Epidemiology of Chagas disease in non-endemic countries: the role of international migration

Gabriel A Schmunis

Pan American Health Organization/World Health Organization, 525 23rd Street, NW Washington, DC 20037, USA

Human infection with the protozoa Trypanosoma cruzi *extends through North, Central, and South America, affecting 21 countries. Most human infections in the Western Hemisphere occur through contact with infected bloodsucking insects of the triatomine species. As* T. cruzi *can be detected in the blood of untreated infected individuals, decades after infection took place; the infection can be also transmitted through blood transfusion and organ transplant, which is considered the second most common mode of transmission for* T. cruzi. *The third mode of transmission is congenital infection.*

Economic hardship, political problems, or both, have spurred migration from Chagas endemic countries to developed countries. The main destination of this immigration is Australia, Canada, Spain, and the United States. In fact, human infection through blood or organ transplantation, as well as confirmed or potential cases of congenital infections has been described in Spain and in the United States.

Estimates reported here indicates that in Australia in 2005-2006, 1067 of the 65,255 Latin American immigrants (16 per 1000) may be infected with T. cruzi, *and in Canada, in 2001, 1218 of the 131,135 immigrants (9 per 1000) whose country of origin was identified may have been also infected. In Spain, a magnet for Latin American immigrants since the 2000, 5125 of 241,866 legal immigrants in 2003 (25 per 1000), could be infected. In the United States, 56,028 to 357,205 of the 7,20 million, legal immigrants (8 to 50 per 1000), depending on the scenario, from the period 1981-2005 may be infected with* T. cruzi. *On the other hand, 33,193 to 336,097 of the estimated 5,6 million undocumented immigrants in 2000 (6 to 59 per 1000) could be infected. Non endemic countries receiving immigrants from the endemic ones should develop policies to protect organ recipients from* T. cruzi *infection, prevent tainting the blood supply with* T. cruzi, *and implement secondary prevention of congenital Chagas disease.*

Key words: Chagas disease - immigration - non-endemic countries - blood supply - prevention - transfusion and congenital transmission

American trypanosomiasis or Chagas disease is caused by the protozoa *Trypanosoma cruzi*. Human infection extends through North, Central, and South America, from Mexico in the north to Argentina and Chile in the south, affecting 21 countries (WHO 1991, 2002, OPS 2006).

Most human infections in the Western Hemisphere still occur when the skin or mucous membranes come into contact with the stool or urine of *T. cruzi* infected bloodsucking insects of the triatomine species (WHO 1991). However, significant advances have been made on this front. Strengthening vector control of the main domiciliary vector in the Southern Cone of South America, *Triatoma infestans*, interrupted vector transmission of *T. cruzi* by that triatomine in Uruguay in 1997, Chile in 1999 (WHO 2002), and Brazil in 2006. That success stimulated countries in Central America to attempt control of their intradomiciliary vector, *Rhodnius prolixus*. Up to now, significant success has been achieved in El Salvador and Guatemala.

E-mail: schmunig@paho.org
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As *T. cruzi* can be detected in the blood of untreated infected individuals, or of those with treatment failure (WHO 1991), decades after infection took place, said infection can be transmitted to an uninfected individual through blood transfusion. As long as blood from infected donors is not discarded, the possibility of transmitting infections through transfusion remains. Transfusion of whole blood, packed red blood cells, platelets, leukocytes, frozen fresh plasma, and cryoprecipitate is dangerous. In contrast, the use of lyophilized products appears to be safe (Schmunis 1991).

Transfusion can be considered the second most common mode of transmission for *T. cruzi*. Fortunately, only a fraction of infected blood recipients will become infected, e.g., between 12 and 20% in Argentina, Brazil, and Chile, and up to 48% in Bolivia (Schmunis 1991). However, this risk might be even less; in the United States, it was shown that 11 individuals who had received blood units positive for *T. cruzi* serology remained seronegative (Leiby et al.1997).

In the last 15 years, most Latin American countries have implemented policies to prevent transmission of Chagas disease by transfusion. Four countries screened 100% of donors for *T.cruzi* in 1993-1995; 5, in 1997; 7, in 2001-2002 (Schmunis et al. 1998, and 2001, Schmunis & Cruz 2005); and 8, in 2004 (PAHO 2006). Another four countries screened ≥ 99% of donors in 2004 (PAHO 2006) (Table I). In fact, the only common mode of transmission of *T. cruzi* to which not enough

TABLE I

Latin America, 1993-2004: number of countries with serological screening of blood donors for *Trypanosoma cruzi*

