2 | *LEISHMANIA* SPECIES

2.1 | Disease agent

- *Leishmania* Species

2.2 | Disease agent characteristics

- Protozoan. Amastigotes are intracellular: 3–6 μm × 1–3 μm; promastigotes quite a bit larger, extracellular, motile, and found in the alimentary tract of sandflies.
- Order: Kinetoplastida.
- Family: *Trypanosomatidae*.
- Intracellular pathogen of macrophages/monocytes.
- Promastigotes are injected into humans by sandflies; amastigotes multiply in cells of various tissues and infect other cells.

2.3 | Disease name

- Leishmaniasis.
- Visceral leishmaniasis is called kala-azar in India and various names elsewhere.
- Cutaneous forms have a variety of colloquial names around the world.
- Mucocutaneous leishmaniasis.

2.4 | Priority level

- Scientific/epidemiologic evidence regarding blood safety: low.
- Public perception and/or regulatory concern regarding blood safety: low.
- Public concern regarding disease agent: Low, but moderate among military personnel deployed in endemic areas.
- Concern among ecotourists and travelers to endemic areas: moderate.

2.5 | Background

- Leishmaniasis is a vector-borne protozoan infection with a wide clinical spectrum, which ranges from asymptomatic infection to fatal disease. Infections in humans are caused by more than 20 species of *Leishmania*. The parasite is found in more than 100 countries around the world—including the New World (Mexico and those in Central and South America), and the Old World (Asia, Africa, the Middle East, and southern Europe). The infection rarely occurs in the United States, although a few cases have been reported to have been acquired in Texas and Oklahoma. Increasing number of travelers, soldiers, and immigrants with leishmaniasis are being observed in the United States. Leishmaniasis is an increasingly common infection in ecotourists traveling to Central and South America.
- Generally limited to tropical and sub-tropical climates.
- Considered stable, but with sporadic outbreaks like those recently observed in Sudan, Ethiopia, Kenya, India, and in South American countries.
- Two million new cases worldwide each year: 1.5 million cutaneous and 0.5 million visceral.
- Nine US soldiers who served in the Persian Gulf area in 1990 were found to have viscerotropic *L. tropica* infections. They experienced a nonspecific febrile illness with fatigue, arthralgia, and diarrhea. Some soldiers recovered spontaneously, whereas others progressed and developed a chronic condition with adenopathy or splenomegaly. These events led to concern about the safety of returnees from the Persian Gulf as blood donors. A survey conducted by the Department of Defense regarding cases of cutaneous leishmaniasis in military personnel deployed to three countries (Afghanistan, Iraq, and Kuwait) and in Southwest/Central Asia during August 2002—February 2004, identified 522 parasitologically confirmed cases.

2.6 | Common human exposure routes

- Bite of infected sandfly

2.7 | Likelihood of secondary transmission

- Minimal.
- Transfusion-transmitted leishmaniasis (TTL) continues to be a problem in areas where kala-azar is endemic, such as India and Brazil. There are fewer than 15 probable or confirmed cases of TTL and 10 reported cases of congenital transmission worldwide. However, these numbers could be higher since there is no ongoing active surveillance of TTL.

2.8 | At-risk populations

- Residents, travelers, and ecotourists to endemic areas.

2.9 | Vector and reservoir involved

- Phlebotomine sandflies: *Phlebotomus* genus (Old World) and *Lutzomyia* genus (New World)

2.10 | Blood phase

- *Leishmania* parasites survive and multiply in mononuclear phagocytes. Parasite circulation in peripheral blood has been reported in asymptomatic *L. donovani, L. tropica, L. major* and *L. infantum* infections, and in treated and inapparent *L. braziliensis* infections.

2.11 | Survival/persistence in blood products

- *Leishmania* species are known to survive in human RBCs under blood bank storage conditions for as long as 25 days at 4°C and longer in experimental animal models.

2.12 | Transmission by blood transfusion

- Transfusion-transmitted leishmaniasis continues to be a problem in areas where kala-azar is endemic, such as India and Brazil.
- Transfusion transmission has been documented in at least three cases in nonendemic areas in which the recipients who received transfusion were either infants or immunocompromised patients. One probable case of *L. donovani* transmission by platelet transfusion has been reported.
- No transfusion cases reported in the United States.
- *Leishmania* species have been transmitted via clinical transfusions from seropositive donor dogs to recipient dogs.

