Prevention of Transfusional *Trypanosoma cruzi* Infection in Latin America

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Trypanosoma cruzi *is a protozoan infection widely spread in Latin America, from Mexico in the north to Argentina and Chile in the south. The second most important way of acquiring the infection is by blood transfusion. Even if most countries of Latin America have law/decree/norms, that make mandatory the screening of blood donors for infectious diseases, including* T. cruzi *(El Salvador and Nicaragua do not have laws on the subject), there is usually no enforcement or it is very lax.*

Analysis of published serologic surveys of T. cruzi *antibodies in blood donors done in 1993, indicating the number of donors and screening coverage for* T. cruzi *in ten countries of Central and South America indicated that the probability of receiving a potentially infected transfusion unit in each country varied from 1,096 per 10,000 transfusions in Bolivia, the highest, to 13.02 or 13.86 per 10,000 transfusions in Honduras and Venezuela respectively, where screening coverage was 100%. On the other hand the probability of transmitting a T. cruzi infected unit was 219/10,000 in Bolivia, 24/10,000 in Colombia, 17/10,000 in El Salvador, and around 2-12/10,000 for the seven other countries.*

Infectivity risks defined as the likelihood of being infected when receiving an infected transfusion unit were assumed to be 20% for T. cruzi. *Based on this, estimates of the absolute number of infections induced by transfusion indicated that they were 832, 236, and 875 in Bolivia, Chile and Colombia respectively. In all the other countries varied from seven in Honduras to 85 in El Salvador.*

Since 1993, the situation has improved. At that time only Honduras and Venezuela screened 100% of donors, while seven countries, Argentina, Colombia, El Salvador, Honduras, Paraguay, Uruguay and Venezuela, did the same in 1996. In Central America, without information from Guatemala, the screening of donors for T. cruzi *prevented the transfusion of 1,481 infected units and the potential infection of 300 individuals in 1996. In the same year, in seven countries of South America, the screening prevented the transfusion of 36,017 infected units and 7, 201 potential cases of transfusional infection.*

Key words: *Trypanosoma cruzi* - Chagas disease - blood transfusion - serology - donors screening - prevention - Latin America

Trypanosoma cruzi is a protozoan infection widely spread in Latin America, from Mexico in the north to Argentina and Chile in south. Years after the infection takes place, *T. cruzi* may be detected in the blood in as many a 50% of those infected (Schenone et al. 1968). Thus, it is not unexpected that *T. cruzi* could be transferred from an infected to a noninfected person by blood transfusion. Fortunately, only some of the recipients of infected blood become infected. Infection rates among blood recipients vary from 1.4% to 18% in Argentina, Brazil, and Chile, and can be up to 48% in Bolivia (Rohwedder 1969, Cerisola et al. 1972, Diaz 1979, Zuna et al. 1985). Transmission by blood transfusion is considered the second most common way of acquiring this infection (Schmunis 1985, WHO 1990).

For the past six decades, economic hardship in Latin America has stimulated migration to urban areas. Therefore, what used to be a rural disease is now often present in cities, where an average, close to 75% of the population of Latin America now lives (Organización Panamericana de la Salud 1998). Migration from rural to urban areas, while decreasing the rural population exposed to infected vectors (Quinteros et al. 1990), increases the possibility of acquiring *T. cruzi* infection by blood transfusion in cities (Schmunis 1985, 1989, 1991, World Health Organization 1990).

Economic hardships and/or political turmoil have increased migration among Latin American countries, and from Latin America countries to the USA (Schmunis 1994). The United States 1990 census indicated that more than 7 million people from countries endemic for *T. cruzi* reside in the United States (Statistical Abstract of the USA

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1992). In addition, 250,000 are living in Europe, 80,000 in Australia, and 150,000 in Japan (Schmunis 1994). Therefore, it is not surprising that transfusion acquired *T. cruzi* infection is a potential problem in non endemic countries.