Percentage of donors screened[a]																			
1993/1995					1997					2001/2002					2004				
100	≥ 80 ≤ 90	≥ 70	≥ 50/ ≤ 70	≤ 50	100	≥ 99	≥ 70 ≤ 80	≥ 50/ ≤ 70	< 50	100	≥ 99	≥ 90 ≤ 98	≥ 70 < 90	< 50	100	≥ 99	≤ 75 < 90	< 50	
ARG HON URU VEN	PAR	CHI GUT	NIC ECU	BOL COL[b] COR[c] ELS PAN	ARG ELS PAR URU VEN	HON COL	CHI ECU	NIC PER	BOL COR PAN[d]	ARG BRA ECU ELS HON URU VEN	COL PAR PER	GUT NIC	BOL CHI	PAN COR MEX	ARG BRA COR ECU ELS NIC URU VEN	COL GUT HON PAR	BOL CHI PER	MEX PAN	

a: Brazil and Mexico reported screening coverage for the first time in 1999. *b*: screening coverage, 1.42 %; *c*: screening coverage, 0 %; *d*: screening coverage, 0.7 %; ARG: Argentina; BOL: Bolivia; BRA: Brazil; CHI: Chile; COL: Colombia; ECU: Ecuador; ELS: El Salvador; GUT: Guatemala; HON: Honduras; MEX: Mexico; NIC: Nicaragua; PAN: Panama; PER: Peru; URU: Uruguay; VEN: Venezuela.

attention has been paid in most endemic countries is the transplacental route. Although infection rates of congenital infection vary widely, it is accepted in the Southern Cone countries of South America that 1 to 12% of newborns from infected mothers could be infected (Carlier & Torrico 2003).

The estimated number of individuals infected with *T. cruzi* in endemic areas of Latin America decreased steadily since the 1980s, from 16-18 million cases in the middle of that decade and early 1990s (WHO 1991) to 11 million in the mid to late 1990s (Schmunis 2004); and to 7.6 million in 2006 (OPS 2006). This decrease may also be observed by comparing the burden of disease caused by several infectious diseases in 1990 with the equivalent data for 2001.

In Latin America, the disease burden produced by Chagas disease was surpassed only by acute respiratory infections, diarrheal diseases, and AIDS (World Bank 1993). Chagas disease had a higher disease burden than tuberculosis in 1990 (Fig. 1). At that time, the disease burden produced by the so called tropical diseases, malaria, schistosomiasis, leishmaniasis, and leprosy together equaled 25% of the disease burden caused by Chagas disease (Schmunis 1994).

In 2001, the disease burden decreased for all the aforementioned diseases, except for tuberculosis; nevertheless, Chagas disease had the greatest decrease when measured in disability adjusted life years (DALYs): 2.7 million to 867,000 DALYs (World Bank 2006) (Fig. 1). The number of deaths attributed to *T. cruzi* infection also decreased, from 45,000 deaths a year in the 1980s (Moncayo 1993) to 14,000 in 2001 (World Bank 2006 a). Indeed Chagas disease is in retreat in Latin America.

On the other hand, the potential for transfusing *T. cruzi*-infected blood or blood products is not exclusive to Latin America. Economic hardship, political problems, or both, have spurred migration from Chagas endemic countries to developed countries. For example, it was estimated that in the United States between 100,000

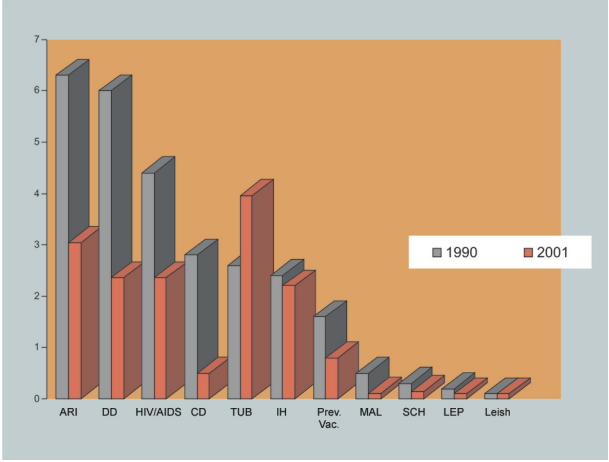

Fig. 1: burden of disease in Latin America and the Caribbean 1990 and 2001. The unit use for measurement is the disability adjusted life years (DALYs) (World Bank 1993). One DALY can be considered as one year of healthy life lost (WHO 2002a). ARI: acute respiratory infections; DD: diarrheal diseases; HIV/AIDS; CD: Chagas disease; TUB: tuberculosis; IH: intestinal helminths; Prev. Vac.: diseases preventable by vaccination; MAL: malaria; SCH: schistosomiasis; LEP: leprosy; Leish: leishmaniasis.

(Skolnick 1989) and 370,000 people (Milei et al. 1992) had chronic *T. cruzi* infection, and that 75,000 of those suffered from chronic myocardiopathy of that etiology (Milei et al. 1992). In Canada, in a recent survey of 102 Latin American refugees and immigrants, the prevalence of Chagas disease was found to be at 1% (Steel et al. 2007). Surprisingly, a similar survey conducted among immigrants in Germany showed 2% prevalence (Hegenscheid et al. 1997). Also as a result of migration, a case of congenital Chagas disease was diagnosed in Sweden (Pehrson et al. 1981).

