35 | PORCINE ENDOGENOUS RETROVIRUS

This fact sheet is archived and will not be further updated without further evidence that the pathogen poses a threat in the context of transfusion medicine.

35.1 | Disease agent

- Porcine endogenous retrovirus (PERV)

35.2 | Disease agent characteristics

- Family: *Retroviridae*; Genus: *Gammaretrovirus*
- Virion morphology and size: Enveloped, icosahedral concentric nucleocapsid, spherical to pleomorphic particles, 80–100 nm in diameter
- Nucleic acid: Linear, positive-sense, single-stranded RNA, ~8.0–8.5 kb in length
- Physicochemical properties: Sensitive to heat, detergents, and formaldehyde

35.3 | Disease name

- None

35.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical.
- Public perception and/or regulatory concern regarding blood safety: Absent, given the current moratorium on xenotransplantation in the United States. However, this is an issue for public health and regulatory agencies based on the perception that xenotransplant recipients or their contacts will become blood donors and may transmit these agents.
- Public concern regarding disease agent: Absent, given the current moratorium on xenotransplantation.

35.5 | Background

- The concern for transmission to humans as a result of xenotransplantation comes from experimental studies disclosing that the virus can be transmitted to human cell cultures in vitro.
- The A and B strains of PERV can infect human cells in vitro, but the C virus appears to be confined to pigs.
- Porcine heart valve and porcine-derived Factor VIII have been shown to contain viral components, but recipients have not been infected.

35.6 | Common human exposure routes

- Xenotransplantation could theoretically transmit to humans. Secondary transmission from these people to their intimate contacts has been hypothesized. Other exposures, such as those related to animal husbandry, would also be theoretical routes.

35.7 | Likelihood of secondary transmission

- Unknown

35.8 | At-risk populations

- See common human exposure routes. There is no documented at-risk human population to date.

35.9 | Vector and reservoir involved

- Pigs

35.10 | Blood phase

- Unknown

35.11 | Survival/persistence in blood products

- Unknown

35.12 | Transmission by blood transfusion

- Not demonstrated; human infection has never been demonstrated by any route, although infection of human cell lines and horizontal transfer among human cells has been shown in vitro.

35.13 | Cases/frequency in population

- Unknown or absent

35.14 | Incubation period

- Not characterized

35.15 | Likelihood of clinical disease

- No human disease has been recognized.

35.16 | Primary disease symptoms

- Not applicable

35.17 | Severity of clinical disease

- Not applicable

35.18 | Mortality

- Not applicable

35.19 | Chronic carriage

- Unknown in humans.
- Virus is integrated into genome of normal host (pig) cells.

35.20 | Treatment available/efficacious

- Not applicable

35.21 | Agent-specific screening question(s)

- No specific question is in use for blood donors; however, questions regarding xenotransplantation are required by FDA for donors of human cell, tissue, and cellular- and tissue-based products (HCT/P).
- Not indicated because human infection by any route, including transfusion, has not been demonstrated, and, currently, there is a moratorium on xenotransplantation in the United States.
- As xenotransplantation studies resume, blood organizations have emphasized that it is the responsibility of the transplant team to provide xenotransplant recipients and intimate contacts with a warning against their providing blood, tissue, and organ donation.

35.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Research tests include NAT and virus expression by cocultivation with cell lines.

35.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists for blood donors.
- Permanent deferral was previously proposed in draft guidance from FDA for xenotransplant recipients and their intimate contacts. However, final guidance has not been issued for blood donors, and there is a continuing moratorium on xenotransplantation.

35.24 | Impact on blood availability

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

35.25 | Impact on blood safety

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

35.26 | Leukoreduction efficacy

- Unknown; theoretically could have an impact if putative human infection is leukocyte associated.

35.27 | Pathogen reduction efficacy for plasma derivatives

- No specific data available but presumed to be robust, as the agent is an enveloped virus that should be sensitive to many measures used in the fractionation process

35.28 | Other preventive measures

- Pathogen reduction would be expected to have efficacy, based on studies with other retroviruses.
- CRISPR-CAS9 technology has been shown to be capable of inactivating PERV allowing the generation of PERV-inactivated pigs via somatic cell nuclear transfer. This may mitigate the risks of xenotransplantation.

SUGGESTED READING

1. Fishman JA, Patience C. Xenotransplantation: infectious risk revisited. Am J Transplant. 2004;4:1383–90.
2. Herring C, Cunningham DA, Whittam AJ, Fernández-Suárez XM, Langford GA. Monitoring xenotransplant recipients for infection by PERV. Clin Biochem. 2001;34: 23–7.
3. Leyh RG, Wilhelmi M, Walles T, Kallenbach K, Rebe P, Oberbeck A, et al. Acellularized porcine heart valve scaffolds for heart valve tissue engineering and the risk of cross-species transmission of porcine endogenous retrovirus. J Thorac Cardiovasc Surg. 2003;126:1000–4.
4. Magre S, Takeuchi Y, Bartosch B. Xenotransplantation and pig endogenous retroviruses. Rev Med Virol. 2003;13: 311–29.
5. Niu D, Wei HJ, Lin L, George H, Wang T, Lee IH, et al. Inactivation of porcine endogenous retrovirus in pigs using CRISPR-Cas9. Science. 2017;357(6357):1303–7.
6. Ogle BM, Butters KA, Plummer TB, Ring KR, Knudsen BE, Litzow MR, et al. Spontaneous fusion of cells between species yields transdifferentiation and retroviral transfer in vivo. FASEB J. 2004;18:548–50.
7. Paradis K, Langford G, Long Z, Heneine W, Sandstrom P, Switzer WM, et al. Search for cross-species transmission of porcine endogenous retrovirus in patients treated with living pig tissue. Science. 1999;285:1236–41.
8. Patience C, Scobie L, Quinn G. Porcine endogenous retrovirus-advances, issues and solutions. Xenotransplantation. 2002;9: 373–5.
9. Winkler ME, Winkler M, Burian R, Hecker J, Loss M, Przemeck M, et al. Analysis of pig-to-human porcine endogenous retrovirus transmission in a triple-species kidney xenotransplantation model. Transpl Int. 2004;17: 848–58.
10. Yoo D, Giulivi A. Xenotransplantation and the potential risk of xenogeneic transmission of porcine viruses. Can J Vet Res. 2000;64:193–203.