9 | *YERSINIA ENTEROCOLITICA*

9.1 | Disease agent

- *Yersinia enterocolitica*

9.2 | Disease agent characteristics

- Gram-negative, facultatively anaerobic, bacillus to coccobacillus, nonmotile, non-spore forming, facultatively intracellular bacterium.
- Order: Enterobacteriales; Family: *Enterobacteriacea*.
- Size: 0.5–0.8 × 1.0–2.0 μm.
- Nucleic acid: The genome of *Yersinia enterocolitica* is 4.6 Mb of DNA.
- Growth of *Y. enterocolitica* is enhanced by cold enrichment and exposure to 4°C for a period of time, and the organism is capable of growth at 4°C.

9.3 | Disease name

- Yersiniosis

9.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Low/Moderate; decreased frequency of transfusion-associated cases over the past 20 years.
- No transfusion related fatalities of *Y. enterocolitica* have been reported in the United States to the FDA since at least 2012; however, fatal cases (26 from 1975 to 2014) have been described outside of the US including the most recent (2015) from contaminated red cells in a post-partum female.
- Public perception and/or regulatory concern regarding blood safety: Very low.
- Public concern regarding disease agent: Absent.

9.5 | Background

- *Yersinia enterocolitica* is identified throughout the world, and is isolated from multiple environmental sources, including water, contaminated foods, and a wide range of wild and domestic animals. Foodborne outbreaks are recognized.
- It is an infrequently recognized cause of diarrhea and abdominal pain in the United States but is relatively more commonly identified in northern Europe. Infections have been documented in other parts of the world, including South America, Africa, and Asia, but *Y. enterocolitica* is not considered an important cause of tropical diarrhea.
- *Yersinia enterocolitica* is highly heterogeneous and can be divided into several bioserotypes, only a few of which are known to be associated with human disease. Most *Y. enterocolitica* strains causing human yersiniosis belong to bioserotypes 1B/O:8, 2/O:5,27, 2/O:9, 3/O:3, and 4/O:3.
- Inefficient isolation methods have compromised accurate estimation of the prevalence of *Y. enterocolitica* disease.

9.6 | Common human exposure routes

- Ingestion of contaminated foods (plants or animal origin)
- Direct contact with animal sources, particularly pigs

9.7 | Likelihood of secondary transmission

- Person-to-person transmission is rare. However, contamination of food by an infected food handler and nosocomial infections have been described.

9.8 | At-risk populations

- Infants and children have the highest risk of symptomatic infection.
- Individuals with advanced liver disease and syndromes associated with iron overload have the highest risk of septicemic disease.
- Rural populations and those living in cooler temperate zones.
- Certain racial and ethnic groups through exposure to particular foods and food preparation methods.

9.9 | Vector and reservoir involved

- Domestic animals (livestock) are the important animal reservoir. The major animal reservoir for strains that cause human illness is pigs.

9.10 | Blood phase

- Prolonged or recurrent bacteremia occurs in some individuals after acute or chronic symptomatic or subclinical infection.

- Persistent infection, when present, lasts for weeks in most instances, but it can persist for several years.

9.11 | Survival/persistence in blood products

- Full shelf life and beyond for whole blood and RBCs.
- Although significant bacterial growth increases over time, sepsis has been described with RBCs stored for as short a period as 14 days.
- Bacteria can survive in phagocytic cells and extracellularly.
- Plasma depletion typical of RBC units reduces or prevents complement-mediated killing of serum sensitive *Y. enterocolitica*.
- Time-dependent lysis of white blood cells releases additional organisms and senescence of RBCs releases iron that stimulates and supports growth.
- Variability in growth and survival in blood products among serotypes may be related to serum resistance at storage temperatures and their capacity to bind iron.

9.12 | Transmission by blood transfusion

- Multiple case reports (>50) of transfusion transmission of *Y. enterocolitica* from asymptomatic donors have occurred since 1975 (lack of reports prior to that may have been a result of shorter storage times in use), including from autologous transfusion. *Y. enterocolitica* accounts for more than half the cases of sepsis arising from transfusion of RBCs. At least one case of a transfusion reaction due to *Y. enterocolitica* contaminating a pooled platelet concentrate has been reported.
- Clinical disease symptoms in transfusion recipients may be a result of endotoxemia and/or subsequent growth of the organism.
- Symptoms usually are consistent with septic shock, less often include atypical symptoms such as diarrhea.

9.13 | Cases/frequency in population

- In 2019, compared with the previous 3 years, the reported incidence of *Y. enterocolitica* infection in the United States population increased by 153%, with an overall incidence of 1.4 per 100,000.
- Advances in laboratory testing to identify bacteria cannot entirely explain the observed increase in foodborne pathogen infections.
- Incidence of subclinical and asymptomatic infections is unknown.
- Transfusion-transmitted *Y. enterocolitica* infection may be decreasing in recent years possibly because of interventions, such as leukoreduction.

