



Disponible en ligne sur

ScienceDirect
www.sciencedirect.com

Elsevier Masson France

EM|consulte
www.em-consulte.com

TRANSFUSION
CLINIQUE ET BIOLOGIQUE

Transfusion Clinique et Biologique xxx (2017) xxx–xxx

State of the art

State of the art: Vest Nile Virus circulation surveillance in Italy and transfusion risk early prevention methods

État de l'art : surveillance de la circulation du virus West Nile en Italie et méthode de prévention précoce du risque transfusionnel

C. Velati^{a,*}, P. Angelini^b, S. Pupella^c

^a Italian Society of Transfusion Medicine and Immunohaematology (SIMTI), via Principe Amedeo 149/D, 00185 Roma, Italy

^b General Direction for Health and Social Policies, Regione Emilia-Romagna, Bologna, Italy

^c National Blood Centre, Istituto Superiore di Sanità Roma, Roma, Italy

Abstract

After the Chikungunya outbreak in 2007 in Italy, a national Plan for the surveillance of human vector-borne diseases has been implemented and annually updated on the basis of the epidemiological changes based-evidences. The transfusion Authorities cooperates, since 2008, with public health services and veterinary (entomological and ornithological) surveillance systems. In some Italian regions, a common protocol for exchanging data is in place to identify the West Nile Virus (WNV) circulation in birds and mosquitoes: the goal is to anticipate the introduction of WNV-NAT screening in blood donors and, on the other hand, to limit testing only in geographic areas where the virus circulation is actual. The integration of surveillance activities and a multidisciplinary approach made it possible to introduce efficient and preventive measures for reducing the risk of transmission of WNV through blood, tissues and organ donation.

© 2017 Elsevier Masson SAS. All rights reserved.

Keywords: West Nile Virus; Transfusional risk; Surveillance; Blood donor screening

Résumé

Après l'épidémie de Chikungunya en 2007 en Italie, un plan national de surveillance des maladies à transmission vectorielle a été mis en œuvre et mis à jour annuellement sur la base des changements épidémiologiques et leur évolution. Les autorités de transfusion coopèrent depuis 2008 avec les services de santé publique et les systèmes de surveillance vétérinaire (entomologique et ornithologique). Dans certaines régions d'Italie, un protocole commun pour l'échange de données est en place pour identifier la circulation du virus West Nile (WNV) chez les oiseaux et les moustiques: l'objectif est d'anticiper l'introduction du dépistage du WNV par NAT/DGV chez les donneurs de sang et aussi de limiter les tests aux zones géographiques où la circulation du virus est réelle. L'intégration des activités de surveillance et une approche multidisciplinaire ont permis d'introduire des mesures efficaces et préventives pour réduire le risque de transmission du WNV par le sang, les tissus et le don d'organe.

© 2017 Elsevier Masson SAS. Tous droits réservés.

Mots clés : Virus West Nile ; Risque transfusionnel ; Surveillance ; Dépistage du donneur de sang

1. Introduction

West Nile Virus (WNV) is a mosquito-borne arbovirus most often transmitted through mosquito bites but which can also be

transmitted through organ transplantation, blood transfusion, in laboratory settings and from mother to fetus during pregnancy.

A bird-mosquito cycle is the condition where WNV is maintained, with birds acting as amplifying hosts. Mosquitoes acquire infection by feeding on viraemic birds and, once infected, remain infectious throughout their life, potentially transmitting the virus to every vertebrate on which it feeds. Humans, horses and other mammals are considered dead-end hosts. Infections in humans

* Corresponding author.

E-mail address: claudio.velati@simti.it (C. Velati).

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.

Approximately 10% of infected horses may show neurological signs. There is no specific treatment for humans or animals, and no vaccine is available for humans, although inactivated and recombinant vaccines for horses are used in Europe [1].

