資料２

日本赤十字社提出資料

シャーガス病の安全対策に係る現状と課題

１．シャーガス病について

- シャーガス病：原虫 *Trypanosoma cruzi* を病原体とする原虫感染症で、主にメキシコを含む中南米に認められる。*T. cruzi* は、媒介昆虫サシガメの糞便中に存在し、サシガメの刺創や擦創から糞便中の原虫がヒトに感染する。
- サシガメは土壁の割れ目、草葺きの屋根、草むらに生息し、夜間這い出してきて吸血する。住環境の整備されていない農村部や貧困地域に多い。
- 上記以外の感染経路：母子感染、輸血、臓器移植、サシガメの糞に汚染されたサトウキビ・アサイなどのジュースによる経口感染
- 潜伏期：１～２週間。
- 虫体は主にトリポマスチゴート（錐鞭毛型）とアマスチゴート（無鞭毛型）があり、トリポマスチゴートは末梢血中に認められ、これがヒトに感染し、網内系や筋組織に侵入してアマスチゴートに分化、分裂し増殖する。その多くが、常在マクロファージ、心筋細胞、腸管平滑筋細胞や交感神経節細胞に侵入する。
- 症状：急性期（１週間～数ヵ月間、主に小児）は、高熱、発疹、リンパ節炎、肝脾腫、片側性眼瞼浮腫（Romaña sign）、その後は無症状で慢性期（10 年～数十年後）に心筋炎、巨大結腸等。
- 現在のところ、有効な薬剤は急性期のみ（ベンズニダゾール、ニフルティモックス）。
- 欧米、カナダの非流行地域では、中南米からの移民の増加が背景にあり、シャーガス病対策が課題となっている。

２．輸血への影響について

- 全血製剤中の原虫は 4℃で 18 日以上生存
- 4℃の赤血球製剤中での生存は、数日～数週間であるが、赤血球製剤中の生存についての報告は全血製剤ほど十分に確認されていない。
- 通常保管条件下での血小板製剤中の生存は最長 5 日間である。
- 凍結血漿中の生存率は 24 時間以下である。
- 冷凍赤血球製剤中の生存率は不明である。
- 白血球除去フィルター又は放射線照射は、リスクを減少させるが完全ではない。
- 輸血による伝播は、米国 7 例、カナダ 2 例及びスペイン 5 例と報告されている。
- 輸血による感染者の多くは、がん、造血幹細胞移植に伴う化学療法により免疫抑制状態の患者である。
- 原因製剤が特定された症例は、すべて血小板製剤によるものである。
- 抗体陽性の感染供血者由来の製剤による受血者への輸血感染率は 1.7%と低い。（製剤別内訳：血小板製剤 13.3%、赤血球製剤 0.0%、血漿・クリオプレシピテート 0.0%）
- メキシコを含む中南米諸国では *T. cruzi* 抗体スクリーニング検査が行われており、米国、カナダ、スペイン等では選択的な *T. cruzi* 抗体スクリーニング検査が行われている。

３．日本の現状について

- ✓ 現在のところ輸血によりシャーガス病に感染した事例は報告されていない。
- ✓ 中南米からの定住者が約 30 万人。

✓ 定住者の中にも *T.cruzi* キャリアがいる（日本人の中南米長期滞在者も含め）
✓ 日本語を理解する日系人などが献血している。
✓ 発症するまで長期間にわたるため、キャリアの人が献血し、輸血による感染の潜在的リスクが存在する。

（1） 中南米居住又は滞在歴を有する献血者の状況
✓ 問診票の取り扱い：シャーガス病の既往がある場合は採血しない。
✓ 渡航歴・居住歴、滞在歴：自由回答（～2011 年 3 月）→2011 年 4 月問診票改訂

1980 年（昭和 55 年）以降、海外に旅行または住んでいたことはありますか。
① それはどこですか。（国、都市名 ）
② いつ、どのくらいの期間ですか。（ ） はい・いいえ
③ 1980 年（昭和 55 年）～1996 年（平成 8 年）の間に英国に通算 1 ヵ月以上滞在しましたか。
（ はい・いいえ）

⇩

1 年以内に外国（ヨーロッパ・米国・カナダ以外）に滞在しましたか。 はい・いいえ
（国名 ）

4 年以内に外国（ヨーロッパ・米国・カナダ以外）に 1 年以上滞在しましたか。 はい・いいえ
（国名 ）

✧ 中南米居住歴を有する献血受付者及び献血者数（2010 年）

国 名	献血受付者数（人）	献血者数（人）
ブラジル	**4,940**	**4,159**
メキシコ	2,448	2,095
ペルー	845	697
アルゼンチン	769	669
チリ	369	325
パラグアイ	361	313
ボリビア	345	285
コロンビア	217	184
エクアドル	180	146
ベネズエラ	195	160
パナマ	260	223
コスタリカ	180	153
グアテマラ	159	132
ニカラグア	133	112
エルサルバドル	99	77
ウルグアイ	70	58
ホンジュラス	1	1
ガイアナ	1	0
スリナム	4	4
ベリーズ	18	12
合 計	**11,594（966/月）**	**9,805（817/月）**

シャーガス病の感染リスクのある中南米諸国の居住歴を有する 2010 年の献血受付者数及び献血者数を集計した。その数は、献血受付者数 11,594 人（966 人/月）、献血者数 9,805 人（817 人/月）であった。献血受付者の 85%が献血していた。その内ブラジル居住歴を有する者が最も多く、献血者数 4,159 人であり、全体の 42%を占めた。

中南米居住歴のある者の都道府県別の献血者数では、東京都 1,503 人、神奈川県 1,375 人、愛知県 1,362 人の順で多かった。ブラジル居住歴のある者の都道府県別の献血者数では、愛知県が最も多く 759 人であり、以下、東京都 559 人、神奈川県 365 人、静岡県 318 人と続いた。

ブラジル居住歴者の男女別年代別の分布では、男女比は約 3:1 と男性の方が多く、年代別では 30 代が最も多かった。全体では 30 代以下が約 6 割、40 代以上が約 4 割であり、シャーガス病の感染リスクの比較的低いと考えられる若い世代が多く献血している状況であった。

献血申込（受付）者 1 万人当たりのブラジル居住歴を有する受付者数は、全国平均では 7.8 人であったが、頻度が高い東海四県では、愛知県 20.0 人、静岡県 19.6 人、三重県 16.7 人、岐阜県 10.3 人であった。

✧ 中南米滞在歴を有する献血受付者及び献血者数（問診票改訂後の状況：2011 年 4 月～12 月）
・献血受付者数 4,471 人（497 人/月）、献血者数 3,581 人（398 人/月）であった。
・国別受付者数は、メキシコ 1,525 人、ブラジル 1,040 人、ペルー626 人、アルゼンチン 376 人、チリ 228 人、ボリビア 105 人、コロンビア 91 人の順であった。これは、改訂前の渡航歴と近似した分布である。
・氏名により日本人・外国人を分類したところ、改訂前の居住歴の 83%、改訂後の滞在歴の 96%が日本人であった。

