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CHAGAS' DISEASE AND BLOOD TRANSFUSION

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The possibility of *Trypanosoma cruzi* transmission to man through blood transfusion was first mentioned by Mazza et al. (1936) and Dias (1949). Pellegrino (1949) detected infected blood donors in Belo Horizonte, Brazil, and soon Freitas et al. (1950) described the first cases of Chagas' disease transmission by this route. In 1951 and 1952 this problem received particular attention in São Paulo, Brazil, when the basis for the chemoprofilaxis of Chagas' transfusional disease in banked blood was established (Nussensweig et al., 1953, 1955).

Since the decade of the 1950 a large number of epidemiological works are showing significant prevalence rates of chagasic blood donors or candidates to blood donation in Health Services of all Latin America. Cerisola et al. (1972) payed attention to important problems related to the risk of *T. cruzi* transmission in blood banks, reporting a direct relationship between the number of transfusions and the positivity of serology in hemophilic patients who received multiple blood transfusions. Theoretically this risk is very high if one considers the existence of free and viable trypomastigotes in at least 50% of the chronic chagasic individuals, as demonstrated by xenodiagnosis and/or hemocultures (Cerisola et al., 1972; Dias, 1979). In follow-ups of patients who have received blood from chagasic donors, the transmission of *T. cruzi* occurred in 18.7% (Nussensweig et al., 1955), 13.0% (Salazar et al., 1962), and 14.3% (Coura, 1966) of the cases; recently, in an hyperendemic bolivian area, Zuna (1984) observed a risk of about 40%. In general, the risk of an effective transmission is of about 12.5 to 25.0% in patients who receive around 500 ml of fresh "chagasic" blood (Dias, 1979).

The number of reported transfusional cases, however, is still small (about 200 cases). This problem has been analysed in Brazil, with the following explanations (Amato Neto, 1968; Dias, 1979):

a) There is a lack of interest of hemotherapeuts about the identification and communication of such transfusional accidents;

b) Frequently the relationship between Chagas' disease and former blood transfusion is not established;

c) There is a significant number of asymptomatic and/or oligosymptomatic cases that makes very difficult the diagnosis of Chagas' disease, mainly in endemic areas, where both technical problems and staff incompetence are present;

d) There is an effective difficulty for the scientifical publication in the endemic countries.

Nevertheless, the theme is becoming more important within last 15 years, according to the increasing number of surveys performed in blood banks of several Latin American countries. Moreover, the problem displayed other implications when it was verified that *T. cruzi* could be also transmitted by organs transplantation (Dias, Brener & Macedo, 1984).

Chagas' disease is a question of political priority, and the problem of the transfusional transmission does not constitute an exception (Dias & Borges Dias, 1979). In spite of the contributions on to basic research on control measures accomplished in the 1950s, in terms of effective programmes very little was improved up to date. There are still some endemic countries with neither epidemiological data, nor vector control programs (PAHO, 1984).

The present work intends to make a short review about the problem of transfusional Chagas' disease, foccusing on some technological and operational advances on the matter. It is also necessary to stimulate more epidemiological research and to try new control schedules. Since the problem depends basically on the health care system, an institutional diagnosis must be performed in order to understand the fundamental involved factors ("contextual epidemiology", Dias & Borges Dias, 1979; Carvalheiro, 1982).

General epidemiology and diagnosis

All the recent expert committees on Chagas' disease have been strengthening the idea that transfusional route is becoming more and more important in Latin America. The problem seems to increase because of the progressive rural-urban migration process, as well as the increasing number of transfusions in all the Continent (Brasil, 1974; PAHO, 1984). Rural-urban migration is an actual very important phenomenon in several parts of Latin America, with deep roots in the social and economic policy of the countries (Dias & Borges Dias, 1979). The working market, the production relationships and the urban-

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industrial model are clearly involved factors that can be observed in typical migratory routes such as from the Northeastern Brazilian states to São Paulo city (Goldbaum, 1978) or from Bolivia to Buenos Aires (Manzullo et al., 1982). In Brazilian large cities such as Rio, São Paulo and Belo Horizonte, detected chagasic blood donors are generally poor, unskilled laborers who have migrated from rural endemic areas (Coura, 1966; Silva et al., 1979; Gontijo, 1981; Dias & Brener, 1984). Today there are about 360,000 chagasic people living in São Paulo, 240,000 in Rio de Janeiro and 90,000 in Belo Horizonte, according to Coura (*in* Dias, 1984a).

