of a large number of West Nile virus infections in the EU/EEA and EU neighbouring countries.

Consulted experts

ECDC contributors: Johanna Young, Agoritsa Baka, Olivier Briët, Sergio Brusin, Dragoslav Domanović, Benedetto Simone and Céline Gossner

External experts consulted (in alphabetical order): Cornelia Svetlana Ceianu (Cantacuzino National Medico-Military Institute for Research and Development, Romania; EVD-LabNet), Mitra Drakulovic (National Institute of Public Health Dr Milan Jovanovic Batut, Serbia), Eszter Mezei (Department of Hospital Hygiene and Epidemiological Control, Hungary), Anna Nagy (National Public Health Institute, Hungary), Anna Papa (Aristotle University of Thessaloniki, Greece; EVD-LabNet), Danai Pervanidou (Hellenic Center for Disease Control and Prevention, Greece), Chantal Reusken (EVD-LabNet, Erasmus University Medical Center), Giovanni Rezza (National Institute of Health, Italy), Flavia Riccardo (National Institute of Health, Italy) and Anca Sirbu (National Institute of Public Health, Romania).

* According to Directive 2002/98/EC, 'blood establishments' are structures or bodies that are responsible for any aspect of the collection and testing of human blood or blood components, whatever their intended purpose, and their processing, storage, and distribution when intended for transfusion.

Disease background information

West Nile fever (WNF) is a zoonotic vector-borne disease caused by a virus that is most often transmitted through mosquito bites (primarily *Culex* genus), but can also be transmitted through organ, cell and tissue transplantation, blood transfusion, laboratory settings, breastfeeding, pregnancy or the peripartum period [4-6]. Humans, horses and other mammals are considered dead-end hosts. Infections in humans are generally asymptomatic. Around 20% of cases develop influenza-like symptoms, while 1% of cases, mainly elderly and immunocompromised people, develop West Nile neuroinvasive disease (WNND), which may lead to death.

In this assessment, we refer to WNV infections that encompass both human WNF cases and asymptomatic infections (i.e. infection detected via blood screening).

In Europe, most cases occur between June and October and are reported by southern and southeastern European countries.

In Europe, the mosquito species *Culex pipiens* and *Culex modestus* are considered to be the main vectors of WNV and are widely distributed [7]. *Aedes albopictus* and *Aedes detritus* are also competent vectors, but have little importance for transmission as these species mainly bite mammals [8,9]. *Culex* mosquitoes bite at night.

While locally acquired WNV infections of humans and equids have been exclusively reported by southern European countries, there are no indications for differences in the susceptibility of birds or vector competence between populations in southern and northern European countries [9,10]. The most plausible explanation for the absence of cases from northern European countries is the generally cooler summer temperatures.

Several EU directives define preventive interventions to mitigate the risk of WNV transmission through substances of human origin (SoHO). Directives 2004/33 EC and Directive 2014/110/EU for blood and blood components stipulate that blood establishments should defer prospective blood donors for 28 days after leaving an area with local transmission of WNV unless an individual nucleic acid test [NAT] is negative [11,12]. Potential blood donors who are diagnosed with an WNV infection may be accepted for blood donation 120 days after diagnosis [13].

Directive 2004/33/EC does not require deferral or screening interventions when plasma is donated for fractionation because the virus is inactivated during the manufacturing process of plasma-derived medicinal products [14].

Directive 2006/17/EC for cells and tissues and Directive 2010/45/EU for organs recommend additional testing of donors depending on the donor's travel and exposure history and the characteristic of tissues and cells donated [15,16].

