Transmission of visceral leishmaniasis through blood transfusions from infected English Foxhounds to anemic dogs

Sean D. Owens, DVM; Donna A. Oakley; Kym Marryott; Wendy Hatchett; Raquel Walton, VMD, MS, DACVP; Tom J. Nolan, PhD; Alisa Newton, VMD; Frank Steurer, MS; Peter Schantz, VMD, PhD; Urs Giger, Dr med vet, PD, DACVIM

Objective—To conduct serologic surveillance for Leishmania spp in English Foxhounds from a kennel, as well as recipients of blood from these dogs, and determine whether Leishmania organisms could be transmitted via blood transfusion.

Design—Serologic prevalence survey.

Animals—120 English Foxhounds and 51 dogs of various breeds receiving blood from these donors.

Procedure—Foxhound blood donors, foxhound non-donors, and nonfoxhound recipient dogs were evaluated serologically for Leishmania spp by indirect fluorescent antibody testing. Dogs that received packed RBC (PRBC) transfusions from foxhound donors from mid-1996 through mid-2000 were identified. Furthermore, dogs were serologically evaluated if they had received fresh frozen plasma (FFP) transfusions in 1999 and 2000 from seropositive foxhound blood donors.

Results—Thirty percent of the English Foxhounds were seropositive for Leishmania spp (titer ≥ 1:16), although the degree of seropositivity varied considerably during the period. Furthermore, 57 foxhounds had been used as donors from 1996 to 2000, and 342 units of PRBC had been transfused to at least 227 patients. All 25 dogs screened that received PRBC from seronegative foxhound donors tested negative, whereas 3 of 7 dogs that received PRBC from seropositive donors tested positive. All 9 dogs that received FFP from seropositive foxhound donors remained seronegative.

Conclusions and Clinical Relevance—To our knowledge, this report documents the first transmission of Leishmania spp by blood transfusion. The use of foxhounds as blood donors may not be advisable in this region where the disease is enzootic and sand flies reside (eg, dogs of military personnel returning from overseas duty). However, since 1980, there have been sporadic reports of visceral leishmaniasis in foxhounds in the United States.

Visceral leishmaniasis is a zoonotic protozoal disease of the mononuclear phagocytic system caused by members of the Leishmania donovani complex, and dogs represent the major reservoir for infections in their species and in humans. Natural transmission of Leishmania spp occurs through the bite of an infected sand fly (Phlebotomus sp in the Old World [eg, the Mediterranean, India, Nepal, and Bangladesh] and Lutzomyia sp in the New World [eg, Latin America]) carrying promastigote forms of the parasite. A diagnosis of leishmaniasis is made through microscopic detection of the parasite in tissue or culture, antileishmanial antibodies in plasma, or parasite DNA isolation.

In the United States, visceral leishmaniasis is generally associated with a history of travel to a region where the disease is enzootic and sand flies reside (eg, dogs of military personnel returning from overseas duty). However, since 1980, there have been sporadic reports of visceral leishmaniasis in foxhounds in the United States.
Materials and Methods

Animals—All English Foxhounds (abbreviated here as foxhounds) reported in this study are from 1 private kennel in southeastern Pennsylvania and are registered with the MFCAA. Foxhounds from this kennel that participated in the PABB volunteer canine blood donor program from mid-1996 through mid-2000 as well as other foxhounds kept in the same kennel in 2000 and 2001 were serologically surveyed and examined for Leishmania spp. One standard unit of blood (450 ml ± 10%) was obtained from each dog up to 6 times/yr. The yearly health screen for foxhound donars was the same as for other donors of the volunteer donor program and included a physical examination, CBC, serum biochemical analysis, serologic testing for Ehrlichia canis, Babesia canis, Rickettsia rickettsii, and Borrelia burgdorferi, and antigenic Dirofilaria immitis testing.

Five nonfoxygened pet dogs on the kennel premises were also serologically examined by IFAT for Leishmania spp.

