# Brief Reports

*Brief reports of new clinical or laboratory observations, cases of unusual importance, and new developments in medical care will be considered for publication in this section. Manuscripts must be typed double-spaced. Text length must not exceed 750 words; not more than ten references and one figure or table can be used. See "Information for Readers and Authors" for form of references. Manuscripts should include an abstract of not over 150 words. Reports will be reviewed by consultants when, in the opinion of the editors, such review is needed. The Editor reserves the right to shorten reports and to make changes in style.*

## Transfusion-Associated Acute Chagas Disease Acquired in the United States

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Although a significant problem in Latin America (1), the transmission of *Trypanosoma cruzi* infection by transfusion has not been unequivocally documented in the United States. We report a case of severe acute transfusion-acquired Chagas disease in a child with Hodgkin disease who had never travelled to an endemic area; however, she had received platelets from an asymptomatic Bolivian immigrant who had serologic evidence of *T. cruzi* infection.

An 11-year-old white girl with Hodgkin disease who had been in remission since May 1987 after splenectomy, radiotherapy, and chemotherapy presented in April 1988 with a temperature of 38.3 °C. Her physical examination was otherwise unremarkable. Her leukocyte count was $14.6 \times 10^9$/L her erythrocyte sedimentation rate was 66 mm/h. After an extensive nondiagnostic evaluation, vincristine was administered on 3 May and cyclophosphamide on 10 May. A Gram stain showed *T. cruzi* in a bone marrow aspirate. (Figure 1). She had always resided in the Bronx and had visited only urban areas in North America.

At admission on 17 May, she complained of fatigue, headaches, myalgia, and tremulousness. She was afebrile with a blood pressure of 88/50 mm Hg, mild cardiac failure, and coarse tremors. Her granulocyte count was $0.4 \times 10^9$/L. There was a moderate pericardial effusion. Cerebrospinal fluid showed seven mononuclear cells; glucose and protein levels were normal. The peripheral blood smear showed many *T. cruzi,* and the serum *T. cruzi* titer was 1:256 by indirect fluorescent antibody technique for total immunoglobulin.

Therapy with nifurtimox (25 mg/kg body weight · d) was instituted. She became febrile and developed myoclonus, generalized seizures, and an enlarging pericardial effusion, as well as progressive hypotension, dyspnea, and anasarca. On hospital day 3, pericardial window placement yielded 300 mL of serosanguineous fluid in which motile trypanosomes were seen. On day 5, because of her deteriorating condition, subcutaneous interferon-gamma was begun on a compassionate basis (30 $\mu g/m^2$ body surface area · d). By day 7, her granulocyte count was $1.3 \times 10^9$/L. On the next day, parasites were absent on peripheral blood smears. She steadily improved. On day 16, nifurtimox was lowered to 15 mg/kg daily. By day 23, she was asymptomatic and discharged on digoxin, phenobarbital, and nifurtimox. She completed 20 days of interferon-gamma therapy and 120 days of nifurtimox therapy. All subsequent blood smears were negative for parasites. *Trypanosoma cruzi* was isolated from blood drawn the day before admission by both hemaculture and inoculation into nude mice; however, the organism was not isolated from blood drawn after 23 days of nifurtimox therapy.

Antibody to *T. cruzi* was not detected by indirect immunofluorescence in a stored serum specimen from 30 March 1987. Between 14 July 1987 and 22 February 1988, she had received blood products from six different donors. Of the five donors tested, one 70-year-old asymptomatic woman had a titer of 1:512 by indirect immunofluorescence. She had emigrated from Bolivia to the United States in 1972. Our patient had received her platelets on 22 February 1988. Five recipients of this donor's blood products who could be tested did not have serologic evidence of infection with *T. cruzi.*

