

Joint UKBTS / NIBSC Professional Advisory Committee (*)

Position Statement

West Nile Virus

01 March 2010

Prepared by: The Standing Advisory Committee on Transfusion Transmitted Infections

This document will be reviewed whenever further information becomes available, and at least annually. Please continue to refer to the website for in-date versions.

1. Background

West Nile Virus (WNV), a mosquito-borne flavivirus recognised since 1937 and widely distributed in Africa, Western Asia, Europe and Australia, emerged for the first time in the Northeast of the United States (US) in 1999. WNV case numbers increased in the US in following years, reaching a peak in 2003. WNV has now spread across the whole of the US and into parts of Canada.

In 2002, cases of transfusion and transplant-transmission of WNV were recognised in the US. The definitive strategy adopted in the US to deal with this issue was the implementation of WNV NAT in 2003. As travel to the USA and Canada is common in UK blood donors, a deferral policy was adopted by UKBS for such donors as a precautionary measure in June 2003. In April 2004 this deferral policy was updated to take account of the availability of WNV NAT tests for donation screening and such screening was applied in NHSBT for the relevant periods of 2004 and 2005.

Data for the 2009 WNV season have been reviewed and for the time being it is recommended that deferral criteria should be continued during the 2010 WNV season (see 1.1). This advice takes account of information contained in FDA CBER Guidance issued in June 2005.¹ A further review will be conducted by SACTTI towards the end of the 2010 WNV season, or earlier, if new information becomes available.

1.1. The recommended deferral criteria are:

Donors who have visited a WNV risk area*:

Defer for 28 days from date of leaving the affected area unless a validated WNV NAT test on the donation is performed and is negative

**Donors who have visited a WNV risk area* and have either:
a history of symptoms suggestive of WNV whilst there or following their return to the UK
or
been diagnosed with WNV whilst there or following their return to the UK.**

Defer. Refer for clinical microbiology follow-up as appropriate.

Donors who are found not to have had WNV may be re-instated.

All donors may be re-instated six months after their return from an affected area.

Donors who are WNV NAT tested and have NAT reactive samples.

Do not use the donation.
Defer. Refer for clinical microbiology follow-up as appropriate.
May be re-instated 6 months after return from affected area.

Joint UKBTS / NIBSC Professional Advisory Committee (*)

Position Statement

West Nile Virus

01 March 2010

*A **WNV risk area** is defined as any part of North America (USA and Canada) during the risk period. FDA CBER specified the “typical WNV season” as falling between **1 May and 30 November** although isolated cases may occur at any time of the year, and the majority of cases occur in the months July to October.

Requirements of EU Blood Safety Directive 2004/33/EC

It should be noted that the EU Blood Safety Directive (and the Blood Safety and Quality Regulations) requires that travellers from an area with ongoing transmission of WNV in humans should be deferred for 28 days. It is assumed that WNV NAT testing, in place of deferral, is an acceptable strategy.

1.2. Post- donation illness (donor) and post-transfusion infection (recipient) reporting

Both types of reporting are routine in the UKBS and standard UKBS procedures should be followed:

- In the case of a donor becoming ill with WNV or suspected WNV within 14 days of donation, relevant blood donations are those 14 days prior to and 120 days after the onset of illness.
- In the case of a recipient becoming ill with WNV/suspected WNV within 120 days of transfusion.

2. West Nile Virus

Background ^{2,3,4}

WNV is an arthropod borne flavivirus, first isolated in 1937. The principal vectors are mosquitoes and the principal hosts are wild birds. Humans and other animals e.g. horses, are infected via mosquito bites. They are considered to be “incidental hosts” as they do not develop sufficient viraemia to maintain transmission cycles.

WNV has also caused sporadic cases and outbreaks of human and equine disease in Europe since the 1960s. Outbreaks have occurred in Romania (1996 and 2008), Russia (1999), Israel (2000), Hungary and Italy (both 2008)

In the USA, WNV was first identified in 1999, and during 2000-2001 spread to over half the country. In 2002 there was a major epidemic which peaked in August – late September; 99% of the human cases occurred between 1 July and 31 October. Since cases are mosquito-related, the numbers are expected to decline over the winter. The 2003 epidemic resulted in 9858 human cases with 262 deaths. The 2009 epidemic resulted in 663 human cases with 30 deaths and 109 presumptive viraemic blood donors. Human case numbers from previous years are shown in the table below. In Canada there were a total of 36 cases in 2008 with the last case reported in mid-September. In 2007, cases continued to be reported well into November.