Dogs that received packed RBC (PRBC) or fresh frozen plasma (FFP) transfusions—The PABB product inventory records and medical case records at VHUP were searched for dogs that received PRBC transfusions from donors from 1996 through 2000. Furthermore, dogs were evaluated serologically when they received FFP transfusions in 1999 and 2000 from foxhound blood donors later found to be seropositive for Leishmania spp. Patient medical records were examined to determine whether transfusion recipients were discharged alive, died, or were euthanatized. If the recipient was discharged alive, the referral veterinarian was contacted to establish the health status of the recipient. If the recipient was believed to be alive or if the health status could not be determined from the medical record or the referral veterinarian, the owner of the recipient animal was contacted via telephone by a member of the PABB staff to gather this information. Owners of living transfusion recipients were asked to take their dog to the VHUP or their primary care veterinarian for physical examination and blood tests.

Leishmania serologic evaluations—One to 3 blood samples (2 to 10 ml) were collected during an 11-month period from donors and recipients at VHUP were searched for infected promastigotes by culture, materials from fine-needle aspirates were prepared and stained with Wright-Giemsa. For isolation, at least 2 slides of aspirated material and tissue imprints were incubated at 26°C in 25-cm² tissue culture flasks. Using the 1:4 dilution, the serum was separated and shipped frozen to the CDC for Leishmania IFAT. All serum samples were screened at 1:4, 1:8, 1:16, and 1:32 dilutions. Samples positive at a 1:32 dilution were further titrated by serial 2-fold dilutions to 1:512. Dogs were considered seropositive if the IFAT titer was ≥ 1:16.1,3 Seropositive foxhounds and blood recipients were also assessed for the presence of specific antibodies against Trypanosoma cruzi, but none tested positive.1,4

Leishmania detection—For direct cytocentrifugation, the serum was separated and shipped frozen to the CDC for Leishmania IFAT. All serum samples were screened at 1:4, 1:8, 1:16, and 1:32 dilutions. Samples positive at a 1:32 dilution were further titrated by serial 2-fold dilutions to 1:512. Dogs were considered seropositive if the IFAT titer was ≥ 1:16.1,3 Seropositive foxhounds and blood recipients were also assessed for the presence of specific antibodies against Trypanosoma cruzi, but none tested positive.1,4

Evaluation of PRBC and FFP recipients—The initial evaluation of recipients of PRBC or FFP from donors consisted of a history, physical examination, and collection of a serum sample for IFAT as described. Recipients that had a positive IFAT result (defined as ≥ 1:16) were reevaluated by repeat IFAT and further examined via CBC, serum biochemical analysis, urinalysis, bacterial culture, urine protein:creatinine ratio, thoracic and abdominal radiography, abdominal ultrasonography, and examination of aspirates of lymph node, liver, and spleen, as permitted by the owners. Representative samples of selected aspirates underwent culturing for Leishmania spp promastigotes as described. All owners declined a bone marrow aspirate for Leishmania spp screening. Any other dogs living in the household with a seropositive recipient were given a complete physical examination, and blood was drawn for Leishmania serologic testing as described.

Treatment protocol—Treatment was offered to Leishmania seropositive foxhounds and transfusion recipients. Allopurinol was administered at a dosage of 15 mg/kg (7 mg/lb) of body weight, PO, every 12 hours, and treated animals were monitored.1,3

Necropsy and histopathology—Complete necropsies were performed on 2 seropositive foxhounds (1 blood donor and 1 seropositive transfusion recipient).

Persons with foxhound contact—The PABB nursing staff who had contact with the foxhound blood donors were serologically tested for exposure to Leishmania spp. The workers and handlers at the foxhound kennel and owners, veterinarians, and nursing staff exposed to seropositive recipient dogs were advised to contact their physician or a human infectious disease specialist.