"Blood-market" practice is another problem related to Chagas' disease transmission. Paid blood donors are common among poor unemployed people in urban centers of Latin America. They are "professional" donors, paid by unscrupulous blood banks that have only profit interests and generally do not make any selection about Chagas or other transmissibles diseases (Amato Neto, 1979). According to Carvalho (*in* Dias, 1979), the simple change of the "selling" to the "responsible" blood transfusion regime could lessen more than 70% of chagasic donors in blood banks of Belo Horizonte, Brazil. The number of blood transfusions is increasing in all the Continent, because of several factors. Among them, the abusive practice of hemotherapy, as disclosed by Amato Neto (1980) and Osório (1984). This problem depends basically on the blood commercial use, but also on the generalized technical unskill on the matter (Jamra, 1984; Dias, 1984c). The correct indication of blood transfusions is a very actual issue in several countries, involving technical and ethical factors, as well as an adequate jurisprudence (Rassi & Rezende, 1976; Osório, 1984).

The incidence of transfusional Chagas' disease is not clearly established because of the factors above mentioned. The available data indicate more or less 200 reported cases up to the present; among 131 published cases before 1979, 72 were described in Brazil (55.0%) and 53 in Argentina (40.5%) (Dias, 1979). Cançado (1980) found 8 transfusional cases among 40 acute patients (20%) studied in Belo Horizonte, Brazil, during 13 years. The estimated incidence only for São Paulo city is of about 1,500 cases per year, considering 10,000 annual transfusions, the risk of 15% for each transfusion with chagasic blood and the prevalence of about 2% of infected donors (Dias, 1979). With similar numbers, Amato Neto (1984) appraises an annual incidence of transfusional Chagas' disease of about 10,000 to 20,000 for Brazil, considering the occurrence of 4,000,000 blood transfusions carried out per year in the country. But, as mentioned above, the effective risk can be greater in other regions, since Zuna (1984) confirmed *T. cruzi* in 4 out of 10 patients from Bolivia who received blood from chagasic donors.

Prevalence of chagasic blood donors: several serological surveys have been carried out in different countries, showing for Latin America between 0.4 to 63.0% of infected blood donors (Dias, 1979); the majority of recent results are between 2.9 and 13.4%, as indicated in Table I.

TABLE I

Seropositiveness for Chagas' disease among blood donors and candidates to blood donation in Latin American countries, in recent years.

Country	Reference (Year)	Examined No.	Positiveness (%)
Mexico	Bayona el al. (1984)	200	16.5
Honduras	Ponce (1984)	364	13.4
Venezuela	Maekelt (1973)	529,883	4.0
Peru	Naquira et al. (1972)	893	5.8
Bolivia	Zuna (1984)	420	46.7
Paraguay	Servin-Blaires (1984)		16.9
Argentina:	Alderette, Torres & Monteban (1984)	5.434	14.7
(B. Aires	" " " "	–	6.1
(S. Estero)	" " " "		23.3
(Chubut)	" " " "		2.9
Chile	Lorca et al. (1983)	1.332	6.0
(Santiago DC)	" " "	478	3.6
(II Region)	" " "	99	10.1
(IV Region)	" " "	492	8.7
(V Region)	" " "	225	3.7
Brazil:			
(São Paulo state)	Waldman et al. (1982)	56,902	2.9
(Minas Gerais state)	Dias & Brener, 1984	2,300	5.7

–: Not avaiable data.