In the late in 1980s, the number of documented Latin American immigrants in the United States from countries endemic for *T. cruzi* was 2,24 million, 1,55 mil-

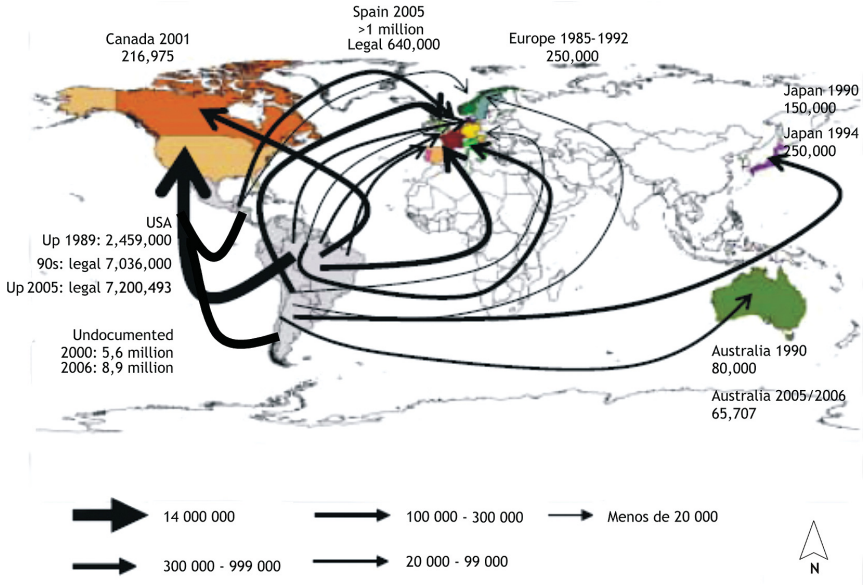

Fig. 2: immigration flow from Latin America. Obtained from the Latin American and Caribbean Center for Demography [Centro Latino Americano y Caribeño de Demografía (CELADE)] and modified. Population Division of CEPAL (División de Población de la CEPAL). Proyect on research of international migration in Latin America [Proyecto de investigación de la migración internacional en Latinoamérica (IMILA)].

lion of whom were from Mexico (Statistical abstract of the United States 1989). The potential for finding *T. cruzi* infected individuals also existed in Europe, Australia, and Japan, where in the late 1980s, 250,000, 80,000, and 200,000 immigrants from Latin America, respectively, were living (Schmunis 1991). Immigrants in Japan were mainly Brazilians of Japanese ancestry whose living conditions in Brazil made them unlikely to have been infected with *T. cruzi*. In the United States, more than 7 million people from *T. cruzi* endemic countries become legal residents between 1981 and 2005 (US Census Bureau 2007). In Europe, Spain has become a magnet for immigrants from Latin America.

We report here, estimates of the number of *T. cruzi* infected individuals in non endemic countries i.e., Australia, Canada, Spain, and the United States, with immigrant populations from Latin American endemic countries. We discuss as well the public health implications of said immigration.

METHOD

Data on the number of immigrants, regardless of their legal status, were obtained from official sources from Australia (Australia Bureau of Statistics 2007), Canada (Canadian Statistics 2005), Spain (General Police Directorate, Interior Ministry (2002), Eurostat Europa, (2006), and the United States (Statistical Abstract of the United States 1989; US Department of Homeland Security 2003 and 2004; US Bureau of Census 2006, 2007; and information from newspapers.

The possibility of getting and infected transfusion from immigrant blood donors depends on the prevalence of infection in the country of origin. Taking into account that serology in blood donors correlated well with serological surveys among the general population (Schmunis 1994), we used the prevalence of *T. cruzi* infection per 1000 blood donors at the time when it was first officially reported by the countries of Latin America (around 1993-1995), as proxy for that prevalence: Argentina, 49 per 1000 donors; Bolivia, 148; Chile and Colombia, 12; Costa Rica, 8; Ecuador, 2; El Salvador, 15; Guatemala, 14; Honduras, 12; Nicaragua, 2; Panama, 1; Paraguay, 45; Uruguay 6; and Venezuela, 13 (Schmunis & Cruz 2005). Two countries, Brazil and Peru, reported country-wide prevalence of *T. cruzi* serology in blood donors for the first time in 1999 and 1997, respectively (8 per 1000 in Brazil, and 2 per 1000 Peru) (Schmunis & Cruz 2005). In Mexico, prevalence of *T. cruzi* infection in blood banks of the public health services in 12 of the 34 Mexican states ranged from 1,7/1000 (Chihuahua) to 17/1000 (in Morelos) from 1978 to 2004 (Cruz Reyes & Pickering Lopez 2006). On the other hand, 1999 was the first year for which data from Mexico on the prevalence of infectious disease markers in blood donors were officially provided; at that time, the prevalence rate for *T. cruzi* (4 per 1000) was based on the screening of only 13% of the total number of donors (Schmunis & Cruz 2005). In 2004 however, screening coverage increased to 34%, and the prevalence for *T. cruzi* also increased to 5 per 1000 (PAHO 2006), the same prevalence found in the state of Veracruz (Ramos-Lingonio et al. 2006). In some instances, information on rates of *T. cruzi* infection among blood donors from non endemic Mexican states (where there is no transmission) indicated high positive rates; such is the case of Puebla in 2001-2002 with a

