Resistance to *Trypanosoma cruzi* Infection in Relation to the Timing of IgG Humoral Response

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**Abstract.** The Biozzi “high” (BH) and “low” (BL) responder mice (Selection III) differed in their susceptibility to *Trypanosoma cruzi*. The BH strain responded quickly to the infection, similar to the reaction of (CBA × C57B1/10)F1 mice but in contrast to the susceptible BL strain. We suggest that the IgG response mounted by the host during the prepatent period of the infection is crucial to the outcome of the infection.

**Introduction**

It is estimated that over 6 million people in Brazil, most of them under 20 years of age, suffer from Chagas' disease. Mortality is not high during acute disease, but cardiac and digestive manifestations of the chronic phase ("mega viscera") are distressing. Inapparent forms account for 50% of individuals infected (Macedo 1980).

Although its causative agent, the stercorarian trypanosome *Trypanosoma (Schizotrypanum) cruzi* (Chagas 1909), infects several mammalian orders (Barretto 1968), an experimental model mimicking the human disease is lacking. Such a model would be a tremendous help to experimental research on Chagas' disease.

As a consequence, important features of the host-parasite relationship are missing in this trypanosomiasis. Thus, the relative contribution of the humoral and cell-mediated immune responses to the acquired resistance as well as their participation in the pathogenesis of Chagas' disease need to be clarified (Trischman et al. 1978; WHO 1979).

We have studied the highly resistant (CBA × C57B1/10)F1 mice, which develop a quite standard infection from the strain Y (Corsini et al. 1980a, 1980b). Furthermore, we verified that the resistance to *T. cruzi* in F1 mice is T-dependent. Thus, T-deprived (thymectomized, irradiated, fetal liver reconstituted) “B” mice were extremely susceptible to *T. cruzi* in contrast...
to normal mice. Moreover, nylon wool purified T cells that were harvested from infected mice at 30 days post-infection, but not from normal mice, were capable of protecting those “B” mice (Corsini and Stelini Jr. 1981). In addition, immune serum protected normal T-cell reconstituted mice but did not protect unreconstituted ones (Corsini and Stelini Jr. 1981 unpublished data).

Since protective antibodies in murine experimental infections have only been found in IgG2a and IgG2b subclasses but not in IgM class (Takehara et al. 1981), we decided to evaluate the participation of the IgG humoral response in the resistance of \((\text{CBA} \times \text{C57B1/10})\text{F}_1\) mice to \(T. cruzi\). \(\text{F}_1\) mice were splenectomized or immunosuppressed and compared with Biozzi mice (Selection III) selected as “high” (BH) and “low” (BL) antibody responder strains against the flagellar antigen of \(Salmonella typhimurium\) and \(Salmonella oranienburg\) (Siqueira et al. 1976).

The experiments described in this paper suggest that the timing of the IgG humoral response is important for host protection. In addition, infected mice were able to mount a secondary IgG response to a lethal challenge and survive reinfection. Furthermore, Biozzi mice Selection III differed in their resistance to \(T. cruzi\), as did Selection I (Kierszenbaum and Howard 1976), the BH being resistant and the BL susceptible.

**Material and Methods**

**Animals**

\((\text{CBA} \times \text{C57B1/10})\text{F}_1\) and Biozzi mice (Selection III) were bred in our laboratory. The female and male mice were 3 months old when infected. The colony of Biozzi mice was initiated from breeders given by Dr. Oswaldo Sant’Anna (I. Biológico – São Paulo – Brazil). These mice were selected according to their antibody response against the flagellar antigen of \(Salmonella typhimurium\) and \(Salmonella oranienburg\) (Siqueira et al. 1976). Biozzi mice were usually heavier (35–40 g) than \(\text{F}_1\) mice (30–35 g).

**Trypanosome**

\(Trypanosoma (Schizotrypanum) cruzi\) strain Y was obtained from Dr. Zigman Brener (Dept. Parasitology – Belo Horizonte – Brazil). It was passaged weekly in Swiss 55 mice as described by Brener (1968).

**Trypanosome Infections and Reinfections**

Mice were infected intraperitoneally (i.p.) with 100 trypanosomes as described previously (Corsini et al. 1980b). Reinfections were performed on different days after the primary infection using \(10^5\) parasites injected i.p.

**Immunosuppressive Drugs**

Cyclophosphamid (N-N-bis (B-creoltil) diamide N',0-propilen-ortophosphoric ester (Enduxan, Pravaz Recordati São Paulo – Brazil) (Cy) and Hydrocortisone (Hydrocortisone hemsuccinate – Flebocortid, Richter São Paulo – Brazil) (Hy) freshly diluted in distilled water were injected intramuscularly into experimental animals. Different schedules and doses were used throughout. Thus, 1.5 or 3.0 mg Cy was given daily either 3 days before infection or for 3 days from the day of infection. Hy was given for 10 days from the day of infection in daily doses of 10 mg.

**Splenectomy**

Splenectomy was performed in both normal and infected mice under ether anaesthesia.