An important aspect is the variation of the prevalence of chagasic donors in the same region, as time goes by. Even being very difficult to compare different surveys made by different researchers, some available data are presented in Table II. It is possible to verify that the general tendency of the problem in different decades can be either to decrease or to be maintained, according to the region. Prophylactical measures against the vector and also those specific for blood banks (screening infected candidates) could be involved in the decreasing of infected candidates (Dias, 1979; Rassi, 1984).

TABLE II

Prevalence (in %) of chagasic blood donors in serological inquiries made in different areas in the last four decades

City or Region	1950	1960	1970	1980
São Paulo City (Brazil)	6.15*	3.04*	–	–
B. Horizonte City (Brazil)	5.56*	2.50 (1)	2.30 (1)	1 to 2.50 (2)
Uberaba Town (Brazil)	15.0 (3)	16.2 (4)	7.70 (4)	6.98 (4)
Minas Gerais State (Brazil)	7.27 (5)	–	–	5.70 (6)
Buenos Aires City (Argentina)	–	5.26 (7)	6.05 (8)	6.10 (9)
Santiago City (Chile)	–	4.66*	2.80 (10)	3.16 (11)

Legend:

*Mean rate among several observations in recent revision (Dias, 1979)

– : Not avaiable data.

(1) = Tavares, 1971; (2) = Gontijo, 1981; (3) = Jatene & Jacomo, 1959; (4) = Souza, 1984; (5) = Salgado & Pellegrino, 1968; (6) = Dias & Brener, 1984; (7) = Cerisola et al., 1964; (8) = Cerisola et al., 1972; (9) = Alderette, Torres & Monteban, 1984; (10) = Schenone, 1983; (11) = Lorca et al., 1983.

Several other factors are involved in the risk of *T. cruzi* transmission by blood transfusions, such as the parasite strain, the parasitemia in the blood donor, the general conditions of the recipient patient, the total amount of transferred blood, etc (Dias, 1979). *T. cruzi* trypomastigotes are viable in total stored blood for at least 18 days (Cerisola et al., 1972). Some blood factors such as immunoglobulins present in the sera of chronic patients can agglutinate circulating forms of the parasite and even to produce its grow inhibition in culture media (Schlemper Jr., 1978; Chiari, Lana & Dias, 1978). The utilization of other blood fractions such as erythrocytes mush, plasma and cryoglobulins also offer some risks of *T. cruzi* transmission, according to Carvalho, Cardoso & Brener (1977). Plasma seems to be the blood fraction less adequate to the parasite permanence, considering chronic patients; the plasma lyophilization is able to prevent completely the transmission risk in plasmapheresis from infected donor (Amato Neto, Leonhardt & Souza, 1966).

"Institutional" epidemiology is an actual theme in transfusional Chagas' disease. It is very important to know where, when, why, how and by whom blood transfusions are being made. The problem can be completely different in small medical centers in comparision with the large hospitals with sophisticated personnel and equipment. Brazilian small towns commonly are not provided with specialized hemotherapy services, or with permanent blood or haemoderivates stocks. Blood transfusions in those places generally occur in emergency situations, when then volunteer or relatives of the patient are required for immediate blood transferences (Dias, 1979; Dias & Brener, 1984). In the Uberaba region (Brazil) blood storage was performed only in 4 out of 12 counties where blood transfusion is being carried out (Jamal & Cunha, 1984). A recent survey about blood transfusion practice was carried out in 631 counties of Brazilian Minas Gerais state, by Dias & Brener (1984). In only 266 counties blood transfusions were performed (42.2%), involving 473 hospitals and 100 blood banks. Among such counties, in only 124 (40.6%) routine serological tests were being carried out to exclude chagasic blood donors. The most employed serological methods was Complement Fixation Test (68.7%), being followed by Immunofluorescence technique (28.3%) and "Chagas-Latex Test" (28.3%) and by Indirect Haemagglutination technique (24.2%). Considering only those services in which serology is performed, the survey showed that in 68.7% only one serological method was being employed; two techniques were simultaneously utilized in 29.2% and three in only 7.3%. The majority of blood donors were "volunteers" (97.9%), only 2.1% being paid, according to this research.

