2 | BORNA DISEASE VIRUS

2.1 | Disease agent

- Mammalian 1 Orthobornavirus; species: Borna disease virus (BoDV-1 and 2)

2.2 | Disease agent characteristics

- Family: Bornaviridae; Genus: Orthobornavirus.
- Virion morphology and size: Enveloped, helical nucleocapsid, spherical, 90–130 nm.
- Nucleic acid: Linear, non-segmented, negative-sense, single-stranded RNA, 8.9 kb in size.
- Physicochemical properties: Cell-free virion infectivity is inactivated by heating at 56°C for 0.5–3 h, but more stable in tissues or in the presence of serum; under in vitro conditions, virions are relatively stable when stored at 37°C, with minimal loss of infectivity after 24 h in the presence of serum; stable after drying and for at least 3 months at 4°C; tolerant of alkaline pH, but inactivated below pH 4; sensitive to treatment with organic solvents and detergents, and infectivity is reduced after exposure to ultraviolet light and irradiation.

2.3 | Disease name

- Borna disease

2.4 | Priority level

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

2.5 | Background

- 1766: Borna disease first described in European sheep and horses.
- The name Borna refers to the city of Borna, Germany where an equine epidemic occurred during the late 1800s, crippling the Prussian cavalry.
- BoDV-1 naturally infects ostriches, horses, cattle, sheep, dogs, cats, shrews, and foxes. It is experimentally transmitted to non-human primates.
- 1996: BoDV-1 isolated from patients with mood disorders.
- 2015: Novel bornavirus initially discovered in variegated squirrels (variegated squirrel bornavirus-1; VSBV-1), and was confirmed in four human cases of fatal encephalitis.
- 2018: BoDV-1 was identified as a causative agent of severe and fatal encephalitis in three recipients of solid organ transplants from the same donor from Southern Germany. Recipients of both kidneys died; liver recipient in remission; 99.3%–99.7% nucleotide sequence identity from brain tissue of one kidney recipient to shrews and horses in Bavaria.
- Only infrequently has viral nucleic acid been found in human blood.

2.6 | Common human exposure routes

- Unknown, but contact with infected domestic animals, such as horses, sheep, and cats has been proposed.

2.7 | At-risk populations

- Unknown

2.8 | Likelihood of secondary transmission

- Unknown

2.9 | Vector and reservoir involved

- Sporadic enzootic disease of horses and sheep, although host range is wide; however, mode of transmission is unknown.
- Neonatal rats experimentally infected with BoDV-1 develop viral persistence, so rodents are a theoretical reservoir and vector; antibodies against BoDV have been detected in a few wild rodents, but specificity of BoDV antibodies is controversial.
- In 2006, the bi-colored, white-toothed shrew (Crocidura leucodon) was identified as a reservoir host in an area of Switzerland and in Southern Germany where BoDV-1 is prevalent in horses and sheep; the existence of other reservoir species has not been ruled out.

2.10 | Blood phase

- Unknown; but transcripts and proteins have been detected in peripheral blood mononuclear cells (PBMC) from patients with acute or chronic
psychiatric disease and in healthy persons. In these studies, cross-contamination and cross-reactivity have not been ruled out.
- BoDV RNA was not detected in 100 white cell pellets and in pools representing 25,000 plasma donations from Scottish blood donors.

2.11 | Survival/persistence in blood products
- Unknown

2.12 | Transmission by blood transfusion
- Never reported. However, the organ transplant cluster justifies continued attention. The organ transplant cluster emphasizes the zoonotic potential of BoDV-1 transmission that can lead to potentially lethal disease, and thus should be considered in cases of viral encephalitis with potential direct or indirect contact with bornavirus reservoirs.

2.13 | Cases/frequency in population
- World-wide natural infection of domestic animals.
- BoDV-1 has been identified as a causative agent in at least 18 naturally acquired sporadic or transplant-associated fatal human encephalitis cases.
- Seroprevalence previously reported in hospitalized patients with psychiatric, neurologic, and/or immunologic disorders ranged from 6% to 37%, but only 1%–2% in healthy volunteers; these data have not been reproduced, and thus may reflect cross-reactivity or non-specificity of the test assay used, or cross-contamination of controls.
- In a study from Bavaria, Germany, brain tissues from 56 encephalitis cases of putative viral origin (1999–2019) were submitted for virological testing and screened for BoDV-1 RNA. BoDV-1 nucleic acid, confirmed with antibodies, was detected in 8 encephalitis cases. Six of the 8 had no record of immunosuppression before the onset of fatal disease, whereas two were immunocompromised after solid organ transplantation. Viral RNA was not detected in any serum sample tested from 7 of the 8 cases. BoDV-1 sequence information and epidemiological analysis indicated spillover transmissions most likely from the local wild animal reservoir.

2.14 | Incubation period
- Approximately 1–3 months for horses and sheep
- Unknown human incubation period

2.15 | Likelihood of clinical disease
- At least 18 BoDV-1 naturally acquired sporadic or transplant-associated fatal human encephalitis cases have been identified.
- There is no information about transfusion transmission.

2.16 | Primary disease symptoms
- Causes severe, frequently fatal neurological disease in horses and sheep.
- Cause of severe often fatal neurologic disorders (encephalitis) in humans.
- Any role in psychiatric diseases remains to be proven.

2.17 | Severity of clinical disease
- Disease in humans believed to be a severe or lethal infection of the central nervous system. For patients with severe neurological disease of unknown etiology, healthcare providers should consider testing for BoDV-1, especially those who reside in, or traveled to, areas endemic for animal Borna disease.

2.18 | Mortality
- Acute Borna disease in animals and humans results in high mortality.

2.19 | Chronic carriage
- Unknown in humans.
- Bi-colored, white-toothed shrews appear to be a natural viral reservoir, with probable lifelong virus persistence. Shrews stay healthy and show no signs of neural inflammation, despite a broad range of infected tissues.
- Horses: Lifelong persistence with short periods of activation and long periods of inactivity.
2.20 | Treatment available/efficacious

- No consensus

2.21 | 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.

2.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Generally accepted standards for diagnosis of human BoDV infection not established.
- Options for laboratory testing include immunofluorescence, immunoprecipitation, and western blot (specific antibodies in serum and cerebrospinal fluid (CSF)), flow cytometry (BoDV nucleic acid and antigens in PBMC), tissue culture (BoDV in CSF), and RT-PCR (saliva, nasal or conjunctival fluid).

2.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.

2.24 | Impact on availability

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

2.25 | Impact on blood safety

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

2.26 | Leukoreduction efficacy

- Unknown. If truly highly cell-associated there would be theoretical interest

2.27 | Pathogen reduction efficacy for plasma derivatives

- Multiple pathogen reduction steps used in the fractionation process have been shown to be robust in the removal of enveloped viruses.

2.28 | Other prevention methods

- None

SUGGESTED READINGS