Transfusional infection is a significant public health problem. Even if most countries of Latin America have laws, regulations and guidelines that make the screening of blood donors for infectious diseases mandatory, including *T. cruzi* (El Salvador and Nicaragua do not have laws on the subject), there is usually no enforcement or it is very lax. While in most countries serology for *T. cruzi* is mandatory throughout, in Chile (Ministry of Health, Chile 1993) and Mexico (Guzman Bracho et al. 1998) serology in blood banks is mandatory only in endemic areas. Furthermore, screening in Mexico is not routinely done in all endemic states. In places like Santa Cruz, Bolivia, where the prevalence of *T. cruzi* antibodies in the population is above 50%, the possibility of acquiring *T. cruzi* infection through a blood transfusion is obvious (Zuna et al. 1985, Carrasco et al. 1990).

PREVALENCE

Serologic surveys of *T. cruzi* antibodies in blood donors have been available since 1949. The results of almost all the surveys carried out between 1949 and 1980, and a few other surveys reported since the 80's have been reviewed elsewhere (Schlemper Jr. 1978, Dias 1979, Schmunis 1991, 1994, Wendell & Dias 1992). Information available from Brazil compares the range of prevalence of *T. cruzi* in different regions with the range of prevalence of other diseases transmitted through blood (Ministry of Health, Brazil 1990-1991).

Available data up to 1992 indicate that prevalence of *T. cruzi* infection in blood donors was around 25% in Bolivia; 5% to 6% in Argentina and Paraguay; 3% to 5% in El Salvador and Guatemala; 1% to 2% in Brazil, Chile, Colombia, Honduras and Venezuela; and, <1% in Ecuador and Nicaragua. Data on serological prevalence of *T. cruzi* in blood donors from Argentina (Schmunis 1985, Perez & Segura 1989, Rosestein Campanini et al. 1993), a Brazilian state (Andrade et al. 1989), Honduras (Ponce 1992) and Uruguay (Franca 1986, Arago 1986) correlated well in most areas with the results of serological surveys, indicating morbidity in the general population of those locations (Segura et al. 1985, Andrade et al. 1989, Salvatella et al. 1989, Ponce 1992).

All of the above were partial data, because national data were not available. Nevertheless these data were extremely useful because establishing the prevalence of *T. cruzi* antibodies in blood donors may provide quick information on the prevalence of the infection in a given geographical area. This is especially the case in countries where knowledge of the status of human infection is lacking, and where control measures for vector or transfusional transmission of *T. cruzi* are not implemented. These data would also indicate the need to implement control strategies for the prevention of transfusional transmission (Schmunis 1991).

INCIDENCE

The real incidence of *T. cruzi* acquired through blood is unknown because most cases are either inapparent or *T. cruzi* is not recognized as the etiological agent (Schmunis 1985, 1991). Danger may come not only from whole blood, but from packed red cells, platelets, white cells, fresh frozen plasma, and cryoprecipitate. On the other hand, the use of lyophilized products seems to be safe (Cerisola et al. 1972, Schlemper 1978, WHO 1990).

In Brazil, where 4 million transfusions are performed yearly, an annual incidence of 10,000 to 20,000 cases has been suggested (Amato Neto 1984, cited in Amato Neto 1993). These estimates correspond to the decade of 1970 (Wendell & Diaz 1992). Only the São Paulo metropolitan area may have contributed 10,000 cases a year (Camargo 1977, cited in Dias 1979). It currently seems that those numbers were exaggerated. The number of donors with positive serology for *T. cruzi* was 55,000; of those, 11,000 were not screened; therefore, it was estimated that between 1,500 to 3,000 individuals, per year, acquired the infection through transfusion (Amato Neto 1993).

The risk of receiving infected blood will be proportional to the prevalence of the infection in the donor population and to the number of transfusions performed. Therefore, polytransfused individuals, like hemophiliacs, patients with other hematologic disorders, or those undergoing dialysis, are at greater risk. In Argentina, 50% of hemophiliacs became infected after receiving 30 or more transfusions each from a blood bank with a 2% prevalence of positive serology for *T. cruzi* (Cerisola et al. 1972). In another study, in Chile, it was found that 15% of individuals who had multiple transfusions, had positive serology for *T. cruzi*, while the general population was 2% positive (Lorca et al. 1988). Polytransfused individuals from a blood bank with 2% positive serology for *T. cruzi* were 8.7 times more likely to be positive than individuals who did not receive transfusions. On the other hand, the theoretical risk of transmission for individuals receiving only one transfusion may vary from 0.15% to 0.6% (Atias et al. 1984) to 20% (WHO 1990) or higher (Zuna et al. 1985).