Diagnosis on transfusional Chagas' disease must consider two main aspects: a) the diagnosis of acute infection in recipients who received infected blood, and b) the "prophylactical" diagnosis in blood donors candidates in order to discard chagasic individuals. The first aspect involves not only the technical laboratory procedures to detect the acute infection, but also the clinical mistrust on patients who received blood transfusions in endemic countries (see Dias, 1984b). Former than the knowledge about the principal symptoms and signs of the acute phase, the physician and the haemotherapeut should have in Latin America

a minimum idea about the epidemiology of Chagas' disease and the problem of transfusional *T. cruzi* transmission.

Besides the available chemoprofilaxis, serology in blood donors is an essential element to control transfusional Chagas' disease. The serological techniques must be highly sensitive and easy to process, even in poor endemic regions. Moreover, since in several times transfusions are made in emergency circunstances, rapid qualitative tests might be improved (Segura, 1984). For such a purpose, the establishment of adequate serological titers is critical. As stressed by Camargo (1979, 1980), the quantitative serological limit between infected and not-infected individuals can vary according to the region. Therefore, the local laboratories ought to perform quantitative serological studies to establish the adequate titer that defines chagasic or non-chagasic populations in the region. Analysing chagasic patients with positive xenodiagnosis, Yanowsky (1979) verified that 1:8 serological dilution was reactive in all these individuals, while titers of 1:16 and 1:32 dilutions would detect 97.5 and 85.0% of the cases. Figure 1 shows the serological quantitative curves of chagasic people and general blood donors in São Paulo, Brazil, that stand out the maximum sensitivity in the titer 1:8 (Yanowsky, 1979).