rate of 77 per 1000 (Sanchez Guillen et al. 2002), or Mexico City in 1998-2000 with a rate of 68 per 1000 (Cabrera et al. 2004). It was considered that the latter were mostly low income donors from 28 out of the 31 states of the country.

Taking into account the variations in prevalence rates among Mexican blood donors and the large numbers of Mexican immigrants in the United States, two scenarios were used for calculations. The first one used the prevalence found in the overall donor pool in 2004 (5 per 1000), and the other, the prevalence found among donors in Mexico City hospitals in Mexico City (68 per 1000). The latter was assumed to be a better estimate of the prevalence among low income populations likely to migrate to the United States.

It was also assumed that blood donors in immigrants' host countries would have been born at least 18-20 years before 2006 in their country of origin (in 1986-1988 or earlier) at a time when the overall *T. cruzi* prevalence rate in the latter country would have been higher (Schmunis 1991). Therefore, immigrant rates shown here are conservative estimates of the potential rate of infection of the immigrant population in the receiving country. All data were rounded to the nearest tenth of a unit by conventional methods.

RESULTS

Australia

Information was available on permanent arrivals from Argentina, Brazil, Chile, El Salvador, and Uruguay from 1975 to 2005. For Colombia and Peru, the information available was the estimated resident population in 2006 (Australian Bureau of Statistics 2007). Overall, the total number of immigrants was 65, 255, and the overall potential number of infected individuals could have been 1067 (Table II) when combining both permanent arrivals and resident population or 16 per 1000 of Latino immigrants in Australia (Table II).

Canada

Among the 29,639,035 individuals that populated Canada in 2001, 216,975 were classified as of Latin American origin. For 131,235 of those, there is information about country of origin. Most came from Mexico, followed, in decreasing order by Chile, El Salvador, Peru, and Colombia (Table II). Another 41,620 were from Central and South America; no information was available on the country of origin. There were also 44,120 individuals considered Latinos born in Canada (Canadian Statistics 2005). Estimates on the number of individuals potentially infected with *T. cruzi* from each country are shown in Table II. In Canada, the rate used to calculate the infection rate among immigrants from Mexico was 5 per 1000. Overall 9 per 1000 immigrants whose country of origin was identified may have been infected with *T. cruzi* (Table II).

Spain

In Europe, Spain is the country with the largest number of immigrants from Latin America. According to the General Police Directorate of the Ministry of the Interior 2002, there were 297,171 legal immigrants from Argentina, Brazil, Chile, Colombia, Ecuador, Peru, Uruguay, and Venezuela in 2002. At that time, there was no information on the number of immigrants from other endemic countries such as Bolivia, Costa Rica, El Salvador, Guatemala, Honduras, Nicaragua, Panama, and Paraguay. In 2003 (Table III), 241,866 immigrants were reported, including those from two countries where Chagas disease was highly prevalent, i.e., Bolivia and Paraguay (Eurostat 2006). It was estimated that 6125 or 25 per 1000 of those immigrants could have been infected.

The Ministry of the Interior (2005) indicated that of the approximate 2 million legal immigrants in Spain, 640,000 (32%) were from Latin America (Gazcon 2006). Of those, 11% were from Ecuador (70,400), 7% from Colombia (44,800); 3.5% from Peru (22,400), and 3%

TABLE II

Estimated number of legal immigrants and potential number of immigrants infected with *Trypanosoma cruzi*, in Australia, 2005-2006, and Canada, 2001, by country of origin

	Australia		Canada	
Country of origin South America	Estimated number of immigrants	Estimated number of infected immigrants	Estimated number of immigrants	Estimated number of infected immigrants
Argentina	10,053	493	NA	NA
Brazil	4225	34	NA	NA
Chile	21,672	260	34,110	409
Colombia	5943	71	15,865	190
El Salvador	10,956	164	26,740	401
Mexico	NA	NA	36,675	183
Peru	7217	14	17,745	35
Uruguay	5189	31	NA	NA
Total	65,255	1067	131,135	1218

NA: no information available.