In any case information available up to 1992 have some limitations. Countries lacked a country

wide information system on the number of donors and the number of screened donors, both needed to calculate screening coverage. If that information had been available, coupled with a knowledge of the prevalence of the infection, it would have been possible to calculate the risk of acquiring *T. cruzi* infection through a transfusion, and the potential number of cases transmitted by blood (Schmunis et al. 1998).

In blood banks, the aim of tests for diagnosis of *T. cruzi* is screening, so as to eliminate all units of blood potentially infected. The purpose of performing more than one serological test for screening, was to avoid introducing false negatives in the blood supply by detecting all potentially positive units (those that could have been negative by one test). In fact, adding tests increases the sensitivity as well as the specificity of the diagnosis. Each methodology and antigen(s) used in the different tests is able to detect antibodies of different specificities. Actually, a limitation of the data obtained, was that different type of tests for *T. cruzi* serology were used in the donor population in the different countries.

Several serological techniques are being used for detection of *T. cruzi* antibodies: complement fixation (CF); indirect hemagglutination (IHA); indirect immunofluorescence (IIF), direct agglutination (DA), and enzyme linked immunoabsorbent assay (ELISA). CF test is the more difficult to standardize and its use must be discouraged. Sensitivity of any single test alone is ≥ 98.91%, and specificity ≥ 98.52%. Using three (CF, IIF and IHA) or the four tests increases sensitivity to 100%, but slightly decreases specificity or the latter remains the same (Takei 1992, Wendell & Gonzaga 1993).

Although ELISA tests are easy to standardize and have the advantage of automatization, they need higher concentration of antibodies in the sample to correlate well with the IIF (Wendell & Gonzaga 1993). Considering as positive only those sera that were positive by IHA and IIF tests, the ELISA gave two false negative and 41 false positive results. The overall sensitivity of ELISA was considered to be 96.3% (Andrade et al. 1992a). In another study in which an ELISA test using a recombinant antigen and four commercially available antigens were compared with conventional serology done by IIF and IHA, it was concluded that ELISA improved the serologic diagnosis of Chagas. In addition, the ELISA best allowed for a considerable reduction in the number of sera in which there was disagreements in the results obtained by different tests in conventional serology (Carvalho et al. 1993). Evaluation of commercial ELISA indicated that the sensitivity varied from 93% to 100% (Oelerman et al. 1998).

In the real world however, another limitation of the data obtained from countries was the unreliability of the commercial kits, whose sensitivity and specificity varied widely as was shown for IFI, IHA, and ELISA in Chile (Lorca et al. 1992, 1994) and for the IHA in Brazil (Saez-Alquezar et al. 1997). This problem is compounded in most countries by the lack of quality control systems. A report from Brazil shows that, in spite of serological screening, 12 of 1,513 samples tested were false-negative (Andrade et al. 1992b) In a performance evaluation of 57 major public blood banks, there were 3.7% false-negative results when testing four panels of sera on a total of 108 samples. Most false-negative results were reported by banks using the IHA (Saez-Alquezar et al. 1997).

A recent report (Schmunis et al. 1998) analyzed national data (OPS 1994, 1995a,b, 1996) on coverage of blood donors screening in four Central American countries (El Salvador, Guatemala, Honduras and Nicaragua) and six countries in South America (Bolivia, Chile, Colombia, Ecuador, Paraguay and Venezuela). With the exception of Chile (Ministerio de Salud, Chile 1996), which reported a fractionation index of 1.85, for all the other countries it was assumed that every blood donation corresponded to a subsequent transfusion to one recipient. Estimates were based on results of screening activities as reported by the countries.

Table I presents the number of donors, screening coverage and prevalence rates for *T. cruzi* antibodies among blood donors in each one of the ten countries. For *T. cruzi* infection, only Venezuela and Honduras screened 100% of donors, prevalence rates per one thousand donors ranged from 0.20% in Ecuador and 0.24% in Nicaragua, to 5.30% in Paraguay, and 14.8% in Bolivia. At that time (1993), Costa Rica, Peru and Mexico had not yet introduced routine screening for *T. cruzi* in blood banks. Information from Argentina indicated that screening coverage for *T. cruzi* was not complete and in Brazil, screening was routinely done in blood banks from the public sector but no information was available from the private sector.