Results

Foxhound Leishmania testing—On the basis of information provided and requests made by the MFCAA, 120 adult English Foxhounds, including 57 used as blood donors, were examined by IFAT 1 to 3 times from June 2000 through May 2001. There were 64 sexually intact females and 56 sexually intact male foxhounds, ranging from 1 to 8 years old. Of the 57 foxhound donors, 31 were sexually intact females, and 26 were sexually intact males. All foxhounds at the kennel from June 2000 to May 2001 were tested at least once, except for 3 foxhounds whose aggressive behavior posed serious risk of injury to the blood bank nursing staff and kennel personnel. On at least 1 of 3 test dates, 36 (30%) dogs tested positive with titers ranging from 1:16 to 1:512 (Table 1). No illness had been reported in the foxhound kennel previously, although a few dogs had been poor performers over the preceding 4 years, and 4 had been euthanatized prior to the survey. Treatment for leishmaniasis was permitted and begun in January 2001 for 5 seropositive foxhounds (titer ≥ 1:32), and the treatment was well tolerated.

Foxhound blood donors—From 1996 through 2000, whole blood obtained from 69 foxhounds was used for a PRBC transfusion. Of these 69 foxhound donors, 12 had been euthanatized prior to June 2000. The remaining 57 foxhound donors were screened for Leishmania infection on at least 1 of the 3 test dates from June 2000 through May 2001. Of the 57 tested foxhound blood donors, 17 (29.8%) had positive Leishmania titers on at least 1 test date. The first test
Packed red blood cell units transfused from foxhounds, mid-1996 through mid-2000—A total of 342 PRBC units was collected during a 4-year period from 69 foxhound blood donors (12 not tested). There were 214 units transfused to dogs that died before June 2000 and 30 units transfused to 40 dogs that were alive and available for follow-up evaluation in 2000 and 2001. None of the recipients found to be deceased appeared to have had any clinical evidence of leishmaniasis. The 31 recipients of 33 PRBC transfusions were lost to follow-up. Information regarding the recipients of these PRBC units was either not recorded in the patient’s medical record or not entered into the PABB product use logbook. The recipients of 45 of the units are unknown, as the referral hospitals that obtained the blood from PABB did not keep records identifying the recipient of the PRBC unit.

Evaluation of recipients of PRBC units from foxhound donors—Forty dogs that received PRBC transfusions from foxhound blood donors were still alive in 2000 and 2001 (Table 2). All 25 of the recipient dogs that received PRBC transfusions from seronegative foxhound donors were examined once, and all had negative IFAT results. All 8 of the dogs that had received PRBC transfusions from foxhounds with an unknown IFAT status (not tested because they were euthanatized prior to June 2000) were seronegative for Leishmania spp. Three of the remaining 7 dogs that received PRBC transfusions from seropositive foxhounds were determined to be seropositive.

Seropositive PRBC recipient evaluation—In December 1998, a 5-year-old spayed female American Cocker Spaniel (recipient 1) with acute anemia received a PRBC transfusion provided by the PABB at a referral clinic. The foxhound donor (donor 1) for this transfusion had a Leishmania titer of 1:256 in 2000. At the referral clinic, the recipient was treated for a presumptive persistent immune-mediated hemolytic anemia with prednisone and azathioprine for the following 2.25 years. The dog remained mildly anemic, became progressively obese, and developed a septic joint in the spring of 2000 that resolved following antibiotic treatment. History of travel outside of the United States was not reported for the recipient dog or owner.

The dog’s health slowly deteriorated in February 2001, as noted by progressive lethargy and reluctance to go on regular walks. In March 2001, the primary care veterinarian performed a physical examination, discovered pyrexia, and treated the dog with cephalexin. Throughout the month, the dog’s appetite remained good. The recipient had a serum antibody titer of ≥ 1:512 against Leishmania spp (confirmed 2 weeks later). Upon receiving these results from the CDC, azathioprine was withdrawn, prednisone was tapered, and treatment with allopurinol was initiated at 15 mg/kg, PO, every 12 hours. Because the dogs condition deteriorated, it was referred to VHUP for further evaluation a week later.

