Torque Teno Virus (TTV) Complex

Disease Agent:

- Torque teno virus (TTV) and SEN virus (SENV)

Disease Agent Characteristics:

- Family: *Circoviridae*; Genus: *Anellovirus*
- Virion morphology and size: Nonenveloped, nucleocapsid of unknown symmetry, 30-50 nm in diameter
- Nucleic acid: Circular, negative-sense, single-stranded DNA, ~3.6-3.8 kb in length
- Physicochemical properties: Not described, but chicken anemia virus is inactivated at 95°C for 30 minutes or 100°C for 10 minutes; resistant to ether and other lipid solvents

Disease Name:

- No confirmed disease associations

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Absent; transmission documented, but no disease associated despite extensive studies
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent

Background:

- In 1997, Japanese investigators discovered TTV using representational difference analysis from a blood sample of a patient with posttransfusion non-A-E hepatitis.
- The name torque teno virus was selected by a working group on the circoviruses after torques (necklace) and tenuis/teno (thin), thereby preserving the widely used term, TTV, which originally employed the initials of the patient (i.e., T. T.).
- Phylogenetic analysis showed TTV to represent the prototype virus for a vast group of heterogeneous agents unrelated to any known human or animal hepatitis viruses.
- SENV was discovered in Italy by using degenerate primers from TTV. Although originally thought to be novel, it was subsequently shown to be a member of a genetically diverse group of viruses in the TT complex.
- Despite their source from hepatitis cases, subsequent studies showed that these viruses are ubiquitous (prevalence rates up to 90% in adults) and that neither agent is a cause of human hepatitis.

Common Human Exposure Routes:

- Parenteral transmission is the major route of transmission, but the fecal–oral route is similarly suspected to contribute to spread of the virus.
- Sexual transmission probable

Likelihood of Secondary Transmission:

- Probably moderate, but the extent of secondary spread is not well defined

At-Risk Populations:

- Blood component recipients
- Injection-drug users
- Household contacts
- Sexual partners

Vector and Reservoir Involved:

- Humans

Blood Phase:

- Persistent viremia is common.

Survival/Persistence in Blood Products:

- Survives refrigeration and freezing

Transmission by Blood Transfusion:

- Well documented in prospective studies

Cases/Frequency in Population:

- The prevalence of viremia ranged from 2-12% in blood donors; however, using primers for highly conserved sequences, TTV DNA has been detected in >90% of some populations.
- Prevalence of TTV ranges from 40-70% in hemophiliacs, dialysis patients and injection-drug users, but could be higher with different primers.

Incubation Period:

- In nonhuman primates, viremia is detected 4-7 days after intravenous injection and 7-10 days after oral inoculation.

Likelihood of Clinical Disease:

- SENV and TTV were originally suspected to be etiological agents for acute and chronic non-A to -E hepatitis, hepatitis-associated aplastic anemia, acute liver failure, or cryptogenic cirrhosis, but these associations have been excluded.

Primary Disease Symptoms:

- No virus-specific symptoms have been identified.

Severity of Clinical Disease:

- No clinical disease established; thus any clinical relevance of the TT complex is speculative.

Mortality:

- None

Chronic Carriage:

- Asymptomatic carrier state frequent

Treatment Available/Efficacious:

- No treatment required
- Interferon treatment has been associated with viral clearance during treatment of coinfections with other hepatitis viruses.

Agent-Specific Screening Question(s):

- No specific question is in use.
- Not indicated because transfusion-transmitted disease has not been demonstrated
- No sensitive or specific question is feasible.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Virus detected by NAT

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- There is no indication for deferral in the absence of disease associations.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable.

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable.

Leukoreduction Efficacy:

- Unknown but unlikely to be effective against a noncell-associated virus.

Pathogen Reduction Efficacy for Plasma Derivatives:

- Not inactivated by solvent-detergent
- No data on other inactivation procedures, but two other circoviruses (porcine circovirus 2 and chicken anemia virus) demonstrated extreme thermal resistance to pasteurization or prolonged dry heat methods similar to those proven effective for plasma products.

Other Prevention Measures:

- None

Suggested Reading:

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8. Umemura T, Yeo AE, Sottini A, Moratto D, Tanaka Y, Wang RY, Shih JW, Donahue P, Primi D, Alter HJ. SEN virus infection and its relationship to transfusion associated hepatitis. Hepatology 2001;33:1303-11.
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