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Chagas Disease: *in vivo* Acute Infection Induces Morphological Changes in Monocytes/Macrophages But Not Nitric Oxide Production

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Chagas disease, caused by intracellular protozoan *Trypanosoma cruzi,* is one of the most important public health problems in Latin America [1]. The acute infection triggers a plentiful production of monocytes from bone marrow precursor cells so as to control *T. cruzi* replication in the target tissues such as the myocardium [2]. Clear monocyte/macrophage activation occurs earlier in the acute *T. cruzi* infection in parallel to a high number of these cells respectively in the blood and heart [2,3].

In the present work, the nitric oxide (NO) production by peripheral blood monocytes (PBM) and peritoneal macrophages was evaluated, *in vivo*, in rats during the acute phase of disease. The ultrastructure of the PBM and peritoneal and heart macrophages was also analyzed. Animals were inoculated with *T. cruzi* ($3x10^5$ tripomastigotes, i.p., Y strain) and sacrificed at days 6, 12 or 20 post-infection (4-6 rats/group).

Acute *T. cruzi* infection did not induce NO synthesis by monocytes and macrophages despite of being found a significant increase in the number of these cells. PBM from infected animals showed ultrastructural signs of activation, being more voluminous with more euchromatic nucleus and a striking increase in cytoplasmic organelles and surface rufflings compared to controls (FIG. 1). Macrophages from infected animals showed clear morphology of activated cells. Many pseudopodia, arrays of rough endoplasmic reticulum, lipid bodies, mitochondrion profiles and vesicles were present (Fig.2). Macrophages were often seen ingesting *T. cruzi* forms and showed many phagolysosomes with varying sizes and electron-densities containing amorphous materials, cell debris and amastigotes. The monocyte and macrophage sizes (diameter measurements taken from electron micrographs) in infected rats were significantly higher than those of the control group cells, especially at day 12 of infection (Table 1).

Our data showing a high number of morphologically activated monocytes/macrophages highlights the importance of innate immunity during the acute Chagas disease. A novel finding is that NO production does not seem essential to control the whole period of the in vivo acute phase of *T. cruzi* infection in rats.

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Table 1. Diameter measurements (μm) from peripheral blood monocytes and peritoneal and heart macrophages in rats with 12 days of infection and controls. Values expressed as mean ± standard deviation. The range is indicated in brackets.Monocyte/macrophage system morphometry at different days of *T.cruzi* infection in rats.

Groups	Peripheral Blood Monocytes	Peritoneal Macrophages	Heart Macrophages
Control	4.8 ± 0.1[3.7-5.5]	6.9 ±0.1[6.2-7.6]	4.9 ± 1.1 [4.0-6.6]
Infected	5.7 ± 0.1[3.2-7.2]	8.5 ±0.2[6.2-10.7]	9.4 ± 3.2 [5.3-16.6]

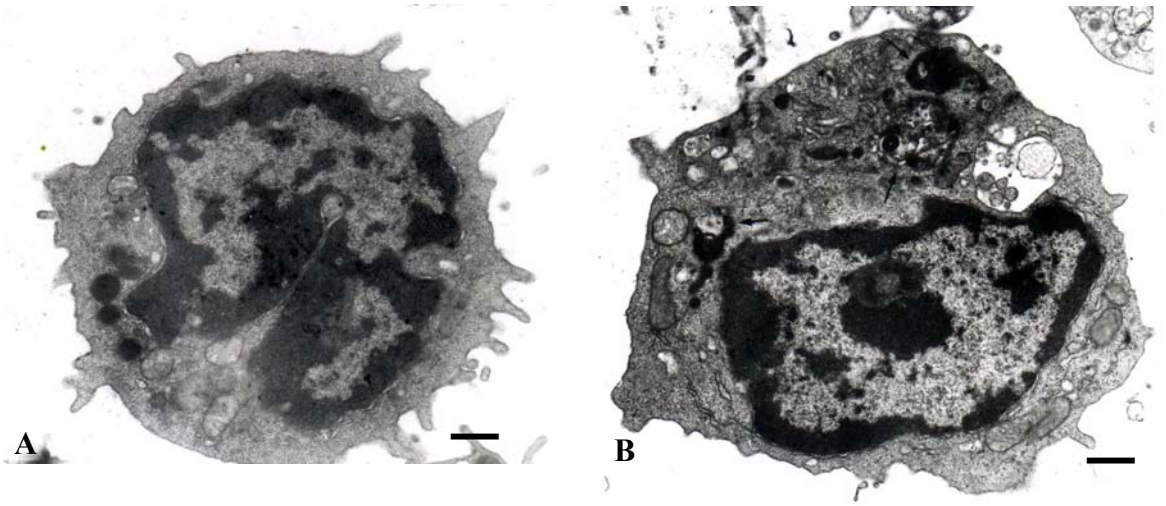

Figure 1. Electron micrographs of peripheral blood monocytes in normal (A) or infected (B) rats at day 12 day of infection with *T.cruzi*. Digestive vacuoles are indicated (arrows).Scale bar = 0.5μm

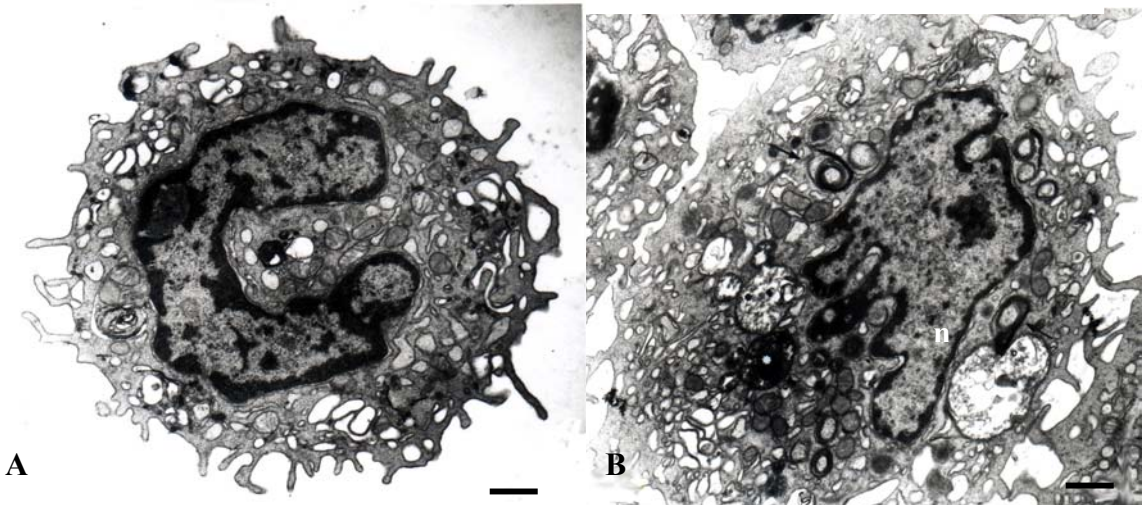

Figure 2. Electron micrographs of control (A) and infected (B) peritoneal macrophages from a rat at day 12 of infection with *T.cruzi*. The cells show nucleus (n) irregular in outline, voluminous cytoplasm rich in organelles and degenerating parasite amastigote forms (arrows). Scale bar = 0.5μm

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