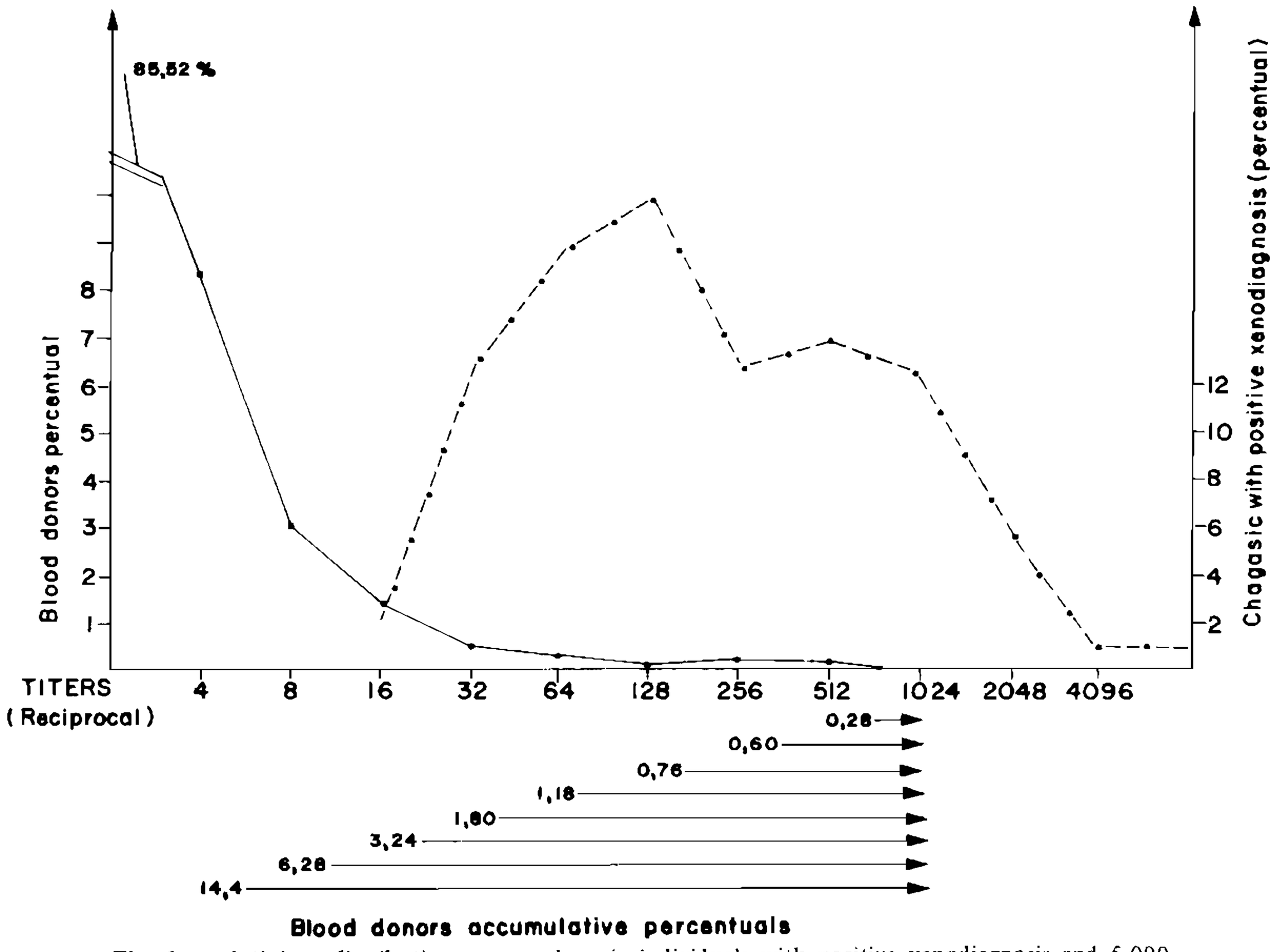

Fig. 1: agglutinines distribution among chagasic individuals with positive xenodiagnosis and 5,000 blood donors of São Paulo city, Brazil. (Yanowsky, 1979).

Since the main problem in blood transfusion is to screen infected donors, the qualitative serological tests employing low titers provide high sensitivity, in spite of an increase of the number of false positives. Yanowsky (1979) estimated an unespecificity of about 3.24% for the maximum sensitivity of Direct Agglutination test in São Paulo. On the other hand, considering the 4,000,000 annual blood transfusions in Brazil, with a mean rate of 1.5% of chagasic donors, with the minimum risk of about 12.5% of *T. cruzi* transmission, we could expect of about 150 annual cases of transfusional Chagas' disease if all the blood donors have been screened by a single serological test with a sensitivity of 98%.

Clinical and therapeutical aspects

Generally, acute Chagas' disease in blood recipients has the same clinical picture described in insect transmission (Amato Neto, 1958; Dias, 1979; Cançado, 1980). It seems that the incubation period can be longer in transfusional than in vectorial route, about 20 to 40 days. One case with an incubation period of 116 days has been described by Amato Neto & Dias (1969). Among the published transfusional cases, about 20% were completely asymptomatic, only being detected through objective researches made among

people who received blood from chagasic donors (Dias, 1979). Fever is the most important and frequently the only manifestation of Chagas' transfusional disease. Generalized adenopathy, hepatosplenomegaly and common electrocardiographical disturbances of the classical acute picture may be present. Portal of entry signs ("chagomas") have not been described. The clinical follow-up of transfusional Chagas' disease seems to be the same of the vector transmitted infection (Amato Neto, 1979; Dias, 1979).

