Hepatitis A Virus

Disease Agent:

- Hepatitis A virus (HAV)

Disease Agent Characteristics:

- Family: *Picornaviridae*; Genus: *Hepatovirus*
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical, 27-32 nm in diameter
- Nucleic acid: Linear, positive-sense, single-stranded RNA, ~7.5 kb in length
- Physicochemical properties: HAV retains most of its infectivity when subjected to pH 1.0 for 2 hours at room temperature and is still infectious at 5 hours. It is highly resistant to detergents and to organic solvents such as ether and chloroform. Autoclaving at 121°C is effective. HAV is inactivated within minutes at 98-100°C. The virus persists for days to months in experimentally contaminated fresh water, seawater, wastewater, soils, marine sediment, live oysters, and cream-filled cookies. Oysters inoculated with contaminated feces, heated at 60°C for 19 minutes and sealed in a can, transmitted HAV. HAV is inactivated by UV radiation, formalin, β-propiolactone, iodine, and chlorine or chlorine-containing compounds (sodium hypochlorite). Infectivity of HAV is substantially decreased by 70% ethanol at 25°C.

Disease Name:

- Hepatitis A

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Low
- Public perception and/or regulatory concern regarding blood safety: Very low/Absent
- Public concern regarding disease agent: Moderate

Background:

- Incidence has fallen by more than an order of magnitude in US since the 1970s in association with immunization in high risk communities. Universal immunization should further lower the risk.
- Produces disease only in humans and nonhuman primates.

Common Human Exposure Routes:

- Ingestion of virus from material contaminated with feces containing HAV (fecal-oral route)

Likelihood of Secondary Transmission:

- Moderate; from infected persons to close contacts

At-Risk Populations:

- Susceptible travelers to or workers in foreign countries (including the military) where the risk of acquiring hepatitis A is enhanced because of living conditions, the prevalence of HAV in the area, and the length of stay
- Native Americans
- Men who have sex with men
- Illegal drug users, injecting or noninjecting
- Persons who work with HAV or with nonhuman primates
- Persons with chronic liver disease (advanced fibrosis or cirrhosis)
- Persons residing in areas where extended community outbreaks exist or children living in states that have high and intermediate rates of disease
- Staff and residents of closed communities
- Refugees residing in temporary camps after catastrophes
- Close personal contacts of a case
- Staff and parents of children in day-care centers
- Common-source exposure to infected food or water

Vector and Reservoir Involved:

- Infected humans and nonhuman primates

Blood Phase:

- Viremia is observed concurrent with fecal shedding and often precedes the development of symptoms by at least 2 weeks; communicability is apparently highest during this interval. Concentrations of virus found in blood are usually relatively low (~$10^{3\text{-}5}$ virions/mL).
- HAV can circulate in the blood enclosed in lipid-associated membrane fragments that may transiently protect the virus from neutralizing antibodies. Viremia may be present during the early stages of jaundice but usually terminates shortly after hepatitis develops.
- Virus-specific nucleic acid may be detected in the blood of HAV-seropositive individuals for 30 days or more from onset of symptoms. This has not been correlated with infectivity.

Survival/Persistence in Blood Products:

- Infectivity preserved for the duration of the product

Transmission by Blood Transfusion:

- HAV transmission through blood is rare but well documented. It can be amplified in neonatal intensive care units where multiple infants develop infection after receiving aliquots of blood components from an infected donor.
- The rarity of transmission in adults is attributed to the short infectious viremic stage, low incidence of HAV in the US, absence of a carrier state, prevalence of immunity in many recipients, and neutralization of virus from a concurrent blood product that may contain specific antibody.

Cases/Frequency in Population:

- Variable in the US from 0 to more than 20 cases per 100,000 population. The rate in the western half of the US was more than 2.5 times the mean rate in other regions of the country. Eleven states in the West comprising only one-third of the US population registered 20 or more cases of hepatitis A per

100,000 during 1987-1997 and accounted for 65% of the reported cases of hepatitis A. These rates are expected to dramatically change with universal immunization.
- Geographic areas of risk are observed in areas of the world with a low level of sanitation or hygiene and where living conditions are crowded.

