

The Outlook for Chagas Disease, Leishmania and Bioterror Agent Testing of Blood

Advisory Committee

Blood Safety and Availability

Department of Health and Human Services

May 17, 2005

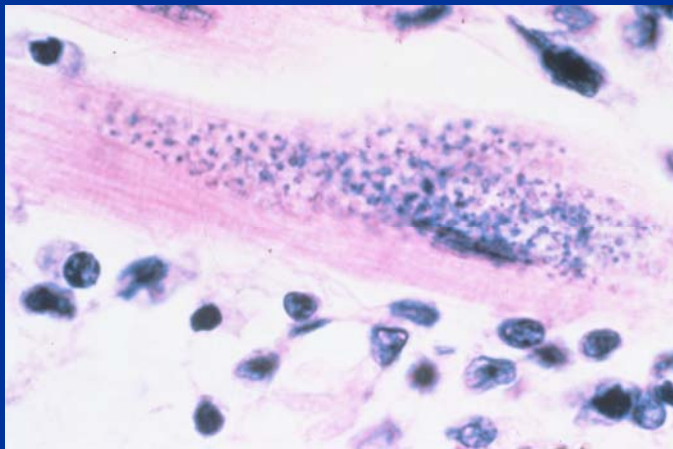
Robert Duncan, PhD

CBER/OBRR/DETTD

***Trypanosoma cruzi*: causative agent of Chagas disease**



- **small protozoan parasite**
- **chronic, asymptomatic infection**
- **Difficult or impossible to treat**
- **endemic to portions of Mexico, Central America, and South America**
- **transmission: vectorial, congenital, organ transplant, blood exposure (transfusion, laboratory accident)**



Blood Donor Screening for Chagas: Background

- 16-20 million people infected with *T. cruzi*, mostly in Central and South America.
- Blood transfusion transmission is a recognized problem in endemic areas. An infected unit causes infection in the recipient 1.4%-48% of the time depending on the geographic area (Schmunis, 1999)
- 7 cases of transfusion transmission documented in US/Canada
- 3 cases of solid organ transplant transmission
- Seroprevalence in US donor population ranges from 0.01-0.2% with the higher rates in areas with large numbers of immigrants from Central and South America.
- Increasing rates of immigration raises concern about the potential for increased transmission.

Chagas Disease After Organ Transplantation --- United States, 2001

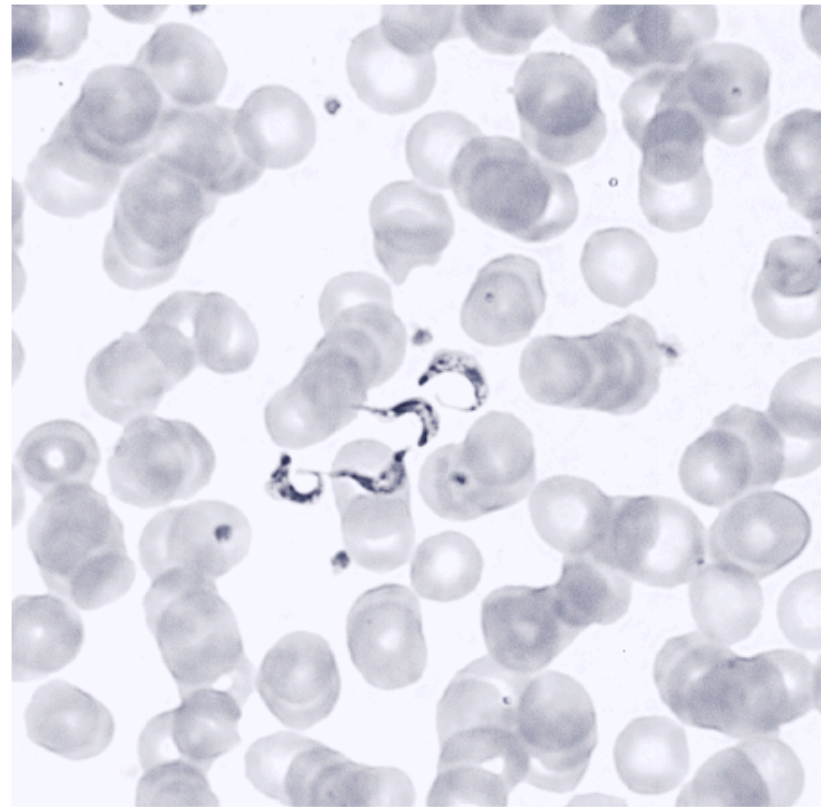
MMWR

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One donor- three
recipients, all infected