Clinical manifestations among chagasic blood donors generally are slight or absent, since the own circunstances of blood donation tends to select healthly individuals. For this reason, some authors assure that anamnesis, clinical examination, EKG and X-rays have not any value as transfusional Chagas' disease prophylactical measures (Tavares, 1971). Nevertheless, clinical evaluation can detect heart and digestive disturbances among chagasic donors, as it was verified in Buenos Aires by Manzullo et al. (1982), in Uberaba, Brazil, by Souza (1984) and in São Paulo city by Medrado Faria et al. (1984). Dias (1984a) found in Belo Horizonte 68.4% of chronic indeterminate form among chagasic blood donors, while 21.1% presented heart involvement and 15.0% had digestive disperistalsys.

Therapeutical aspects in transfusional disease consider basically the specific treatment of the recipients in acute Chagas' phase. Both Benznidazole and Nifurtimox are effective drugs in this phase and must be employed precociously during at least 60 days in all the detected cases (Rassi, 1984). The cure control must take into account that repeated serological tests must remain permanently negative, as stressed by Cançado & Brener (1979). Chagasic candidates to blood donation must be forbidden to give their blood, and be advised of the need to receive medical attention. It does not make sense to try the specific treatment in chronic chagasic blood donors, since the available drugs in this phase not provide a parasitological cure, nor a clinical improvement in these patients (Macedo, 1984). An exception can be made in order to obtain temporary decrease of the parasitemia in chagasic kidney donors, before the transplantation. This measure was recently tried by Dias, Brener & Macedo (1984) as well as the preventive treatment of the recipient immediately after the surgery, with no important side effects and no *T. cruzi* transmission to the recipient.

Prophylatic aspects

The control of transfusional Chagas' disease was established many years ago, being based upon the serological screening of blood donors and in the chemoprophylaxis of stored suspected blood with effective parasiticidal drugs (Nussensweig et al., 1953). Unfortunately there is a long time lapse between technological advances and medical practice in endemic countries, resulting in several blood banks without any control (Amato Neto, 1979; Dias, 1984c). The prophilactical basis on transfusional Chagas' disease still remain the same, but today we know that the problem involves also political, ethical and institutional aspects (Osório, 1984; Dias & Brener, 1984).

As mentioned above, transfusional Chagas' disease is not absolutely restricted to blood banks and big cities, but widely spread in all the endemic area. The problem then might be foccused at least in two angles: a) The political and institutional angle, in which the concientiousness of the problem is fundamental in order to reach adequate priority; b) The technical question (chemoprophylaxis and diagnosis). In the first aspect, is useful to remember Osório (1984), when she sets the ethical and correct blood policy in a tripod mainly destinated to the developing countries: 1) The creation of an official "blood system" to collect and to distribute blood, but also to make an effective supervision on hemotherapic practice; 2) The strong stimulation on behalf the voluntary blood donation, and, 3) The enactment of specific laws about hemotherapy, "chiefly to prohibit profitering with human blood".

In correlation to these theoretical propositions there are already some practical experiments in endemic countries that are important to mention. In Argentina, the Human Health Programme (BID/Health Ministry/Del Salvador University) is improving the chain of regional laboratories involved in serological screening of blood donors (Alderette, Torres & Monteban, 1984). In Minas Gerais state, Brazil, the Health Secretary and Oswaldo Cruz Foundation are developing an integrated diagnosis system with central and regional laboratories able to select blood donors. The Central Laboratory (in Ezequiel Dias Foundation) is a Reference Centre that checks and supervises the regional laboratories, produces reagents and prepares human resources (Dias & Brener, 1984). In Brazil, major centers are being improved the "Hemocenters", official institutions set in strategic geographical points in order to make massive blood collection and distribution to associate peripheric services. Also very important was the recent *Chagas' disease law* enacted by Argentine Congress, that established in 1983 clear responsabilities about the transfusion Chagas' disease.

