38 | RABIES VIRUS

38.1 | Disease agent

- Rabies virus

38.2 | Disease agent characteristics

- Family: *Rhabdoviridae*; Genus: *Lyssavirus*.
- Morphology and size: Enveloped, bullet-shaped, 45–100 nm in diameter, 100–430 nm in length.
- Nucleic acid: Single-stranded, linear, negative-sense RNA genome, ~11.9 kb in length.
- Physicochemical properties: Susceptible to 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol, formaldehyde, and quaternary ammonium compounds. Inactivated on exposure to ultraviolet radiation, by heat (1 h at 50°C), and by lipid solvents. Rabies virus is inactivated rapidly in sunlight and does not survive for long periods out of the host unless protected in a cool, dark area.

38.3 | Disease name

- Rabies

38.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Absent
- Public perception and/or regulatory concern regarding blood safety: Very low
- Public concern regarding disease agent: Moderate to high

38.5 | Background

- Rabies is a neglected zoonotic disease that causes an estimated 60,000 human deaths annually worldwide. Rabies virus is transmitted by contact membranes; most human and animal viral exposures result from the bite of an infected animal.
- Pathogenesis involves transport of virus centripetally along peripheral nerves to the central nervous system where virus replicates, followed by centrifugal transport via peripheral nerves to multiple organs and tissues. The latter is responsible for transmission via transplantation.
- The pathogenesis of rabies is associated with the inability to deliver immune effectors across the blood-brain barrier and to clear virulent rabies virus from CNS tissues.

38.6 | Common human exposure routes

- While rabid dogs are the source of approximately 99% of global human infections, in the United States, 70% of reported cases were attributed to bats, whereas dog bites during international travel were the cause of 28% of cases.
- Aerosol exposure has been recognized in laboratory spread and natural settings (e.g., bat caves).
- From 1978 to 2017, at least 13 cases of rabies transmission via organ and tissue transplants have occurred globally resulting in reported fatalities from both high or low-risk countries.

38.7 | Likelihood of secondary transmission

- Low; the rare cases from transplanted tissues and organs involved in rabies transmission were corneas, kidneys, liver, heart, lungs, pancreas, and iliac artery from donors with unrecognized rabies.

38.8 | At-risk populations

- Animal handlers (veterinarians, etc.).
- Individuals living in proximity to infected mammals, especially bats.
- Those at risk include urban residents as well as rural populations.

38.9 | Vector and reservoir involved

- Wild animals in the United States: bats, raccoons, skunks, foxes.
- Domestic animals (cats, cattle and dogs) can be infected following contact with infected feral species and are the most frequently reported rabid domestic animals in the United States.

38.10 | Blood phase

- Viremia has not been demonstrated (this is contested)

38.11 | Survival/persistence in blood products

- No data

38.12 | Transmission by blood transfusion

- Rare cases of transmission by organ/tissue transplantation probably associated with infection of neurologic components in transplanted allografts.
- There has never been a reported case of rabies infection via a blood transfusion. Viremia has not been demonstrated in New World nonhuman primates, but viremia remains contested in humans. Viremia has been detected in mice and rabbits prior to the development of neutralizing antibody, and the virus is intraneuronal during the incubation period. There is no evidence to suggest that an apparently healthy blood donor can transmit rabies, even if incubating clinical rabies.

38.13 | Cases/frequency in population

- 128 cases of human rabies have been reported in the United States from 1960 to 2018 accounting for two deaths per year.
- Approximately 55,000 people in the United States seek postexposure prophylaxis each year after contact with a potentially rabid animal.

38.14 | Incubation period

- <30 days (25%)
- 30–90 days (50%)
- 90 days (about 3 months)-1 year (20%)
- >1 year (5%)

38.15 | Likelihood of clinical disease

- High after significant exposure without postexposure prophylaxis

38.16 | Primary disease symptoms

- Fever, malaise, anorexia
- Paresthesia or pain at wound site
- Rapid progression to cerebral dysfunction and death
- Two polar clinical syndromes: "furious" or encephalitic rabies and "dumb" or paralytic rabies

38.17 | Severity of clinical disease

- High

38.18 | Mortality

- Virtually 100% in the absence of postexposure prophylaxis

38.19 | Chronic carriage

- None, although incubation period may last >1 year

38.20 | Treatment available/efficacious

- Investigational and anecdotal
- Since the introduction of cell-based vaccines in the mid-1970s postexposure prophylaxis has never failed in the United States, when used promptly postexposure.

38.21 | Agent-specific screening question(s)

- No specific question is in use, except for recent immunizations
- Not indicated because transfusion transmission has not been demonstrated
- No sensitive or specific question is feasible.

38.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Multiple tests are available to diagnose rabies antemortem in humans.
- Direct viral detection tests are performed on samples of saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck. Saliva can be tested by virus isolation or reverse transcription followed by RT-PCR.
- Serum and spinal fluid can be tested for antibodies to rabies virus.

38.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- No deferral after possible rabies exposure is required.
- Some facilities may require temporary deferral for prophylaxis because of confusing infectious disease test serologies that may occur following receipt of hyperimmune globulin (e.g., anti-HBc).

38.24 | Impact on blood availability

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

38.25 | Impact on blood safety

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

38.26 | Leukoreduction efficacy

- Unknown

38.27 | Pathogen reduction efficacy for plasma derivatives

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

38.28 | Other prevention measures

- Postexposure prophylaxis with hyperimmune globulin and vaccine
- Vaccination (with inactivated vaccine)
- Education

SUGGESTED READING

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