Hepatitis E Virus

Disease Agent:

- Hepatitis E virus (HEV)

Disease Agent Characteristics:

- Family: *Hepeviridae*; Genus: *Hepevirus*
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical particles, 30-34 nm diameter
- Nucleic acid: Linear, positive-sense, single-stranded RNA, ~7.2 kb in length
- Physicochemical properties: Less stable to heat than HAV; most strains totally inactivated at 60°C although a Mexican strain was moderately more resistant; stable to multiple cycles of freezing and thawing

Disease Name:

- Hepatitis E

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Very low in the US but probably higher in other countries where transfusion-transmitted cases have been reported
- Public perception and/or regulatory concern regarding blood safety: Absent in the US
- Public concern regarding disease agent: Absent in the US

Background:

- Not recognized until 1980; virus visualized in infected volunteer by immune electron microscopy of feces in 1983 and transmitted to Cynomolgus monkeys
- Serologic studies distinguished an enterically transmitted hepatitis virus distinct from hepatitis A virus.
- HEV cloned and sequenced in 1990

Common Human Exposure Routes:

- Most epidemics water-borne, some food-borne from a fecally contaminated cause
- Exposure source for sporadic cases usually unknown; may be fecal-oral, but epidemiology different from other fecal-oral agents (e.g., HAV)
- Person-to-person spread relatively uncommon; sexual spread unproved
- Blood transmission is rare, but has been reported in endemic areas and rarely in nonendemic areas presumably resulting from an extended asymptomatic viremic period.

Likelihood of Secondary Transmission:

- Very low, most likely from fecal shedding

At-Risk Populations:

- Endemic and epidemic in residents of Southeast and Central Asia plus Japan, Middle East, North and West Africa, Mexico, Brazil
- Travelers to these areas
- Sporadic cases occur in developed nations; no identified risk group

Vector and Reservoir Involved:

- Five genotypes: Humans (1 and 2), humans and swine (3 and 4), and avian (5)
- Zoonotic spread may occur from swine or other domestic and wild animals (Sika deer, wild boar) to humans through consumption of uncooked meat products or close environmental contact.

Blood Phase:

- Viremic phase of 4-6 weeks with nucleic acid being detected up to 112 days.
- Longer duration of nucleic acid detection has been reported in immunocompromised organ-transplant recipients following acute HEV.

Survival/Persistence in Blood Products:

- No data, but should survive refrigeration

Transmission by Blood Transfusion:

- Documented in endemic areas (e.g., Saudi Arabia and Hokkaido in Japan) and rarely in industrialized regions (UK and France)

Cases/Frequency in Population:

- Antibody prevalence in endemic regions is 20-40%.
- HEV seroprevalence in the US during 1988-1994, as measured in the 3rd NHANES survey, was 21% with the highest prevalence in the Midwest and metropolitan areas.
    - For US-born individuals increased odds of HEV seropositivity were found among males, non-Hispanic whites, or if a pet was in the home, or liver and other organ meats were consumed more than once monthly.

Incubation Period:

- Usually 3-8 weeks, but longer and shorter periods have been reported.

Likelihood of Clinical Disease:

- Severity can range from inapparent to fulminant hepatitis.
- In nonhuman primates, severity is related to dose.

Primary Disease Symptoms:

- Indistinguishable from other forms of hepatitis: nausea, vomiting, abdominal pain, anorexia, fatigue, jaundice

Severity of Clinical Disease:

- Usually not severe except in those with chronic liver disease or in pregnant women where fulminant hepatitis may occur
- High incidence of fetal wastage

Mortality:

- 0.2-4% overall except in pregnant women during third trimester where rates of 10-20% have been reported

Chronic Carriage:

- While no cases of chronic HEV have been reported among immunocompetent potential donors, several cases of acute hepatitis leading to chronicity and cirrhosis have been described in immunocompromised patients following liver and/or kidney transplants and in a patient undergoing chemotherapy for a T cell lymphoma.

Treatment Available/Efficacious:

- No established treatment

Agent-Specific Screening Question(s):

- None specifically for hepatitis E; however, questions from the Donor History Questionnaire concerning a history of clinical hepatitis and possible exposure to hepatitis viruses are relevant. These specific questions are as follows: Have you ever had hepatitis after the age of 11 years? In the past 12 months, have you lived with a person who has hepatitis?

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- IgG and IgM antibody assays have been developed but vary widely in sensitivity and specificity.
- Virus detected by RT-PCR

Currently Recommended Donor Deferral Period:

- The FDA requires an indefinite deferral for a clinical history of viral hepatitis (regardless of the specific viral agent) after age 11.

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:

- None expected

Pathogen Reduction Efficacy for Plasma Derivatives:

- HEV would not be affected by the solvent-detergent process.
- Heat-inactivation by commercial plasma processes has not been evaluated, but the virus may be susceptible, based on recent thermal stability studies.

Other Prevention Measures:

- A vaccine has been shown to be efficacious in animals and in phase III human clinical trials. The vaccine will presumably only be used in endemic areas, the military or in travelers to high-risk areas.

Suggested Reading:

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