

What's Eating You? Sand Flies

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PRACTICE POINTS

- Sand flies cause a wide array of cutaneous and systemic diseases worldwide.
- Identification and treatment of leishmaniasis and other diseases transmitted by sand flies requires a high degree of clinical suspicion.
- With the increase in global travel and the rise of autochthonous disease in the United States, American physicians must increase their awareness of diseases for which sand flies serve as vectors.

As thousands of Americans descended upon Brazil for the Olympic games in the summer of 2016, the mosquito-borne Zika virus became a source of great concern among the countless athletes and travelers in Rio. As is often the case, the media frenzy that ensued drew travelers' attention away from a lesser known flying vector that often carries with it grave consequences. The Phlebotominae, commonly known as sand flies, are biting insects known for their ability to transmit the protozoa *Leishmania* as well as a number of other viruses and bacteria. As the impact of sand flies continues to grow in the United States and worldwide, knowledge of the vector is important for proper treatment and prevention of the diseases they carry.

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Identification

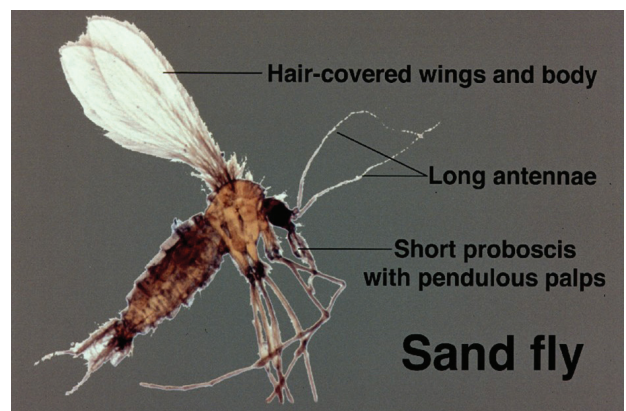
Phlebotomine sand flies are the only member of the Psychodidae family that are capable of taking blood.¹ The mouthparts of the sand fly are toothed distally, and the maxilla and mandible are utilized in a sawtooth fashion to take a bloodmeal.² The flies are very small (ie, only 1.5–3.5 mm in length), which makes their identification difficult.¹ Sand flies can be distinguished by the appearance of their wings, which often are covered in hair and extend across the back in a V shape.³ The adult sand fly is hairy with a 6- to 8-segmented abdomen, and the color can range from gray to yellow to brown.² Phlebotomine

sand flies can be further identified by their long antennae, dark eyes, and small heads (Figure).²

As is the case with all Diptera, the sand fly goes through 4 complete life stages from egg to larva to pupa to adult.³ Female sand flies will lay their eggs following a blood meal and have been found to take multiple blood meals in a single cycle.² On average, the eggs will hatch in 6 to 17 days but are temperature dependent.³ The subsequent larvae and pupa stages last 20 to 30 days and 6 to 13 days, respectively.¹ The larvae are white in color with short antennae and dark heads.⁴ Sand flies prefer to lay their eggs in areas where adequate resting places are available and where their larvae will thrive.^{4,5} The larvae require warm moist environments to succeed and thus are commonly found in animal burrows.³ Once fully developed, the adult sand fly can live up to 6 weeks.²

Sand Fly Vector

Although it is more common in rural forested areas, the sand fly also can be found in urban areas, including heavily populated cities in Brazil.⁶ Sand flies are most active during hot humid seasons but depending on the local



Sand fly anatomy.

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climate may remain active year-round.^{1,7} For example, in tropical regions of Asia, the number of sand flies increases substantially during the monsoon season compared to the dry season.² Phlebotomine sand flies are most active at dusk and during the night⁵ but may become agitated during the daytime if their environment is disturbed.¹

Host selection usually is broad and includes a wide variety of vertebrates.² In the United States, host species are thought to include small rodents, foxes, armadillos, and opossums.⁸ One study found that visceral leishmaniasis in foxhounds is able to develop fully in sand flies, thus posing an emerging risk to the American population.⁹

Distribution

The Phlebotominae family contains approximately 700 different species of sand flies but only 21 are known vectors of disease.¹⁰ The great majority belong to 1 of 3 genera: *Phlebotomus*, *Sergentomyia*, and *Lutzomyia*.¹¹ The vectors are commonly divided into Old World species, dominated by the *Phlebotomus* genus, and New World species, which exclusively refers to the *Lutzomyia* genus.³ The Old World and New World distinction helps to classify the various vectors and subsequently the diseases they transmit. Old World refers to those vectors found in Southwest and Central Asia, the Indian subcontinent, the Middle East, and East Africa, as well as Southern Europe.⁶ New World refers to vectors found predominantly in Brazil and other parts of Latin America but also Mexico and the United States.⁶ Sand flies are found to be endemic in 90 countries and on each continent, except Australia.⁵ Although the vector can be found in a variety of environments, sand flies prefer moist environments that typify tropical and subtropical climates, thus it is not surprising that the highest diversity of Phlebotominae in the world can be found in the Amazon basin.¹²