FIGURE 1. *Trypanosoma cruzi* trypomastigotes on a peripheral blood smear from a patient aged 37 years



Photo/CDC file

U.S./Canadian Transfusion Cases

1987: California - Mexican donor

1989: New York City - Bolivian donor
Manitoba - Paraguayan donor

1993: Houston - unknown donor

1999: Miami - Chilean donor

2000: Manitoba - German/Paraguayan donor

2002: Rhode Island – Bolivian donor

Blood Donor Screening for Chagas: Previous Discussions

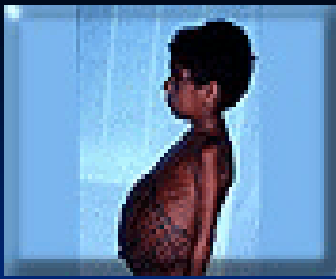
- 1989- BPAC recommended donor screening for Chagas provided there were a suitable test available.
- 1995-BPAC responded to the question, “are the available tests appropriate for donor screening?” by voting yes=3, no=0, and abstain=10.
 - Committee Members were unclear about requirements for approval of a donor-screening test.
- 2002-FDA outlined expectations of a Chagas test to BPAC who informally reaffirmed recommendation for universal screening provided a suitable test is available

Chagas Tests in Development

- *T. cruzi* lysate-based ELISA
- Recombinant antigen-based serological assay
 - Available published results indicate high sensitivity and specificity
- Confirmatory test?

Confirmatory tests

- FDA has requested that BLAs for licensing a blood screening assay for Chagas Disease should be accompanied by validation of a confirmatory test
- Radio Immune Precipitation Assay (RIPA), recognized as the most specific and sensitive test, involves difficult and hazardous methodology
- Other promising methodologies need further development and validation



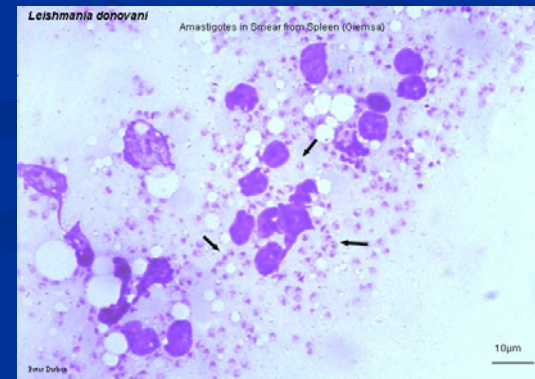
Visceral

Leishmaniasis



Cutaneous

- Disease caused by infection of macrophage cells with protozoan parasite, *Leishmania*
- Infection acquired by bite of an insect vector
- Endemic to subtropical and tropical areas in the Middle East, Asia, Africa, Central and South America and Mediterranean Coast of Europe
- *Leishmania* transmission by blood transfusion has been demonstrated
 - 15 cases worldwide-all visceral



Leishmaniasis Deferral

Discussed at Dec 2003 BPAC

- Large number of potential US donors exposed in endemic areas (Iraq and Afghanistan)
- >900 Reported cases of disease in US troops
- DoD and AABB recommendations for deferral for travel to Iraq have been issued
 - Travelers to Afghanistan are deferred for malaria exposure
- BPAC voted to recommend 1 year deferral for travel to Iraq, lifetime deferral for diagnosis of leishmaniasis, consistent with DoD and AABB recommendations

