

MEASURES TAKEN TO REDUCE THE RISK OF WEST NILE VIRUS TRANSMISSION BY TRANSPLANTATION IN ITALY

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For the first time in Italy, two patients with meningoencephalitis were diagnosed with West Nile virus (WNV) infection in September 2008 [1]. The patients live in the Bologna and Ferrara provinces of Emilia Romagna where WNV infections had previously been noted in horses, crows and magpies [2].

The Italian National Transplant Centre (CNT), which is responsible for the procurement, processing and distribution of organs and tissues in Italy, has now reviewed the risks of transmission of WNV by organ, tissue and cell transplantation and, taking into account the advice and recommendations of the relevant authorities in other countries, issued guidance to the transplant community.

Background

Although there are no known cases of WNV transmission by tissue transplantation, both blood transfusion and organ transplantation have resulted in transmissions [3-6]. Transmission by transplantation of tissues such as bone, heart valves, skin and corneas is theoretically possible, particularly when the tissues have been minimally processed and/or they contain blood.

European Union Directive 2006/17/EC, Annex 1, defines the criteria to be applied for the selection of tissue and cell donors and Annex 2 defines the testing requirements [7]. Annex 1 states that donors must be excluded from donation if there is evidence of "risk factors for transmissible diseases on the basis of a risk assessment, taking into consideration donor travel and exposure history and local infectious disease prevalence". This requirement is reflected in the CNT's Guidelines for the Procurement, Processing and Distribution of Tissues for Transplantation (19/06/2007), which demand the exclusion of donors who have "a risk of infection associated with travel to endemic areas or exposure to infective agents that cannot be excluded by testing".

The Food and Drug Administration (FDA) in the United States issued draft, non-binding guidance for blood, cell and tissue donations in April 2008 [8]. They recommend that blood specimens from all human cell and tissue donors be tested year-round for WNV by individual donor Nucleic Acid Testing (NAT) using a licensed screening NAT test, and that only donors whose specimens are non-reactive may be considered eligible.

The American Association of Tissue Banks has raised concerns about the necessity for universal testing seeing as there are as yet no reports of transmission by tissue transplantation. They have

also raised concerns regarding the reliability of the kits that have been licensed for use with post-mortem samples: They report an unacceptable rate of abnormal initial tests that give a weak positive result but are negative when repeated for the same sample [9].

Apart from these concerns, it is relevant that in the case of the first donor that transmitted WNV by organ transplantation, two serum samples collected at the time of admission did not contain any detectable WNV IgM antibody or nucleic acid. Neither did a serum sample obtained from the patient on the following day, after receipt of transfusions contain detectable levels of WNV nucleic acid. However, serum and plasma samples collected a day later at the time of organ recovery yielded WNV nucleic acid in a quantitative PCR, and WNV could be recovered in culture [4]. In the second case of transmission by organ transplantation, the donor tested negative for WNV RNA, although serum samples were positive for WNV IgG and IgM [5].

These findings underline the problems that can arise when relying on testing and the importance of accurate documentation of the donor's history in the prevention of donor-transmitted infections such as West Nile fever.

It is notable that in the United Kingdom, 18,700 blood donors returning from high-incidence WNV areas during the epidemic season were tested between mid-June 2004 and the end of November 2005 and no positive result was obtained [10]. It can be concluded that the risk of transmission by those who have travelled to affected areas is very low.

Guidance issued for transplantation in Italy

In the light of the recently reported infections, and taking a precautionary approach, the Italian National Transplant Centre has issued guidance that all potential donors of organs, tissues and cells from the Bologna and Ferrara provinces in the Emilia-Romagna region should be tested to exclude infection. Where there is evidence of infection, organs, tissues and cells will not be used.

In the rest of Italy and in the other Emilia-Romagna provinces, the following rules apply:

- Investigation of the history of potential **tissue donors** will include enquiries regarding a possible overnight stay in the provinces of Bologna and/or Ferrara during the previous 28 days. If a potential donor has visited one of these provinces, they will

not be considered eligible for donation, unless laboratory test results for WNV are negative;

- For **organ donors**, a case by case evaluation is conducted in order to assess the infection risk, which is acknowledged to be very low, taking into account the nature and benefits of transplantation and the health status of the patient on the waiting list.