・外国人の滞在歴受付者数は 169 人で、国別内訳は、ブラジル 125 人、メキシコ 17 人、チリ 8 人、コロンビア 7 人、ペルー5 人、エクアドル 2 人、アルゼンチン、ベネズエラ、パラグアイ、グアテマラ、エルサルバドル各 1 人であった。
・滞在歴上位のメキシコ、ペルー、アルゼンチンの殆ど 99%は日本人であった。

✓ 滞在歴のある受付者数の減少：震災の影響よりも問診票の改訂が大である。
✓ 日系人が日本人の中に含まれている可能性はあるものの、問診票改訂後に中南米滞在歴のある外国人を捕捉できていないと推測される。
✓ 中南米滞在歴のある外国人では、ブラジル人が最も多いことから、ブラジル人の動向を把握することが重要である。

（2）東海 4 県の中南米居住歴を有する献血者における研究的 *T. cruzi* 抗体検査
- *T. cruzi* 抗体検査：迅速法（イムノクロマト法）及び ELISA 法
- 132 名全員 *T. cruzi* 抗体陰性（未成年 2 名含む）
- ブラジル 112 名、ペルー6 名、コロンビア、パラグアイ、メキシコ各 1 名、日本人 11 名
- 日本人除く 121 名（男性 83 名、女性 38 名）の年齢分布（中央値 32 歳；10 代 2 名、20 代 38 名、30 代 53 名、40 代 23 名、50 代 5 名）10～30 代が 77%を占めている。平均滞日年数 10 年。

4．欧米の対応

1）英国
・永久制限：中南米での出生（本人又は母）、輸血、4 週間以上農村部に居住又は就労
・最終曝露から 6 カ月以上経過し、認証された *T.cruzi* 抗体検査が陰性ならば可

2）スペイン
・流行地域で、本人が出生した、母が出生した、輸血を受けた供血者に対しスクリーニング検査（義務）
・流行地域で居住した供血者にもスクリーニング検査実施

3）米国
・シャーガス病の既往のある者、繰り返し *T.cruzi* 抗体検査陽性者は永久排除
・スクリーニング検査の最初の 1 回が陰性であれば可。

4）カナダ
・中南米での 6 ヵ月以上の滞在歴がある場合、本人、母又は祖母が中南米で出生した場合には血小板製剤や凍結血漿には使用しない。
・上記の該当者に対して *T.cruzi* 抗体検査を実施する。

5）オーストラリア
・シャーガス病の既往のある者は永久制限
・流行地域で出生した、又は流行地域で新鮮な血液成分の輸血を受けた供血者からは分画原料のみ可

5．日本の対策案

1）中南米滞在歴の正確な把握：質問項目追加
上記実施の上で、①～③の案

①中南米滞在歴のある者の献血制限
②中南米滞在歴のある献血者の血液の製造制限
③中南米滞在歴のある献血者の *T.cruzi* 抗体スクリーニング

2）中南米からの定住者が多い地域でのパイロットスタディの継続と対象地域の拡大

6．課題と検討事項

- 日本語によるコミュニケーションを徹底するか（献血制限）
- 中南米滞在歴の正確な把握
  - ✓ 当面の間は受付窓口での別紙質問票による捕捉。
    - ・国籍の質問は難しい
    - ・国や地域、都市部、農村部の区別も難しい
    - ・中南米での出生地、居住歴、一定期間以上（3 カ月、6 カ月、1 年）の滞在歴
    - ・母子感染を考慮するならば母系既往歴？母系出生地？
  - ✓ ポスターなどによる事前周知の徹底
  - ✓ いずれは問診項目にする。

（例）私は、以下のいずれかに該当します。 □　中南米諸国で生まれました、又は育ちました。 □　私の母が、中南米諸国で生まれました、又は育ちました。 □　（日本人の場合）中南米諸国に３ヵ月以上滞在しました。

- 滞在歴を把握した上で①～③の対応案
- ①中南米滞在歴のある者の献血制限：
  - ✓ 数は多く見積もっても１万人なので、採血・製造への影響は少ないが、一律制限することの妥当性。
- ②中南米滞在歴のある献血者の血液の製造制限：

（選択案） ・全血製剤、血小板製剤のみ不可（△） ・ＦＦＰ、分画原料可（△） ・分画原料のみ可（○）

  - ✓ 検査なしでＦＦＰ可、ＲＣＣ不可の理解が得られるか。
  - ✓ 「輸血用は不可、分画原料は可」は理解を得やすく、製造の流れとしては一部製剤のみ製造可の対応は、従来実施していないので工夫が必要である。
- ③中南米滞在歴のある献血者の *T. cruzi* 抗体スクリーニング：
  - ✓ 検査件数が少ない
  - ✓ 国内で認可されている試薬がない、研究用として使用。（米国での認可試薬は 2 社；アボット社 CLIA 法、オーソ社 ELISA 法）
  - ✓ スクリーニング検査ではなく、②で制限した後、研究的（疫学研究）に抗体検査を実施するならば、まとめて検査が可能。別途同意書が必要か。

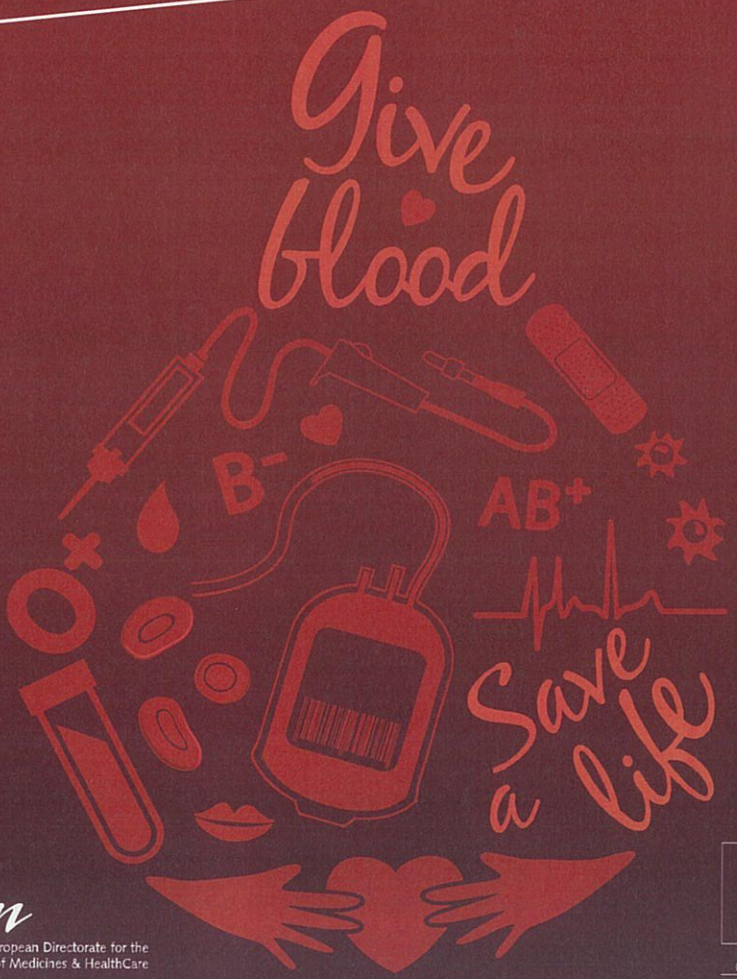
- パイロットスタディの継続と対象地域の拡大:
  - ✓ 埼玉、群馬ほかブラジル人コミュニティの集住地域にも拡大し継続検討

別添 1

16th Edition 2010

Guide to the Preparation, Use and Quality Assurance of Blood Components

European Committee (Partial Agreement) on Blood Transfusion (CD-P-TS)



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European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Prophylactic immunisations

See *Standards*.