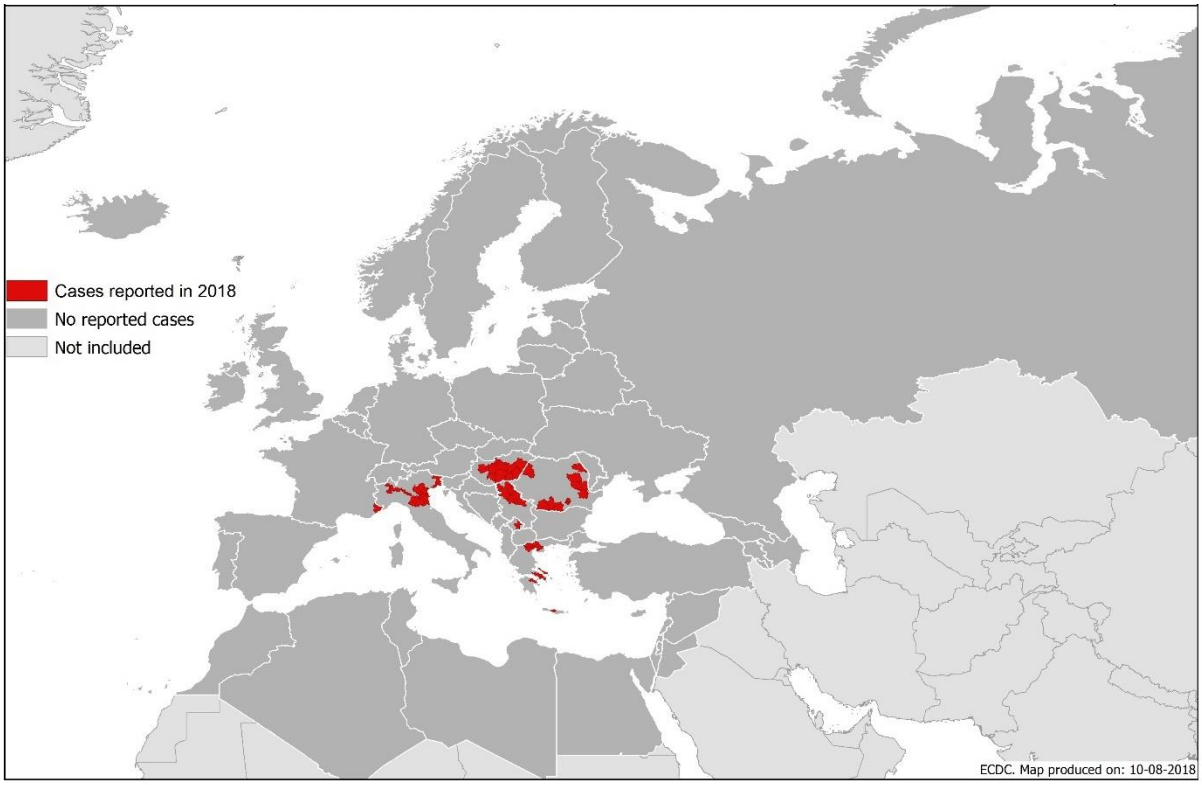
Additional information can be found in the Council of Europe's professional guides for blood [13], cells and tissues [17] and organs [18]. Regional and national laboratories providing different types of WNV diagnostics can be found in the EVD-LabNet directory [19].

More information on WNF is available from ECDC's factsheet available at https://ecdc.europa.eu/en/west-nile-fever/surveillance-and-disease-data/historical [4].

Event background information

In 2018, as of 9 August, 335 confirmed and probable autochthonous human WNV infections were reported by European countries: 231 in EU/EEA Member States and 104 in EU neighbouring countries. Italy reported 123 cases, Serbia 102 cases, Greece 59, Hungary and Romania 23 each, France 3 and Kosovo 2 (Figure 1). Seventeen deaths due to WNF were reported: 9 in Serbia, 3 each in Greece and Italy and one each in Kosovo and Romania. In comparison, in the same time period between 2014 and 2017, 5 to 45 cases were reported each year.

Figure 1. Distribution of West Nile fever cases in humans by affected areas in EU/EEA Member States and EU neighbouring countries in 2018 as of 9 August 2018



In 2018, the first WNV infections were notified by Greece in week 26 (25 June to 1 July), with the earliest disease onset on 31 May (week 22). In comparison, in 2014, 2016 and 2017, the first cases were notified from week 28 onwards while in 2015, one case was reported by Bulgaria in week 25 (Figure 2).