2.13 | Cases/frequency in population

- Unknown frequency in nonmilitary, nonexpatriate US population.
- Worldwide, leishmaniasis is found in 100 countries.
- WHO estimates that more than 1 billion people live in areas endemic for leishmaniasis and are at risk of infection. The estimated annual number of new cases of visceral leishmaniasis is about 500,000, of which 90% are found in India, Bangladesh, Nepal, Sudan, and Brazil. Approximately 10 million annual cases of cutaneous infection are estimated worldwide.

2.14 | Incubation period

- Weeks to months following bite of infected sandfly

2.15 | Likelihood of clinical disease

- Variable depending upon infecting *Leishmania* species, host genetics, immune status, and nutritional status.

2.16 | Primary disease symptoms

- Cutaneous leishmaniasis: cutaneous lesion/ulcer at the bite site, variable in size, can be active for months but usually self-healing (caused by *L. major, L. tropica, L. aethiopica*, and *L. mexicana* subspecies). Diffuse cutaneous leishmaniasis with lesions that do not heal has been reported in Ethiopia and South America and has been attributed to *L. aethiopica* and *L. mexicana amazonensis*, respectively. In 2018, over 85% of new cutaneous leishmaniasis cases occurred in 10 countries: Afghanistan, Algeria, Bolivia, Brazil, Colombia, Iran, Iraq, Pakistan, the Syrian Arab Republic and Tunisia.
- Visceral leishmaniasis: caused by *L. donovani, L. infantum*, and *L. chagasi*; characterized in diseased individuals by intermittent fever, hypergammaglobulinemia, massive hepatosplenomegaly, and anemia. However, a significant proportion of the population in areas of endemic infection shows subclinical infection (*L. infantum*). In 2018, more than 95% of new cases reported to WHO occurred in 10 countries: Brazil, China, Ethiopia, India, Iraq, Kenya, Nepal, Somalia, South Sudan and Sudan.
- Mucocutaneous leishmaniasis: (e.g., *L. braziliensis*) the initial skin lesion may cure spontaneously, but metastatic lesions develop in the mucosa of the nasopharynx. Over 90% of mucocutaneous leishmaniasis cases occur in Bolivia, Brazil, Ethiopia, and Peru.

2.17 | Severity of clinical disease

- Visceral leishmaniasis: fatal if not treated.
- Other forms: can be severely disfiguring (social impact).

2.18 | Mortality

- 20,000–50,000 deaths each year

2.19 | Chronic carriage

- Viable parasites can remain in the host for months to years, if not a lifetime, in both visceral and cutaneous infections. Disease can be reactivated by immunosuppression. Visceral leishmaniasis is a common reactivating syndrome in acquired immunodeficiency syndrome patients.

2.20 | Treatment available/efficacious

- When treatment is needed, antimonial compounds (e.g., sodium stibogluconate) are efficacious, but have toxic side effects. Amphotericin B and miltefosine are alternative therapies being used with increasing frequency. Oral miltefosine was approved by the US FDA in 2014 for specific cases of cutaneous, mucosal, and visceral leishmaniasis. FDA-approved liposomal amphotericin B is given intravenously for visceral leishmaniasis.

2.21 | Agent-specific screening question(s)

- Direct queries about leishmaniasis are not in wide use in the developed world.
- Of the 100 countries endemic for leishmaniasis, most are also endemic for malaria, and travelers to malaria-endemic areas are currently deferred for three months after travel, which may affect the number of *Leishmania*-infected presenting donors.

2.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- There are several FDA-licensed diagnostic tests.
- Options for laboratory testing include blood smear microscopy, culture, immunofluorescence assay, enzyme immunoassay, western blot, nucleic acid test, and antigen-based rapid diagnostic tests.

2.23 | Currently recommended donor deferral period

- Historically, there was a 1-year deferral from the last date of departure from Iraq.
- Deferral for a history of leishmaniasis has been discussed, but no regulation or standard exists covering civilian blood banks.

2.24 | Impact on blood availability

- Agent-specific screening question(s): Prior deferral for travel to Iraq negatively impacted blood availability, especially for the military. A deferral for travel to or immigration from other endemic countries could have a significant impact.
- Laboratory test(s) available: Not applicable.

2.25 | Impact on blood safety

- Agent-specific screening question(s): The impact of the Iraq deferral was unmeasured, and the potential deferral for travel to or immigration from other endemic countries are unknown.
- Laboratory test(s) available: Not applicable.