Conditions requiring individual assessment

As donors may present with a variety of medical problems, past or present only some of the more common examples are considered here.

Condition requiring individual assessment	Criteria for deferral
Allergy	Individuals with a documented history of anaphylaxis should not be accepted as donors.
Auto-immune diseases	If more than one organ is affected this leads to permanent deferral.
Beta thalassaemia trait	Heterozygote carriers of beta-thalassaemia trait may give blood provided they are in good health and have a haemoglobin level within acceptable values.
Bronchitis	Persons with symptoms of severe chronic bronchitis should not be accepted as donors.
Common cold	Accept, if asymptomatic and feels well on the day of donation.
Hypertension	A person who presents with a systolic blood pressure of more than 180 mm Hg or a diastolic blood pressure of more than 100 mm Hg should not be accepted as a blood donor. A mild hypertensive whose diastolic blood pressure is maintained at less than 100 mm Hg may be accepted.
Jaundice and hepatitis (see *Standards*)	Hospital staff coming into direct contact with patients with hepatitis are accepted at the discretion of the physician in charge of the blood-collecting unit providing they have not suffered an inoculation injury or mucous membrane exposure, in which case they must be deferred.
Chagas disease see *Standards*)	In some countries, donors who were born or have been transfused in areas where the disease is endemic are deferred or tested. The blood of persons who were born or have been transfused in areas where the disease is endemic should be used only for plasma fractionation products unless a validated test for infection with *T. cruzi* is negative.

Post donation information

Blood donors must be instructed to inform the blood establishment when signs or symptoms occur after a donation, indicating that the donation may have been infectious (see *Standards*). A donor may also inform the blood establishment that he or she previously donated blood, but should not have done so in the light of donor selection criteria aimed at the health protection of recipients, e.g. in retrospect did not fulfil criteria mentioned in the donor questionnaire.

Infectious diseases

For infectious diseases not specifically addressed elsewhere in this guide, generally a deferral period of at least 2 weeks after cessation of symptoms should be respected.

If there was contact with an infectious disease, the deferral period should equal the incubation period, or if unknown, the nature of the contact and the deferral period has to be determined by the responsible physician.

Some emerging infectious diseases may represent a threat to the safety of blood transfusion. A risk/benefit analysis should be carried out on a country by country basis. Precautionary measures, which should be proportionate to the risk, should be implemented in a timely fashion in line with the emerging evidence. Donor selection policies to address the risk may include deferral for a suitable period of donors exposed in geographic areas where the disease is occurring. The introduction of appropriate testing strategies may have to be considered.

It is recommended that national authorities develop detailed guidance based on prevailing epidemiology in the populations they serve.

Variant Creutzfeldt-Jakob disease

A new variant of Creutzfeldt-Jakob disease (vCJD) has been described. It is accepted that BSE and vCJD are caused by the same agent, and that vCJD is acquired by eating contaminated beef. Transmission of vCJD by transfusion of blood components has also been documented.

antigen either manually or on blood grouping machines, or a test employing a variant of the *Treponema pallidum* haemagglutination assay (TPHA). An ELISA test is occasionally used. Positive syphilis screening results must ideally be confirmed by TPHA, fluorescent Treponemal antibody test (FTA), or an immunoblot test.

Anti-HTLV testing

The approach to confirmation is similar to HIV and includes nationally established algorithms as well as specific assays including immunoblotting and NAT. Sensitive tests for genome detection including typing may be helpful in defining the infection status of the donor.

Chagas testing

The blood of persons who were born or have been transfused in areas where the disease is endemic can be selected to be tested for *T. cruzi* antibodies. Plasma for fractionation is exempt from such a test procedure.

Paragraph 4. Nucleic acid screening (HCV- and HIV-NAT) in mini-pools

The Committee for Medicinal Products for Human Use (CHMP) recommended for HCV a strategy of pretesting by manufacturers of mini-pools (of donations or of samples representative of donations) in order to avoid the loss of a complete manufacturing pool and to facilitate tracing back to the donor in the event of a positive test result.

In order to achieve a sensitivity which will detect 5000 IU/mL of HCV RNA for donations which are tested in mini-pools of say 100; 50 IU/mL should be detected with 95% confidence by the NAT assay. Each assay run should include an external run control (usually at 3 times the 95% detection limit). This reagent must be reactive in every run. The external run control may be omitted if the test is licensed (CE marked) with other procedures to warrant robustness.

Table 2-1. Conditions leading to permanent deferral (rejection)

Cancer/ Malignant Diseases	Individuals with a malignant disease, or a history of such, are usually permanently deferred. The physician in charge may make exceptions to this rule in selected cases (see *Principles*).
Creutzfeldt-Jakob Disease	All individuals who have in the past been treated with extracts derived from human pituitary glands, have been recipients of dura mater or corneal grafts or who have been told of a family risk of Creutzfeldt-Jakob Disease or any other Transmissible Spongiform Encephalopathy[1].
Diabetes	If requiring insulin therapy.
Drugs	Any history of injectable drug abuse.
Heart and blood vessel disease	Persons with a history of heart disease, especially coronary disease, angina pectoris, severe cardiac arrhythmia, a history of cerebrovascular diseases, arterial thrombosis or recurrent venous thrombosis (see also *Hypertension*).
Infectious conditions	There are infectious states and diseases necessitating permanent deferral: Carriers of HIV 1/2, HTLV I/II, HBV, HCV Babesiosis[2] Leishmaniasis (Kala-Azar)[2] Chronic Q fever[2] Trypanosomiasis cruzi (Chagas disease)[2] (see also *Infectious diseases*) Persons, whose sexual behaviour puts them at high risk of acquiring severe infectious diseases that can be transmitted by blood.
Xenotrans-plantation	All recipients.

1 A family history of CJD carries a presumption of family risk unless it is determined that: (a) the affected family member had vCJD, not CJD; or (b) the affected family member did not have a genetic relationship to the donor; or (c) the cause of CJD in the affected family member was iatrogenic; or (d) the donor was tested and is known to have a normal genetic polymorphism for PrP^c.

2 Deferral requirements may be waived by the blood establishment when the donation is used exclusively for plasma for fractionation.

Infectious diseases

a. HIV/AIDS

Persons whose sexual behaviour puts them at high risk of acquiring severe infectious diseases that can be transmitted by blood must be permanently deferred.