TABLE III

Estimated number of legal immigrants and potential number of immigrants infected with *Trypanosoma cruzi*, in Spain, by country of origin, 2003

	Legal immigrants	
Country of origin South America	Estimated number of immigrants	Estimated number of infected immigrants
Argentina	30,313	1485
Bolivia	24,433	3616
Brazil	10,107	81
Chile	7105	85
Colombia	15,998	192
Ecuador	99,380	199
Paraguay	3335	150
Peru	18,519	37
Uruguay	11,834	71
Venezuela	13,117	171
Total	234,141	6087
Central and North America		
Costa Rica	NA	NA
El Salvador	487	7
Guatemala	340	5
Honduras	1368	16
Mexico	4918	25
Nicaragua	319	1
Panama	293	0
Total	7725	38
Grand total	241,866	6125

NA: no information available.

from Argentina (19,200). Following the same estimation method as above, the number of infected individuals would have been 141 from Ecuador, 538 from Colombia, 45 from Peru, and 941 from Argentina. Taking into account only those legal immigrants from those four countries, it can be estimated that there were 1665 individuals infected with *T. cruzi* in Spain. There are indications that illegal immigration is even greater than legal immigration. For example, 550,000 tourists from 17 Latin American countries entered Spain in 2002, but only 86,000 have a registered departure. Ecuador is at the extreme of this situation, with 101,432 Ecuadorian tourists entering Spain and only 874 returning to their country of origin. Among those who stayed, there could be 203 estimated cases of *T. cruzi* infected individuals. In addition, it was recently estimated that there were 400,000 Bolivian immigrants in Spain (El Deber Santa Cruz 2007). Given the prevalence of *T. cruzi* positive serology in blood banks in Bolivia, it could be expected that 59,200 of Bolivian immigrants in Spain may also turn out to have positive serology for *T. cruzi*. A survey done for the Interamerican Development Bank, estimated that in Spain there were 1,820,000 Latin American immigrants; including 262,000 from Argentina, 269,000 from Colombia, 414,000 from Ecuador, 126,000 from Peru (Ultima Hora 2007), and 37,000 from Paraguay (La Nacion 2007). Estimates of those infected were 12,838, 3228, 828, 252, and 1665 respectively.

United States

Up to late 1980s, the United States was by far the main destination for immigrants from Latin America, mostly from Mexico. At the time, of a total of 2439 million legal immigrants, 1,55 million were from Mexico (Statistical Abstract of the United States 1989). Since then, these numbers have increased significantly. In 1990, there were 7 million legal immigrants from Latin America (Schmunis 1994). According to data from the 2000 Census, 35 million Hispanics lived in the United States, and in 2004, that number was estimated at 41 million. A significant number of these immigrants came from countries endemic for *T. cruzi* infection (US Department of Homeland Security 2003, US Census Bureau 2006).

In the United States, the potential number of infected Latinos who could transmit *T. cruzi* infection through blood transfusion cannot be estimated based on the total Latino population, whose members were mostly born in that country. Also, the social and economic conditions of the rural population are not such as to allow intimate contact between the sylvatic vector of *T. cruzi* and humans. In consequence, only five cases of vector transmission of the infection have been reported (Herwald et al. 2000). Nevertheless, an approximation of the number of potentially infected Latinos may be based on the number of legal immigrants from the period 1981 to 2005, i.e., 7,200,493 (Table IV); estimates of the number of undocumented immigrants arriving in the United States from *T. cruzi* endemic countries in Latin America (5.6 million in 2000) (Table IV) (Department of Homeland Security 2003 & 2004, US Census Bureau 2006), and the prevalence of infection in the respective country of origin, as mentioned in the method section. As a result, it could be estimated that 56,028 to 357,205 legal immigrants or 8 to 50 per 1000 population might be expected to have *T. cruzi* infection, depending on the scenario used to estimate the infection rate among Mexican immigrants. On the other hand, 33,193 to 336,097 undocumented immigrants or between 6 and 59 per 1000 population might also be infected.

In 2006, it was estimated that there were 11 million undocumented immigrants in the United States, of which 57% (6,270,000) came from Mexico, 24% (2,640,000) from other Latin American countries, and the rest, from Africa, Asia, Canada, and Europe (The Wall Street Journal 2006). By applying the same method as above, one might expect to find between 31,350 and 426,360 *T. cruzi* infected individuals among those undocumented Mexican immigrants. Documented or undocumented, the real number of those infected from Mexico may lie somewhere between the aforementioned numbers.

In summary, there is ample evidence that non endemic countries harbor a population of individuals infected with *T. cruzi*, and that, sooner or later, nations should have to confront the prevention of transfusion or organ-acquired infection, as well as secondary prevention of congenital infection.