Discussion

In the case of organ donation, decisions have to take into account the shortage of organs available for transplant and the great, usually life-saving, benefit that can result from this type of transplantation. The available time is very limited and it may not always be possible for WNV testing to be performed in a particular area of Italy where a donor is identified in time before the transplantation would need to proceed. Under such circumstances, the risk posed by a potential donor who may have spent a night in a WNV-affected area in the previous month and has had no symptoms of infection would be very low and would probably not justify depriving the recipients of the opportunity for transplantation. For this reason, it is necessary to consider each case individually, weighing the risks and potential benefits that face each individual recipient in a balanced and pragmatic way.

In the case of tissue donation, the potential donor pool is much larger and shortages are therefore not a major challenge in the system, particularly in Italy where tissue donation rates are high. In general, tissue transplants result in improved quality of life and are rarely life-saving, so it is important to maintain risk at a very low level. On the other hand, many donated tissues are processed by washing, freezing, freeze-drying and in some cases subjected to gamma irradiation or other types of sterilisation. The tissues that are not highly processed, such as corneas, heart valves and skin, contain very little blood. The risk of an infected tissue transmitting a virus is therefore significantly lower than for blood or organs. Overall, it is considered appropriate to take a precautionary approach to the selection of tissue donors until there is a clearer picture of the extent of the problem.

The guidance described here will be reviewed should further infections be reported, also taking into account changing seasons.

References

1. Rossini G, Cavrini F, Pierro A, Macini P, Finarelli AC, Po C, et al. First human case of West Nile virus neuroinvasive infection in Italy, September 2008 – case report. *Euro Surveill.* 2008;13(41):pii=19002. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19002>
2. Macini P, Squintani G, Finarelli AC, Angelini P, Martini E, Tamba M, et al. Detection of West Nile virus infection in horses, Italy, September 2008. *Euro Surveill.* 2008;13(39):pii=18990. Available from: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=18990>
3. Centers for Disease Control and Prevention (CDC). Update: West Nile Virus Screening of Blood Donations and Transfusion-Associated Transmission – United States, 2003. *MMWR Morb Mortal Wkly Rep.* 2004;53(13):281-4.
4. Iwamoto M, Jernigan DB, Guasch A, Trepka MJ, Blackmore CG, Hellinger WC, et al. Transmission of West Nile virus from an organ donor to four transplant recipients. *N Engl J Med.* 2003;348(22):2196-203.
5. Centers for Disease Control and Prevention (CDC). West Nile Virus Transmissions in Organ Transplant Recipients – New York and Pennsylvania, August – September 2005. *MMWR Morb Mortal Wkly Rep.* 2005;54(40):1021-3.
6. Centers for Disease Control and Prevention (CDC). West Nile Virus Transmission through Blood Transfusion – South Dakota, 2006. *MMWR Morb Mortal Wkly Rep.* 2007 Feb 2;56(4):76-9.
7. European Commission. Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells 2006/17/EC. Brussels; 2006. Available from: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2006:038:0040:0052:EN:PDF>
8. Center for Biologics Evaluation and Research. Draft Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of transmission of West Nile Virus from Donors of Whole Blood and Blood Components Intended for Transfusion and Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS). US Department of Health and Human Services, Food and Drug Administration; April 2008 Available from: <http://www.fda.gov/cber/gdlns/natwnvhctp.htm#iv>
9. American Association of Tissue Banks. Comments in response to the FDA publication " Draft Guidance for Industry: Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus from Donors of Whole Blood and Blood Components Intended for Transfusion and Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/PS)". McLean, Virginia; July 2008. Available from: <http://www.aatb.org/files/fdacommments72508.pdf>
10. The Standing Advisory Committee on Transfusion Transmitted Infections. Position Statement West Nile Virus 05 February 2008. Joint UKBTS/NIBSC Professional Advisory Committee. Available from: <http://www.transfusionguidelines.org.uk/index.asp?Publication=DL&Section=12&pageid=801>

This article was published on 16 October 2008.

Citation style for this article: Nanni Costa A, Grossi P, Porta E, Venettoni S, Fehily D. Measures taken to reduce the risk of West Nile virus transmission by transplantation in Italy. *Euro Surveill.* 2008;13(42):pii=19009. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19009>