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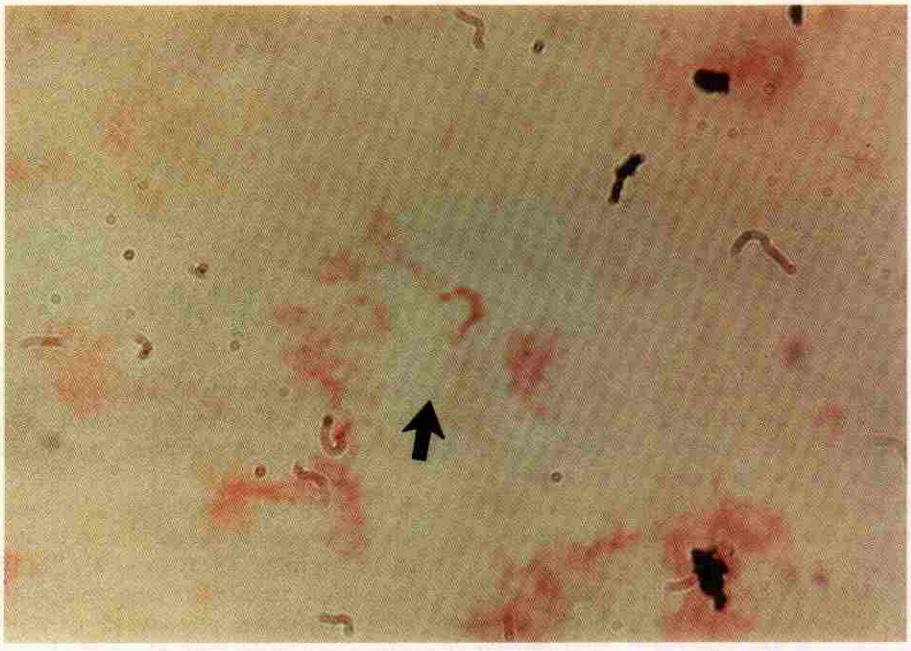

**Figure 1.** *Trypanosoma cruzi (arrow)* in bone marrow aspirate. (Gram stain; original magnification, × 1000.)

Transfusion-associated Chagas disease has not been previously recognized in the United States; however, transfusion is the second most important mode of transmission of Chagas disease in Latin America, where *T. cruzi* is endemic; there is an estimated attack rate after transfusion of seropositive blood products ranging from 12% to 50% (1). Because acute Chagas disease is often unrecognized, chronic infection is usually unsuspected. Untreated persons remain potentially infectious for life (2); low-grade parasitemia is found on xenodiagnosis in up to 50% of seropositive persons (1, 3).

It is estimated that 10 to 12 million persons in Central and South America are infected with *T. cruzi* (4). In Santa Cruz, Bolivia, where our patient's donor came from, 62% of blood donors and 71% of transfusion recipients were found to be seropositive for *T. cruzi* (1). The prevalence of infection in immigrants to the United States has not been thoroughly assessed. In a seroprevalence study done in Los Angeles, 1 of 1027 blood donors had clear serologic evidence of *T. cruzi* infection (5). In Washington, D.C., 4.9% of 205 immigrants from Nicaragua and El Salvador were seropositive for *T. cruzi* (3).

Acute Chagas disease may be more severe in immunocompromised persons. Our patient had a splenectomy and developed severe myopericarditis and possible meningoencephalitis while neutropenic. Fulminant Chagas myocarditis developed in a recipient of a bone marrow transplant who had both travelled in endemic areas and received seropositive transfusions (6).

It has been claimed that nifurtimox is associated with elimination of parasites in 90% of patients with chronic Chagas disease (7). Cure rates in patients with acute infection and in immunosuppressed patients are uncertain. Therapy with interferon-gamma reduced morbidity and eliminated mortality in mice that had received a lethal *T. cruzi* infection (8). Improved chemotherapeutic responses in children with refractory visceral leishmaniasis have been observed. (Johnson W. Personal communication.) Although the contribution of interferon-gamma to our patient's recovery cannot be assessed, no toxic effects were observed.

Blood donors from endemic areas may transmit *T. cruzi.* With large population influxes, tranfusion-associated transmission may occur with increasing frequency. Policies for identifying potentially infected blood products may be needed. At Memorial Sloan-Kettering Cancer Center, we currently ask patients about exposure to conditions favoring contact with reduviid insects and defer such persons as donors. *Trypanosoma cruzi* is another infection that should be considered in the febrile patient who has received blood products.

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**References**

1. **Schmunis GA.** Chagas' disease and blood transfusion. In: Dodd RY, Barker LF, eds. *Infection, Immunity and Blood Transfusion:* Proceedings of the XVIth Annual Scientific Symposium of the American

Red Cross, Washington, D.C., May 9-11, 1984. New York: Alan R. Liss;1985;127-45.
2. **Kirchhoff LV, Neva FA.** Chagas' disease in Latin American immigrants. *JAMA.* 1985;**254:**3058-60.
3. **Kirchhoff LV, Gam AA, Gilliam FC.** American trypanosomiasis (Chagas' disease) in Central American immigrants. *Am J Med.* 1987;**82:**915-20.
4. **Brener Z.** Recent developments in the field of Chagas' disease. *Bull WHO.* 1982;**60:**463-9.
5. **Kerndt P, Waskin H, Steurer F, et al.** *Trypanasoma cruzi* antibody among blood donors in Los Angeles [Abstract 669]. Program and Abstracts: Twenty-Eighth Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, D.C.: American Society for Microbiology; 1988.
6. **Geiseler PJ, Ito JI, Tegtmeier BR, Kerndt PR, Krance R.** Fulminant Chagas' disease in bone marrow transplantation [Abstract 418]. Program and Abstracts: Twenty-seventh Interscience Conference on Antimicrobial Agents and Chemotherapy. Washington, D.C.: American Society for Microbiology; 1987.
7. **Gutteridge WE.** Existing chemotherapy and its limitations. *Br Med Bull.* 1985;**41:**162-8.
8. **Reed SG.** In vivo administration of recombinant IFN-Gamma induces macrophage activation, and prevents acute disease, immune suppression, and death in experimental *Trypanosoma cruzi* infections. *J Immunol.* 1988;**140:**4342-7.