TABLE IV

Estimated number of legal (1981-2005) and undocumented (2000) immigrants from Latin America, and potential number of immigrants infected with *Trypanosoma cruzi*, in the United States, by country of origin

	Legal immigrants		Undocumented immigrants	
Country of origin South America	Estimated number of immigrants	Estimated number of infected immigrants	Estimated number of immigrants	Estimated number of infected immigrants
Argentina	71, 998	3528	NA	NA
Bolivia	38, 232	5658	NA	NA
Brazil	127, 942	1024	77, 000	616
Chile	49, 625	595	NA	NA
Colombia	349, 742	4197	141, 000	1692
Ecuador	179, 847	360	108, 000	216
Paraguay	6624	298	NA	NA
Peru	229, 926	460	61, 000	122
Uruguay	17, 175	103	NA	NA
Venezuela	79, 093	1028	NA	NA
Total	1, 150, 204	17, 251		
Central and North America				
Costa Rica	37, 823	303	NA	NA
El Salvador	573, 425	8601	189, 000	2835
Guatemala	270, 753	3791	144, 000	2016
Honduras	146, 411	1757	138, 000	1656
Mexico	4, 780, 588	23, 903 to 325, 080	4, 808, 000	24, 040 to 326, 944
Nicaragua	180, 316	361	NA	NA
Panama	60, 973	61	NA	NA
Total	6, 050, 289	38, 777 to 339, 954	5, 666, 000	33, 193 to 336, 097

NA: no information available.

DISCUSSION

Migration from Latin America has occurred for economic and/or political reasons. As of the 1970s, the country receiving the largest number of immigrants was the United States (Schmunis 1991, 1994). In the late 1990s, and early in the new century, immigration to Spain grew exponentially.

Since the 1980s, there have been several signs warning that, in time, non endemic countries would have to face the problem of transfusion *T. cruzi* infection (Schmunis 1985, Kirhoff et al. 1987). In Spain, a case of infection was reported in a bone marrow transplant recipient in 1992 (Villalba et al.1992), but worries about *T. cruzi* tainting the blood supply coincided with the increase in the number of immigrants around 2000. A survey conducted in Valencia among 705 blood donors at potential risk of infection because of their ethnic Latin American origin or residence in Latin America, found a positive infection rate for *T. cruzi* of 1.56% by indirect hemagglutination test, and 0.85% positive rate by indirect immunofluorescence (IIF). Of the six positive blood donors, two were from Bolivia and one each from Chile, Ecuador, Mexico, and Nicaragua (Parada et al. 2005).

Another survey was conducted in Cataluña in 2005 among 1770 blood donors, 1524 (86%) of them born in endemic areas of Latin America. The screening used was the ID-PaGIA antibody test (Rabello et al. 1999), and confirmation of positive samples was done by two different ELISA tests. The results yielded 21 positive samples by screening (1.2%), of which 11 were confirmed by ELISA (0.62%). Most positive samples came from Bolivian blood donors (Piron et al. 2007). In 1996, and also in Cataluña, testing for *T. cruzi* was conducted among 70 children 0-14 years of age and 98 women of child bearing age. In this survey, 18 of 168 (10.65%) samples were positive (Soriano et al. 2007), when serology was done using the Stat-Pak screening test (Chembio Diagnostic Systems 2000, Ponce et al. 2005). However, when tested for confirmation with two different ELISA tests, five positive samples from children and four from the women tested turned out to be false positive. The prevalence rate among the women tested was 4% (Soriano et al. 2007). Therefore, when a case of congenital Chagas disease was detected in Barcelona (Guarro et al. 2007), it was not an unexpected event.

In the late 1980s in the United States there were reports of transfusion-transmitted infection among immunosuppressed patients who had received blood or platelets in Canada and the United States (Geiseler et al.1987, Grant et al.1989, Nickerson et al.1989). Two other cases were detected later (Cimo et al. 1993, Leiby et al. 1999). Five of the seven cases identified were reported in the United States and two in Canada (Nickerson et al. 1989, Lane et al. 2000). There probably are many more undi-

agnosed cases among immunocompetent hosts, whose onset of symptoms is four or five weeks after transfusion, whose symptoms are mild and may disappear after symptomatic treatment, or whose infection is indeed completely asymptomatic (Bergoglio 1984). Detectable parasitemia is uncommon. In most cases, diagnosis is made because serology for *T. cruzi* becomes positive. Transfusional *T. cruzi* infections in immunocompromised hosts may present with fever, hepatosplenomegaly, global signs of heart failure and detectable parasitemia.

A case of transmission of *T. cruzi* through solid organ transplantation, in which three organ recipients were infected from one donor, has been also documented (CDC 2002). Another two patients who received heart transplant were also infected, but in both cases recipients of other organs from the same donor were apparently not infected (Mascola et al. 2006).

