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ACTUAL ASPECTS AND EPIDEMIOLOGICAL SIGNIFICANCE OF CONGENITAL TRANSMISSION OF CHAGAS' DISEASE

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The congenital transmission of Chagas' disease occurs by transplacentary via when trypomastigotes present in the intervillous space gain access through the trophoblast. Besides parasitemia, other factors are certainly involved in the congenital transmission of this infection. We have observed patients with several positive xenodiagnosis during gestation who did not transmit their infection to the fetus.

Why the fetal infection occurs only in a small proportion of infected mothers is a matter to be clarified. Andrade (1982) observed experimentally a striking difference in the rate of placental parasitism with three different strains of *Trypanosoma cruzi*. Delgado & Santos Buch (1978) verified in mice that the transplacental passage of trypomastigotes was dependent on pathogenicity of the strain of *T. cruzi* and on the placental phagocytic activity. Otherwise it has been observed in human cases that stocks of *T. cruzi* enzymically indistinguishable (zimodeme II, highly prevalent in patients in Bahia) can have different behaviors with respect to transplacentary transmission (Bittencourt, 1984). Certainly, the congenital transmission of Chagas' disease depends on the infectious agent and the immunological competence of the placenta. The macrophages of the placenta are the Hofbauer cells, present in the stroma of the villi, in the chorium and in the amnion; these cells have well established immunophagocytic function (Moskalewski, Ptak & Czarnik, 1975; Loke et al., 1982). Otherwise, it is also know that the trophoblastic epithelium has phagocytic capacity (Smith & Wilson, 1974; Schlafke & Anders, 1975; Myagkaya & Vreeling-Sindelarova, 1976). When trypomastigotes penetrate the villi necrosis of the trophoblast occurs and secondaryly a collection of maternal mononuclear cells is formed around the necrotic area determining a perivillositis; in the chorium the trypomastigotes transforme into amastigotes within the Hofbauer cells (Fig. 1). Parasitism of the trophoblastic epithelium (Fig. 2) has been reported in only three placentas up to date, associated or not to parasitism of Hofbauer cells (Rassi et al., 1958; Medina, 1983; Bittencourt, 1984); in these three cases however the conceptuses were free of infection. There are also a few cases referred in literature of placentas with parasitized Hofbauer cells without fetal infection (Moya, Villagra & Risco, 1979; Bittencourt, 1984). Certainly, both Hofbauer cells and trophoblastic epithelium are involved in the defense mechanism of placenta to *T. cruzi*.

In a study of 33 cases of congenital Chagas' disease the following patterns were considered peculiar to the congenital form of Chagas' disease when compared with the noncongenital acute disease: 1. The presence of parasitized giant cells with a single and hyperchromatic nucleus; 2. Pneumonitis, in almost all the cases associated with parasitism of the amnionic epithelium; 3. Parasitized supepidermal granulomas also associated with parasitism of the amnionic epithelium; 4. Presence of early digestive manifestations with development of megaesophagus in the acute phase of disease (Bittencourt, 1984).

These giant cells (Fig. 3) have been observed in several tissues and in different organs, including the placenta and adnexae. As these cells appear only in cases with prominent parasitism of the macrophagic system, it was suggested that this pattern may be related to the strain of *T. cruzi* (Bittencourt, 1976). Bittencourt et al. observed a case with this type of cells whose isolate of *T. cruzi* showed enzymically a triple banded GPI pattern (Bittencourt, 1984); this pattern has not been described in Bahia but has been registered in Bolivia and Chile where congenital cases with giant cells have also been found (Rubio & Howard, 1963; Azougue, 1982; Miles, 1983).

The simultaneous observation of parasites in the macrophages of the alveolar wall (Fig. 4) and in the amnionic epithelium (Fig. 5) indicates without doubt parasitism of the amnionic fluid. This fact has epidemiological importance since the amnionic fluid once infected may be a vehicle of accidental transmission of *T. cruzi* to professionals involved in obstetrical care (Bittencourt et al., 1981).