Incubation Period:

- 10-50 days with a mode of ~1 month from exposure to symptoms regardless of the route of infection. Higher doses of virus lead to a shorter incubation period.

Likelihood of Clinical Disease:

- From 21 to 53% of those with overt hepatitis A are hospitalized, being lowest among children and highest among persons 60 years of age or older. Over 70% of the adult clinical cases are jaundiced.

Primary Disease Symptoms:

- Anicteric or icteric hepatitis
- Prodrome of anorexia, fever (usually <39.5°C), fatigue, malaise, myalgia, nausea, and vomiting; relatively abrupt transition from well-being to acutely ill (within 24 h) in more than 60% of the cases; weight loss with disorder of taste and smell; right upper quadrant abdominal pain followed by an icteric phase within 10 days of the initial symptoms

Severity of Clinical Disease:

- Low to moderate
- Atypical manifestations include prolonged cholestasis (5%), relapsing hepatitis (3-20%), autoimmune chronic hepatitis, and extrahepatic manifestations (rash, arthritis, arthralgia, hemolytic anemia, pancreatitis, leukocytoclastic vasculitis, and renal disease).
- Fulminant hepatitis (encephalopathy within 6-8 weeks of illness or 1-4 weeks after jaundice) is associated with high fever, marked abdominal pain, vomiting, and jaundice and occurs in <1.5% of hospitalized icteric patients. Overall survival ranges between 33 and 63%.

Mortality:

- Overall mortality rate is estimated to be <0.015%. However, in hospitalized patients with icteric hepatitis, the mortality rate is reported to be 0.23% in those < 29 years old, 0.3-0.6% in those 30-49 years old, and 1.8-2.1% in those > 49 years old.

Chronic Carriage:

- None

Treatment Available/Efficacious:

- Supportive
- Liver transplant for acute fulminant hepatitis

Agent-Specific Screening Question(s):

- None specifically for hepatitis A; however, questions from the Donor History Questionnaire (DHQ) concerning a history of clinical hepatitis and possible exposure to hepatitis viruses are relevant. These questions are concerned with: hepatitis after the age of 11 years, use of needles to take drugs not prescribed by a physician, and sexual contact with a person who had hepatitis or having lived with a person who has hepatitis in the past 12 months?
- Blood collection facilities should consider the need to prospectively elicit information from donors who may have been exposed to HAV during a common source outbreak. This information could be elicited from donors using one or more mechanisms such as:
  - Temporarily providing written information to all presenting blood donors about the name of the involved establishment or food outbreak and the dates of possible exposure
  - Asking an additional question during the health history interview regarding exposure in the past 4 months to the local hepatitis A outbreak

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- FDA-cleared diagnostic assays: total IgG/IgM anti-HAV and IgM-specific anti-HAV
- HAV RNA testing is available but not approved by the FDA.
- Plasma used for further manufacture is generally tested for HAV RNA by pooled NAT using research tests.

Currently Recommended Donor Deferral Period:

- FDA requires an indefinite deferral for a clinical history of viral hepatitis (regardless of the specific viral agent) after age 11.
- In the US, most viral hepatitis before the age of 11 is a result of HAV; consequently, individuals with a history of hepatitis prior to the age of 11 are allowed to donate.
- AABB recommends deferral of 120 days following appropriately documented exposure to a community HAV outbreak; this is a result of potential for transmission from secondary HAV cases.

Impact on Blood Availability:

- Agent-specific screening question(s): Questions regarding exposure to a common source outbreak could have a moderate effect in a local community
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening question(s): Probably would have minimal effect because risk is already low
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- Unknown but not likely to be effective against a virus that is not strongly cell associated in blood

Pathogen Reduction Efficacy for Plasma Derivatives:

- Efficacy is high, except cases of HAV transmission have been reported from coagulation factor concentrates prepared using the solvent-detergent (SD) method.

Other Prevention Measures:

- Routine vaccination of children aged ≥1 year in the US
- Vaccination of persons in groups at increased risk for hepatitis A or its adverse consequences and the administration of hepatitis A vaccine and/or immune serum globulin to protect persons who are exposed to HAV within the previous 2 weeks (postexposure prophylaxis).

Suggested References:

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