In the United States, blood donors more likely to harbor *T. cruzi* are in areas with the largest Latino populations. In Los Angeles, California, 1.1% of 988 donors were found to have positive serology for *T. cruzi*; 0.1% of the total were positive by two diagnostic techniques in 1987 (Kerndt et al. 1991). A questionnaire to identify high-risk donors in California, found that 543 of 3492 donors (15.5%) came from areas endemic for *T. cruzi* in 1989-1990. Seventy-two were regarded as high-risk donors, and *T. cruzi* serology was performed on 45 of them; of those, two (4.4%) were positive when tested by two serological techniques (Appleman et al. 1993). Using another risk assesment questionaire, 988 donors were tested by EIA beginning in 1993. One in 299 eligible donors were seroreactive, and one in 524 appeared infected with *T. cruzi.* Of the donors who admitted to birth or travel history to endemic areas for Chagas disease one in 141 had a positive serology, and one in 247 were apparently infected (Shulman 1995). In another study of 13,309 donors living in California, New Mexico, and Texas, including 7835 of Hispanic origin, 0.10% tested positive for *T. cruzi* (Brashear et al.1995). And of 49,465 donors tested in Miami and California in 1994-1995, 105 (0.21%) were seroreactive. After conducting a second test using a different technique, only 34 of the 49,465 samples (0.06%) remained positive (Leiby et al. 1997). Positive samples were also detected among blood donors from the Southwestern United States considered to be at moderate risk (0.14% was considered repeatable reactive and 0.003% of 100,089 donors was confirmed positive (Leiby et al. 1999a). Nationwide estimates suggest that 1 in 25,000 blood donors are infected with *T. cruzi*. However, when a risk screening questionnaire was applied to more than 1.1 million donors in Los Angeles and 181,000 in Miami, 7.3 and 14.3% of respondent, respectively, reported risk. Serology indicated that one per 7500 donors were positive in Los Angeles and one per 9000 in Miami. In addition, the donors showed an increase in the positive rates for *T. cruzi* from 1996 to 1998 (Leiby et al. 2002).

When ELISA testing for *T. cruzi* antibodies was conducted in Houston, Texas, among 3765pregnant women (2107 Hispanic and 1658 non Hispanic), 22 women (0.6%) were reactive. Eleven were also positive by indirect hemagglutination (IHA) (0.3%); nine of the latter (0.4%) came from the Hispanic group, and two (0.1%) were non Hispanic (Di Pentima et al. 1999). This is further indication that congenital Chagas disease, which in endemic countries is mostly asymptomatic, has the potential of going undiagnosed and, consequently, untreated in the United States. In fact, two potential cases of congenital Chagas disease have been detected in the United States (Leiby et al. 1999a).

Prevention

Regarding *T.cruzi* infection in countries at the receiving end of migration, the riskier blood or organ donors are those who come from areas where the prevalence of infection is high; there is also an increased risk in places with a great number of immigrants. Such is the case, with immigrants from Mexico, Chile, and El Salvador in Canada; those from Argentina, Bolivia, Colombia, Ecuador, and Peru in Spain; and those from Argentina, Colombia, El Salvador, Guatemala, and Mexico, in the United States.

The only effective form of prevention is to avoid the use blood from donors from countries where Chagas disease is endemic, or to perform serological screening for *T. cruzi* exclusively on donors from these countries. In endemic countries, the administration of a questionnaire prior to donation to determine place of birth (rural area), housing characteristics (unsanitary), and/or familiarity with the vector (positive identification in a picture) yields warning signs to rule out donors. Such questionnaires could also be employed in non endemic countries. However, even when experts implement the questionnaire, some infected individuals will not be detected, and only through serology will it be possible to determine whether a potential donor for whom the questionnaire yielded no warning sign is infected or not. On the other hand, one could question the need for blood from donors from areas where the prevalence of *T. cruzi* infection is high, such as the departments of Santa Cruz de la Sierra, Tarija, Sucre or Cochabamba, in Bolivia (prevalence between 29 and 51% in blood donors) (Carrasco et al. 1990), or may be not as high, but still much higher than in the rest of the country, as is the case the Argentinean provinces of El Chaco, Jujuy, La Rioja, Salta, and Santiago del Estero (prevalence between 16 and 21% in blood donors) (Perez & Segura 1989).

In Latin America, the most commonly tests for screening, and sometimes for confirmation, are the enzyme immunoassays using conventional (crude antigens) or non conventional reagents (mixture of peptides or recombinant antigens) (Luquetti 1990, Ferreira et al. 2001, Umezawa et al. 2003). The IHA is also used for screening and, on occasions, as a second test for confirmation. However, sensitivity and specificity of commercial reagents available varies widely (Saez-Alquezar et al. 1997) other non conventional tests that has been used for confirmation are an Immunoblot (Umezawa et al. 1996), the TESA (Silveira-Lacerda et al. 2004), the INNOLIA Chagas (Saez-Alquezar et al. 2000), and the RIPA (Leiby et al. 2000), all aimed at replacing the IIF as the gold standard.