Bittencourt (1984) observed three congenital cases of chagasic infection with digestive symptoms since birth; all these babies died before six months of age and on post-mortem examination it was found a marked reduction in the number of neurons or even absence of these cells in the myoenteric plexus of the esophagus. One of these children had a radiographically proven megaesophagus (Fig. 6) at four months of age (Fig. 5) and at autopsy a marked dilatation of this organ was observed. Another case of megaesophagus due to congenital chagasic infection was diagnosed radiographically by Tafuri, Lopes & Nunan (1973) but this patient did not present digestive manifestations and, at post-mortem examination esophageal dilatation was not found. It is known that the neuronal lesions of the digestive tract occur mainly in the acute phase of Chagas' disease (Koeberle, 1974; Rezende & Rassi, 1983; Andrade, 1983) but the digestive symptomatology and the megaesophagus appear usually in the chronic phase, 10 or more years after the infection (Rezende, 1979); in the congenital cases referred above the esophageal lesions were so marked that led to the develop-

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ment of megaesophagus during the acute phase of disease (Bittencourt, 1984). These cases constitute examples of digestive chagasic disease occurring in the acute phase of infection.

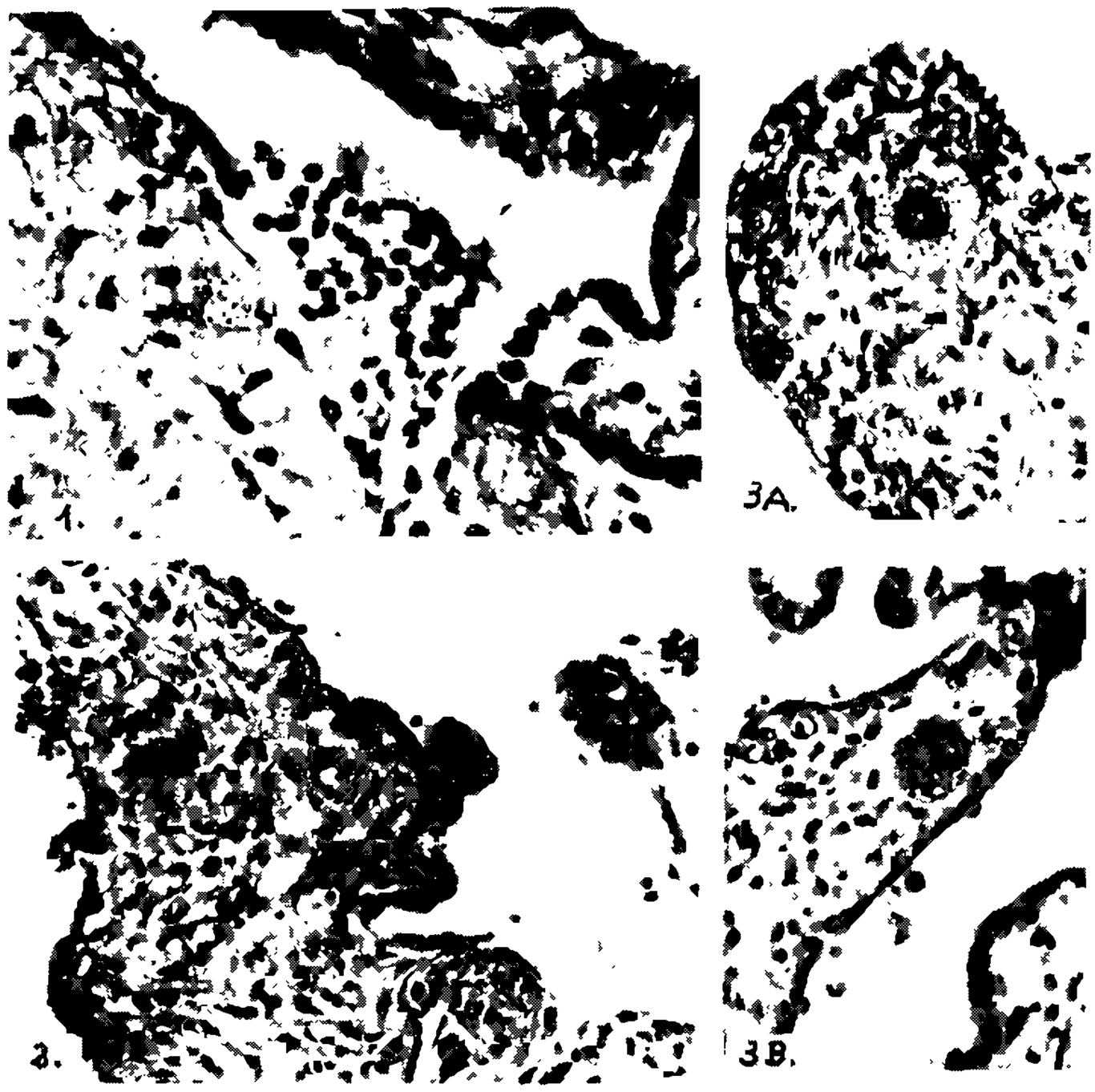


Fig. 1 – Placenta. A villus with an area of recent infection. There are necrosis of the trophoblast and a collection of polimorfonuclear leucocytes and mononuclear cells around the necrotic area; in the chorium, a parasitized Hofbauer cell is seen. H & E, x 400. Fig. 2 - Placenta. A villus with parasitism of the trophoblastic epithelium. H & E, x 400. Fig. 3 - Mucosa of the bladder. A: see a parasitized giant cell with a hyperchromatic nucleus. B: placental villus with the same type of cell. HE x 400.

