Update on West Nile virus and Blood Safety
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Background Information

- WNV is an enveloped single stranded RNA virus
- WNV is a mosquito-borne Flavivirus
  - Primarily infects birds
  - Occasionally infects humans and other animals
- About 80% of human infection is asymptomatic, and 20% develop mild febrile illness (flu-like illness)
- Approximately 1 in 150 infections results in meningitis or encephalitis
  - Advanced age is by far the most significant risk factor for severe neurologic disease
- Viremic period can occur up to 2 weeks prior to symptoms and last up to a month from the initiation of the infection

Background Information……

- The 2002 US outbreak of WNV resulted in the identification of other modes of transmission including:
  - blood transmission (RBCs, plasma and platelets), transplantation, breast-feeding, transplacental and occupational by percutaneous injury
- The magnitude of the risk of WNV from transfusion is unknown.
- Virus titer in blood is low compared to other transmissible viruses.
  - Viremia in encephalitis patients can be as high
- IgM can persist for a long time in some cases up to 2 years
- No chronic stage of WNV infection has been reported

WNV Blood Safety Measures

- **FDA's Office of Blood Research and Review has provided guidance to blood establishments on donor screening and unit management to prevent transmission of WNV by blood transfusion as follows**:
  - August 17, 2002, FDA issued an alert to blood establishments to exercise vigilance to exclude potential donors with flu-like symptoms even though there had been no reports that it could be transmitted by blood.
  - October 25, 2002, FDA issued a guidance document, "Final Guidance for Industry on Recommendations for the Assessment of Donor Suitability and Blood and Blood Product Safety in Cases of Known or Suspected West Nile Virus Infection" to prevent donors with symptoms from donating and to manage implicated products.
  - May 1, 2003 FDA issued a revised guidance to include deferral of donors who are healthy but had symptoms of fever with headache within the week before donation.

WNV Blood Safety Measures

- **FDA has encouraged and worked with manufacturers to develop suitable WNV blood-screening tests**
  - In cooperation with the Department of Health and Human Services, FDA issued a call to industry to rapidly develop blood donor screening tests in September 2002.
  - FDA sponsored a public workshop in November 2002, and discussed issues in development of WNV donor screening at various public forums including meetings of FDA's Blood Products Advisory Committee
  - FDA is developing reference materials and standards that companies can use to validate their tests similar in format.
  - FDA is participating in meetings with AABB task force to coordinate the epidemiological data on WNV infection and to monitor the outcome of nation wide testing.

WNV Blood Safety Measures

- **WNV testing:**
  - The experimental kits in use are nucleic acid amplification tests, which detects WNV RNA in the human blood sample, are similar to those already licensed for screening blood donors for HIV and hepatitis C virus infection.
  - WNV NAT testing of whole blood, blood components source plasma, bone marrow, cord blood, hematopoietic progenitor cells, tissue and organ donors is being done under IND.
  - Nationwide testing started as of July 1, 2003 using Roche and Gen Probe tests.
  - Clinical trials are being performed in both pooled (16 for GenProbe and 6 for Roche) and individual samples.
  - The regulatory pathway for WNV testing includes testing all donors under IND, link product release to WNV test results, require confirmatory testing (alternate NAT and IgM), unit donor management (follow up, counseling and look back).

WNV Blood Safety Measures

FDA's current recommendations for donor deferral

- FDA most recent recommendations targeting prevention of transmission by donors with current or recent symptoms (about 20% of infected individuals) was issued on May 1, 2003.
- FDA regulations already require that blood establishments determine donors to be in good health at the time of donation and defer donors with current clinical symptoms.
- During the epidemic season of June 1 to November 30:
  - Donors who report a medical diagnosis of WNV infection are deferred for at least 28 days from onset of symptoms or until 14 days after the condition is resolved whichever is longer.
  - Donors who report fever and headache in the week before donation are deferred for 28 days from the date of the interview.