2.26 | Leukoreduction efficacy

- Moderate to high. Because *Leishmania* are found in blood cells of the monocyte/macrophage lineage, leukocyte reduction could be an efficient method to reduce the risk of transfusion-transmitted leishmaniasis. Laboratory spiking studies indicate that not all parasites are removed, particularly if found extracellularly.
- Universal leukocyte reduction has been implemented in at least 15 countries, including France and Spain, that have regions of high prevalence of *Leishmania* seropositivity. Although surveillance for transfusion-transmission of *Leishmania* is of unknown quality, there have been no reported cases of *Leishmania* transmission by blood transfusion in these countries.

2.27 | Pathogen reduction efficacy for plasma derivatives

- No specific data are available, but it is presumed that the agent should be sensitive to many measures used in the fractionation process.

2.28 | Other prevention measures

- Avoidance of the sandfly vector.
- *Leishmania* parasites were reduced 5–7 logs in platelets and plasma using riboflavin and ultraviolet light (Mirasol PRT System).
- A second study showed *Leishmania* inactivation in human apheresis platelets by a psoralen and a long

wavelength ultraviolet irradiation (inactivated both metacyclic promastigotes and amastigotes to undetectable levels, more than a 10,000-fold reduction in viability).
- No vaccine available, but some communities intentionally infect children to provide protection.

SUGGESTED READING

1. Aronson NE, Copeland NK, Magill AJ. Leishmania Species: Visceral (Kala-Azar), Cutaneous, and Mucosal Leishmaniasis. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. Volume 275; 2019. p. 3321–39.e6.
2. Cardo LJ. *Leishmania*: risk to the blood supply. Transfusion. 2006;46:1641–5.
3. Cardo LJ, Rentas FJ, Ketchum L, Salata J, Harman R, Melvin W, et al. Pathogen inactivation of *Leishmania donovani infantum* in plasma and platelet concentrates using riboflavin and ultraviolet light. Vox Sang. 2006;90:85–91.
4. Cardo LJ, Salata J, Harman R, Mendez J, Weina PJ. Leukodepletion filters reduce *Leishmania* in blood products when used at collection or at the bedside. Transfusion. 2006;46:896–902.
5. Chung H, Chow HK, Lu JP. The first two cases of transfusion kala-azar. Chinese Med J. 1948;66:325–6.
6. Kaplanski G, Farnarier C, Durand JM, Soubeyrand J, Bongrand P, Kaplanski S. Leishmaniasis acquired in Belgium. Lancet. 1991;338:128.
7. Eastman RT, Barrett LK, Dupuis K, Buckner FS, Van Voorhis WC. Leishmania inactivation in human pheresis platelets by a psoralen (amotosalen HCl) and long-wavelength ultraviolet irradiation. Transfusion. 2005;45:1459–63.
8. Grogl M, Daugirda JL, Hoover DL, Magill AJ, Berman JD. Survivability and infectivity of viscerotropic *Leishmania tropica* from operation desert storm participants in human blood products maintained under blood bank conditions. Am J Trop Med Hyg. 1993;49:308–15.
9. Herwaldt BL. Leishmaniasis. Lancet. 1999;354:1191–9.
10. le Fichoux Y, Quaranta JF, Aufeuvre JP, Lelievre A, Marty P, Suffia I, et al. Occurrence of Leishmania infantum parasitemia in asymptomatic blood donors living in an area of endemicity in southern France. J Clin Microbiol. 1999;3:1953–7.
11. Mathur P, Samantaray JC. The first probable case of platelet transfusion-transmitted visceral leishmaniasis. Transfus Med. 2004;14:319–21.
12. Owens SD, Oakley DA, Marryott K, Hatchett W, Walton R, Nolan TJ, et al. Transmission of visceral leishmaniasis through blood transfusions from infected English foxhounds to anemic dogs. J Am Vet Med Assoc. 2001;218:1076–83.
13. Singh S, Chaudry VP, Wall JP. Transfusion transmitted kala-azar in India. Transfusion. 1996;36:848–9.
14. Giger U, Oakley DA, Owens SD, Schantz P. *Leishmania donovani* transmission by packed RBC transfusion to anemic dogs in the United States. Transfusion. 2002;42:381–3.
15. WHO. Global health observatory data repository. Accessed 28 Sept 2022. https://apps.who.int/gho/data/node.main.NTDLEISH?lang=en
16. WHO. Leishmaniasis. Accessed 28 Sept. 2022 https://www.who.int/health-topics/leishmaniasis