Estimates of the potential infectivity of the blood supply are shown in Table II. The probability of receiving a potentially infected transfusion unit in each country varied from a maximum of 1096 per 10,000 transfusions in Bolivia, to 1,048 in Nicaragua or around 13 per 10,000 transfusions in Honduras and Venezuela, where screening coverage was 100%. On the other hand, the probability of getting an infection through an infected unit was 219 per 10,000 in Bolivia, 24 per 10,000 in Colombia, 17 per 10,000 in El Salvador, and between 2 and 12/10,000 for the seven other countries (Schmunis et al. 1998).

TABLE I

Latin America 1993
Serology for *Trypanosoma cruzi* in blood donors[a]

Country	No. of donors	Screening coverage (% of donors with serology)	Prevalence (00)
Bolivia	37,948	29.40	14.81
Chile	217,312	76.70	1.20
Colombia	352,316	1.40	1.20
El Salvador	48,048	42.50	1.47
Ecuador (1994)	98,473	51.0	0.20
Guatemala	45,426	75.00	1.40
Honduras	27,885	100.00	1.24
Nicaragua	46,001	58.40	0.24
Paraguay (1994)	32,893	95.47	5.30
Venezuela	203,316	100.00	1.32

a: countries that provided national information.

Infectivity risks, defined as the likelihood of being infected when receiving an infected transfusion unit, were assumed to be 20% for *T. cruzi* (WHO 1990). Based on these estimates, the absolute number of infections induced by transfusion was 832, 236, and 875 in Bolivia, Chile and Colombia, respectively. In all the other countries this number varied from seven in Honduras to 85 in El Salvador. The ratio infection/donation for each country indicated that one *T. cruzi* infection might have been transmitted for every 46 (Bolivia) to 4,924 (Ecuador) donations (Table II) (Schmunis et al. 1998).

However, even in those countries with 100% screening coverage there is a potential for receiving an infected transfusion, because of the residual infectivity originated in the lack of sensitivity of the reagents available for diagnosis (Schmunis et al. 1998).

In all countries there is a risk that blood recipients may become infected with *T. cruzi*. Even in those countries where official data was not available, like for Costa Rica, Mexico and Peru it is possible to speculate on the status of *T. cruzi* as a danger for the blood supply. Previous data on the seroprevalence of *T. cruzi* in blood donors from Costa Rica from 1983-1985 (Schmunis 1994), suggest that a risk may exist. Information from Mexico, where there are approximately 850,000 donations yearly, suggests that 12,750 donors are infected with *T. cruzi*. Assuming that only 15% of donors are infected, would indicate that 1912 recipients were potentially infected with *T. cruzi* (Guzman Bracho et al. 1998). Data from a survey among donors in Lima indicated a prevalence of 2.36% (OPS 1994). If this is the real prevalence in that city, the number of tainted units transfused would have been 1,872 in 1993, while the number of infected individuals through blood transfusion could have been 375. On the other hand, if blood had not been screened at all in the ten countries that reported *T. cruzi* prevalence, the number of infected units transfused would have amounted to several thousands.

This 1993 report provided an overview of the potential risk of receiving tainted blood in different Latin American countries. However, some limitations of the data must be taken into account. As the laboratory procedures employed in the ten countries may differ in sensitivity and specificity, comparisons among them are not straightforward. In addition, results of the screening are influenced by the existence of an organized system of quality

TABLE II

Trypanosoma cruzi transfusion transmitted infection[a]

Country	Probability of receiving an infected transfusion (X0000)[b]	Probability of getting a transfusion transmitted infection (X0000)[b]	Absolute no. of transfusion transmitted infections	Ratio infections/ donations
Bolivia	1096.38	219.28	832	1:46
Chile	29.36	5.87	236	1:92
Colombia	124.24	24.85	875	1:403
Ecuador	10.29	2.06	20	1:4,924
El Salvador	88.75	17.75	85	1:565
Guatemala	36.75	7.35	33	1:1,377
Honduras[c]	13.02	2.60	7	1:3,984
Nicaragua	10.48	2.10	10	1:4,600
Paraguay	62.37	12.47	41	1:802
Venezuela[c]	13.86	2.77	57	1:3,584

a: Schmunis et al. 1998. All data from 1993, except for Ecuador and Paraguay that were 1994; *b*: probability for 10,000 transfussions. *c*: residual infection only as screening coverage is 100%.

