

## Influenza A Virus (Highly Pathogenic Avian Influenza-H5N1)

### Disease Agent:

- Influenza A virus (H5N1)

### Disease Agent Characteristics:

- Family: *Orthomyxoviridae*; Genus: *Influenzavirus A* (subtype H5N1)
- Virion morphology and size: Enveloped, helical nucleocapsid, spherical to pleomorphic virions, 80-120 nm in diameter
- Nucleic acid: Linear, segmented, negative-sense, single-stranded RNA, ~13.6 kb in length
- Physicochemical properties: Virions are sensitive to treatment with heat, lipid solvents, nonionic detergents, formaldehyde, oxidizing agents; infectivity is reduced after exposure to radiation.

### Disease Name:

- Highly pathogenic avian influenza (HPAI)

### Priority Level:

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

### Background:

- Transmission to humans from domestic fowl was first described in Southeast Asia in 1997 with high mortality among both birds and humans.
- Transmission to humans is inefficient, and human disease is rare after 10 years of potential exposures.
- Global spread of H5N1 by birds may constitute a pandemic threat.

### Common Human Exposure Routes:

- Almost all recent exposures have had close contact with poultry.
- Unsustained H5N1 transmission from human to human has been documented rarely, under conditions of crowding.

### Likelihood of Secondary Transmission:

- Rarely occurs
- If circulating strains adapt for human-to-human transmission, an influenza pandemic could occur.

### At-Risk Populations:

- Usually, but not exclusively, occurs in children and young adults with very close contact to infected domestic fowl in Southeast Asia and Egypt.

- If adaptation to human-to-human transmission were to occur, the world's population is immunologically naïve and would be nearly universally susceptible.

### Vector and Reservoir Involved:

- Birds are the reservoir, although a number of mammalian species have been shown to be susceptible to infection.

### Blood Phase:

- Animal models of influenza A demonstrate viremia after experimental infection.
- Ferrets infected with HPAI develop disseminated infection, with virus isolated from nonrespiratory sites.
- Other human influenza A strains have been demonstrated to cause disseminated infection to organs outside the respiratory tract that suggests viremia occurs.
- A single case report describes influenza A H3N2 (Hong Kong) viremia in a naturally infected, asymptomatic patient, which would be most relevant to concerns about transfusion transmission.
- Influenza A virus has been isolated in blood and from extrapulmonary sites from patients with symptomatic H5N1.

### Survival/Persistence in Blood Products:

- Unknown

### Transmission by Blood Transfusion:

- This has never been documented, but there has been concern in the blood and regulatory communities in the context of pandemic planning.

### Cases/Frequency in Population:

- No sustained transmission of H5N1 in humans has been observed.
- H5N1 has now spread in birds from Asia to Europe and Africa with human cases detected as far west as Turkey and Egypt.
- 429 confirmed cases and 262 deaths reported to WHO from 2003 to May 2009
- Mutation of virus could allow human-to-human transmission that would increase concern.

### Incubation Period:

- Usually 2-9 days

### Likelihood of Clinical Disease:

- Ratio of asymptomatic to symptomatic disease is currently unknown.

**Primary Disease Symptoms:**

- Severe, with most patients presenting with an influenza-like illness of fever, cough, and shortness of breath
- Fulminant pneumonia and multiorgan failure develop in a high proportion of patients and are associated with poor outcomes.

**Severity of Clinical Disease:**

- Infections result in frequent hospitalization and death from respiratory and multiorgan failure.
- Median time from onset of illness to acute respiratory distress syndrome is 6 days.

**Mortality:**

- The mortality rate is over 60% for cases reported to WHO as of May 2009.
- High death rates are seen among infants and children.

**Chronic Carriage:**

- No

**Treatment Available/Efficacious:**

- Neuraminidase inhibitors (e.g., oseltamivir) that have in vitro activity are available, but clinical efficacy has not been proven.
- Resistance to neuraminidase inhibitors has already developed in Southeast Asia.
- Ventilatory support and other ICU care, with or without corticosteroids, and broad-spectrum antibiotics for bacterial superinfection are widely used.

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

- No specific question is in use, but symptomatic donors are excluded by current donor criteria ("Are you feeling well and healthy today?").
- No question is feasible for exposure to influenza A during a community outbreak or a pandemic.

**Laboratory Tests Available:**

- No FDA-licensed blood donor screening test exists.
- Antemortem diagnosis confirmed by viral isolation, experimental nucleic acid testing for H5N1-specific RNA, and the less sensitive antigen detection tests
- All tests have been validated for sputum/pharyngeal secretions but not for blood or blood fractions. Isolation may be higher from pharyngeal samples (at a median of 5.5 days).
- An RT-PCR assay in minipools has been evaluated in 10,272 blood donor samples. All were negative.

**Currently Recommended Donor Deferral Period:**

- No FDA Guidance or AABB Standard exists.

- Prudent practice would be to defer donor until signs and symptoms are gone.

**Impact on Blood Availability:**

- Agent-specific screening question(s):
  - Symptomatic infection is already cause for deferral.
  - If there is a concern about asymptomatic viremia, and a deferral for contact with influenza is considered during a seasonal outbreak or pandemic, the impact could be major.
- Laboratory test(s) available: No screening test is currently available; if screening for viremia by NAT were implemented, additional impact on availability is unknown.

**Impact on Blood Safety:**

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

**Leukoreduction Efficacy:**

- Unknown
- Likely to be minimal because of hemagglutinin antigen on influenza A and high levels of virus in RBC fractions in experimental models

**Pathogen Reduction Efficacy for Plasma Derivatives:**

- Virus inactivation steps used to manufacture derivatives (including pasteurization for albumin, solvent-detergent treatment for intravenous immunoglobulin, vapor heating for Factor VIII inhibitor bypassing activity, and incubation at low pH for intravenous immunoglobulin) were effective in one study using a reassortant strain of H5N1 influenza A.

**Other Prevention Measures:**

- Vaccines are under development and likely to be efficacious

**Suggested Reading:**

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