Epidemiological and institutional researches are still very important in the transfusion issue, in order to produce information and operative support to Governments and Health authorities. In several endemic countries, the *T. cruzi* problem in blood transfusions remains unknown; the very worst is the absence of specific transfusion programmes in official health systems of the majority of these countries (PAHO, 1984). In Brazil, CNPq (National Research Council) is now supporting at least three research lines on the matter, considering the action of Gentian violet upon blood components (Souza, 1984), the epidemiology of transfusion disease and the problems related to transfusion practice is two endemic areas (Carvalheiro, 1982; Dias & Brener, 1984).

The technical question involves the recent advances in diagnosis and chemoprophylaxis. It is important to consider that serology and chemoprophylaxis are not mutually exclusive, but complementary measures in transfusion Chagas' disease control. Research lines must be stimulated in both aspects.

The principal advances in serology applied to the transfusional system could be summarized:

a) Blood collection procedures are being simplified by Camargo (1984) and Yanowsky (1984), utilizing microtechniques to collect blood in capillary tubes. When preserved in pure Glycerin (concentration 1:1) this material can be easily stored and processed. Moreover, it facilitates blood collection in small health centers, taking blood drops from finger tips and mailing the tubes in blokhead covers.

b) Simple, sensitive and rapid haemagglutination tests are being developed by Segura (1984) and Yanowsky (1984), to be processed in unsophisticated laboratories, as screening tests for emergency transfusions. These techniques employ simple, disposable kits and can be read in about two hours.

c) New serological tests are being improved, either to detect circulating immunecomplexes in acute disease (see Dias, 1984b) or to put in evidence specific IgG antibodies in chronic phase (reviewed by Camargo & Takeda, 1979). Lytic antibodies, being studied by Krettli, Cançado & Brener (1982), are demonstrating the presence of these immunoglobulins in 100% of chronic, untreated patients. This non-conventional serology employs a complement-mediated lysis technique, and is being very useful in the cure control of the infection.

Finally it must be considered that the creation of strategic serological reference centers in all America* is an auspicious new step in the fight against Chagas' disease.

Chemoprophylaxis of Chagas' disease in blood banks began with Nussensweig et al. (1953) and was carefully reviewed by Rassi & Rezende (1976) and by Schlemper Jr. (1978). Two main reasons support the chemoprophylactical practice in transfusion Chagas' disease: the difficulties found in selecting donors and the problem in hyperendemic areas, where the number of non-chagasic blood donors could be small (Nussensweig et al., 1953; Rassi & Rezende, 1976). On the other hand, sometimes "the use of crystal violet for eliminating *T. cruzi* from blood is not accepted and, as long as there is no drug to take its place, serology must be employed" (PAHO, 1984).

The great limitation of Gentian violet and other available trypanocide dyes in blood banks is not really the color change of the blood (or of the recipient), but chiefly the mercenary blood bank system (Amato Neto, 1979; Osório, 1984). In small health centers, besides the lacking of blood banks, it is often impossible to maintain stored blood with the drug for the minimum requirement of 24 hours (Dias, 1979; Dias & Brener, 1984).

Gentian violet is still the most available and effective drug to employ in chemoprophylaxis of transfusion Chagas' disease. Its effectiveness has been proved in a volunteer studied by Amato Neto & Mellone (1959) who received 300 ml of blood obtained from a donor with acute Chagas' disease. This blood was treated with Gentian violet at a concentration of 1:2,000 for 48 hours before the transfusion. The recipient did not acquire *T. cruzi* infection (3 months of clinical, parasitological and serological follow-up), while a control group of mice transfused with the same blood without Gentian violet became infected. Moreover, routine employment of Gentian violet has been carried out in some important hemotherapic services in endemic areas, with very successful results: in Goiânia (Brazil), where the dye is added to plastic bags for blood collection in hemotherapy, more than 49,000 transfusions have been carried out without any case neither of *T. cruzi* transmission nor of intoxication by the drug (Rassi, 1984; Rezende, 1984). Similar results were recently reported by Ciancio (1984) for Argentine experience with about 10,000 transfusions performed with crystal violet, and by Souza (1984) for 30,000 blood transfusions with Gentian violet in the endemic area of Uberaba, Brazil.