The outbreaks of WNV in the United States (US) in 1999 has been responsible for more than 38,000 reported clinical cases, of which 16,453 presented with neuroinvasive disease, 20,876 with West Nile fever and 1579 with a fatal outcome. [2].

In addition to the risk of vector-borne transmission, the high proportion of asymptomatic persons with the virus relative to those presenting with WNND, estimated at more than 100:1, poses a risk of WNV transmission via blood transfusion or organ transplantation [3].

The complex interactions of multiple factors involved makes difficult to predicting West Nile virus (WNV) circulation and the risk of WNV epidemics.

The virus may remain undetected for long periods, but during hot seasons and in places with suitable ecological conditions, the virus circulation may increase to affect humans and equids. Generally, in temperate regions, it has been shown that the virus may over winter in infected female mosquitoes as well as in residential birds, so there is no need for continuous reintroductions by migrating birds [4].

Although WNV circulation has been observed in several European Union (EU) countries since the early 1950s, large WNV outbreaks have only been documented starting from the mid-1990s [1,5].

In Italy, cases of WNV infection have been registered regularly since 2011 and have been distributed in several regions. Cases occur mostly in the summer and autumn following an annual seasonal pattern. To prevent WNV transmission by blood transfusion and organ donation, a national surveillance plan has been in place since 2008.

Since 2008, an integrated surveillance targeting mosquitoes, birds and humans, has been put into effect starting in the Emilia-Romagna region, where the outbreak of Chikungunya virus was previously observed, and, in the following years, by other 4 regions (Veneto, Friuli Venezia-Giulia, Lombardia, Piemonte, all in northern Italy). The main goals of this regional WNV surveillance were to contain the spread of WNV infections in humans and to more effectively reduce the probability of virus transmission through blood, tissue and organ donation systems [6].

The development of the surveillance plan in Italy and, particularly, in these 5 regions is presented showing also the results of the two scenarios for preventing WNV transmission by transfusion and/or organ transplantation: the basic scenario which follows the WNV Italian national plan and the second scenario based on evidence from a surveillance integrating environmental observations where blood unit and organ screening is initiated at the province level when the mosquito or the bird active surveillance show WNV circulation in this province. Should a WNND human case occur before the detection of WNV circulation by

the entomological or ornithological surveillance in the province, the measures to be taken are as in the national surveillance plan for this particular situation.

2. Methods

2.1. Entomological surveillance

Following the detection of human cases of WNV infection in 2008 in the Emilia-Romagna region, a surveillance network was designed and operated in the summer period (June–October). In the 2009 season, mosquito collections were conducted partially in fixed stations and partially in occasional stations, with weekly to monthly periodicity. From the 2010 season, the mosquito collections were standardised in fixed geo-referenced stations with fortnightly periodicity. Female mosquitoes were trapped using CO₂ baited traps (and gravid traps from 2012), activated one night per collection. The network was initially designed to cover the regional plain area using a grid with cells of ca 110 km².

Collected mosquitoes were counted, identified at the species level and pooled according to date, location, and species, with a maximum number of 200 individuals per pool and was submitted to the laboratory for biomolecular analysis (real-time polymerase chain reaction (RT-PCR).

2.2. Ornithological surveillance

According to the WNV national surveillance plan, an active surveillance was started since 2006 on corvid species, which are considered as agricultural pests and therefore the target of population control programmes. Birds were trapped in the plain and low hill areas (up to 600 m above sea level (a.s.l)). The culling programme was performed from May to October, dividing the surveyed area into quadrants sized 1600 km² and collecting 15 to 20 specimens in each quadrant every month.

2.3. Blood donation system

The national strategy for prevention of WNV transmission by transfusion indicates that, in regions where no virus circulation was observed in the previous year only blood donors with a single overnight stay in affected areas (defined at the province level) are to be deferred for 28 days or tested for WNV RNA. Moreover a WNV RNA screening of all blood units in a given province shall start as soon as possible following the first WNND human or equine WNV infection case detection.