Current sexual partners of people with HIV must be deferred.

Previous sexual partners of people with HIV are acceptable after 12 months since the last sexual contact.

b. Brucellosis (confirmed)

Deferral for at least two years following full recovery.

The deferral period does not apply when the donation is used exclusively for plasma fractionation.

c. Chagas disease

Individuals with Chagas disease or who have had Chagas disease must be deferred permanently.

The blood of persons who were born or have been transfused in areas where the disease is endemic should be used only for production of plasma that is used exclusively for fractionation into plasma derivatives unless a validated test for infection with *T. cruzi* is negative.

d. Jaundice and hepatitis

Individuals with a history of jaundice or hepatitis may, at the discretion of the appropriate competent medical authority, be accepted as blood donors provided a CE marked test for HBsAg and anti-HCV is negative.

Persons who have been in close household contact with a case of hepatitis B infection (acute or chronic) must be deferred for six months from the time of contact unless demonstrated to be immune.

Current sexual partners of people with HBV must be deferred unless demonstrated to be immune.

別添2

Emerging Infectious Disease Agents and their Potential Threat to Transfusion Safety (Transfusion, vol 49, Aug 2009 supplement)

APPENDIX 2

Trypanosoma cruzi

Disease Agent:

- *Trypanosoma cruzi*

Disease Agent Characteristics:

- Protozoan, 16-20 μm (trypomastigotes) 1.5 × 4.0 μm (amastigotes)
- Order: Kinetoplastida
- Family: Trypanosomatidae
- Metacyclic trypomastigotes and amastigote life-cycle stages found in human hosts.
  - Metacyclic trypomastigotes (hemoflagellates) are intermittently found in the peripheral blood and are the stage that transmits the infection to vectors or blood recipients.
  - Amastigotes are intracellular, tissue-dwelling forms, often associated with cardiac tissue.

Disease Name:

- Chagas' disease
- American trypanosomiasis

Priority Level:

- Scientific/Epidemiologic evidence regarding blood safety: Low since the implementation of blood donor screening test
- Public perception and/or regulatory concern regarding blood safety: Moderate; regulatory concern is increasing.
- Public concern regarding disease agent: Low

Background:

- Agent is naturally limited to American continent (North, Central, and South).
- Stable in endemic countries, but with decreased frequency in rural areas because of vector control and improvements in housing. However, large reservoir populations throughout parasite's range ensure that *T. cruzi* will never be completely eradicated.
- Emergent in nonendemic countries (US, Canada, Europe) because of increase in immigration
- Infected vector insects are present in the southern US, and autochthonous transmission is described infrequently. CDC reports that the insect vector is present in 27 states in the US; the northern range extends from Pennsylvania and New Jersey in the east to California and Nevada in the west. In the US, the parasite is restricted to latitudes below 40°.

Common Human Exposure Routes:

- Exposure to feces from infected vector
- Blood transfusion and organ transplantation
- Congenital transmission and breast-feeding
- Oral ingestion of insect-contaminated food or beverages

Likelihood of Secondary Transmission:

- Moderate
- Transmitted congenitally, by blood transfusion and organ transplant
- Five cases of organ-transmitted *T. cruzi* in the US including one cluster of 3 cases from a single donor

At-Risk Populations:

- Residents of, or immigrants from endemic regions particularly from impoverished rural communities with unplastered walls and thatched roofs
- Recipients of untested blood in Latin America
- Children of infected mothers

Vector and Reservoir Involved:

- Triatomine or reduviid bugs, particularly those from the genus *Triatoma*, *Rhodnius*, and *Panstrogylus*; 11 species reported in the US
- Large sylvatic reservoir populations exist in endemic countries. In the US, *T. cruzi* is found in 18 mammal species including opossums, raccoons, and other sylvatic animals.

Blood Phase:

- Parasitemia occurs during symptomatic acute phase lasting from weeks to months.
- Parasitemia is intermittently detectable during asymptomatic indeterminate and chronic phase.

Survival/Persistence in Blood Products:

- Parasites persist and remain in whole blood at 4°C for at least 18 days.
- Survival in RBCs at 4°C is days to weeks but is less well documented than survival in whole blood.
- Survival in platelets under normal storage conditions for up to 5 days
- The viability of the parasite in frozen plasma components is 24 hours or less.
- The viability in frozen RBC components is unknown.

Transmission by Blood Transfusion:

- Seven cases documented in the US and Canada but more are likely to have occurred and been undetected.
- In Latin America, 12-25% of recipients of seropositive units were infected following the transfusion of fresh, whole blood.
- Infection leading to detectable clinical disease is more common in immunocompromised recipients.
- Components with the greatest risk of transmission are whole blood and platelets. In four of the US cases where an implicated donor was identified (based on

history of having resided in a Chagas' endemic area), the component responsible for transmission was a platelet unit. In a fifth case, transmission from a platelet unit was also likely. The transmitting component in the other two North American cases was not identified in the case report.

Cases/Frequency in Population:

- 100 million people at risk in endemic areas and 7.7 million infected in 18 Latin American countries. It is estimated that 1-2 million exhibit chronic features (cardiac or gastrointestinal), with 14,000-45,000 annual deaths.

Incubation Period:

- 20-40 days, usually manifested by fever of unknown origin

Likelihood of Clinical Disease:

- Generally asymptomatic, but 20-30% of infected individuals develop clinically relevant complications

Primary Disease Symptoms:

- Fever, hepatosplenomegaly, and cardiac symptoms

Severity of Clinical Disease:

- Severe, particularly in immunocompromised recipients, where some lethal cases are described in the acute phase

Mortality:

- In Latin America, 14,000-45,000 deaths annually
- Mortality high in acute transfusion-transmitted infection when recipients are immunocompromised. True mortality rate from transfusion transmission is unknown.

Chronic Carriage:

- Lifetime

Treatment Available/Efficacious:

- Benznidazole or nifurtimox are used for therapy, but effectiveness varies and greatest success is in treating acute stages. In the US, nifurtimox can be obtained through CDC.

Agent-Specific Screening Question(s):

- Currently in use as part of Donor History Questionnaire: "Have you ever had Chagas' disease?"
- Potential risk-factor questions (e.g., birth/residence in an endemic country) have been shown to have a low positive predictive value so have not been recommended.

Laboratory Test(s) Available:

- In the US, one EIA for blood donor screening has been licensed but not required by FDA. Some, but not all blood organizations, are using the test to screen donations.
  - After 2 years of mainly universal screening in the US, testing strategies will likely be modified to a selective strategy based upon at least one-time testing of every donor.
- In Latin America, there are more than 100 tests approved for blood screening.
- IHA, IFA, EIA, western blot, RIPA, chemiluminescence, and NAT methods are available, but a true gold standard remains controversial. Direct parasite detection can be made by smear, xenodiagnosis, and culture; PCR has also been used as direct evidence of the presence of parasites.

Currently Recommended Donor Deferral Period:

- History of Chagas' disease is a lifetime/permanent deferral.

