Enteroviruses

Disease Agent:

- Human enteroviruses, species A-D (Polioviruses, Coxsackieviruses, Echoviruses), and Rhinoviruses

Disease Agent Characteristics:

- Family: *Picornaviridae*; Genus: *Enterovirus* (Poliovirus 1 is the type species.)
- Virion morphology and size: Nonenveloped, icosahedral nucleocapsid symmetry, spherical particles, 30 nm in size
- Nucleic acid: Linear, nonsegmented, positive-sense, single-stranded RNA, 7.4-7.5 kb in length
- Physicochemical properties: Labile to heat at 60°C for 60 minutes or 100°C for 5 minutes; sensitive to guanidine and disoxaril; relatively resistant to 70% ethanol, 5% Lysol, quaternary ammonium compounds; insensitive to ether, chloroform, and deoxycholate (a bile acid) at room temperature; retains infectivity at pH 3.0 but labile at pH 1.0; sensitive to 0.3% formaldehyde, glutaraldehyde, sodium hypochlorite, and UV light; drying on surfaces significantly reduces virus titers

Disease Name:

- Many; see "Primary disease symptoms."

Priority Level

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

Background:

- Ubiquitous with wide variety of clinical manifestations; sporadic epidemics; many show seasonal variation

Common Human Exposure Routes:

- Predominantly fecal/oral transmission but also may spread via respiratory secretions and by direct contact (e.g., conjunctivitis)

Likelihood of Secondary Transmission:

- Moderate/high via gastrointestinal/respiratory shedding. This may not apply to parenterally acquired infection.

At-Risk Populations:

- Neonates, young children, patients with congenital and acquired B cell deficiencies (including acquisition following treatment with rituximab)
- Possibly patients undergoing hematopoietic cell transplant

Vector and Reservoir Involved:

- None

Blood Phase:

- Not well characterized for majority of serotypes
- Based on polio model, primary infection occurs with viral replication in the GI tract and draining lymph nodes. A brief period of viremia with very low levels of virus occurs approximately 2-9 days following infection in about 25% of all infections. However, a major viremia occurs following amplification of the virus in the reticuloendothelial tissues with subsequent development of clinical manifestations in target organs.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- Theoretically possible but not demonstrated
- Enterovirus RNA sequences were detected by RT-PCR in 19 minipools containing 95 component donor samples from 83,600 Scottish blood donors corresponding to a donor prevalence of at least 0.023%. Infectivity was not evaluated, and transmission was not investigated. Sequences were not detected in clotting factor concentrates.

Cases/Frequency in Population:

- Ubiquitous with regional and seasonal epidemics
- Young children are the most important transmitters of enteroviruses, especially within households although the incidence is low in the first 4-6 months of life in developing countries as a result of maternal protective antibody. As a result, children are more likely to develop significant symptomatology.
- Disease is more prevalent among lower socioeconomic populations and those living in urban areas. Disease is more common among males at a male-to-female ratio between 1.2 and 2.5:1.

Incubation Period:

- Not well characterized; major viremia thought to occur 6-9 days after exposure but may occur earlier and persist longer. Major symptoms occur after the viremia, which disseminates infection to target organs.
- For poliovirus, the incubation period is estimated to be 9-12 days (range: 5-35 days) and 11-17 days (range: 8-36 days) until the onset of paralysis.

Likelihood of Clinical Disease:

- In adults, the majority of infections are asymptomatic.
- The incidence and severity of symptoms is higher in children, especially neonates.
- Among susceptibles, only about 1 in 200 poliovirus infections result in paralytic disease.

Primary Disease Symptoms

- Enteroviruses can cause many clinical syndromes, including:
  - Poliomyelitis, paralysis, aseptic meningitis, encephalitis
  - Pleurodynia, myositis, myocarditis, pericarditis, chronic heart disease
  - Exanthems, herpangina, hand, foot, and mouth disease
  - Upper and lower respiratory illness
  - Hemorrhagic conjunctivitis
  - Diabetes mellitus
  - Severe neonatal infection with hepatitis.

Severity of Clinical Disease:

- Acute infection: Severity varies with age and immunocompetence of patient.
  - Adults: Usually asymptomatic or only mild symptoms
  - Neonates: Usually mildly symptomatic but may be severely affected and infection may be fatal. Enteroviruses are a common cause of fever in neonates. The likelihood of severe sequelae varies.
- Implicated as a cause of insulin-dependent diabetes mellitus, possibly via an immune response mechanism, although it is unclear how often this occurs
- Chronic infection: Suspected to occur in some target organs, e.g., polio, heart disease. Frequency and clinical significance is undetermined, except chronic enteroviral meningoencephalitis in B cell immunodeficiency can be lethal.

Mortality:

- It varies with age and agent but is uncommon where critical care medicine is available. Mortality occurs mainly in neonates; it may occur in immunodeficient patients.

Chronic Carriage:

- Unknown, but may occur in immunosuppressed patients.

Treatment Available/Efficacious:

- None

Agent-Specific Screening Question(s):

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

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- NAT increasingly used for diagnosis (generic enterovirus and subtype-specific assays are available in research and public health labs)
- Serologic assays available but not useful as screen
- Culture possible for some agents, not useful as screen

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer donor until signs and symptoms are resolved.

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:

- Unlikely to be effective, as RNA has been detected in plasma.

Pathogen Reduction Efficacy for Plasma Derivatives:

- Nonenveloped viruses, so solvent/detergent would be ineffective.
- Probably susceptible to heat inactivation

Other Prevention Measures:

- With the exception of poliovirus, no widely available vaccine.

Suggested Reading:

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