TABLE V
Sensitivity and especificity of ELISA commercial tests for screening of blood donors

Commercial kits	Kappa	% sensitivity	CI 95%	% specificity	CI 95%
Adaltis	0.71	100	94.0 - 100.0	60	46.0 - 73.2
Bio-manguinhos [a]	0.95	100	94.0 - 100.0	93	82.2 - 97.7
Bio-manguinhos [b]	0.97	97	89.7 - 99.5	98	89.7 - 99.9
Biomerieux	0.97	100	94.0 - 100.0	95	85.4 - 98.7
Biochile	0.98	99	91.9 - 99.9	98	89.9 - 99.9
Biozima Chagas	0.98	100	93.9 - 100.0	97	87.3 - 99.4
Ebram	0.97	99	91.5 - 99.9	97	87.5 - 99.4
Hemagen	0.98	100	93.9 - 100.0	97	87.5 - 99.4
Patozime-Chagas	0.97	99	91.3 - 99.9	97	87.5 - 99.4
REM Gold	0.97	99	91.8 - 99.9	97	87.0 - 99.4
Wama diagnosyica	0.98	99	91.5 - 99.9	98	89.9 - 99.9
Wiener	0.97	100	94.0 - 100.0	95	85.4 - 98.7

a: recombinante; *b*: conventional; CI: confidence interval.

The Ministry of Health of Brazil tested several reagents used for *T. cruzi* antibody testing in that country (Tables V, VI). The recommendation was to use screening reagents that have a 99% or higher sensitivity, and 97% or higher specificity (Ministry of Health, Brazil, 2006). Up to now, the perfect reagent for the perfect high sensitivity and high specificity test, that is easy to use and inexpensive, has yet to be developed.

Chagas disease among immigrant populations, most of whose members do not know they are infected, represents a challenge for non endemic countries. First, this is a disease that the health services in non endemic countries are not accustomed to manage, so that specialized services with appropriate infrastructure and trained staff would need to be developed. For countries at the receiving end of migration that offer free medical care, services for Chagas are going to be expensive, and should be planned for. If immigrants are going to be allowed to become blood donors, blood donor screening policies should be adjusted to prevent tainting the blood supply. In fact, several European governments have already begun implementing such policies. For instance, the French Government has halted blood collection in the overseas territory of French Guiana, and implemented *T. cruzi* screening among French blood donors at risk, such as those born in an endemic area or from a mother from an endemic area; and donors traveling in endemic areas, regardless of the length of stay. When returning from those areas, donors are deferred for four months.

In addition, a performance evaluation of different ELISA tests was done. Two of them were selected for further testing. One was made from a crude antigen and another from a recombinant antigen, both to be used simultaneously in routine blood screenings. An IIF test will be used as a confirmatory test (Assal & Aznar 2007).

In Spain, Royal Decree 1088 (Real Decreto 2005) on hemodonation, automatically and permanently deferred donors with Chagas disease. If screening tests were not available, donors born in the endemic area, those born from mothers born in endemic areas, and persons who received transfusions in endemic areas are excluded from donating blood labile components (red cells and platelets). However, if these donors have a negative screening test, they may donate blood.

TABLE VI
Sensitivity and especificity of indirect hemagglutination and particle agglutination commercial tests for screening of blood donors

	Indirect hemagglutination	
Kit	% sensitivity	% especificity
Imunoserum	94.64	95.42
Ebran	88.69	59.92
Wama	100.00	95.80
Hemagen	93.45	87,79
Biolab	99.40	97.33
	Particle agglutination	
Serodia	100	97.71
ID PaGIA	98.81	98.85

In the United States, the Food and Drug Administration for the first time approved a test (ELISA) to screen for Chagas disease (US Food and Drug Administration 2007). Although the use of this test to screen for *T. cruzi* antibodies in blood donation centers is not required, organizations responsible for collecting approximately 65% of the country's blood supply began screening donors in January 2007. The American Association of Blood Banks (AABB) recommended that blood donations that are repeatedly reactive by ELISA should be removed from distribution, and its donor deferred (Stramer et al. 2007). Recipients of blood from positive donors (repeat positive by ELISA and RIPA positive) collected previously should be investigated. Moreover, deferred donors, at risk family members, and infected recipients that received components from infected donors should be referred to health services for medical care.

The tests use as antigen a lysate of epimastigotes (Tobler et al. 2007). In 2005, 40,000 blood samples were tested; only one sample turned out positive, but the same was negative by RIPA. Further testing by ELISA conducted by the American Red Cross in 146, 969 samples, detected 63 positive from 61 positive donors (Stramer et al. 2007). Thirty two of these samples were positive by RIPA. Overall, the test is considered to have a sensitivity of ≥ 99% detecting 198 out of 199 positive samples from individuals believed to be infected. Field trials of more than 70,000 donor samples revealed that the likelihood of obtaining a false positive result was small (2 to 3 per 100,000 tests) (US Food and Drug Administration 2007).

Last, but not least, legislation might have to be modified so that immigrants are not discriminated against at their places of employment due to their infection.

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