Influenza A and B Viruses (Other Than H5N1)

Disease Agents:

- Influenza A and B viruses

Disease Agent Characteristics:

- Family: *Orthomyxoviridae;* Genera: *Influenzavirus A* or *Influenzavirus B*
- 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 for influenza A and ~14.6 kb in length for influenza B
- Physicochemical properties: Virions are sensitive to treatment with heat, lipid solvents, nonionic detergents, formaldehyde, oxidizing agents; infectivity reduced after exposure to radiation.

Disease Name:

- Influenza

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: Moderate

Background:

- Seasonal epidemics are characteristic of influenza A and B. These are primarily in the late fall and winter in temperate climates.
- When major changes (antigenic shift) occur in influenza A antigens, pandemics occur with high attack rates and variable morbidity and mortality.
- Influenza B does not undergo shifts but evolves by antigenic drift and is not associated with severe pandemics.
- Depending on vaccine efficacy and other factors associated with epidemic activity , epidemics occur annually and pandemics every few decades
- Influenza A viruses infect avian species, humans, and several other mammalian species (especially swine). Influenza B infects only humans.

Common Human Exposure Routes:

- Person-to-person spread primarily via contact with droplets expelled during coughing and sneezing
- Virions are present in high titers in nasal secretions starting about 2-3 days after exposure and just before symptoms.
- Preschool and school-age children are major contributors to transmission of influenza A viruses.

Likelihood of Secondary Transmission:

- Characteristic of influenza following exposure to secretions from infected persons

At-risk Populations:

- Elderly individuals (>65 years)
- Infants and pregnant women
- Those with a variety of chronic medical conditions
- During pandemics, much larger segments of the population are immunologically naïve, and susceptible to infection.

Vector and Reservoir Involved:

- Influenza A viruses circulate in birds and mammalian species, especially pigs, where they undergo antigenic drift and shift with eventual transmission to humans.
- Influenza B infection is confined to humans.

Blood Phase:

- Animal models of influenza A demonstrate viremia after experimental infection.
- Virus isolation at autopsy from organs outside the respiratory tract (heart, CNS, kidney, spleen, liver, fetus) is indirect evidence of dissemination during natural infection that suggests viremia.
- Viremia and influenza A "RNA-emia" are described in a small series of symptomatic patients (who would have been disqualified as donors because of symptoms).
- 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.
- Experimental human infections have been accompanied by viremia during the incubation period, but the relevance of the high-dose intranasal inoculation (as opposed to the natural droplet route) has been questioned.
- Influenza B viremia was detected in 4 of 11 pediatric patients 2-4 days after symptom onset.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- Never documented

Cases/Frequency in Population:

- The incidence varies from season to season, but population attack rates during a pandemic first wave can approach 40%. During seasonal epidemics, rates of up to 18% are seen (higher in children) and up to 70% in confined or selected populations.

- Worldwide prevalence: Up to 10% of weekly mortality attributable to influenza during outbreaks
- In March-April 2009, a new strain of influenza A H1N1 was isolated in Mexico and then rapidly worldwide. The spread of the virus and disease soon qualified as a level 5 of 6 (the highest indicating a pandemic) using the WHO influenza pandemic definitions. Although formally achieving the existing WHO criteria for level 6, by community spread of the new H1N1 virus in a second region by the end of May, the WHO did not raise the pandemic alert to level 6 until June 11, 2009. This is the organization's first flu pandemic declaration in more than 40 years. Raising the alert to level 6 does not indicate the disease is more fatal or riskier than at level 5, but that it has spread to an increasing number of countries. As of June 11, 2009:
  - 74 countries reported 28,774 cases including 144 deaths
  - 94% of global cases are from the Americas with most from Mexico
  - Cases of disease have been milder than expected based on initial reports from cases in Mexico
- Phylogenetic cluster analyses using the new H1N1 strain and its closest relatives support the fact that the 2009 worldwide H1N1 virus derived from one or multiple reassortments between influenza A viruses circulating in swine in Eurasia and in North America (H1N1, H1N2 and H3N2).
- Receipt of recent (2005-2009) seasonal influenza vaccines is unlikely to elicit a protective antibody response to the novel H1N1 virus
  - 2-fold increase in cross-reactive antibody in those aged 18-64 (compared to a 12- to 19-fold for the seasonal H1N1 influenza strain)

Incubation Period:

- 1-5 days (longer for influenza B virus)

Likelihood of Clinical Disease:

- Based on experimental infection, most influenza A cases are symptomatic, with high fever in 60-90% of subjects.
- Asymptomatic influenza A infection does occur and was documented in 4 of 34 infected prisoners.
- While some authorities suggest that influenza B is milder than A, most believe they closely resemble each other.

Primary Disease Symptoms:

- Abrupt onset of fever of 38-40°C but can reach 41°C when symptoms first develop; usually continuous but may come and go; may be lower in older adults than in children and younger adults
- Myalgias, commonly occurring in the back, arm, or legs
- Headache, chills, dry cough
- Retro-orbital pain, conjunctivitis
- Fatigue, malaise, anorexia
- Tracheobronchitis with rhinorrhea; cough can persist for 1 or 2 additional weeks after fever and upper respiratory tract symptoms resolve.

Severity of Clinical Disease:

- Symptoms can be severe and associated with increased hospitalizations during epidemics (1/2900 infected for 1- to 44-year-old group and 1/270 infected for those older than 65 years).
- During the past four influenza seasons, the peak percentage of patient visits for influenza-like illness ranged from 4.0 to 7.6%.

Mortality:

- Influenza is the cause of excess mortality each year, especially in persons >65 years (1/2200 infected increasing to 1 in 300 infected during a pandemic)
- During pandemics mortality is generally highest at the extremes of age; however, during the 1918 pandemic, there was a mortality peak in young adults.

Chronic Carriage:

- No

Treatment Available/Efficacious:

- Several antiviral drugs (amantadine and rimantadine) and neuraminidase inhibitors (zanamivir, oseltamivir) are available that have both prophylactic and clinical efficacy, although resistance, including transmission of primary resistant strains, is a major concern.

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 or B during a community outbreak.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Antemortem diagnosis confirmed by viral isolation, experimental nucleic acid testing for virus-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 for the associated influenza A H5N1 subtype 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 a 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, but thought to be minimal because of hemagglutinin moiety of influenza and high levels of virus in plasma and 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 developed annually have moderate impact on tempering seasonal epidemics.

Suggested Reading:

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