control and proficiency testing for the serology and for the evaluation of the diagnostic kits, which most countries lacked in 1993-1994. In some cases, the risk of transfusion related infection is overestimated considering that recipients might be already infected. This is most significant for *T. cruzi* infection in Bolivia where the seroprevalence in the general population is sometimes higher than 20% (Zuna et al. 1985, Carrasco et al. 1990).

In any case, the findings stress the importance of having an information system that allows for determining the status of the screening process for infectious diseases in the blood supply. This information, which was only partially available before (Linares & Vinelli 1991, Schmunis 1991, Wendell & Dias 1992), serves as baseline to which future achievements could be measured.

Since 1993, the situation has improved in several countries. Table III shows the screening coverage in 17 countries of the Americas, from 1993 to 1997. The following conclusions are based on data from 1993-1996 already published (OPS 1997, 1998, Schmunis et al. 1998b), analyzed following the methodology reported previously (Schmunis et al. 1998). They also assume the best scenario: sensitivity and specificity of diagnostic test to be 100%; that all test were made correctly; that a system of quality control was in place; and that prevalence of donors screened were the same as in unscreened donors. Consequently, in Central America, except for Guatemala, the screening of donors for *T. cruzi* prevented the transfusion of 1,481 units and the potential infection of 300 individuals (Table IV). In the same year, in seven countries of South America, screening prevented the transfusion of 36,017 infected units and 7, 201 potential cases of transfusional infection (see Table IV). The bottom line is that two countries, Honduras and Venezuela, screened 100% of donors in 1993, while seven countries, Argentina, Colombia, El Salvador, Honduras, Paraguay, Uruguay and Venezuela, did the same in 1997.

PREVENTING *T. CRUZI* TRANSMISION THROUGH TRANSFUSION

Some governments do not have the will or the capacity for implementing prophylactic measures or to enforce them. On the other hand, while the number of transfusions is unjustifiably high, the medical profession at large, and even those devoted to blood banking, seem not to pay enough attention to the possibility that *T. cruzi* could be transmitted by this mean (Dias 1979, Diaz & Brener 1984, Schmunis 1991, Dias 1992). Therefore, health personnel, in particular, and the public, in general, must be educated on the possibility that *T. cruzi* could be transmitted by blood.

Mandatory serology must be implemented in all countries where *T. cruzi* is endemic ideally using at least two serological tests. There should be a ban on paid blood donors; voluntary altruistic donations must be promoted; and a program of quality control for serology must be implemented (Dias 1979, 1992, Diaz & Brener 1984, Schmunis 1991).

TABLE III

Number of blood donors and screening coverage in countries of the Americas

Countries	Year(s)	No. of donors	% screening coverage
Argentina[a]	1993-1997	742,000 – 850,000	58-100
Belize	1997	2,796	0
Bolivia	1993-1996	19,987 - 40,056	30-71
Brazil[b]	1997	1,605,001	100
Chile	1993/1996/1997	217,312 – 228,801	60-77
Colombia+	1993-1997	332,540 – 422,300	1.40-100
Costa Rica	1995-1997	44,754 - 58,436	0-13
Ecuador	1994-1997	98,473 – 110,619	51-91
El Salvador	1993-1997	34,091 - 55,069	42-100
Guatemala	1993	45,026	75
Honduras	1993-1997	27,660 - 33,958	85-100
Nicaragua	1993-1997	43,887 - 48,030	51-68
Panama	1994-1996	26,333 - 41,888	1.14-24
Paraguay	1994-1997	32,893 - 39,904	83-100
Peru	1997	203,690	0-60
Uruguay	1994-1997	110,319 – 115,490	52-100
Venezuela	1993-1997	204,316 – 262,295	100

a: information not available for 1994; *b*: information on percentage of screened donors and prevalence not available for 1,044,673 donors from the private sector; *c*: information not available for 1996.