Impact on Blood Availability:

- Agent-specific screening question(s): Current question has no impact.
- Laboratory test(s) available: Low because of the low prevalence of *T. cruzi* antibody in the US blood donor population and the high specificity of the FDA-licensed EIA

Impact on Blood Safety:

- Agent-specific screening question(s): Current question has no impact.
- Laboratory test(s) available: Will significantly decrease the transmission of *T. cruzi*

Leukoreduction Efficacy:

- Low; though parasites are partially retained by leukocyte filters, there is no evidence to support protection of blood recipients when receiving leukoreduced units. At least one transfusion-transmitted case has been documented from a leukoreduced platelet concentrate.

Pathogen Reduction Efficacy for Plasma Derivatives:

- No specific data are available, but it is presumed that the agent would be sensitive to many measures used in the fractionation process.
- Freezing plasma kills the parasite.

Other Prevention Measures:

- First agent for which chemical treatment of whole blood was shown to be effective (crystal violet). More recently, platelet inactivation by amotosalen

and UV light (INTERCEPT) or riboflavin and ultraviolet light (Mirasol PRT System), and for plasma either INTERCEPT or methylene blue have been shown to be effective.

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ORIGINAL ARTICLE

Trypanosoma cruzi infection in North America and Spain: evidence in support of transfusion transmission

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BACKGROUND: The United States, Canada, and Spain perform selective testing of blood donors for *Trypanosoma cruzi* infection (Chagas disease) to prevent transfusion transmission. The donor, product, and patient characteristics associated with transfusion-transmitted infections are reviewed and the infectivity of components from donors with serologic evidence of infection is estimated.

STUDY DESIGN AND METHODS: A systematic review of transfusion-transmitted *T. cruzi* cases and recipient tracing undertaken in North America and Spain is described. Cases were assessed for the imputability of the evidence for transfusion transmission.

RESULTS: *T. cruzi* infection in 20 transfusion recipients was linked to 18 serologically confirmed donors between 1987 and 2011, including 11 identified only by recipient tracing. Cases were geographically widely distributed and were not associated with incident or autochthonous infections. Index clinical cases were described only in immunocompromised patients. All definite transmissions (n = 11) implicated apheresis or whole blood–derived platelets (PLTs), including leukoreduced and irradiated products. There is no evidence of transmission by red blood cells (RBCs) or frozen products, while transmission by whole blood transfusion remains a possibility. Recipient tracing reveals low component infectivity from serologically confirmed, infected donors of 1.7% (95% confidence interval [CI], 0.7%-3.5%) overall: 13.3% (95% CI, 5.6%-25.7%) for PLTs, 0.0% (95% CI, 0.0%-1.5%) for RBCs, and 0.0% (95% CI, 0%-3.7%) for plasma and cryoprecipitate.

CONCLUSIONS: *T. cruzi* is transmitted by PLT components from some donors with serologic evidence of infection. Evidence of transmission before the implementation of widespread testing in the countries studied is sparse, and selective testing of only PLT and fresh whole blood donations should be considered.

Universal serologic testing of US blood donors for *T. cruzi* infection was initiated by the two largest blood collecting systems, the American Red Cross (ARC) and Blood Systems, Inc., in early 2007, after the US Food and Drug Administration's (FDA's) approval of a screening assay in December 2006 and a recommendation by the FDA's Blood Products Advisory Committee (BPAC).[1] The decision to implement blood donation screening was based on accumulated evidence that a substantial number of donors nationwide had evidence of prior exposure; reported transmission rates of 12% to 20% based on historical findings from South America; and case reports of transfusion transmissions in the United States, Canada, and Spain.[2-17] FDA draft guidance recommending universal blood donation screening was released for comment in March 2009. After 16 months of testing, serologic evidence of infection was confirmed in approximately 1:27,500 donors overall but was especially concentrated in areas with large Latin American immigrant communities.[1,18] With an observed low rate of transfusion transmission and apparent absence of incident infections in the US donor pool, many blood centers moved to selective one-time testing of all donors.[19-21] Final FDA guidance released in December 2010 endorsed this approach. In September 2005, Spain implemented selective qualification by testing or

ABBREVIATIONS: ARC = American Red Cross; BPAC = Blood Products Advisory Committee.

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TRANSFUSION **;**:**-**.

exclusion of donors who revealed histories during donor questioning suggesting *T. cruzi* infection risk, after documentation of transfusion-transmitted cases implicating immigrant donors from South America.[22] Both blood providers in Canada implemented similar selective testing models in 2009 to 2010.[23]

After more than 4 years of screening for *T. cruzi* infection in blood donors and recipient tracing of prior donations from serologically confirmed-positive donors, it is timely to reexamine the evidence for transfusion-transmitted *T. cruzi* outside of endemic areas to evaluate the impact of testing on patient safety. It is especially important to assess the imputability of reported cases, as many are described only in case reports of varying quality and completeness. Therefore, we embarked on a systematic review of published reports of transfusion-transmitted *T. cruzi* and of recipient tracing investigations, to assess the characteristics of the donors, patients, and products involved.

MATERIALS AND METHODS

Publication inclusion criteria

This review seeks to summarize all reported cases of transfusion-transmitted *T. cruzi* in North America (Canada, United States, and Mexico) and Spain, with an evaluation of imputability to assess the reliability of each report. Cases were diagnosed either as index clinical infections that were subsequently linked to transfusion or through identification of infected blood donors by serologic screening and tracing of recipients of blood products derived from earlier donations from those donors (recipient tracing). Reports were obtained by literature review and PubMed searches; however, some cases are reported in abstract form only and the authors relied on personal communications with experts in the United States and Spain to assist in identifying reports. A PubMed search between January 1980 and August 2011 on the terms "*Trypanosoma cruzi*" and "transfusion" revealed 377 abstracts that were reviewed for evidence of transfusion transmission and/or recipient tracing studies occurring in the United States, Mexico, Canada, or Spain. Included are all cases identified in the United States by recipient tracing and reported to the BPAC on August 2, 2011.[24]

Imputability

Each case of suspected transfusion-transmitted *T. cruzi* was assessed for imputability based on the available published data using a classification scheme consistent with the Centers for Disease Control and Prevention's National Healthcare Safety Network criteria.[25] To be considered transmission by transfusion, a case had to describe a patient with a clinical or laboratory diagnosis of *T. cruzi* infection (with or without clinical symptoms) and a history of transfusion. Possible cases included any patient where no donor was identified as a potential source of infection but transfusion transmission was thought likely on epidemiologic grounds, or recipient tracing cases where an infected donor and recipient were identified but recipient infection before transfusion could not be excluded and the infected patient had a major risk factor for prior infection, such as having lived in and/or being born in a *T. cruzi*–endemic area. Probable cases included those in which an infected blood donor was identified through serologic testing, with or without further confirmatory testing, but the patient may have at least one other weak risk factor for prior *T. cruzi* infection such as travel to endemic areas; however, transfusion transmission was thought likely on epidemiologic grounds.[26] For the purposes of this study, definite cases included infected patients with no other recorded risk factors and who were transfused with a blood product from a donor shown to be infected with *T. cruzi*.