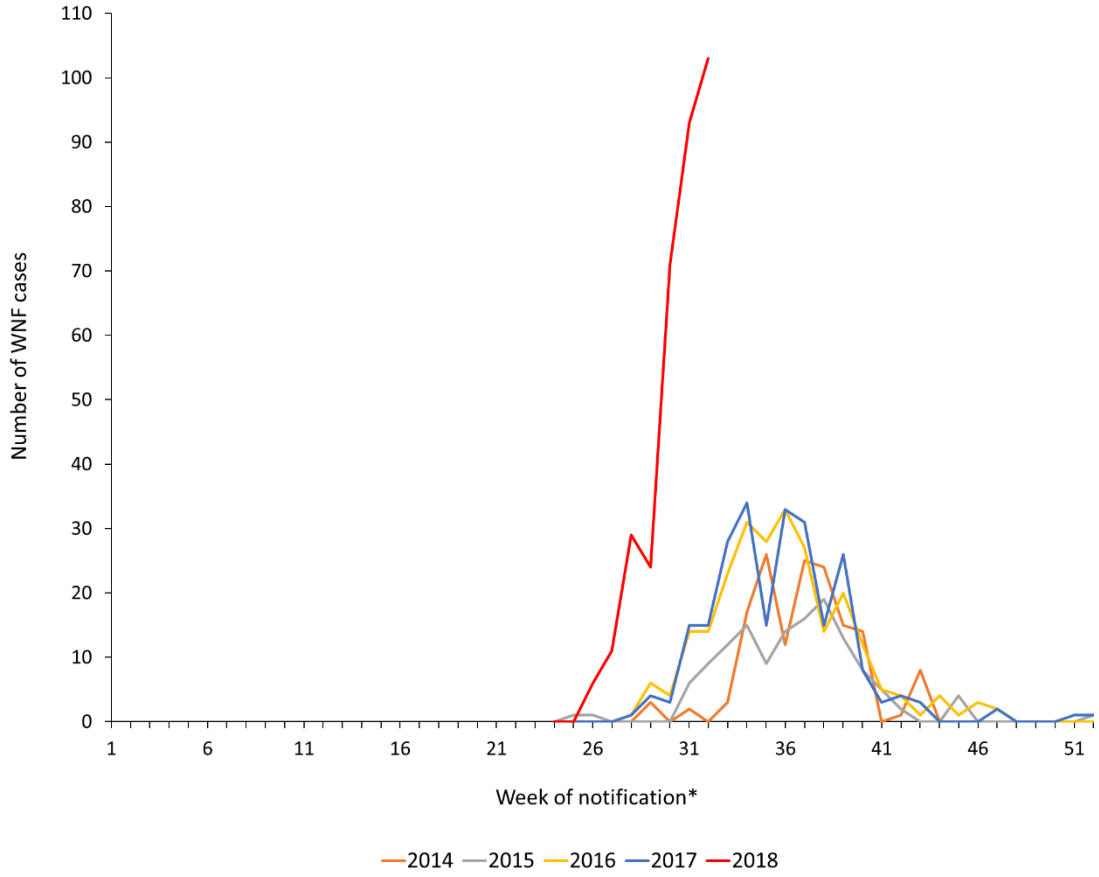
Among the 64 affected areas in 2018, 13 areas in Greece, Italy and Serbia did not report any WNV infections between 2014 and 2017. It should be noted that while these areas were not affected in the past four years, they may have reported WNV infections prior to 2014.

In 2018, the median age among confirmed and probable cases to date is 64 years old and the male-female gender ratio is 2.0. Both values are comparable to those observed in the previous four years (median age between 62 and 65.5 years and gender ratio between 1.4 and 2.6).

Greece and Italy detected WNV lineage 2 (WNV-2) in 2018, which has been identified regularly throughout southern, eastern and central Europe since its first detection in humans in Hungary in 2008 [20].

In addition to the human cases described above, 16 outbreaks among equids (11 in Italy, 3 in Hungary and 2 in Greece) have been reported to the Animal Disease Notification System (ADNS) [21]. In the same time period between 2014 and 2016, one to two outbreaks were reported. In 2017, 10 outbreaks were reported in this time period. So far, all outbreaks among equids reported in 2018 occurred in areas that were affected at least once in the past four years. In addition, in 2018, all outbreaks among equids occurred in areas where human cases were reported.

Figure 2. Number of West Nile fever confirmed and probable cases in EU/EA and EU neighbouring countries by week of notification to ECDC, 2014 to 2018 as of 9 August 2018



** Week of notification to national authorities or if missing, week of notification to ECDC.*

ECDC threat assessment for Europe

As of 9 August 2018, the total number of confirmed and probable WNV infections reported this year has been higher compared with the same period in previous years. In addition, these cases were reported earlier in the season. This may indicate a high level of virus circulation in affected countries, which could potentially result in the occurrence of a high number of cases during the coming months.

People residing or travelling in an affected area are at risk of WNV infection. The elderly and immunocompromised are especially at high risk of developing WNND (e.g. meningitis and encephalitis).

There is no available evidence of any change in the surveillance systems in place in affected countries, the reporting of cases at the national level or to ECDC and in the transmissibility or pathogenicity of the virus or viruses circulating in Europe. Further epidemiological and microbiological investigations should be conducted to better understand this increase in the number of cases.

Data on outbreaks among equids reflect a similar pattern, also indicating an early start of the transmission season among equids.

The majority of areas affected in 2018 were areas with cases between 2014 and 2017. It is likely that the virus will spread to more areas in the coming months, including areas where no human autochthonous cases were reported in previous years, hence affecting a population that is potentially immunologically naïve. The observed weather pattern this year, including increased temperatures, is indicative of an early spring season in the southeastern part of Europe and is expected to favour the geographical spread of the virus.

Considering the usual high number of asymptomatic cases among WNV infections (80%), most infections remain undetected. Therefore, the number of cases reported is largely under-representing the actual number of infections. This is of concern particularly with regards to SoHO donations as infectious but asymptomatic people may donate SoHO and recipients are often immunocompromised patients. In order to avoid blood donor shortages, especially in urban areas, most EU countries experiencing local WNV transmission apply NAT screening of blood donations

instead of temporary deferrals or interruption of blood donations in affected areas. Blood safety measures in the EU seem to be highly effective as only one case of transfusion-transmitted WNV has been reported in the EU since 2012 [22].

Laboratories performing NAT screening should be aware of possible cross-reactivity with Usutu virus [23]. Blood donations positive for Usutu virus should be discarded.

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