Prevalence of Antibodies to *Trypanosoma cruzi* among Solid Organ Donors in Southern California: A Population at Risk

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Trypanosoma cruzi, a parasite that causes Chagas' disease, is endemic in parts of Mexico, South America, and Central America. Transmission of *T. cruzi* infection by solid organ transplantation has been reported in Latin America and recently in the United States. To determine the prevalence of *T. cruzi* antibodies in Southern California organ donors, 404 samples from deceased organ donors between May 2002 to April 2004 were screened using a qualitative enzyme-linked immunosorbent assay (EIA) and confirmed with an immunofluorescence assay (IFA) available through the Centers for Disease Control (CDC). Six donors were initially reactive by EIA. Three donors were repeatedly reactive after repeat testing and were sent to the CDC for confirmation. One donor (0.25%) had an IFA-confirmed reactivity to anti-*T. cruzi* antibodies. In areas where there is a high number of immigrants from *T. cruzi* endemic countries, screening for anti-*T. cruzi* donor antibodies may be beneficial.

Keywords: Organ transplantation, Chagas' disease, *Trypanosoma cruzi.*

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Chagas' disease is a parasitic infection caused by *Trypanosoma cruzi.* It is endemic in Mexico, South America, and Central America, where an estimated 16–18 million people are infected with the disease (*1*, *2*). Parasitemia follows a bite by an infected kissing (reduviid) bug. In the acute phase fever is the most common clinical manifestation of the disease, although approximately 20% of those infected are completely asymptomatic (*3*). Rarely, patients succumb to the acute phase of infection secondary to severe heart failure or encephalomyelitis (usually children and immunocompromised patients) (*1–3*). Infection leads to T cell activation as well as antibody formation. These immune responses promote a latency or indeterminate phase in most patients, while a susceptible minority develops chronic infection leading to potentially lethal cardiomyopathy and megasyndromes (megacolon, megaesophagus).

Trypanosomes circulating in the blood make blood-borne transmission a possibility. The first transmission by blood transfusion occurred in Brazil in 1952. Since then, nearly 200 cases have been reported in Latin America, which is assumed to be a severe underestimation (*3*). The dangers of transmission are increased because this disease is often subclinical, causing many donors to be unaware of their infection status. In 1993, a study of 318 blood donors in Morelos, Mexico showed that 17% of donors had antibodies to *T. cruzi* detected by a commercial enzyme immunoassay (EIA) (*4*). Reports of transmission of *T. cruzi* by organ transplantation inevitably followed, although screening in Latin America for the parasite is standard practice (*1*, *2*, *5–8*).

Reports of blood and donor organ transmissions have surfaced in the United States and Canada. There have been three reported cases of transfusion transmission of *T. cruzi.* Two cases were in the United States, occurring in a patient with Hodgkin's disease and a bone marrow transplant patient, both with clinical manifestations of infection (*3*, *9*). The third case was from Canada, in a patient with acute lymphocytic leukemia who developed acute Chagas' disease (*10*). In all cases the suspected blood donors had emigrated from *T. cruzi* endemic areas.

In March of 2002, the Centers for Disease Control (CDC) reported a case in which three solid organ transplant recipients were infected with *T. cruzi* from a single organ donor (*1*). The donor was an immigrant from Central America assumed to have been infected with *T. cruzi.* One of the recipients, a 37-year-old female, developed a febrile illness and continued to suffer bouts of symptomatic parasitemia despite treatment for *T. cruzi.* She eventually died from acute Chagasic myocarditis. The other kidney recipient was successfully treated, and the recipient of the liver died of unrelated causes. This recent report has increased awareness of the possibility of organ transplant transmission of a potentially fatal disease.

Chagas' disease is of special concern in Southern California, where there is a large immigrant population from countries where *T. cruzi* is endemic. According to the year 2000 Census, nearly 7 million respondents in the relevant Southern California counties considered himself or herself Hispanic or Latino (*11*). In the entire state of California, from 1988 to present, 25% of organ donors were Hispanic (*12*). In addition to this large population there are frequent contacts of non-Hispanics with areas where *T. cruzi* is endemic.

