

Variola Virus

Disease Agent:

- Variola virus

Disease Agent Characteristics:

- Family: *Poxviridae*; Subfamily: *Chordopoxvirinae*; Genus: *Orthopoxvirus*; Species: Variola
- Virion morphology and size: Enveloped, biconcave core with two lateral bodies, brick shaped to pleomorphic virions, 360 × 270 × 250 nm in size
- Nucleic acid: Nonsegmented, linear, covalently closed, double-stranded DNA, ~18.6 kb in length
- Physicochemical properties: Stable in dried condition (survives at room temperature in crusts for over a year and for ~3 months in the dark and over a month in the light when dried on slides); killed by heating at 60°C for 10 minutes when moist, but can withstand 100°C for 5-10 minutes when dry; sensitive to UV light (sunlight); inactivated by sodium hypochlorite or by formaldehyde at a concentration of 0.2% in 24 hours at room temperature; resistant to 1% phenol for weeks at 4°C but inactivated within 24 hours at 37°C; may retain infectivity for several hours even if aerosolized

Disease Name:

- Smallpox (variola major and variola minor or variola alastrim)

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Absent; there is no risk to the blood supply in the absence of accidental or intentional release of variola, or a threat of bioterrorism sufficient to require a significant and widespread reintroduction of smallpox immunization.
- Public concern regarding disease agent: Very low; natural variola has been eradicated, and risk remains low but not absent because of the risks of a bioterrorism event or accidental release of the virus.

Background:

- Natural transmission eradicated in 1977. Remains a bioterrorism threat because of archived stocks in the US and former Soviet Union.
- Classified among the highest priority for bioterrorism agents by the CDC (Category A)

Common Human Exposure Routes:

- Inhalation of large airborne respiratory droplets usually through close contact
- Lower transmissibility from fomites or contact with infectious material in scabs.

Likelihood of Secondary Transmission:

- Significant by direct contact or inhalation (58% in unvaccinated close or household contacts or 3.8% in previously vaccinated close contacts)
- Parenteral transmission has not been recognized.

At-Risk Populations:

- All unimmunized people and those with waning immunity from prior vaccination in the event of reintroduction of the virus
- A threat as a bioterrorist weapon for populations not previously considered being at risk

Vector/Reservoir Involved:

- None

Blood Phase:

- By the third or fourth day after infection, virus-infected macrophages enter regional lymph nodes and possibly the blood stream. This is before prodromal symptoms develop at 7-17 days after infection.
- Secondary viremia (which is also largely cell associated) occurs with the onset of symptoms.

Survival/Persistence in Blood Products:

- Unknown

Transmission by Blood Transfusion:

- None observed or documented

Cases/Frequency in Population:

- Zero at this time

Incubation Period:

- 7-17 days after exposure

Likelihood of Clinical Disease:

- High; may be even higher (greater mortality) with engineered bioterrorism strains

Primary Disease Symptoms:

- Initial onset of symptoms is 7-17 days after exposure. Starts with 3-day prodrome: fever (38.3-40°C up to 3 days before the rash), prostration, headache, backache, vomiting
- Toxemic phase including a rash that typically begins centrally and spreads peripherally to the extremities (primarily upper) and face. Typically, by 14 days after

infection, the characteristic progression of skin lesions is observed: macules, papules, vesicles, pustules, umbilication (classic and characteristic), and crusting

- All lesions are in a single stage of development.

Severity of Clinical Disease:

- Severity of disease is correlated with rash burden; it is more severe in children or pregnant women.

Mortality:

- Variola major: 10-30%; variola minor: <1%; may be higher with engineered bioterrorism strains

Chronic Carriage:

- None

Treatment Available/Efficacious:

- There is no specific chemotherapeutic agent for smallpox. Antibiotics may be used for coincident secondary infections, and vaccinia immune globulin may modify the disease course.

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.
- Under circumstances of accidental or deliberate release, the need for, and potential effectiveness of, specific donor screening questions would need to be addressed.

Laboratory Test(s) Available:

- No FDA-licensed blood donor screening test exists.
- Serology, NAT, and virus isolation are available, but primarily in specialized labs, and there are no assays currently suitable for high throughputs screening. Generic orthopox PCR and negative stain electron microscopy (EM) identification of a pox virus in a clinical specimen are suggestive of an orthopox virus infection but not diagnostic for smallpox.
- Laboratory diagnostic testing for variola virus should be conducted in a CDC Laboratory Response Network facility utilizing approved PCR tests and protocols for variola virus.

Currently Recommended Donor Deferral Period:

- No FDA Guidance or AABB Standard exists.
- Not applicable as there is no likelihood of exposure in the absence of an accidental or deliberate release of virus.
- Guidance will likely be issued should disease activity become recognized.

Impact on Blood Availability:

- Agent-specific screening question(s): Not applicable; in response to an accidental or deliberate release, impact of a local deferral would be significant.
- Laboratory test(s) available: Not applicable

Impact on Blood Safety:

- Agent-specific screening question(s): Not applicable; unknown impact in response to an accidental or deliberate release
- Laboratory test(s) available: Not applicable

Leukoreduction Efficacy:

- Unknown
- Cellular tropism studies using primary hemato-lymphoid cells suggest some viral clearance by leuko-reduction can be anticipated.

Pathogen Reduction Efficacy for Plasma Derivatives:

- Inactivation of the closely related vaccinia virus below the limit of detection was demonstrated in one study (that used 6 logs of virus) with pasteurization, caprylate, and solvent-detergent treatments. Filtration of plasma reduced titers approximately 4 logs in one study. Efficacy for variola virus is expected to be similar to vaccinia.

Other Prevention Measures

- Smallpox (vaccinia) vaccination for at-risk persons

Suggested Reading:

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- virus after smallpox vaccination in Italy. *J Gen Virol* 2005;86:2955-60.
6. Schmidt M, Roth WK, Meyer H, Seifried E, Hourfar MK. Nucleic acid test screening of blood donors for orthopoxviruses can potentially prevent dispersion of viral agents in case of bioterrorism. *Transfusion* 2005; 45:399-403.
 7. Smith SA, Kotwal GJ. Immune response to poxvirus infections in various animals. *Crit Rev Microbiol* 2002; 28:149-85.
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