At admission, the dog was grossly obese (24.5 kg [53.9 lb]), had difficulty rising, and was tachycardic and tachypneic. Physical examination revealed hepatomegaly, generalized lymphadenopathy with all lymph nodes at least twice normal size, and bilateral conjunctivitis. Leukocytosis (25,560 WBC/μl) characterized by a mature neutrophilia (19,000 cells/μl) with a left shift (3,400 band neutrophils/μl) was detected. Coombs’ negative regenerative anemia was also detected (Hct, 23%; reticulocyte count, 183,000

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Table 1—Serum indirect fluorescent antibody test (IFAT) titers in English Foxhounds tested at a hunt kennel in southeastern Pennsylvania in 2000 to 2001

<table>
<thead>
<tr>
<th>Leishmania serologic titer</th>
<th>English Foxhounds</th>
<th>No. of dogs</th>
<th>No. of donors</th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>117</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>113</td>
<td>25</td>
<td>0</td>
<td>25</td>
<td></td>
<td></td>
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<tr>
<td>Unknown</td>
<td>32</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>42</td>
<td>0</td>
<td>37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2—Leishmania IFAT results during 2001 for recipients of PRBC from English Foxhounds, mid-1996 through mid-2000

<table>
<thead>
<tr>
<th>Leishmania IFAT status</th>
<th>Positive</th>
<th>Negative</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dead/ not tested</td>
<td>11</td>
<td>113</td>
<td>32</td>
<td>155</td>
</tr>
<tr>
<td>Alive/ tested</td>
<td>7</td>
<td>25</td>
<td>8</td>
<td>42</td>
</tr>
<tr>
<td>Positive</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Negative</td>
<td>113</td>
<td>4</td>
<td>8</td>
<td>125</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>42</td>
<td>37</td>
<td>234</td>
</tr>
</tbody>
</table>

*Tested on 1 or 2 occasions.
ND = Not determined at that test date. PRBC = Packed red blood cell. FFP = Fresh frozen plasma.
Total No. of dogs equals 136, including 16 dogs not tested at any of the 3 test times. Highest titers are indicated by boldface.
found throughout the myocardium. Similarly, multiple ranging in size from approximately 0.5 to 1.8 cm were in the parenchyma of all lung lobes. Numerous multi-
cavity. Multifocal-to-coalescing round firm areas with 150 ml of straw-colored fluid was found in the thoracic
immunocompromised individuals was restricted. The with other animals, and contact with children and
continued, the dosage of prednisone was gradually for 3 days yielded many promastigotes confirmed to intrahistiocytic protozoal organisms. The left
leukocytes contained clusters of 1- to 3-µm round-to-oval deeply basophilic protozoal organisms. Frequently, the parenchyma adjacent to these areas was necrotic. Examination of the spleen and bone marrow revealed severe histiocytosis, and many of the histiocytes contained intracytoplasmic amastigotes. A sec-
tion of skin from the ventral portion of the abdomen had mild plasmodytic and histiocytic dermatitis with intrahistiocytic protozoal organisms. The left precapsular and right mandibular lymph nodes had a moderate subcapsular sinus histiocytosis with intrahistiocytic protozoal organisms. Morphologic features of the protozoal organisms were consistent with *Leishmania* spp. Additional microscopic lesions includ-
ed severe bilateral adenocortical atrophy, diffuse hair follicle atrophy, and a focal leptomeningeal thromboembolus. The cause of death was most likely the pyogranulomatous infiltrative myocarditis and pneu-
oma.