Despite good experience with Gentian violet, several studies are still being made on the drug toxicity towards blood components. Moreover, researches are looking for other soluble trypanocidal chemicals that are cheaper, less colored and less toxic than Gentian violet, and, most importantly, with more rapid activity. Gentian violet has not shown toxicity for man in the usual 1:4,000 concentration, even with enormous amounts of violet added blood. Rezende, Zupelli & Bafutto (1965) reported one case that received 4,000 ml of violet-added blood in 24 hours without toxic phenomena, besides another one that received 36,000 ml over 6 months, also without intoxication. Although Gentian violet can sometimes cause microagglutination and rouleaux formation of erythrocytes (ib.), Ciancio (1984), employing marked blood cells exposed to the drug and injected in volunteers, found that 90% remained alive for 7 days, 88% for 14 and 86% for 22 days. Studying several characteristics of stored blood with added Gentian violet, Souza (1984) found no important changes, apart from an insignificant rise in plasma potassium. In contrast, Pereira Barretto et al. (1983) found a significant increase in plasma potassium and a decrease of sodium when the blood was treated with another trypanocidal drug, the Amphotericin B.

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* UNDP/WB/WHO – Special Programme for Research and Training in Tropical Diseases. Continental Group for Studies on Chagas' disease serology. Executive staff: M.E. Camargo (Chairman), I.S. Kagan & E.L. Segura. Foundation date: 1981.

The trypanocide mechamism of Gentian violet and other cationic compounds is still not clear. Recently Docampo (1984) verified that intracellular reduction process followed autoxidation yielding O_2 and H_2O_2 could be involved in the action of several trypanocidal agents active both *in vitro* (e.g. naphtoquinones) and *in vivo* (nifurtimox). Moreover, the oxygen-reduction products have been implicated in the mechanisms of killing of *T. cruzi* by phagocytic cells (Docampo & Moreno, 1984).

Since high amounts of Gentian violet might be toxic for the recipients, some authors have been studying the possibilities for improving drug effectiveness at lower concentrations. It has been found that ascorbic acid (0.1 mM) added to a Gentian violet/blood solution produced rapid increase of trypanocidal power of the dye, especially in the presence of light (Docampo, 1984). It seems that such a procedures raises the parasites' permeability through the formation of free radicals in the media, thus increasing the action of Gentian violet at lower dose (ib.).

Other drugs have been tested in order to replace Gentian violet in blood banks. Simple *in vitro* tests have been improved by Schlemper Jr. (1978) and Cover & Gutteridge (1982) to study drug activity against *T. cruzi.* But Schlemper Jr., Chiari & Brener (1977) warned that culture forms of the parasite are not suitable for screening additives to Chagas' transfusion disease prevention. Recently, Hammond, Cover & Gutteridge (1984) have tested about 500 existing drugs for trypanocidal activity at 4°C. They reported that 69 of such compounds were active at a concentration of 1mM or less, after exposure for 24 hours; most of these were amphilic cationic drugs, of which many are marketed as antidepressants and adrenergic bloking agents. Three polyene and two anthracycline antibiotics were also in this group. These drugs and others (e.g. Amphotericin B) could be useful in the prevention of transfusion Chagas' disease, but Gentian violet still seems to be the most simple and safe compound. On the other hand, we need to find a manner (or a drug) that be able to sterilize chagasic blood more rapidly than 24 hours, since this time is really an important limitation factor in several conditions.

Finally it must be emphasized that in many times the drug activity and/or toxicity depends on its administration route. Unfortunatelly, not always an active trypanocidal oral drug can be useful *in vitro* to prevent transfusion Chagas' disease in banked blood (Brener, 1985).

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