13 | HEPATITIS A VIRUS

13.1 | Disease agent

- Hepatitis A virus (HAV)

13.2 | 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 h at room temperature and is still infectious at 5 h. 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 pastries. Oysters inoculated with contaminated feces, heated at 60°C for 19 min 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.

13.3 | Disease name

- Hepatitis A

13.4 | Priority level

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

13.5 | Background

- Although incidence decreased more than 95% from 1995 to 2011, it increased 10-fold from 2014 to 2019, primarily due to person-to-person outbreaks among people who use drugs and people experiencing homelessness.
- Universal immunization of children in the United States, recommended in 2006 by the Advisory Committee on Immunization Practices, should lower the risk of infection generally, and of transfusion transmission specifically as a fully immunized cohort enters the donor base.
- Produces disease only in humans and nonhuman primates.

13.6 | Common human exposure routes

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

13.7 | Likelihood of secondary transmission

- Moderate; from infected persons to close contacts

13.8 | At-risk populations

- International travelers
- Men who have sex with men
- Persons who use injection or noninjectable drugs (i.e., primarily those who use illegal drugs)
- Persons with occupational risk for exposure
- Persons who have had close personal contact with someone from an endemic country or area undergoing an outbreak
- Persons experiencing homelessness
- Persons at increased risk for severe disease from HAV infection
  - Persons with chronic liver disease
  - Persons with human immunodeficiency virus infection

13.9 | Vector and reservoir involved

- Infected humans and nonhuman primates

13.10 | Blood phase

- Viremia is observed concurrent with fecal shedding and often precedes the development of symptoms by at least 2 weeks; communicability is highest during this interval. Concentrations of virus found in blood are usually relatively low (~10^{3-5} 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 due to the coexistence of specific neutralizing antibody.

13.11 | Survival/persistence in blood products

- Infectivity maintained for the storage duration of the blood component/product

13.12 | 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 transfusion-transmission in adults in the United States is attributed to the availability of an effective vaccine and the prevalence of immunity in many recipients old enough to donate, a short infectious viremic stage, low incidence of HAV, absence of a carrier state, and neutralization of virus from a concurrent blood product that may contain specific antibody.
  - At least 40 cases have been reported since the early 1970s. The reports range from single cases to outbreaks involving as many as eleven recipients (with secondary spread to more than 40 contacts). Neonatal intensive care units, where exposure of multiple babies to aliquots from a single infectious unit can occur, may be particularly problematic.

13.13 | Cases/frequency in population

- Following years of decline, HAV activity increased starting in 2016–2017, peaking in 2019 with nearly 40,000 infections, more than 10 times the rate in 2013. In 2020 the rate declined by 47% but remained 7-fold higher than in 2015. The impact of the COVID-19 pandemic on infection and reporting is not clear. The increase was driven primarily by person-to-person transmission among people who use drugs and those experiencing homelessness.
- 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.

13.14 | 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.

13.15 | Likelihood of clinical disease

- The likelihood of symptomatic illness from HAV infection is correlated with age. In children younger than 6 years of age, 70% of infections are asymptomatic. In older children and adults, infection is usually symptomatic, with jaundice occurring in more than 70% of patients. 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.

13.16 | 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.

13.17 | 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 of these patients ranges between 33% and 63%.

13.18 | 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.

13.19 | Chronic carriage

- None

13.20 | Treatment available/efficacious

- Supportive
- Liver transplant for acute fulminant hepatitis

13.21 | Agent-specific screening question(s)

- None specifically for hepatitis A
  - Questions from the AABB Donor History Questionnaire (DHQ) include whether the donor is feeling well and healthy, has used needles to take drugs not prescribed by a physician, or has had sexual contact with a person who had hepatitis, and/or lived with a person who had hepatitis in the past 3 months.
  - Requiring an address for all donors reduces the HAV risk associated with homelessness.
  - During a common source outbreak, blood collection facilities should consider the need to prospectively solicit information from donors who may have been exposed to HAV. 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 possible association with an 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 a local hepatitis A outbreak

13.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- FDA-cleared diagnostic assays: total IgG/IgM anti-HAV and IgG or IgM-specific anti-HAV
- HAV RNA tests are available as validated assays to screen plasma for further manufacture.
  - Validated duplex tests for human plasma are available to quantify parvovirus B19 and detect HAV in a single assay.

13.23 | Currently recommended donor deferral period

- AABB recommends a deferral of 120 days following appropriately documented exposure to a community HAV outbreak that takes into account the potential for transmission from secondary HAV cases.

13.24 | 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.

13.25 | 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.

13.26 | Leukoreduction efficacy

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

13.27 | Pathogen reduction efficacy for plasma derivatives

- Efficacy is variable; cases of HAV transmission have been reported from coagulation factor concentrates prepared using the solvent-detergent (SD) method. Plasma used for further manufacture is required to be tested for HAV RNA; pooled NAT is used in combination with parvovirus B19 using validated tests.

13.28 | Other prevention measures

- Hepatitis A virus is generally not susceptible to pathogen inactivation treatments available for labile blood components.

- In addition to risk avoidance, vaccination is advised under the following circumstances: Universal immunization of children in the United States was recommended in 2006 by the Advisory Committee on Immunization Practices.
- Catch-up vaccination is recommended for those at risk who were not immunized in childhood and for certain children ages 6 through 11 months who are traveling outside of the US. Postexposure prophylaxis is available with vaccine and/or immune serum globulin under appropriate circumstances.

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