Joint UKBTS / NIBSC Professional Advisory Committee (*)

Position Statement

West Nile Virus

01 March 2010

The number of human WNV cases, deaths and viraemic blood donors, USA 1999 – 2009*

Year	Case numbers	Deaths	Presumptive viraemic blood donors
1999	62	7	
2000	21	2	
2001	66	9	
2002	3893	254	
2003	9862	264	818
2004	2539	100	224
2005	3000	119	417
2006	4269	177	361
2007	3510	109	326
2008	1356	44	174
2009	663	30	109

*Data source: ww.cdc.gov/ncidod/dvbid/westnile/surv&control.htm

The incubation period in humans is reported to be 3-15 days. Most human infections are either asymptomatic (80%), or result in only mild flu-like symptoms with full recovery (20%), but 1 in 150 –200 develop a more severe form of the disease which may culminate in fatal encephalitis, particularly if elderly or immunosuppressed.

In general the risk of transmission by transfusion relates to a few days of viraemia starting 1-3 days after infection. Viraemia lasts a mean of 6 days. During the 2002 epidemic 23 patients were confirmed to have acquired WNV through transfusion of red cells, platelets or fresh frozen plasma. Transmission has also been reported following organ transplantation from a donor who initially acquired the infection through a blood transfusion. Information from the US has shown that, depending on the sensitivity of the NAT assay used, the virus may take up to 104 days to clear¹. Additionally it was reported that live virus can be demonstrated in some individuals who are seropositive for WNV antibodies. It was also noted that symptoms of headache and fever were poor indicators of WNV infection.

A 2005 report from the US of WNV in organ transplant recipients indicated that WNV transmission through solid organ transplantation can occur from donors who are seropositive for WNV (IgM and IgG antibodies) and WNV NAT negative⁵ but there had been no such reports of transmission from blood donations

There is a report¹⁰ from the US of two cases of probable transfusion-transmitted WNV from a common blood donor in 2006 despite a negative MP-NAT result at the time of donation. The source of infection could not be proven because blood samples or co-components from the implicated donation were unavailable for testing; however, evidence of WNND in two recipients of blood products from a common donor with serologic evidence of recent infection (IgM antibody) at follow-up makes WNV transfusion-transmission probable. Because the two transfusion recipients were hospitalized for at least 2 weeks each before onset of WNND, neither patient was likely to have acquired infection from a mosquito bite. Furthermore, for the recipient who also underwent transplant surgery, transmission through the transplanted

Position Statement

West Nile Virus

01 March 2010

kidney is unlikely, given that neither the organ donor nor the other organ recipient had evidence of WNV infection.

A pragmatic approach is needed in the UK. Donors with a history of WNV and/or a positive WNV NAT should be temporarily deferred pending investigation but may be returned to the donor panel after 6 months without the necessity for a further test. No UK donors were found to be WNV NAT positive during the period when routine WNV NAT screening of blood donors with relevant travel history was performed in the NBS.

3. Risk of transfusion-transmitted WNV in the UK

There are two situations to be considered for UK blood services:

The importation of FFP (from US) for clinical use

The risk from UK donors who may have been exposed in the US.

3.1. Risk of WNV transmission by imported plasma.

USA/Canada introduced mini-pool WNV NAT testing of donations from July 2003. This includes plasma supplied to the UK. This routine NAT screening for WNV has resulted in the removal of many viraemic blood donations from the US blood supply although a small risk of transfusion-transmitted WNV remains from low titre viraemic donations which are not detectable by mini-pool NAT.⁷

The period of asymptomatic viraemia is short-lived with rapid development of IgG and IgM antibodies to WNV. Methylene blue treatment is applied to FFP imported from the US. It has been shown to reduce the WNV load by at least 6.5₁₀ logs to below the detection limit and WNV appears to be one of the most rapidly inactivated viruses studied⁶. The risk of transmission by methylene blue treated FFP of US origin must therefore be considered negligible.