Statistical analysis

Infectivity by transfusion is expressed as the percentage of cases identified by recipient tracing and the 95% confidence interval (CI), as determined by the Mid-P Exact method.[27]

RESULTS

Fifteen reports were identified that document suspected *T. cruzi* transfusion transmission in 20 patients, including six in abstract form only (Table 1). Seven reports were from the United States, five reports were from Spain, two from Canada, and one from Mexico. Eleven patient cases met the imputability definition of definite transfusion transmission, with six of these identified only by recipient tracing of which one was linked by genetic analysis of donor and recipient *T. cruzi* isolates.[2-16]

Five definite cases were discovered on clinical grounds, all in immunocompromised patients undergoing chemotherapy for cancer and/or stem cell transplant. Definite cases were widely distributed geographically with three cases in New York; one each in Florida, Rhode Island, and Canada; and five cases in four separate regions of Spain. Distribution did not correlate with areas known to harbor vectors capable of transmitting *T. cruzi* infection. Additionally, there were no cases ascribed to autochthonous infections or recently infected donors. The donors involved were born most commonly in Bolivia (six cases), but others came from Argentina, Brazil, Chile, and Paraguay. All donors involved in US cases were long-term residents of the United States (16-40 years). No implicated donors came from Mexico or Central America. All definite cases implicated transfusion of a platelet (PLT) product,

TABLE 1. Patient, donor, and product characteristics involved in transfusion-transmitted *T. cruzi* infections

Reference, year, recipient location	Recipient condition	Other risk factors	Donor implicated	Donor origin	Products	Transfusion transmission
1. Grant et al., 1989,[11] New York	Hodgkin's disease	No	Yes	Bolivia	PLTs	Definite
2. Leiby et al., 1999,[4] Florida	Multiple myeloma*	No	Yes	Chile	PLTs (whole blood)	Definite
3. Nickerson et al., 1989,[12] Canada	Acute lymphoblastic leukemia	No	Yes (2)	Paraguay (2)	PLTs	Definite
4. Young et al., 2007,[15] Rhode Island	Neuroblastoma	No	Yes	Bolivia	PLTs (irrad. & leuko.)	Definite
5. Kessler et al., 2010,[8] New York	Unknown*	No	Yes	Argentina	PLTs (irrad. & leuko. apheresis)	Definite
6. Kessler et al., 2010,[8] New York	Unknown*	No	Yes	Argentina	PLTs (leuko. apheresis)	Definite
7. Flores-Chavez et al., 2008,[13] Madrid	Leukemia	No	Yes	Brazil	PLTs	Definite
8. Perez et al., 2008,[5] Malaga	Aplastic anemia	No	Yes	Bolivia	PLTs	Definite
9. Perez et al., 2008,[5] Malaga	Choroid plexus papilloma*	No	Yes	Bolivia	PLTs	Definite
10. Abalo et al., 2007,[7] Galicia	Unknown*	No	Yes	Bolivia	PLTs	Definite
11. Ozaeta Orrono et al., 2008,[9] Basque	Unknown*	No	Yes	Bolivia	PLTs	Definite
12. Lane et al., 2000,[3] Canada	Promyelocytic leukemia	Travel to Mexico	Yes	Paraguay	Not defined (299 PLT units, 8 RBC units)	Probable
13. Geiseler et al., 1987,[6] California	Leukemia	Travel to Mexico	Yes	Not stated	Not defined	Probable
14. Stramer et al., 2008,[20,28] Tennessee	Pregnancy*	Born in El Salvador	Yes	El Salvador	PLTs	Possible
15. Kirchhoff et al., 2006,[16] Mexico	Unknown*	Endemic region	Yes	Mexico	Fresh whole blood or PLTs	Possible
16. Kirchhoff et al., 2006,[16] Mexico	Unknown*	Endemic region	Yes	Mexico	Fresh whole blood or PLTs	Possible
17. Kirchhoff et al., 2006,[16] Mexico	Unknown*	Endemic region	Yes	Mexico	Fresh whole blood or PLTs	Possible
18. Kirchhoff et al., 2006,[16] Mexico	Unknown*	Endemic region	Yes	Mexico	Fresh whole blood or PLTs	Possible
19. Cimo et al., 1993,[10] Texas	Colon cancer	Travel to Mexico	No	No donor identified	~500 RBC, PLT, and plasma units	Possible
20. Villalba et al., 1992,[14] Cordoba	Leukemia	No	No	No donor identified	20 products, not defined	Possible

* Found on recipient tracing.
Irrad. = irradiated; leuko. = leukoreduced.

either from a whole blood or an apheresis donor. In two of these cases, the implicated PLT product was documented to have been both leukoreduced and irradiated[8,15] (D. Kessler, personal communication, 2011). Donations from some of the donors whose PLT products were associated with definite transmissions of *T. cruzi* were subjected to recipient tracing. Overall six definite transmissions were linked by recipient tracing from five donors identified either by donor screening (four) or as an index clinical case (one).[4,5,7-9]

Two cases met the definition of probable transfusion transmission. In both cases, the patient's risk factor involved "travel to Mexico"; recent travel to endemic countries is considered a weak risk factor given improved vector control, along with a requirement for sustained residence in an endemic setting to successfully transmit the parasite.[24,26] Lane and coworkers[3] described a case in Canada in which an implicated donor was born in Germany, but lived extensively in Paraguay. The recipient, who had prolymphocytic leukemia, had received 299 PLT concentrates and eight red blood cell (RBC) units; no specific component was implicated in this transmission case. A second case described by Geiseler and colleagues[6] did not define a component type although a directed donor was implicated by serologic testing (father who had lived in Mexico).

Seven cases were considered to be possible transfusion transmission. The ARC had one possible case associated with a serologically confirmed-positive donor identified by routine blood donation screening. The ARC implemented routine universal screening of all blood donors for *T. cruzi* infection by enzyme-linked immunoassay (ELISA; ORTHO *T. cruzi* enzyme-linked immunosorbent assay test system, Ortho Clinical Diagnostics, Raritan NJ) in January 2007, with confirmation of repeat reactivity by radioimmunoprecipitation assay (RIPA; Quest Diagnostics, Chantilly, VA). Recipient tracing was performed for all repeat donors confirmed positive by RIPA.[18,20,28] During the first year of screening, a donor with a history of birth in Brazil donated a whole blood unit to the Tennessee Valley Region Blood Center and was found to be ELISA repeatedly reactive, RIPA positive, but *T. cruzi* PCR and hemoculture negative by in-house methods.[4] Components from four prior whole blood donations were investigated for transmission. The 28-year-old female recipient of a leukoreduced whole blood PLT unit transfused in August 2006 was found to be *T. cruzi* ELISA repeat reactive, RIPA positive, and PCR and hemoculture negative. This recipient had a history of birth in El Salvador, an endemic region for *T. cruzi*.[28] Conclusive evidence of transfusion transmission was not possible through genetic characterization, as parasites could not be recovered from either the donor or the recipient. A prior recipient of a fresh-frozen plasma (FFP) unit was found to be negative for all tests. The other recipients of the donors' blood were either deceased or lost to follow-up. This case meets our definition of a possible transfusion transmission. Since that time and covering 4 years of screening, the ARC has not identified another infected recipient of a blood product from a confirmed-positive donor (110 total recipients tested; however, only nine received PLTs).