At regional level in 2013, the integrated regional surveillance system requires that WNV nucleic acid testing (NAT) screening is applied to all blood donors in a province after reports of at least two positive mosquito pools by the entomological surveillance network, or one positive bird, within the limits of the province without waiting for human cases. Since 2014 NAT screening was introduced after one positive mosquito pool, and if the positive mosquito pool was detected in a border area (at least 5 km²) between two different provinces, screening was introduced in both the interested provinces.

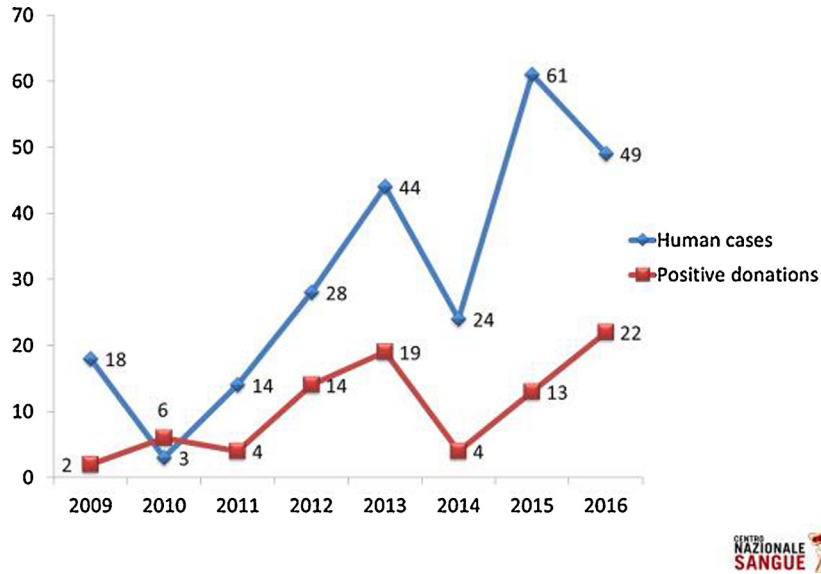


Fig. 1. WNV human cases and positive donors per year in Italy.

Synthesis of the measures for the prevention of WNV trans- fusion transmission:

- blood donor selection and haemovigilance:
 - a) strengthening pre-donation questionnaire, medical inter- view and donor physical examination on (even mild) flu-like symptoms,
 - b) strengthening post-donation information on (even mild) flu-like symptoms,
 - c) implementation of ad hoc haemovigilance procedures;
- trigger criteria for the implementation of WNV NAT testing from June until October/November:
 - a) notification by the Public Health Department to the Regional and National Blood Centres of WNV circulation through entomological (vector mosquitoes) and veterinary

- b) notification of WNV human case (neuro-invasive and non neuro-invasive disease),
 - c) notification of WND equid case,
 - d) in case of a) and/or b): WNV NAT testing shall be timely introduced in the interested provincial areas (administra- tive districts) and shall be performed by ID technique according to the Directive 2014/110/EC,
 - e) testing shall be continued until the end of the surveillance season;
- blood donor deferral:
 - a) nationwide: all donors having been for at least one night in the provinces where WNV NAT testing is introduced as a consequence of the trigger criteria a) and/or b) shall