# Transfusion-Associated *Trypanosoma cruzi* Infection in a Non-Endemic Area

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Opportunistic infections have become a major cause of morbidity in the immunocompromised host. In patients with neutropenia, such infections often arise from their own indigenous flora; however, another potential mode of infection is the transmission of blood-borne organisms by transfusions. Patients with granulocytopenia who receive multiple blood products during chemotherapy are especially prone to transfusion-associated infections. We describe the first case of transfusion-associated acute Chagas disease in a non-endemic area of North America.

## Case Report

In June 1986, a 1-year-old infant presented with a cerebral thrombosis and was subsequently found to have protein S deficiency. When the family was screened, the 21-year-old Cree Indian mother was found to have both protein S deficiency and acute lymphoblastic leukemia. At that time her only complaint was minor fatigue. Induction chemotherapy with doxorubicin, vincristine, L-asparaginase, and prednisone was initiated; after 2 weeks of treatment, she was pancytopenic and febrile. She developed *Escherichia coli* bacteremia and septic shock, which required antimicrobial therapy with vasopressor and ventilator support. Additionally, she received erythrocyte, granulocyte, and platelet transfusions. During the next 2 weeks, she recovered and completed the course of induction chemotherapy; by mid-August 1986, a remission had been achieved. Consolidation chemotherapy, along with cranial radiotherapy, was started. After 2 weeks of treatment, however, she was again neutropenic and febrile.

Physical examination at that time was within normal limits; blood tests and urinalysis, as well as chest and sinus roentgenograms, were persistently normal. Amikacin and pipercillin were empirically started. After 3 days of antimicrobial therapy she remained febrile, and antifungal therapy with amphotericin B was instituted. After 7 days of this therapy, congestive heart failure was apparent: an examination showed an elevated jugular venous pressure, bi-basilar crepitations, a third heart sound, pedal edema, and hepatosplenomegaly. At this time her cumulative doxorubicin dosage was 190 mg, an amount that is infrequently associated with heart failure. An echocardiogram showed global heart dysfunction with four-chamber dilatation and an ejection fraction of 15%. The electrocardiogram was normal. Laboratory findings included a total bilirubin of 59 μmol/L (normal range, 3 to 18 μmol/L), an aspartate aminotransaminase level of 4.93 μkat/L (normal, < 0.83 μkat/L), a lactate dehydrogenase level of 47.43 μkat/L (normal, 1.67 to 3.75 μkat/L), and a creatine kinase of 41.07 μkat/L (normal, 0.06 to 3.13 μkat/L). In a buffy coat smear, analyzed to assess the leukocyte differential, many flagellates were seen. Spindle-shaped, 20 μm long, U- and C-shaped protozoa were identified as trypomastigotes of *Trypanosoma cruzi* (Figure 1). In reviewing previous buffy coat smears obtained at the onset of pyrexia, we observed smaller numbers of *T. cruzi*. Nifurtimox, 10 mg/kg body weight, was administered daily in four divided doses. Within 5 days the patent parasitemia had resolved, the neutrophil count had increased, and the patient was no longer in cardiac failure. At this time the echocardiogram showed an ejection fraction of 65%. Unfortunately, 9 days after receiving nifurtimox, she developed pancytopenia, and a bone marrow aspirate showed aplasia. Therapy with nifurtimox was discontinued, and 5 days later the peripheral blood counts began to return to normal. Three years later, she remains in remission, having received no further chemotherapy; and she has also delivered a normal second child. There have been no cardiac or gastrointestinal manifestations of Chagas disease to date.

*Trypanosoma cruzi* is not endemic to Manitoba, and our patient had not been outside the province. Thus, a transfusion-associated infection was suspected. Between June and September the patient had received blood and blood products from 103 blood donors. We were able to recall 96 of these donors to screen them for *T. cruzi* antibodies. Procedures for an enzyme-linked immunosorbent assay (ELISA), as previously described (1), were adapted to the diagnosis of *T. cruzi*. Briefly, epimastigotes of *T. cruzi* were used at a protein concentration of 10 μg/mL. Significant antibody levels have not been determined for the

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