Kirchhoff and colleagues[16] describe a serologic screening study in Mexico that revealed an overall 0.75% prevalence of *T. cruzi* infection in blood donors at five regional blood centers. Recipient tracing investigations were performed at one center in Guadalajara where the prevalence in blood donors was 0.79%. Four of nine (44%) recipients of either whole blood (two) or PLTs (two) from infected donors were found to be serologically positive. The authors concluded that transfusion transmission had occurred based on a significant difference between the rate of positive findings in the tested recipients and that in the donor population, of which 83% were less than 35 years old. No further details on the donors or recipients, including the recipients' pretransfusion serologic status, age, and underlying disease, or the prevalence of *T. cruzi* in the general patient population, were provided. Direct demonstration of *T. cruzi* infection by PCR or microscopy was not performed in either the donor or the recipient populations in this study. Thus, evidence for transfusion transmission is regarded as possible in these cases.

Two other cases of suspected *T. cruzi* transmission are reported by Villalba and colleagues[14] in Cordoba, Spain, and by Cimo and colleagues[10] in Houston, Texas, based on the detection of clinical infection in multiply transfused patients with no reported history of other risk factors for infection. However, investigation of the blood donor population was incomplete and no infected donors were identified, leading to the conclusion of possible transfusion transmission.

The relatively sparse number of reports of transfusion-transmitted *T. cruzi* in North America and Spain, and the absence of definite cases implicating transfusions involving blood products other than PLTs, raises a question regarding the relative infectivity of components from infected donors. In addition to the transfusion-transmitted cases identified by recipient tracing described above, at least six other reports of recipient tracing studies have failed to identify additional cases of transfusion transmission.[18,19,21,29-32] In total, it is noteworthy that only six definite transfusion transmission cases have been identified through recipient tracing of 350 recipients, suggesting an overall infectivity of 1.7% (95% CI, 0.7%-3.5%) for recipients exposed to blood components from seropositive donors (Table 2). While the full breakdown of component type is incomplete, available data allow us to calculate the infectivity risk for 0 of 197 RBC units (0.0% [95% CI, 0.0%-1.5%]); 6 of 45 PLTs (13.3% [95% CI, 5.6%-25.7%]); and 0 of 80 frozen plasma or cryoprecipitate units (0.0% [95% CI, 0%-3.7%]).

TABLE 2. Outcomes of successful recipient tracing investigations on prior donations from donors found to be infected with *T. cruzi* either after identification of an index clinical case or by serologic screening of blood donors in the research or routine operations setting

	Transfused and investigated				
Report	Total† components	RBCs	PLTs	Plasma or cryoppt	Whole blood
1. Grant et al., 1989[11]	5				
2. Kerndt et al., 1991[31]	7			1	
3. Leiby et al., 1999[4]	1		1*		
4. Leiby et al., 1999[30]	1		1		
5. Leiby et al., 2002[2]	18	11	2	5	
6. Abalo et al., 2007[7]	2	1	1*		
7. Kessler et al., 2008[8]	4	2	2*		
8. Perez de Pedro et al., 2008[5]	8		1*		
9. Ozaeto Orrono et al., 2008[9]	2	1	1*		
10. Fearon et al., 2011[32]	48	30	6	12	
11. FDA BPAC, 2011[24]	254	152	30‡	62	3
Totals	350	197	45	80	3

* Positive recipient tracing investigations with definite infected recipients identified.
† Total component count does not correspond to the individual component count due to missing data in the referenced publications.
‡ A single possible transfusion transmission case is excluded from this analysis.
Cryoppt = cryoprecipitate.

DISCUSSION

In December 2006, the FDA licensed the first blood screening test for antibodies to *T. cruzi* that has been used with a laboratory-developed test (RIPA) for confirmation of repeat reactivity.[1,33] The BPAC met to discuss the development of guidance for blood donation screening in April 2007. The FDA released draft guidance for universal testing in March 2009 and then final guidance in December 2010 allowing a selective testing model where donors need only test negative one time to be qualified for all future donations. Evidence in favor of blood donation screening includes a significant prevalence of *T. cruzi* seropositivity in blood donors, especially in regions of the United States with substantial Latin American immigrant populations. In the late 1990s prevalence rates were as high as 1 in 7500 in Southern California donors and 1 in 9000 in donors in Miami;[29,30] current data reflect rates of 1 in 6800 and 1 in 5000, respectively (ARC internal data). Furthermore, prior reports from endemic countries suggested that approximately 12% to 20% of components from seropositive donors transmit infection, including whole blood, RBCs, PLTs, white blood cells (WBCs), FFP, and cryoprecipitate.[34] Selective one-time testing of all US blood donors was supported by BPAC and incorporated into final FDA guidance based on the paucity of evidence for incident or autochthonous infections in the United States and the low overall rate of transfusion transmission demonstrated by recipient tracing following the first 4 years of testing.[1,21]

In Spain, a European country with a high immigration rate from South America, a Royal Decree was issued in 2005 whereby the Spanish Ministry of Health required the exclusion or testing of donors born in endemic countries, the children or grandchildren of mothers born in those countries, or donors with a history of having resided or being transfused in those areas.[22,35] Both blood providers in Canada recently implemented similar measures, after the report of two transfusion-transmitted cases.[3,12]

Since January 2007, more than half of the US blood supply, consisting of more than 20 million transfused components derived from approximately 10.9 million donors each year,[36] has been tested. A total of 1456 RIPA–confirmed-positive donors were identified by August 2011, according to the AABB Chagas Biovigilance Network,[37] for a mean rate of approximately 1:25,000 to 1:30,000 donors tested, consistent with prior reports.[18,20,28] Substantially higher rates are apparent in areas of the country with larger immigrant populations from Mexico and South and Central America.

Despite the relatively high prevalence of *T. cruzi* infection in the United States, evidence of transfusion transmission is sparse. Only five cases (three definite, one probable, and one possible transmission case) were reported in the United States between 1987 and 2011, with recipient tracing identifying another two definite and one possible case after the introduction of routine donor testing. It has been suggested that acute *T. cruzi* infection may often be subclinical and that it may only be recognized in highly immunocompromised patients. Thus, transfusion transmission may be significantly underreported.[38] Clinical cases confirm the propensity for diagnosis in immunocompromised patients; however, recipient tracing has failed so far to identify a substantial number of seropositive recipients, recognizing that the number of PLT recipients tested is limited (e.g., only nine over 4 years at the ARC). In any event, it is desirable to reassess the available data in support of *T. cruzi* transfusion transmission and resulting screening policies.

