

West Nile virus in Italy: a further threat to blood safety, a further challenge to the blood system

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The first two cases of human WNV neuroinvasive infection ever occurred in Italy

On 20th September 2008, the Regional reference centre for microbiological emergencies (RRCMEs) in Bologna, Emilia Romagna region, reported the detection of specific IgM and IgG antibodies against West Nile virus (WNV) in the serum of a female patient living in a rural area of the district of Bologna, near the border with the district of Ferrara¹.

On 29th September 2008, the disease was confirmed to be the first human case of WNV neuroinvasive infection ever occurred in Italy. The presence of WNV-specific antibodies was confirmed by additional serological tests performed by the National reference centre for arboviruses at the National Institute of Health and the laboratories of the National Institute of Infectious Diseases (NIIDs), Rome¹.

On 3rd October 2008 a second human case of suspected WNV neuroinvasive disease was identified in a male patient living in an area of the district of Ferrara where WNV-positive horses and birds had been identified¹. Serum and cerebrospinal fluid samples of this patient were tested at the RRCMEs of Emilia Romagna region giving positive results for IgG and IgM antibodies against WNV; two different RT-PCRs performed on the serum gave positive results as well. Confirmatory testing was obtained from the laboratories of the NIIDs on 8th October 2008¹, thus allowing to confirm the second human case of WNV neuroinvasive infection.

Epidemiological surveillance

As of 10th October 2008, the National reference centre for exotic animal diseases (c/o Zoo-prophylactic Institute of Teramo, Italy) reported 20 horses affected by neurological

disorders referable to West Nile Disease (WND) in 14 different stables, 10 of which diffusely located in the province of Ferrara, 2 in the province of Bologna, 1 in the province of Mantova, and 1 in the province of Rovigo at the border with the province of Ferrara².

Moreover, WNV had been detected in wild birds in the Emilia Romagna region³. Although no anomalous mortality was found, surveillance of wild birds carried out between 19th August and 14th September through planned capture within a general monitoring of the regional wild fauna, resulted in the detection of WNV in six crows and seven magpies, all in the district of Ferrara³. Animal surveillance continues to be actively carried out and is planned to last until December 2008. Active surveillance of all cases of human meningo-encephalitis was started on 16th September all over the Emilia Romagna region³. A forthcoming circular of the Ministry of Health will extend active surveillance to all human neurological syndromes possibly related to WNV infection, and include the southern areas of the regions of Lombardy and Veneto.

Precautionary measures adopted for blood safety

In the United States, human-to-human transmission of WNV through blood transfusion and transplanted organs, as well as mother-to-child transmission through breast feeding or transplacental infection, were identified in 2002⁴⁻⁸. The documentation of WNV transmission through transfusion led to the rapid development of nucleic acid tests (NATs) for blood screening and, as of August 2003, all blood products in the United States were tested for WNV by NAT in a unique nationwide testing trial that took place in advance of test licensure⁹. At the moment year-round WNV NAT is performed in the United States because the WNV

season appears to have lengthened, and isolated human infections occur in late autumn and early spring¹⁰.

On 23rd September 2008 the National Blood Centre (NBC) was alerted by the Regional blood centre (RBC) of Emilia Romagna about the first suspected human case of WND in the district of Bologna. The application of specific precautionary measures was preliminarily shared among NBC, RBC, RRCMEs, Blood donor associations' representatives and the Public Health Service of the Emilia Romagna region, in case the diagnosis should be confirmed, as it actually happened a few days later.

The epidemiological criteria reported in the French Ministry of Health's guidelines on the procedures against the circulation of WNV were adopted¹¹. Hence, grading of the risk was as follows:

- 1) grade 1: bird mortality due to WND;
- 2) grade 2: horse morbidity;
- 3) grade 3: human morbidity.

According to the above guidelines, it is recommended that precautionary measures for blood safety be applied only at grade 3 risk. Therefore, precautionary measures for blood safety were introduced by the regional health authority of Emilia Romagna on 1st October 2008, following the confirmation of the first human case in Bologna.

Based on the 2007 experience on the Chikungunya epidemic in the same region¹²: a) precautionary measures were balanced between blood safety and maintenance of the blood inventory, in order to prevent blood component loss; b) timely co-operative interventions were promptly put in place.

Deferral for 28 days of WNV potentially infected donors is mandatory according to the Decree of the Minister of Health of 3rd March 2005¹³, which transposes Commission Directive 2004/33/EC¹⁴. Having been for at least one night in affected areas represents a commonly accepted minimum criterion for deferral.

WNV NAT was promptly introduced to test all blood donations from donors living in the areas of Bologna and Ferrara, at the same time testing all available samples from blood donations collected from 16th September until the systematic introduction of NAT. The latter is being carried out at the Blood Transfusion Centre of the Maggiore Hospital in Bologna using the Cobas T/SCRN WNV US-IVD test (Roche Diagnostics, Indianapolis, IN, USA), and at the RRCMEs by the Procleix® WNV assay (Novartis Vaccines and Diagnostics, Emeryville, CA, USA). Non CE marked, FDA approved tests (Cobas T/SCRN WNV US-IVD) were allowed to be used by the regional health

authority. Partial validation of the above tests was carried out by the RRCMEs using a home-made reverse transcription RT-PCR test; complete validation is ongoing.

On 3rd October, the NBC indicated to blood transfusion centres and collection units nationwide a 28-day deferral for blood donors who have spent at least one night in the provinces of Bologna and Ferrara, starting from the day after leaving the interested areas. As to cord blood donations, WNV NAT test was indicated for all mother-donors resident or having been for at least one night in the above provinces during the 28 days preceding the day of delivery.

All precautionary measures are still in place at the moment this report is being written and they will last according to epidemiological data from the active surveillance system.

Conclusion

Emerging infections have been defined as "new, re-emerging or drug-resistant infections whose incidence in humans has increased within the past two decades or whose incidence threatens to increase in the near future"¹⁵. Multiple agents, among which WNV, fall under this definition and are known to be, or have the potential to be transmitted by blood transfusion.

Since the 1950s, temporally and regionally limited outbreaks of WNV infections in humans and horses have been observed in Europe¹⁶, where migratory birds kept a direct vector contact with WNV endemic areas in Africa for a long time. WNV has emerged - as other microbial agents - due to changing population dynamics or altered migration patterns of intermediate hosts and vectors¹⁵.

The reported experience once more shows that new emerging pathogens may be a threat to public health, not only because of their impact on the population, but also because they have a relevant potential to threaten blood safety and to be a challenge to the maintenance of the blood inventory and to the comprehensive management of a regional and national blood system.

Key words: West Nile virus, blood transfusion, blood system, blood safety.

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