

## *Anaplasma phagocytophilum*

### Disease Agent:

- *Anaplasma phagocytophilum* (formerly referred to as *A. phagocytophila*, *Ehrlichia phagocytophila* and *Ehrlichia* species)

### Disease Agent Characteristics:

- Obligate, intracellular, Gram-negative bacterium with tropism for neutrophils
- Order: Rickettsiales; Family: Anaplasmataceae
- Size: 0.5-0.8  $\mu\text{m}$   $\times$  1.2-3  $\mu\text{m}$
- Nucleic acid: A circular DNA of about 1500 kb
- Physicochemical properties: The rickettsiae are susceptible to 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formaldehyde, and quaternary ammonium disinfectants and are sensitive to moist heat (121°C for at least 15 min) and dry heat (160-170°C) for at least 1 hour.

### Disease Name:

- Human granulocytic anaplasmosis (HGA); previously known as human granulocytic ehrlichiosis (HGE)

### Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Very low
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Absent, but low in focal endemic areas

### Background:

- Emergent; first described in 1994 as the causative agent of HGE

### Common Human Exposure Routes:

- Transmitted by the same vectors as those that transmit Lyme disease and babesiosis: *Ixodes scapularis* ticks in the Northeast and upper Midwest (also known as the deer tick or the black-legged tick); year-round seasonal occurrence peaks are synchronized with tick seasons in affected areas.
- *I. pacificus* transmits the infection in the western US, and *I. ricinus* transmits the infection in Europe.

### Likelihood of Secondary Transmission:

- None documented

### At-Risk Populations:

- Individuals at enhanced risk for exposure to infected ticks through outdoor activity, including those involved in hiking, gardening, clearing brush, etc.

### Vector and Reservoir Involved:

- Ticks of genus *Ixodes* (*I. scapularis*, *I. pacificus*, *I. ricinus*)
- The tick nymph is primarily responsible for transmission of Lyme disease, babesiosis, and HGA; because of its small size, the bite may not be noticed and consequently the tick not be removed before disease transmission occurs.
- White-footed mice (*Peromyscus leucopus*) and white-tailed deer (*Odocoileus virginianus*) serve as reservoir hosts.

### Blood Phase:

- The bacteremia lasts for days to a few weeks after the occurrence of symptoms.
- The duration and frequency of asymptomatic bacteremia have not been documented.

### Survival/Persistence in Blood Products:

- Viable organisms have been recovered from anticoagulated, refrigerated whole blood from infected patients for 2 weeks and transmitted by transfusion in animal models (sheep) after 13 days. In a single case (abstract), RBCs stored for 30 days from a seropositive/PCR-negative donor transmitted the organism to a recipient who at diagnosis was seroconverting, PCR positive, and febrile. In the one fully published case (see below), *A. phagocytophilum* survived for 15 days in packed RBCs.

### Transmission by Blood Transfusion:

- Two cases from asymptomatic donors were reported in the US. In neither were the blood components leukoreduced. In the one fully published case, the implicated donor unit was retrospectively identified as PCR positive for *A. phagocytophilum*; in this case, *A. phagocytophilum* was also isolated from the recipient by PCR, and antibody titers of 1:512 and 1:256 were detected by IFA at 50 and 81 days after donation.
- A cluster of cases of human-to-human transmission of *Anaplasma phagocytophilum* infection (and the first report of human granulocytic anaplasmosis [HGA] in China) associated with blood contact was reported in 2008. The infection was not confirmed by blood smear or culture in the index patient, but *A. phagocytophilum* DNA was amplified from and sequenced from the index patient who had been bitten by a tick, and nine family members or health-care workers who had been in close contact. All nine reported contact with the patient's blood; seven had contact with respiratory secretions. The index patient died before seroconversion, but all nine contacts seroconverted.

**Cases/Frequency in Population:**

- Seroprevalence:
  - Blood donors: 11.3% of Westchester County, New York donors, 0.5% of Wisconsin donors, and 3.5% of Connecticut donors had antibodies to *A. phagocytophilum*.
  - Residents: 0.4% in northern California, 3.4% in New York, 14.9% in northwestern Wisconsin had antibodies to *A. phagocytophilum*.
  - Patients: The seroprevalence of *A. phagocytophilum* in 271 South Korean patients with high fever is 8.9% by the western blot assay.
- Incidence: The reported annual US incidence is 1.4 per million population, with annual rates in parts of the Midwest above 4 per million. In 2007, 332 cases were reported to the Minnesota public health department (rate of 6.2/million population). The actual rates are certainly much higher in light of underreporting and lack of recognition of this often nonspecific infection.

**Incubation Period:**

- 7-10 days from tick bite to bacteremia and acute symptoms

**Likelihood of Clinical Disease:**

- Low to moderate
- Males outnumber females by a 2:1 ratio
- Immunocompromised and elderly patients may be at greater risk to develop more severe manifestations of disease.

**Primary Disease Symptoms:**

- Nonspecific febrile illness characterized by high-grade fever (>39°C), rigors, generalized myalgias, severe headache, and malaise often accompanied by thrombocytopenia, leukopenia, and elevated liver transaminases occurs approximately 5-21 days after a bite from an infected tick.
- Anorexia, arthralgias, nausea, nonproductive cough, and rash are sometimes present.
- Median duration of illness is 9 days (1-60 days).

**Severity of Clinical Disease:**

- Generally not severe
- Severe cases are characterized by prolonged fever, acute renal failure, gastrointestinal bleeding, septic shock-like illness, rhabdomyolysis, respiratory insufficiency, and secondary opportunistic infections.

**Mortality:**

- <1% mortality

**Chronic Carriage:**

- Not documented

**Treatment Available/Efficacious:**

- Tetracyclines (e.g., doxycycline) and rifamycins are therapeutically effective.

**Agent-Specific Screening Question(s):**

- No specific question is in use.
- Not indicated at this time because only two cases of transfusion transmission have been reported.
- No sensitive or specific question is feasible. In endemic areas, a question on exposure to tick bites has been shown to be ineffective in distinguishing *Babesia*-infected from *Babesia*-uninfected donors. This question probably also lacks sensitivity and specificity for *A. phagocytophilum*.

**Laboratory Test(s) Available:**

- No FDA-licensed blood donor screening test exists.
- Options for laboratory testing include blood smear microscopy, cell culture, IFA, EIA, and NAT.

**Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.
- In an individual who receives treatment, prudent practice would be to defer donor until signs and symptoms are gone and treatment is complete.
- Based on the natural history of infection, it may be prudent to defer an untreated individual for a minimum of 90 days (30 days beyond the longest duration of illness).

**Impact on Blood Availability:**

- Agent-specific screening question(s): Not applicable
- Laboratory test(s) available: Not applicable; serologic testing, if implemented in the future, could result in a deferral rate of 3-5% in selected collection areas.

**Impact on Blood Safety:**

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

**Leukoreduction Efficacy:**

- Unknown; however, based on studies with a related organism (*Orientia tsutsugamushi*) and location within WBCs, efficacy would likely be moderate to high.

**Pathogen Reduction Efficacy for Plasma Derivatives:**

- Not expected to be transmitted by plasma derivatives

**Other Prevention Measures:**

- Tick avoidance measures (e.g., long pants, long sleeves, insect repellent)
- Riboflavin/Light has been effective in inactivating *Orientia tsutsugamushi*, a related organism.

**Suggested Reading:**

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