WNV Blood Safety Measures

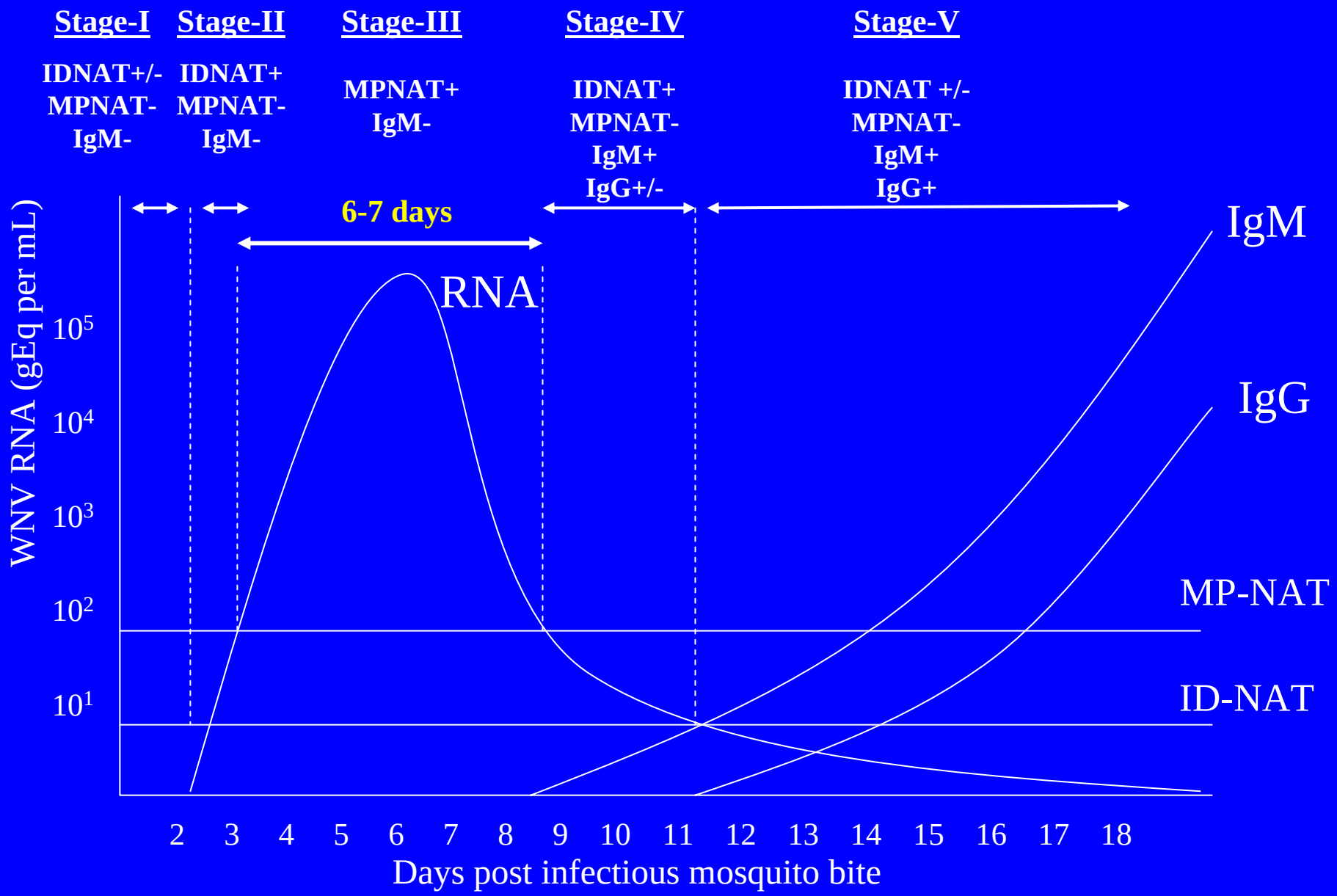
Pathogen inactivation

- Available information indicates it is unlikely that WNV is transmitted through plasma derivatives.
  - Approved procedures for pathogen inactivation such as solvent/detergent will inactivate lipid-enveloped viruses. Model flaviviruses such as BVDV served as models for HCV and have been shown to behave similarly to WNV.
- Experimental use of psoralins, riboflavin, and Inactine for viral inactivation in plasma, platelets, and red cells also showed high level inactivation of WNV (> 4 log reduction).

West Nile Virus and Blood Safety:

- **Nationwide testing of WNV under FDA approved INDs resulted in:**
  - **Donations interdicted from asymptomatic donors with confirmed or suspected WNV infections**
  - **In 2003, 818 WNV presumptive viremic blood donors officially reported to CDC's ArboNet**
    - 6 confirmed T-T cases (4/6 had low viremia ~0.11 pfu/ml)
  - **As of January 11, 2005; 199 presumptive viremic donors officially reported to CDC's ArboNet using MP-NAT as well as ID-NAT in select areas starting May '04**
    - one reported case of T-T (detectable only by ID-NAT)

Proposed model for stages of WNV infection based on results found on MP-/ID-NAT and IgM/IgG EIA



WNV and Blood Safety: Gaps in current knowledge

- **Donor and product management recommendations:**
  - donor follow up identified a period of viremia of 49 days
  - Donor deferral period extended from 28 days to 56 days, what next?
  - Entry of donors after testing ID-NAT (-): time limit
- **Symptoms with WNV infectivity**
  - Correlations of headache with fever in the week before donation
- **Trigger for ID-NAT testing**
  - ID-NAT vs MP-NAT to further reduce risk of WNV T-T

West Nile Virus and Blood Safety: Gaps in knowledge

- **Genetic variations in WNV strains – limited data in human disease cases**
  - Detection by currently available WNV assays
- **Determination of residual risk of WNV infection in the presence of antibody**
  - MP-NAT low titer, MP-NAT (-), ID-NAT (+) units
- **Usefulness of WNV surveillance data to predict epidemic**
  - Detection in birds, mosquitoes, equines, symptoms in human, etc.
  - Severity of epidemic from year to year

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