Leishmania Donor Screening

- No assays approved or proposed
- Diagnostic tests available are species restricted, sensitivity and specificity inadequate for screening
- Transmission risk is low
 - 15 cases of transfusion transmission worldwide associated with visceral disease in the donor
 - Endemic countries do not uniformly screen blood

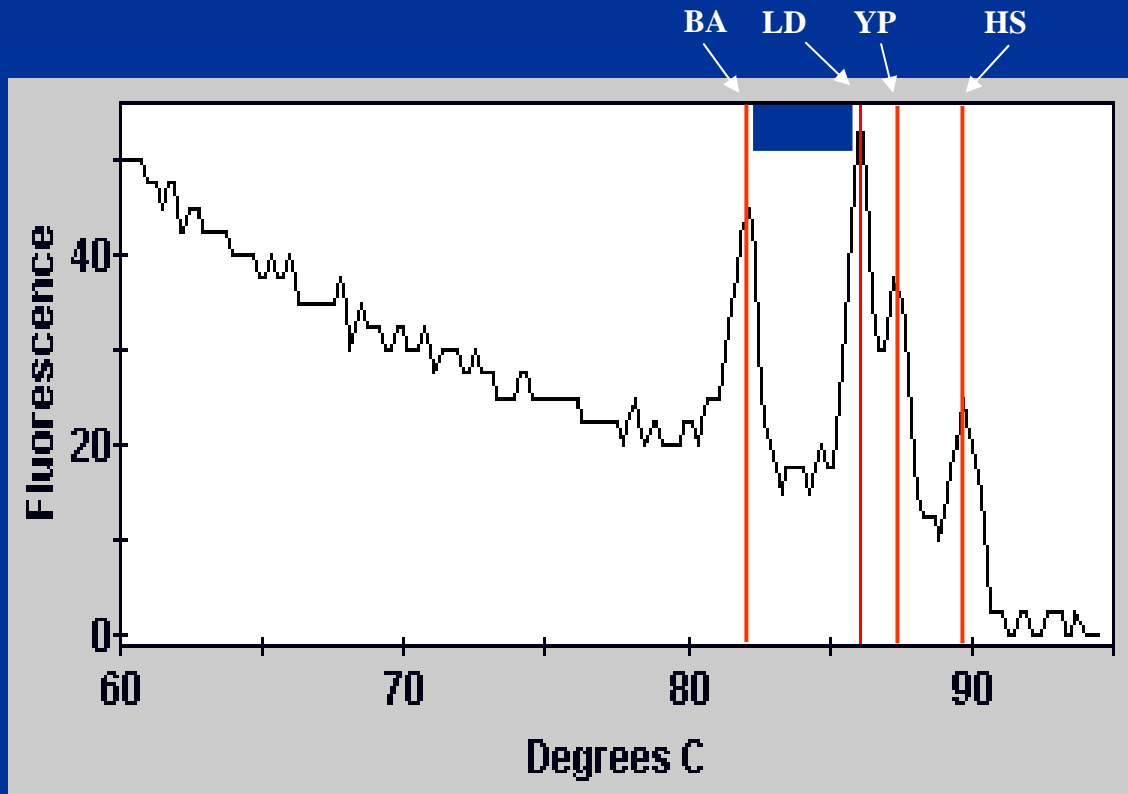
Blood Donor Screening for Bioterror Agents

- No approved assays
- No submissions for blood screening
- BT pathogen presence in blood of asymptomatic donor unlikely-suggests low risk of transfusion transmission.
- For preparedness in event of attack:
Research assays
 - Multiplex Real time PCR assay
 - Multiplex PCR microarray assay

Multiplex Real time PCR

Pathogens spiked into whole blood at 50 CFU/ml

Melt Curve analysis



Pathogens **TM value**

BA: B. anthracis : 82.03

LD: L. donovani : 86.08

YP: Y. Pseudo' : 87.45

HS: Human : 89.5

Microarray for detection of Blood-borne and BT pathogens

Group 1: Bacteria, and Parasites

Ba: *Bacillus anthracis* (**anthrax**)

Ft: *Francisella tularensis* (**tularemia**)