Review of 20 cases derived from 15 reports confirms that there is strong evidence for transfusion transmission; however, all cases where a component was identified involved either PLTs (from both whole blood and apheresis) or whole blood. Leukoreduction and/or irradiation of PLT components do not appear to prevent transmission. The patients detected clinically were immunocompromised and under treatment for oncologic diseases and thus more likely to receive PLT products. Donors involved in transmission cases were invariably born in endemic areas of South and Central America or Mexico and donated blood across the geography of North America or Spain. In the United States and Canada, there is little evidence of increased transmission risk from donations in those areas of the country having the highest proportion of immigrant donors from endemic countries, or from areas at risk for autochthonous transmission, as evidenced by cases in New York, Rhode Island, Manitoba, and Tennessee versus a high concentration of infected donors in California, Florida, and Texas.

There is no evidence in this review of published cases and recipient tracing that plasma, cryoprecipitate, or RBCs transmit *T. cruzi* infection. The evidence for whole blood transmission relies on statistical comparisons of infection rates in donors and patients in Mexico, but transmissibility cannot be excluded. It should be noted that in Mexico, as in much of Latin America, the use of replacement donors remain and the transfusion of "fresh" whole blood within days of collection is much more common than in the United States.

The relative paucity of reports of transmission in Mexico is difficult to understand. *T. cruzi* is endemic in many parts of Mexico and screening of blood donors has revealed a seroprevalence that varies from 0.37% to 7.7%, with a mean of 1.5% in 18 government blood centers in various states.[16,39-44] It seems reasonable to assume that this is due to underreporting and the difficulty in diagnosing transfusion transmission in endemic areas.

The risk of a donor with serologic evidence of *T. cruzi* infection transmitting infection is unknown, but appears to be low. In aggregate, recipient tracing has identified only six confirmed cases in 350 patients transfused and tested, for an overall infectivity rate of 1.7% (95% CI, 0.7%-3.5%). How do we reconcile the data from nonendemic countries suggesting low transmissibility with historical reports of higher transmissibility in endemic countries? It may be that prior estimates are incorrect, that the risk has changed over time, that the risk of transmission varies with different geographical strains of *T. cruzi*, or a combination of the above. First, we must acknowledge the difficulty in assessing transmission in endemic areas. The widely quoted rate of 12% to 20% transmission is based on estimates published by the World Health Organization in 1980 followed by a review of the evidence basis by Schmunis in 1991.[17,38,45]

The early studies often relied on comparisons of infection rates in donor and multiply transfused patient populations as evidence of transmission. The assertion that recipients with higher rates of infection reflected transfusion transmission is likely to be confounded by the fact that infection may have occurred decades ago in rural areas of endemic countries before effective vector control. In addition, because Chagas disease is a chronic infection with long-term sequelae that may require transfusion, and that most blood is transfused to the elderly, infection is more likely to be recognized in transfused patients versus blood donors who are generally much younger.[16,17] These studies cannot confirm infection because there was no pretransfusion sample, which is necessary to prove seroconversion indicative of transmission.[46] In addition, proof of transfusion transmission is especially difficult as serologic conversion may occur 3 or more months after transfusion transmission, requiring PCR testing or hemoculture to make a diagnosis.[4] Thus, the accuracy of early reports of infectivity from endemic areas should be questioned. Indeed, at least one study stated the risk of transmission from a single transfusion is 0.15% to 0.6%, which is consistent with our current observations.[47,48]

Second, the assumed 12% to 20% rate of transmission was established by studies performed before 1980.[17] During that period, the use of paid and/or replacement donors and the transfusion of fresh whole blood or nonleukoreduced blood was more likely than is currently the case. With the move to modern RBC storage solutions, prolonged storage times, and widespread leukoreduction by filtration, the risk of transfusion transmission may have changed over time. Transmission by PLTs shows that *T. cruzi* organisms can survive in anticoagulant solution with storage up to 5 days at room temperature and that leukoreduction and irradiation may reduce but do not eliminate the risk. The absence of transmission by RBCs or noncryopreserved frozen products suggests that the organisms are either removed during whole blood processing and/or do not survive storage or freezing well.[49] *T. cruzi* exists exclusively as an extracellular parasite in the blood and may be particularly susceptible to processing and storage conditions. Dzib and coworkers[50] showed that leukoreduction by centrifugation reduces but does not eliminate *T. cruzi* contamination from RBC, buffy coat, and PLT fractions while Moraes-Souza and colleagues[49,51] showed similar data for leukoreduction by filtration. Alternatively, Hernandez-Becerril and coworkers[41] found that while 41% (12 of 29 donors) of seropositive donors in Mexico City were also positive by PCR and 10% (2 of 29 donors) by hemoculture, suggesting active parasitemia, they were unable to detect any parasitemia in 70 RBC and PLT components prepared from blood donations from similar donors. The authors suggest that processing of whole blood may diminish the parasite burden in blood components by eliminating the WBC-

rich fraction. Given that RBCs are usually transfused after longer storage periods than PLTs, it is entirely possible that the decreased infectivity for RBC products compared to PLTs is due to organism attrition during processing and storage.

Finally, Leiby and colleagues[52] suggest that different strains of *T. cruzi* may pose varying risks of transmission. Most of the immigrant population in Spain where a number of cases of transfusion transmission have been documented is derived from South America where *T. cruzi* (Tc) Lineages II to VI predominate, whereas the immigrant population in the United States, where the rate of transmission is low, is more likely to hail from Mexico and Central America where Tc Lineage I is found. The authors report a significantly higher rate of hemoculture positivity with Tc Lineage II to VI (11 of 24 [45.8%]) versus Tc Lineage I (2 of 90 [2.2%]). Higher levels of parasitemia with Tc Lineages II to VI may explain the higher rates of transmission in countries where immigration from South America predominates. A study conducted by the Centro de Transfusión de Cruz Roja Española en Madrid provides further support for this hypothesis: 15 of 49 (30.6%) blood donors found to be *T. cruzi* antibody positive were also positive by hemoculture, with parasite levels between 1 and 10 parasites/mL. These donors were all born in South America and most were from Bolivia (E. Castro, unpublished data).

Serologic testing for *T. cruzi* adds significantly to the cost of providing blood products to patients while adding little safety benefit, given the sparse evidence for transfusion transmission. For these reasons, Spain and Canada have restricted testing to the small subset of donors who acknowledge risk factors for infection. In US studies, Leiby and colleagues[29] showed that donor country of birth and time in endemic countries were informative donor history determinants, but Custer and colleagues[53] found that they were only able to identify 75% of confirmed *T. cruzi* infections, suggesting that donor history would have limited utility as a safety measure in the United States.

The FDA has released guidance recommending selective donor testing on one occasion, based on the absence of evidence for incident infections in the US donor population.[21] Our analysis now suggests that before any testing, the risk of transfusion transmission was restricted to PLT (and possibly fresh whole blood) transfusions. Selective testing of only these donations would constitute a level of safety that could eliminate any measurable risk of transfusion transmission of *T. cruzi*, while conserving resources for other interventions with higher recipient impact (e.g., *Babesia microti*).

CONFLICT OF INTEREST

None.

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