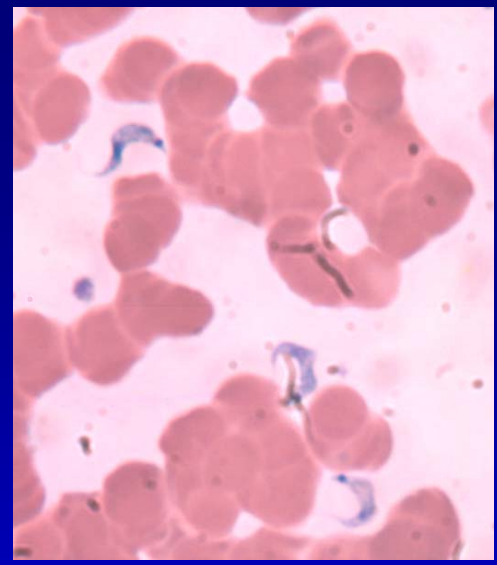
Issues Related to Implementation of Blood Donor Screening for Infection with *Trypanosoma cruzi*

Presentation to ACBSA
May 10, 2007
Robert Duncan, PhD

Background

Trypanosoma cruzi: causative agent of Chagas disease



- **Small protozoan parasite**
- **Chronic, asymptomatic infection**
- **Difficult or impossible to treat, severe symptoms late in about 30% of cases**
- **Endemic to portions of Mexico, Central America, and South America, 16-20 million people infected**
- **Transmission: feces of an infected triatomine insect, congenital, organ transplant, transfusion, oral (breast milk), via conjunctiva, laboratory accident**
- **Blood transfusion transmission is a recognized problem in endemic areas. An infected unit is estimated to have a 12-20% probability of causing infection in the recipient (WHO TRS 905, 2002)**

Background: Risk and Epidemiology in the US

Triatomine bug

- **7 cases of transfusion transmission documented in US/Canada**
- **5 cases of solid organ transplant transmission**
- **Rare natural transmission of *T. cruzi* in the US**
- **Seroprevalence in US donor population has been estimated in the range of 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.**

Background (Continued)

- December 2006- FDA approves the first blood donor screening assay (the Ortho® *T. cruzi* ELISA Test System)
- No FDA licensed supplemental test for *T. cruzi* antibodies is currently available
- April 26, 2007 – Issues related to implementation of blood donor and cell/tissue donor screening presented and discussed with BPAC:
  - Donor management, product management, areas needing additional research, potential for cell/tissue transmission

BPAC Session Agenda

- Introduction and Issues Related to Implementation of Blood Donor Screening for antibodies for *T. cruzi* Infection
  - Robert Duncan, Ph.D., DETTD, OBRR, FDA
- Introduction of Issues Related to the Potential Transmission of *T. cruzi* by Human Cells, Tissue and Cellular and Tissue-Based Products
  - Melissa A. Greenwald, M.D., DHT, OCTGT, FDA
- Ortho *T. cruzi* ELISA Test System Experience
  - Susan Stramer, Ph.D., American Red Cross
- Public Health Impact of Donor Screening for *T. cruzi* infection
  - Susan Montgomery, M.D., CDC
- Potential Strategies for Targeted Testing for *T. cruzi* Infection in Repeat Donors
  - Michael Busch, M.D./ Brian Custer, Ph.D., M.P.H., Blood Systems Research Institute
- Open Public Hearing, Questions and Discussion

Blood donor screening for Chagas disease

- Chagas screening with the Ortho ELISA initiated by ARC and BSI on January 29, 2007 other centers have followed. Through April 17, 2007, 1.8 million donors had been screened, resulting in detection of 265 repeatedly reactive (0.015%).
- Retested on a more specific, unlicensed *T. cruzi* RIPA: 174 non-reactive, 50 reactive, 41 pending.
  - 99.990% specificity, 0.003% prevalence
- Voluntary industry recommendations: AABB issues recommendations for implementation to member establishments. (Bulletin #06-08, Dec. 2006)

Issues for Implementation of Blood Donor Screening : Donor Management

- We are considering whether blood establishments should:
  - Test donations for antibodies to *T. cruzi*
    - Universal screening
    - Potential for selective testing if appropriately validated
  - Defer (indefinitely) and notify all donors repeatedly reactive by the licensed test

Donor Management (Continued)

- Counseling:
  - inform all repeatedly reactive donors about likelihood and medical significance of infection; referral for additional medical diagnostic testing may be useful
  - Medical follow up for cross-reacting diseases
    - Specific counseling of repeatedly reactive donors with no apparent exposure or negative results on more specific medical diagnostic tests for further medical follow up based on risk factors

Issues for Implementation of Blood Donor Screening : Product Management

- We are considering whether blood establishments should:
  - Index donations: quarantine and label all repeatedly reactive
  - Prior collections: retrieve, quarantine and label
  - Recipient tracing: notify consignees to enable notification of recipients of prior donations from repeatedly reactive donors
  - Autologous donations: test and label (21CFR 610.40)

BPAC response to issues presented

- Universal blood screening for *T. cruzi* for one to two years to acquire more data on epidemiology, test performance, understanding of the window period and F/U testing, reentry of deferred donors

- Additional time for test development could lead to a licensed supplemental test that would permit establishing a donor reentry algorithm

Areas where research is needed?

- Possible targeted screening of repeat donors
  - Necessity for continued universal screening?
  - Validation of strategies for retesting selected repeat donors for *T. cruzi* antibodies
  - Presentation was made by Brian Custer, BSRI, outlining plans for a validation strategy

Research on possible targeted screening of repeat donors: BPAC response

- General consensus that research on selected testing should be pursued
  - Validation of the donor questions for selective screening is critical
  - Multiple years of universal screening data would be beneficial for evaluating the selective testing strategies

- FDA will continue to work within the AABB Chagas Task Force to facilitate effective research strategies

Additional areas where research is needed?

- Possibility of cross-reactive antibodies of medical significance: indications from Ortho's performance evaluation study
- *Leishmania*
  - Test reacts with samples from individuals with leishmaniasis (74/100 samples from area non-endemic for *T. cruzi*)
- Other pathogens
  - Test can react with samples from individuals with malaria (1/100)
  - Test may react with *Paracoccidioides* antibodies (2/5 from *T. cruzi* endemic area)

Possible studies to evaluate cross-reactivity of Chagas blood screening tests

- Test a panel of serum/plasma samples from individuals well characterized as infected with *Leishmania* with licensed *T. cruzi* blood screening assay
  - CDC repository
  - Other US repositories of infected samples
  - Acquire additional samples from *Leishmania* endemic countries
- Prospectively follow up for leishmaniasis all donors repeatedly reactive on licensed *T. cruzi* blood screening assays
  - *Leishmania* serology
  - Risk factors for exposure to *Leishmania*
  - Other medical diagnoses
- Similar studies of *Plasmodium* or *Paracoccidioides* cross-reactivity could also be proposed

Cross-reactivity of Chagas blood screening tests: BPAC response

- Concern that the lack of evidence from *T. cruzi* blood screening and follow up *Leishmania* testing of over 300 repeatedly reactive donors indicates no pressing need for more research

- Concern that more research needs to be done to understand how to counsel repeatedly reactive donors that are non-reactive on a more specific test or other medical follow up

- Committee suggested that investigation of cross reactivity to other agents should be focused in medical diagnosis setting