LT: *Leishmania* /*Trypanosoma*

Yp: *Yersinia pestis* and *pseudotuberculosis* (**plague**)

Group 2: Bioterror Viruses

POX: Pox viruses

VAC: Vaccinia

VAR: Variola (**Smallpox**)

MPV: Monkeypox Viruses

CPV: Cowpox Viruses

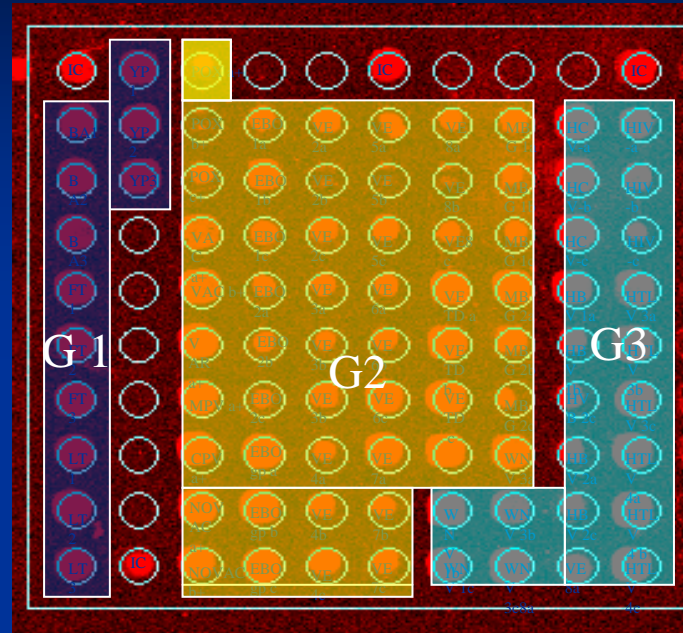
NOVAC: All Pox viruses but Vaccinia

EBO: Ebola Viruses

VE: Venezuelan Equine Encephalitis Viruses

VETD: VE Trinidad Donkey

MBG: Marburg Viruses



 4 internal control probes (Human rRNA gene)

Group 3: Blood Borne Viruses

WNV: West Nile Viruses

HCV: Hepatitis C Viruses

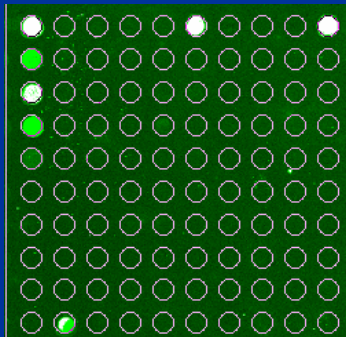
HBV: Hepatitis B Viruses

HIV: Human Immunodeficiency Viruses

HTLV: Human T-cell Leukemia Viruses

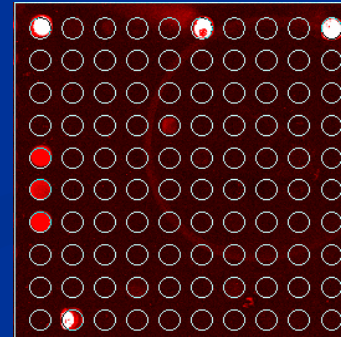
Results of detection in pathogen-spiked blood – 50 cells/ml

Bacillus anthracis



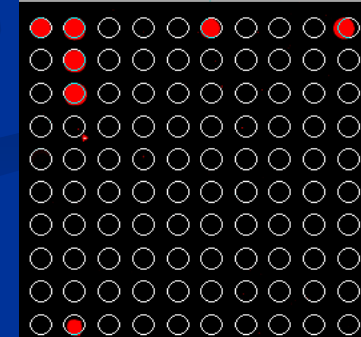
livestock vaccine strain

Francisella tularensis



Live Vaccine Strain

Yersinia pseudotub.



Summary

- Chagas Disease: blood screening tests in development
- Leishmaniasis: vigilance for shifting epidemiology, adjustments in deferral policy, no blood screening envisioned
- Bioterror agents: blood screening not likely mode of early detection, preparedness at the research level