Currently there is no United Network for Organ Sharing (UNOS) policy or CDC recommendations concerning the serologic screening of potential organ donors for *T. cruzi* in the United States. However, EIA have been used in research

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and clinical application in the United States for several years and confirmatory immunofluorescence assay (IFA) is available at the CDC. As the proportion of Hispanic organ donors is very high in our population, we decided to evaluate the seroprevalance of anti-*T. cruzi* antibodies among the cadaver solid organ donors to determine the risk of infection.

MATERIALS AND METHODS

We tested all 404 archived serum samples from deceased organ donors sent to our laboratory by the Organ Procurement Organization (OPO) between May 2002 and April 2004. This OPO recruits donors from the Southern California area (Kern, Santa Barbara, Ventura, Los Angeles, Orange, Riverside, San Bernadino). The composition of our cohort reflects the ethnic diversity of the population living in this area. Median age was 34 years and 41% of donors were Hispanic. All serum samples from prospective organ donors were screened for antibodies to *T. cruzi*, using a commercial EIA (Hemagen Diagnostics, Columbia, MD). The assay was carried out following the manufacturer's instruction. In Figure 1, we provide the distribution of sample absorbance to cut-off ratios (S/CO) for all tested specimens. The figure shows the separation of S/CO for reactive and nonreactive samples. Because of the poor separation between reactive and nonreactive samples, we decided to repeat in duplicate all specimens with absorbance within 10% above and below the cutoff value. Cross-reactive antibodies against Leishmania species and other trypanosomal agents were not determined. All repeatedly reactive specimens were sent for confirmatory testing to the CDC Microbial Disease Laboratory (Atlanta, GA), where a confirmatory testing was performed. The confirmatory assay has a cut off of ≥1:32 dilution and utilizes fixed epimastigotes to confirm specificity of anti-*T. cruzi* EIA reactivities.

RESULTS

In Table 1 we provide results from our screening. From 404 cadaveric donor specimens available for testing, six were initially reactive or gray zone reactive with the EIA. Three specimens were repeatable reactive when re-tested in duplicate and were sent to the CDC for confirmatory testing. One specimen's initial EIA reactivity was confirmed to be weakly reactive (titer 1/64) by IFA. The ages for the initially reactive donor specimens ranged from 40–61 years old. The majority was male (5/6), and three out of the six specimens were from Hispanic donors. The confirmed reactive specimen was from a 45 year-old male Hispanic donor. The OPO has been notified of the results of our study, and tracking of the organs from the positive donor specimen is in progress.

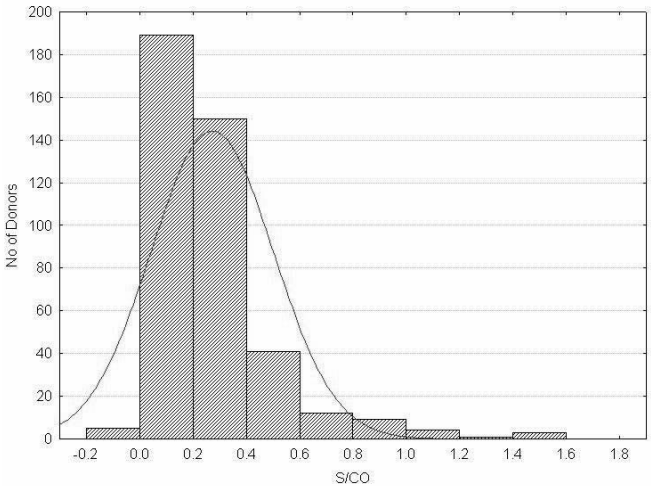

FIGURE 1. Distribution of sample to cutoff ratios (S/CO) for all tested specimens. Ratio equal to 1.0 indicates the assay's cutoff.