TABLE IV

Prevention of *T. cruzi* infection by blood screening in Latin America, by country, 1993-1996

Country	1993	1994	1995	1996
Argentina				
No. of infected units discarded	27,809	?	38,189	27,591
No. of cases prevented	5,561	?	7,638	5,518
Bolivia				
No. of infected units discarded	1,650	2,872	2,002	3,003
No. of cases prevented	330	574	400	600
Chile				
No. of infected units discarded	2,000	?	?	1,305
No. of cases prevented	400	?	?	261
Colombia				
No. of infected units discarded	59	658	2,217	?
No. of cases prevented	12	132	443	?
Costa Rica				
No. of infected units discarded	?	?	47	47
No. of cases prevented	?	?	9	9
Ecuador				
No. of infected units discarded	1,004	100	76	67
No. of cases prevented	201	20	15	13
El Salvador				
No. of infected units discarded	300	741	1,192	1,211
No. of cases prevented	60	748	238	242
Guatemala				
No. of infected units discarded	417	?	?	?
No. of cases prevented	95	?	?	?
Honduras				
No. of infected units discarded	346	357	489	98
No. of cases prevented	69	71	98	24
Nicaragua				
No. of infected units discarded	64	122	122	-
No. of cases prevented	13	24	24	-
Paraguay				
No. of infected units discarded	1,603	1,288	1,647	1,486
No. of cases prevented	321	251	329	297
Panama				
No. of infected units discarded	?	?	9	9
No. of cases prevented	?	?	2	2
Uruguay				
No. of infected units discarded	458	684	658	697
No. of cases prevented	92	136	132	139
Venezuela				
No. of infected units discarded	2,697	2,690	1,701	1,868
No. of cases prevented	539	538	340	373

Few countries use more than one test for blood donor screening. Data from Argentina indicated that 50% of 423 centers performed one serological technique for screening (Perez & Segura 1989). A similar survey done in Brazil, covering 850 counties in 1988-1989, indicated that there were 1,525 health services that provided some sort of blood transfusion services. Of these 882 did serology for *T. cruzi*. Of the latter, 55% performed one serological test for diagnosis, while 26.8 and 12.2%, respectively, did two or three tests (Dias 1992, Morales-Souza et al. 1994).

The situation, however, did improve. In the State of São Paulo, 95.3% of 64 blood services

performed serology for *T. cruzi* in 1990, while only 69% did so in 1988. The percentage of services that made serology for syphilis, hepatitis B and HIV were 92.2%, 92% and 90%, respectively, in 1990, against 70.4%, 67.6%, and 63.4% in 1988. On the other hand, from 61 services that did *T. cruzi* serology in 1990, 11.5% did only one test, 55.7% performed two, and 32.8%, three or more tests (Valerio-Wanderley et al. 1992).

In areas with a high percentage of potential donors infected, even when the facilities to do serological tests are available, blood with positive serology cannot be discarded, because the blood supply may be reduced. In those areas, the only measure capable of preventing transfusional infection is the addition of gentian violet to the blood. This dye kills trypomastigotes *in vitro* at 4°C (Nussenzweig et al.1953, Diaz 1992). When used in concentrations of 125 mg/500 ml, and the blood is stored for 24 hr before use, transmission is avoided (Nussenzweig et al. 1953, Shlemper Jr 1978, Diaz 1979, 1992, Diaz & Brener 1984). This strategy has been used extensively in some countries, like Brazil, without apparent side effects, except that patients may become stained for short periods of time (Schmunis 1985, 1989).

The Aids epidemic has increased the awareness of national authorities from endemic countries of the need for serological screening to prevent transfusionally transmitted diseases. This will also improve the situation in relation to *T. cruzi* (as well hepatitis B and C). Meantime, the number of infected individuals with *T. cruzi* will decrease slowly because the full impact of the measures implemented to interrupt vectoral and blood transmission will take years to materialize. Therefore, implementation of measures to prevent blood transmission of *T. cruzi* as well as the presence of patients with Chagas disease, still will constitute a burden for the health services for the years to come.

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