In November 1999, a 12-year-old castrated male mixed-breed dog (recipient 2) was referred to VHUP for transfusion with a 1-day history of acute anemia, anorexia, vomiting, melena, lameness, and aspirin exposure. The dog also had a pansystolic heart murmur, a hepatic mass, dental disease, and a small (1-cm) mass on the dorsolateral portion of the thorax. The dog received 3 PRBC units from 3 foxhound donors (donors 2, 3, and 4) and recovered uneventfully. One of the donors (donor 2) tested negative, and 1 (donor 3) was not available for testing (the dog was euthanized because of poor performance). The third unit was from a foxhound (donor 4) that tested positive at 1:256 on April 1, 2001.

The recipient's blood was examined 4 times at monthly intervals beginning in February 2001. The IFAT titers for *Leishmania* spp increased from 1:16 to 1:256 over the 4-month period. In April 2001, after a thorough diagnostic evaluation, the dog was bright, alert, afebrile, and in excellent body condition. Abnormal clinical signs included dental calculus, a grade-II/VI systolic heart murmur attributed to mitral valve insufficiency without heart failure (as determined by echocardiography), and an open raised circular skin mass (3 cm in diameter) on the right dorsolateral portion of the thorax. Results of a CBC and

![Image](image-url)

**Figure 1**—Photomicrograph of a fine-needle aspirate of a popliteal lymph node from a dog that received a packed RBC transfusion from a foxhound seropositive for *Leishmania* spp. A cluster of 7 extracellular *Leishmania* amastigotes is evident near the plasma cell. Notice the characteristic kinetoplast perpendicular to the nucleus that is visible in the organisms. Wright-Giemsa stain; bar = 5 µm.
serum biochemical analysis were normal. Bacteriologic culture of urine yielded Escherichia coli susceptible to amoxicillin-clavulanic acid. The urinary tract infection resolved following 3 weeks of antibiotic therapy (confirmed by subsequent urinalyses and negative urine culture results). The urine protein-to-creatinine ratio after antibiotic treatment was 5.8 (normal, < 0.5). Abdominal and thoracic radiography revealed spondylolysis L1-L2, L7-S1, mild cardiomegaly, and degenerative joint disease of the left shoulder. A 6-cm anechoic mass with hyperechoic septae was located in the central portion of the liver by abdominal ultrasonography, and the spleen appeared poorly defined, with slightly hypoechoic mottling throughout the parenchyma. Pyelectasia was identified in both kidneys. Leishmania organisms were not identified by cytologic evaluation or culture of fine-needle aspirates from the popliteal lymph nodes. Permission to aspirate the bone marrow, spleen, and liver for similar evaluations was not granted. The Leishmania IFAT result of the only other dog in the household (a 4-year-old castrated male mixed-breed) was negative, and physical examination findings were unremarkable.

Dental prophylaxis was performed, and the skin mass on the thorax was removed under anesthesia. Histologic examination of the mass revealed a low-grade fibrosarcoma without evidence of Leishmania organisms. Because of the rising serum titers, treatment with allopurinol (15 mg/kg, PO, q 12 h) was started in April 2001. The owner was advised to limit the recipient’s interactions with other dogs and avoid contact of the recipient with children and immunocompromised people. Treatment was well tolerated, but the Leishmania titer remained at 1:256, as of last testing in August 2001.

In January 1999, a 5-year-old castrated male Doberman Pinscher (recipient 3) underwent surgical correction of gastric dilatation-volvulus. Approximately 1 week later, the dog was determined to be anemic and was given a PRBC transfusion from a foxhound (donor 5) that was screened by IFAT in June 2000 with a Leishmania titer result of 1:32 on 1 occasion. The recipient dog recovered uneventfully and has had no illnesses since. The recipient’s blood was initially tested in May and again in June 2001 and had a serum antibody titer of 1:16 and < 1:16, respectively. A thorough diagnostic evaluation by the primary care veterinarian in May 2001 revealed the dog to be bright, alert, and alert. Abnormalities were not detected by physical examination, and results of the CBC, serum biochemical analysis, urinalysis, and urine protein:creatinine ratio were normal. Permission was not granted for fine-needle aspirates of lymph nodes and other internal organs.