DISCUSSION

Organ donor screening algorithms for the prevention of common communicable diseases are well described. However, in the past few years, the transmission of other rare, but potentially fatal diseases has raised the question of whether current screening policies are adequate. The first report of transmission of West Nile virus (WNV) by blood and solid organs occurred in 2002 (*13*). Three organ recipients developed encephalitis and one developed a febrile illness following transplantation. Blood banks have begun using nucleic acid amplification testing to screen for WNV, and potential blood donors are asked about fever and headache symptoms during mosquito season. Organ donors, however, do not undergo serological screening for WNV.

In 2004, a single donor transmitted rabies virus to three solid organ recipients and one recipient of a vascular graft (*14*). All four recipients experienced neurological symptoms and died within 2 weeks of onset of symptoms. Rabies virus, although not spread hematologically, is a risk for organ transplantation. Screening should entail detailed questions about a history of mammalian bites.

To our knowledge, our study is the first evaluation of anti-*T. cruzi* antibodies seroprevalence among cadaveric organ donors from the United States West Coast. With increased emigration to the United States the risk of Chagas' disease transmission is no longer a problem limited to Latin America. A study of 1024 consecutive blood donors at the Los Angeles County blood bank showed a seroreactivity to *T. cruzi* of 1.1%, and a confirmed reactivity of 0.1%. Donors from *T. cruzi*-endemic countries composed 38% of the sample donor population (*15*). We found one donor (0.25%) with a confirmed level of anti-*T. cruzi* reactivity. All initially reactive specimen S/CO ratios were low which is compatible with old exposure (*1*). Our data suggest that screening for *T. cruzi* should be triggered by donor risk factors like the strength of the ethnic ties with endemic areas to avoid unnecessary exclusion of donors due to unconfirmed EIA screening results. There is currently no accepted screening or confirmatory tests for *T. cruzi*. Although EIA screening is not time or cost-prohibitive, future studies are needed to determine the suitability of these tests in both endemic and nonendemic areas.

Our data is in contrast with the previously published data from the United States. Bryan et al. from the Midwestern United States found no organ donors with antibodies to *T. cruzi* over a 6.5-year period (*16*). Barrett et al. screened 8000 random blood donor samples in the Southeast United States and had no samples with *T. cruzi* antibodies (*17*, *18*). This discrepancy is likely secondary to differences in pop-

TABLE 1. Demographics of organ donor samples initially reactive to anti-T.cruzi antibodies by ELISA

Donor	Age	Sex	Ethnicity	ELISA (S/CO)[a] Initial test	Repeat test #1	Repeat test #2	IFA Titer	Confirmed
1	61	F	African-American	1.02	0.91	0.55	1/32	No
2	45	M	Hispanic	0.91	1.03	1.05	1/64	Confirmed
3	40	M	Caucasian	1.56	1.51	1.51	1/32	No
4	55	M	African-American	1.36	0.62	0.67	Not tested	Not tested
5	52	M	Hispanic	1.06	0.77	0.66	Not tested	Not tested
6	35	M	Hispanic	0.96	0.88	0.91	Not tested	Not tested

[a] Absorbance of sample divided by cut-off value; positive value = 1.00 ± 10%.
IFA, immunofluorescence assay.

ulation composition, as Southern California has a large Hispanic and Latino immigrant population. Similar to the issues discussed with the documented transmission of WNV and rabies, the organ transplant transmission of *T. cruzi* raises the question of adequate screening of donors for this disease. The risks involved with possible transmission are high in transplant patients, as immunosuppression has been shown to exacerbate *T. cruzi* infection (*19*). Transmission infection with *T. cruzi* has led to death in previous cases of immunosuppressed patients. According to our data and previous case reports, screening donors from *T. cruzi*-endemic countries for anti-*T. cruzi* antibodies may be beneficial in areas with a high frequency of these organ donors.

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