Disease Transmission

Leishmania refers to a genus of intracellular protozoa found in both the Old World and the New World that causes a variety of clinical syndromes.⁵ Approximately 20 *Leishmania* species are known to cause human disease that includes localized cutaneous, diffuse cutaneous, mucosal cutaneous, and visceral infections.¹³ Cases of all forms of leishmaniasis worldwide have increased rapidly over the last few decades from multiple factors including war in endemic regions, increased numbers of immunodeficient individuals, and increased travel to endemic areas.¹⁴ In the United States, leishmaniasis is caused by both imported and autochthonous forms of transmission and often mirrors recent travel and immigration patterns.^{14,15}

Sand flies also serve as vectors for sandfly fever, also known as Pappataci fever. Although sandfly fever commonly causes a mild febrile illness, it has been shown to be a considerable cause of aseptic meningitis.¹⁶ A number of novel Phlebotoviruses have been isolated as causes of sandfly fever, including Massilia virus, Granada virus,

and Punique virus.¹⁶⁻¹⁸ A form of sandfly fever caused by the Toscana virus has a predilection for the nervous system and can cause encephalitis.¹⁹ Sandfly fever can be found in both the Old World and New World and thus poses a global risk.² Additionally, Phlebotominae also have been found to transmit the Changuinola virus, a type of bunyavirus that is known to cause febrile illness in Panama.²⁰ Vesicular stomatitis, also carried by sand flies, is a known cause of febrile disease in North and South America, including the United States.² In 2013, the Niakha virus, a novel type of *Rhabdoviridae*, was isolated from Phlebotominae in Senegal.²¹ The sand fly is noted to transmit another type of *Rhabdoviridae* in India and Africa, known as the Chandipura virus.²² Although originally thought to cause mild febrile disease, it was the primary cause of multiple outbreaks of fatal encephalitis in India in 2003^{23,24} and again in 2012.²²

Sand flies also are known to serve as vectors for the bacterium *Bartonella bacilliformis*, which is responsible for bartonellosis.²⁵ The disease is divided into 2 forms, which can occur separately or in succession, and is endemic to the Andes region of Peru, Ecuador, and Colombia. The first form is Oroya fever, an acute febrile hemolytic anemia that is fatal in 40% to 88% of cases without intervention.²⁵ This bacterium also causes verruga peruana, an endemic form of bacillary angiomatosis that can persist for years.² Two reports suggested that bartonellosis also can be caused by *Bartonella rochalimae* and *Candidatus Bartonella ancashi*.^{26,27}

Vector Control

Prevention is key to reducing the risk of the various diseases caused by the Phlebotominae vector. Vector control often falls into a few categories, including residual sprays, barriers, and topical repellants.³ It appears that residual sprays applied to houses and animal shelters are the most utilized and effective form of control, with the pyrethroid insecticides having the highest sand fly-specific toxicity.^{3,28} Insecticides also have been applied to animal burrows where sand flies are known to reproduce; one study in Kenya showed a 90% reduction in the sand fly population following treatment of termite and animal burrows with a pyrethroid spray.²⁹ Studies by Perich et al^{30,31} in 1995 and 2003 showed that using barrier sprays can be an effective protective measure. The investigators applied a 100-m barrier using a pyrethroid spray on vegetation and reported a notable decrease in sand flies for over an 80-day period.^{30,31}

For personal protection, barrier methods are important adjunct methods of preventing individual exposures. Due to the small size of sand flies, ordinary bed nets are not effective and those treated with insecticides should be used,¹⁵ which may ultimately prove to be the most sustainable way to prevent sand fly-borne disease.³² Protective attire also should be worn, as sand flies are not able to penetrate clothing.² N,N-diethyl-meta-toluamide (DEET)-based repellants should be applied to exposed

skin.¹⁵ Finally, it is important to avoid exposure from dusk to dawn when sand flies are most active.¹⁵

Rise in Autochthonous Cutaneous Leishmaniasis in the United States

With the increased amount of worldwide tourism, especially to endemic areas, providers will continue to see rising numbers of leishmaniasis in the United States. It is difficult to determine the incidence of the disease in the United States, but one study has shown that leishmaniasis accounts for 143 of every 1000 dermatologic diseases acquired by South American tourists.^{33,34} In addition, the number of autochthonous cases reported in the United States continues to grow. Although only 29 cases were reported between 1903 and 1996, 13 cases were reported between 2000 and 2008.³⁵ Another report in 2013 described an additional 3 cases in the states of Texas and Oklahoma.³⁵ The cases have continued to move in a northeasterly pattern, suggesting a possible shift in the location of sand fly populations. Each of these cases in which a specific species of *Leishmania* was identified showed transmission of *Leishmania mexicana*.³⁵ Most cases of cutaneous disease have occurred in Texas and Oklahoma. The first known case outside of this region was reported in 2014 in North Dakota.⁸ *Leishmania donovani*, brought into the United States with European foxhounds, also is spreading.⁸ One species of sand fly, *Leishmania shannoni*, has now been discovered in 16 states,³⁶⁻⁴² where it serves as a potential vector for *L. mexicana*.^{43,44}

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