Number of units of FFP collected from seropositive foxhound blood donors from 1999 through 2000—Between January 1999 and August 2000, 48 FFP units were obtained from 11 foxhound blood donors later found to be seropositive by IFAT for exposure to Leishmania spp. Thirty-three units had been transfused to dogs that died before 2001, and 13 units were transfused to 11 dogs determined to be alive for follow-up evaluation; however, 1 unit was transfused to a recipient dog whose owner declined testing, and 1 unit was transfused to a dog lost to follow-up. The 9 screened dogs that received FFP from seropositive foxhounds with titers of 1:512, 1:32, and 1:16 had negative IFAT results for Leishmania infection. On the basis of this observation and experimental evidence, we elected not to screen other dogs that received FFP from seropositive foxhound donors prior to 1999.

Results of PABB nursing staff Leishmania testing—All PABB nurses tested (n = 4) had negative serologic test results for exposure to Leishmania spp. Known results of testing of referring veterinarians, nursing staff, and owners of seropositive recipients have been seronegative.

Foxhounds with leishmaniasis—Two seropositive foxhounds (donors 6 and 7) with 1:128 titers were presented for euthanasia because of poor performance, failure to thrive, and acute weight loss. On physical examination, a thin hair coat, several skin abrasions, mild generalized lymphadenopathy, and hepatomegaly were noticed in both dogs. One foxhound was anemic (donor 6; Hct, 34%), and both were hyperglobulinemic (5.4 and 4.7 g of globulin/dl, respectively). Promastigotes were cultured from fine-needle aspirates of popliteal lymph nodes of these foxhounds. The L donovani complex species was identified as L infantum MON-1. Splenic impression smears made at necropsy from donor 6 revealed the presence of Leishmania amastigotes. However, histopathologic examination of tissue specimens failed to reveal pyogranulomatous lesions or Leishmania amastigotes in the mononuclear phagocytic system of either foxhound.

Discussion Following the request of the MFAA and the CDC in May 2000, we tested 120 English Foxhounds (some used as blood donors) from 1 kennel in southeastern Pennsylvania for Leishmania spp infection. On the basis of Leishmania IFAT, 30 and 7.5% of the foxhounds tested were seropositive at ≥ 1:16, and ≥ 1:64, respectively. These percentages are similar to those initially described (49.3% at ≥ 1:16 and 8.6% at ≥ 1:64) in an English Foxhound kennel in Dutchess County, NY.11,12 However, no recent direct contact between the 2 kennels could be established; there had been no travel history to other shows or hunts in the southern United States for the past 3 years, and no new foxhounds from the United States were introduced to the kennel in Pennsylvania. Although only isolated reports12,13 of foxhounds with visceral leishmaniasis have appeared in the literature during the past 2 decades, the survey done by the CDC in 2000 and 2001 revealed many infected foxhound kennels throughout the United States, particularly on the east coast. This suggests a wide distribution and long-standing Leishmania spp infection in foxhound kennels in the United States.

Approximately 15% of the kennel’s English Foxhounds, which were seronegative on initial PABB serologic screening in 2000, became seropositive after 4 to 11 months, possibly indicating recent exposure or infection. These dogs may have been incubating the
infection or been recently infected, as clinical signs of leishmaniasis may develop over a period of 3 months to 7 years following infection.12 Several of these dogs performed poorly when hunting and were, therefore, euthanatized. In 2 dogs with mild clinical signs of leishmaniasis characterized by lethargy, skin lesions, alopecia, and lymphadenopathy, *L. infantum* MON-1 organisms were isolated, but, interestingly, no histopathologic changes consistent with leishmaniasis were found. Thus, documentation of *Leishmania* infection may be difficult when not suspected, and disease may only develop in immunocompromised animals. *Leishmania infantum* MON-1 has been found in foxhounds throughout the United States, where tested, and is the serotype typically encountered in the Mediterranean.14 Treated foxhounds remained seropositive, but there were 3 untreated foxhounds with titers of 1:16 or 1:32 that converted to seronegative. These dogs may have had false-positive results or cleared the infection and spontaneously converted to seronegative status.7 Although the IFAT for *Leishmania* spp may cross-react with *T. cruzi*, there has been no evidence suggested that *T. cruzi* is in the studied kennel; the tested seropositive foxhounds and recipients had no antibody against *T. cruzi*.11,13 There is reason ed evidence from the CDC that *T. cruzi* is present in other foxhound kennels, which may pose an additional transfusion concern, as *T. cruzi* can be transmitted by blood in people. Additionally, infected dogs may not develop *Leishmania*-specific antibodies.23 Therefore, serologic tests may underestimate the true prevalence of *Leishmania* infection.21,22 Recently, polymerase chain reaction (PCR)-based tests have been used to document the presence of leishmanial DNA and thereby confirm infection in dogs, but PCR testing was not used in the present study.11,26