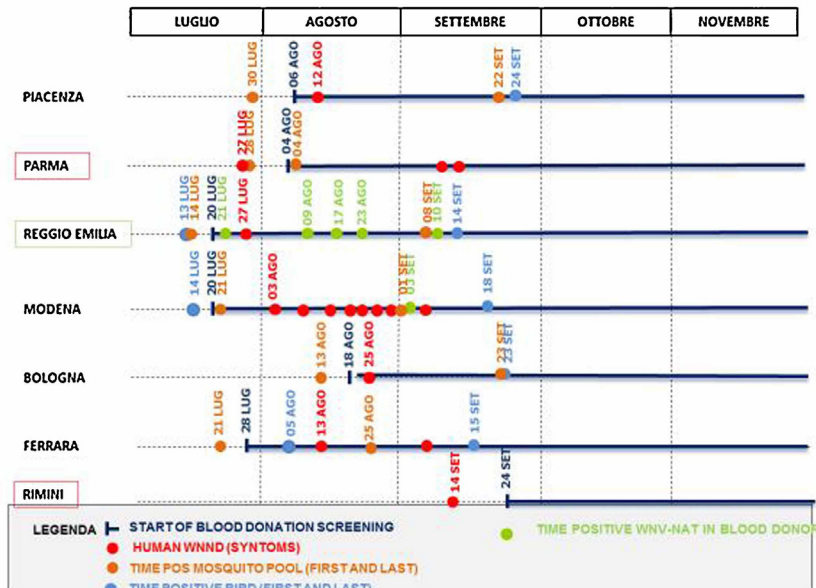


Fig. 2. Timing of events in Emilia-Romagna region.

be deferred for 28 days. Alternatively, in order to avoid critical blood shortages, donors can be admitted to donate provided their donations are tested by ID WNV NAT,

- b) nationwide: 28 days deferral remains applied year round to all donors coming back from the USA and Canada. Alternatively, in order to avoid critical blood shortages, donors can be admitted to donate provided their donations are tested by ID WNV NAT.

3. Results

Fig. 1 reports the number of human cases and blood donors WNV RNA positive in Italy in the years 2009–2016.

Fig. 2 shows, for the year 2015, the timing of: WNV RNA positivity in birds and mosquito pools, symptoms of WNND in humans, start of blood donor NAT screening and blood donor NAT positivity.

4. Discussion

The integrated surveillance programme, which enabled to estimate virus circulation in the range of three to four weeks, with some exceptions, before the appearance of the first human WNND cases at the province level, may support a more evidence-based policy of blood screening, thus avoiding blood units' analyses, and costs, in case of virus absence, even in areas which were affected in the previous year. As the WNV epidemiology is largely unpredictable by modelling, an integrated surveillance is required to support the risk assessment.

It will be possible to better identify the seasonal period of surveillance and blood donor screening on the basis of actual

data about the virus circulation obtained from the entomological and ornithological surveillance system.

A strength integrated surveillance system and an interdisciplinary approach among public health services, entomological and ornithological network and transfusion system is a valid support to guaranteed transfusion safety.

Disclosure of interest

The authors declare that they have no competing interest.

References

- [1] Gossner CM, Marrama L, Carson M, et al. West Nile virus surveillance in Europe: moving towards an integrated animal-human-vector approach. *Euro Surveill* 2017;22 [pii = 30526].
- [2] Lanteri MC, Lee T-H, Wen L, et al. West Nile virus nucleic acid persistence in whole blood months after clearance in plasma: implication for transfusion and transplantation safety. *Transfusion* 2014;54:3232–41.
- [3] Bellini R, Calzolari M, Mattivi A, et al. The experience of West Nile virus integrated surveillance system in the Emilia-Romagna region: five years of implementation, Italy, 2009 to 2013. *Euro Surveill* 2014;19 [pii = 20953].
- [4] Calzolari M, Bonilauri P, Bellini R, et al. Usutu virus persistence and West Nile virus inactivity in the Emilia-Romagna region (Italy) in 2011. *PLoS ONE* 2013;8:e63978.
- [5] European Centre for Disease Prevention Control (ECDC). Annual epidemiological report 2016–West Nile fever. Stockholm: ECDC; 2016 [Available from: http://ecdc.europa.eu/en/healthtopics/west_nile_fever/Pages/Annual-epidemiological-report-2016.aspx, accessed 8 Sep 2016].
- [6] Rizzo C, Napoli C, Venturi G, et al. West Nile virus transmission: results from the integrated surveillance system in Italy, 2008 to 2015. *Euro Surveill* 2016;21 [pii = 30340].