9.14 | Incubation period

- Food-borne gastroenteritis, typically 2–5 days.
- In most cases of transfusion-associated yersiniosis, fever and hypotension occurred 1–2 h after the start of transfusion of contaminated blood.

9.15 | Likelihood of clinical disease

- Rate of asymptomatic gastrointestinal infection is unknown.
- High in blood recipients who received a transfusion with a unit containing *Y. enterocolitica*.

9.16 | Primary disease symptoms

- *Yersinia enterocolitica* typically causes mild disease. Symptoms can include acute diarrhea, terminal ileitis, mesenteric lymphadenitis, and pseudoappendicitis.
- Enterocolitis accounts for two-thirds of reported cases of symptomatic *Y. enterocolitica* infections. This is characterized by fever, diarrhea, nausea, vomiting, and abdominal pain lasting 1–3 weeks. Patients with mesenteric adenitis and/or terminal ileitis have fever, right lower quadrant pain and tenderness, and leukocytosis, and as many as 10% may undergo operation for suspected appendicitis.
- A reactive polyarthritis, lasting less than a year in general, has been specifically related to the presence of HLA-B27 in individuals with yersiniosis. Ankylosing spondylitis rarely develops. Reiter's syndrome (arthritis, urethritis, and conjunctivitis) also has been reported and is associated with HLA-B27 antigen.
- Exudative pharyngitis is seen with *Y. enterocolitica* infections. In one enteritis outbreak in the United States, 8% of patients presented with acute pharyngitis and fever, without accompanying diarrhea.
- *Yersinia enterocolitica* septicemia is uncommon but severe and often fatal. It is most often reported in patients with underlying immunocompromising conditions, the elderly, and patients with iron overload. Septicemic patients may develop metastatic abscesses, endocarditis, and mycotic aneurysms.

9.17 | Severity of clinical disease

- Primary septicemic transfusion-related *Y. enterocolitica* infection is a severe disease.

9.18 | Mortality

- Death is uncommon with naturally acquired infection.
- High for *Y. enterocolitica* bacteremia related to transfusion; based on a recent review that included 55 published cases, the fatality rate is approximately 54%.

9.19 | Chronic carriage

- Metastatic infections after bacteremia can cause subacute and chronic infections, especially among high-risk individuals.
- Chronic infection after acute gastrointestinal infection has been alleged based on persisting gastrointestinal signs and symptoms, persistently positive serologies, and the development of rheumatic syndromes. Microbiologic documentation that viable organisms persist in these patients is not generally provided.

9.20 | Treatment available/efficacious

- Susceptible to a variety of antimicrobial agents including aminoglycosides, fluoroquinolones, chloramphenicol, tetracyclines, and trimethoprim-sulfamethoxazole.
- Clinical data do not support the efficacy of antimicrobial therapy for mild infections, although fecal shedding may be decreased. Treatment decisions must be individualized.

9.21 | Agent-specific screening question(s)

- No specific question is in use.
- Not indicated because of the low incidence of transfusion-associated *Yersinia* sepsis.
- Questions about recent gastrointestinal illness have been documented to lack sensitivity and specificity.

9.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Options for serologic tests include enzyme immunoassays that screen for antibody, especially IgM, directed to virulence plasmid-mediated outer proteins.
- Direct detection: *Yersinia* species grow well on media that support the growth of *Enterobacteriaceae*.
- Culture of whole blood and RBCs for *Y. enterocolitica* may be negative despite spiking of the blood with viable organisms. Intracellular sequestration has been hypothesized to account for such negative cultures.
- Other techniques that have been used include immunofluorescence assay, electrochemiluminescence, and nucleic acid test-based detection methods.

9.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- The length of a deferral period for a donor with diagnosed and resolved *Y. enterocolitica* gastroenteritis is unclear. In the absence of any chronic disease manifestations, it may be acceptable to consider such a donor as eligible when fully recovered, either spontaneously or after treatment.

9.24 | Impact on blood availability

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

9.25 | Impact on blood safety

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

9.26 | Leukoreduction efficacy

- The effectiveness of leukoreduction in reducing transmission and clinical cases of *Y. enterocolitica* is unknown.
- In laboratory studies, leukocyte reduction filtration can reduce *Y. enterocolitica* contamination by removing bacteria-laden phagocytic cells. Prefiltration storage at room temperature allows for free organisms to be phagocytized by white blood cells prior to filtration.

9.27 | Pathogen reduction efficacy for plasma derivatives

- Specific data indicate that the multiple steps in the fractionation process are robust and capable of

inactivating and/or removing bacteria at concentrations that may be present in plasma.

9.28 | Other prevention measures

- Visual examination of units of blood looking for gross contamination is unlikely to be sensitive.
- Testing of RBC units of 25 days or older for endotoxin or screening for bacteria by stained smear has been proposed, but rapid and reliable tests are not available.
- Storage of RBCs at 0°C has been proposed to possibly delay and reduce growth of *Y. enterocolitica*.

SUGGESTED READING

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