The route of *Leishmania* spp transmission in foxhounds in this country remains unknown. Species of *Lutzomyia* sand flies capable of transmitting *Leishmania* spp exist in the United States, particularly *L. shannoni*, whose pattern of distribution appears to overlap with the geographic distribution of infected foxhound kennels in the southeastern United States. Thus far, no infected sand flies have been identified.11,12 This may not explain infections of foxhounds in the northern United States unless the dogs have traveled to the southeast for a show or hunt. Vertical transmission of *Leishmania* spp has been documented,22,26 and transmission through direct contact (eg, bite wounds) may also need to be considered, as these dogs are housed closely together in packs and may often fight, resulting in injury.19 Furthermore, as many foxhounds throughout the United States were documented to be infected, and as no other breed of dogs (wild or domesticated) has been found to be infected in this or the New York kennel, the possibility that a hereditary/primary immunodeficiency may be predisposing the breed to *Leishmania* spp infection needs to be considered.

Because of the potential risk of transmitting *Leishmania* spp via blood products, patients that received blood transfusions from these English Foxhounds were screened by IFAT. All 25 tested dogs that received PRBC from seronegative foxhounds tested negative, whereas 3 of 7 dogs that received PRBC from seropositive donors tested positive. Although the number of dogs studied is small, the risk of *Leishmania* spp transmission through PRBC transfusion from seropositive foxhound donors appears to be high. Blood samples obtained from the donors at the time of transfusion in 1998 and 1999 were not banked for comparison. Thus, archived samples of donor serum could prove helpful for future infectious disease investigations. Two of the seropositive recipients’ donors tested strongly positive in 2000 and 2001, whereas the other seropositive recipients’ donor’s titer was only 1:32 on 1 testing occasion followed by 1 negative test result. Detailed recording of the donor and recipient for each blood product transfusion is crucial for the accurate investigation and follow-up of emerging infectious diseases. Fortunately, detailed records were available to trace most recipients; however, this information was missing for 13% of the PRBC units.

On the basis of results of this investigation, any foxhound from the United States should be considered a potential risk as a blood donor. The PABB ceased using any foxhounds in the donor program in the summer of 2000, following receipt of the first test results. Furthermore, these dogs may serve as a reservoir of infection for other dogs via the sand fly, and these reservoirs and vectors may pose a human health hazard.13 Therefore, the treatment and maintenance of seropositive dogs needs to be carefully evaluated, and there may be a need for further monitoring and surveillance of seronegative foxhounds.30,31 Although direct transmission of *Leishmania* spp infection from dogs to humans has not been documented thus far, the managers and handlers of the foxhounds at the kennel and the veterinarians, nurses, and owners with a history of contact with seropositive dogs were referred to their physicians. Fortunately, all individuals tested had negative titers against *Leishmania* spp.