3.2. The risk from UK donors

The UK situation is as follows:

- There have been only two human WNV cases reported in the UK (this includes travellers returning from endemic areas). One case each in 2006 and 2007 was reported. The 2006 case was in an UK resident, who was a member of the armed forces and stationed in Canada. The diagnosis was made on his return to the UK. The 2007 case was a Canadian resident who became ill when visiting the UK. No human cases have been reported in the UK in 2008 or 2009.
- There were no WNV viraemic blood donors identified among over 20,000 donations made to NBS centres by donors returning from WNV at risk areas during 2004 and 2005.
- In enhanced surveillance of encephalitis patients in England between November 2005

Joint UKBTS / NIBSC Professional Advisory Committee (*)

Position Statement

West Nile Virus

01 March 2010

and June 2007 found no cases of WNV

http://www.hpa.org.uk/infections/topics_az/encephalitis/study.htm.

- A study of the UK bird population showed the presence of neutralising antibodies in a relatively high proportion of resident birds⁸. The absence of an obvious reduction in the bird population suggests that either the strain detected is avirulent or that birds have been exposed for many years and have developed herd immunity.
- The only known risk is therefore in returning travellers from high incidence areas, in the appropriate season, who may be incubating WNV. However, on this point it is noteworthy that during the period of selective WNV NAT testing of NBS donors, out of approx. 18,700 tests performed between 14 June 2004 and the end on November 2005, none were found WNV positive. The risk of WNV transmission via blood transfusion in the UK is considered to be very small but cannot be quantified at present. Nevertheless, assessment of the threat to blood safety of this pathogen using criteria developed by SACTTI⁹ suggests that the preventative measures adopted to date are appropriate.
- There were no imported cases of WNV in the UK in 2008 or 2009.

4. Conclusion

- 4.1 As required by UK Statutory Regulations a 28-day deferral period applies to asymptomatic donors returning from an area with ongoing transmission of WNV in humans unless a validated WNV NAT test on the donation is negative.
- 4.2 The possibility of prolonged WNV viraemia, which may be low-level and not detectable by mini-pool WNV NAT, requires a pragmatic approach in the UK as testing is not routinely applied to blood donations. Donors with a history of WNV and/or a positive WNV NAT should be temporarily deferred pending investigation but may be returned to the donor panel after 6 months without the necessity for a further test. To date, no UK donors have been found to be WNV NAT positive.

References

1. Guidance for Industry. Assessing donor suitability and blood and blood product safety in cases of known or suspected West Nile Virus infection. US Department of Health and Human Science, Food and Drug Administration Center for Biologics Evaluation and Research. June 2005.
2. PD Crook, NS Crowcroft, DWG Brown, West Nile Virus and the threat to the UK, Commun Dis Public Health 2002, 5(2):138-143.
3. CV Prowse, An ABC for West Nile Virus, Transfusion Medicine 2003, 13:1-7.
4. Lisa N Pealer et al, NEJM 2003, 349: 1236-1245. Transmission of West Nile Virus through blood transfusion in the United States in 2002.

Joint UKBTS / NIBSC Professional Advisory Committee (*)

Position Statement

West Nile Virus

01 March 2010

5. West Nile Virus Infections in Organ Transplant Recipients - New York and Pennsylvania, August-September 2005. MMWR Weekly October 5 2005.
6. Immunol Investig 1995; 24: 73
7. Update: West Nile screening of blood donations and transfusion-associated transmission – United States, 2003. MMWR Weekly 2004, 53 (13): 281-284.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5313a1.htm>
8. Alan Buckley et al. Serological evidence of West Nile virus, Usutu virus and Sindbis virus infection of birds in the UK, Journal of General Virology 2003: 84: 2807.
9. SACTTI 05/63 Transfusion Transmissible Infectious Agents: basis for a policy framework: Final working draft, version 1.4, 4 July 2005, Brian McClelland, Roger Eglin, Peter Simmonds.
10. Kightlinger L et al. West Nile Virus Transmission Through Blood Transfusion --- South Dakota, 2006. MMR Weekly, February 7 2007/ 56(04); 76-79.

(*) **Joint United Kingdom Blood Transfusion Services and National Institute for Biological Standards and Control Professional Advisory Committee**