The fact that 3 of 7 dogs became seropositive following PRBC transfusion suggests that *Leishmania* spp infection could readily occur when blood from seropositive donors is transfused. It has been shown that *L. tropica* can be experimentally transferred in the hamster model via blood transfusion.31,32 Because unfiltered PRBC units also contain WBC, and *Leishmania* spp amastigotes reside in the mononuclear macrophages,33,34 transmission of *Leishmania* spp via blood transfusion appears likely.50 Mounting evidence exists that *L. infantum* may be transmitted via blood transfusion in people.50,51 Many human blood donors in endemic regions such as Marseille, France (13%) have been found to be seropositive for *Leishmania* spp.35 However, current blood banking standards in endemic areas or in the United States fail to address this issue. Grogl et al36 found that *L. tropica*- or *L. donovani*-contaminated transfusable blood products are a risk to the blood supply for at least 25 days after donation under standard blood bank storage conditions, indicating that storage conditions do not inactivate or kill *Leishmania* organisms. However, it is important to note that FFP was not implicated as having the potential for disease transmission in their study.51 In our study, all 9 dogs that received FFP from seropositive donors remained seronegative.
A positive serum titer indicates exposure to or infection with *Leishmania* spp, but only 1 (recipient 1) of the 3 seropositive recipients in our study developed clinically apparent leishmaniasis. This recipient was a chronically immunosuppressed dog that developed severe leishmaniasis after receiving a PRBC transfusion from a seropositive donor more than 2 years earlier. Disseminated pyogranulomatous lesions were found, with cardiopulmonary lesions the likely cause of death. In contrast to the typical wasting syndrome, this dog was morbidly obese, likely secondary to administration of prednisone, had a good hair coat, and had no gross skin lesions consistent with leishmaniasis. Although not well documented in dogs, immunosuppressed human patients are much more susceptible to clinical disease secondary to *Leishmania* spp infection than are immunocompetent individuals.42,43 In fact, *Leishmania* spp has become an important opportunistic infection in HIV-infected people. On the basis of the rising and persistently high *Leishmania* spp titer, it is likely that recipient 2 is infected. Although the dog did not have evidence of disease, it has been treated with allopurinol. Recipient 3 initially tested positive at 1:16 2.5 years after transfusion but on retest evaluation approximately 5 weeks later had a test result of < 1:16. In this instance, it is possible that the initial 1:16 test result was false-positive, or the titer was falling after spontaneous cure; however, because of the limitations of the serologic test, *Leishmania* spp infection cannot be ruled out in this recipient. Further investigations are required to confirm or rule out *Leishmania* spp infection in this recipient.

To our knowledge, the infected canine PRBC recipients described here represent the first documentation of transfusion-transmitted *L. infantum* in any species. There have been 6 possible *Leishmania* spp transmissions in humans through blood transfusions reported. The hematogenous spread of *Leishmania* spp was first described in 2 girls who received IM injections of maternal blood for measles prophylaxis; however, the mother had not been evaluated for *Leishmania* spp infection.44 The remaining cases involved immunosuppressed patients such as children with leukemia, recurrent infections, or cardiac surgery who had received blood transfusions. Because the blood donors were never serologically tested for *Leishmania* spp, these cases of transfusion transmission remain presumptive.41,45

Although blood transfusions are also used in the treatment of anemic dogs in endemic areas, there are no reports of *Leishmania* spp transmission via blood transfusion. It is reasonable to assume that some of the canine blood donors in endemic regions are likely to have been screened for *Leishmania* spp infection, thereby reducing the risk of transmission. However, it appears prudent to screen all potential blood donors living in endemic areas for *Leishmania* spp and to use only seronegative donors. In the United States there appears to be no imminent need to screen all canine blood donors for *Leishmania* spp infection at this time; however, it appears crucial to screen all foxhounds and possibly other hound and hunting dog breeds used as blood donors.

In conclusion, this report serves as a reminder of the potential risks of infectious disease transmission through blood transfusions. With this in mind, blood donors need to be carefully screened for known and emerging infectious diseases, and transfusion therapy should be reserved for those patients in which there is a clear clinical indication for blood component therapy.47

References