Congenital chagasic infection may be responsible for severe neurologic sequelae with early manifestations. Stagno & Hurtado (1971) describe microcephalic newborn with chagasic infection who had the diagnosis of cerebral palsy at two months of age. Pearson, Wahlgren & Bengtsson (1982) observed another microcephalic newborn who had the diagnosis of chagasic meningoencephalitis at one month of age; this child had cerebral palsy and a computerized X-ray of the brain showed a seriously disarranged brain with dilated ventricles and multiple calcifications. Another case of cerebral palsy caused by congenital chagasic meningoencephalitis has been recently observed in Bahia (Bittencourt, 1984). Besides other cases of late sequelae of congenital chagasic meningoencephalitis have been also described (Howard, 1976).

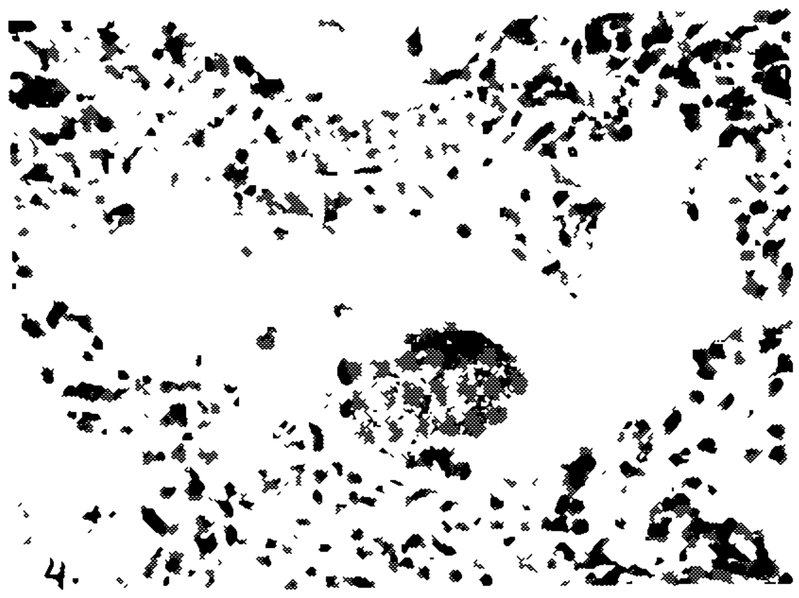
The chronic form of Chagas' disease occurs many years after the acute phase and manifests itself as cardiac, digestive and nervous form (Andrade & Andrade, 1979). In the chronic form of Chagas' disease the parasites are scanty and the lesions are not directly related to a parasite-induced cells destruction, as occur in the acute phase. The myocarditis of the chronic phase is of late onset, is progressive and leads to diffuse fibrosis, but this type of lesion in Chagas' infection is exclusive of the myocardium (Andrade, 1983). By contrast, the digestive alterations are certainly sequelae of lesions occurring during the acute infection (Koeberle, 1974; Andrade, 1983). On the other hand, there is no comprovation that the lesions of the nervous form of chronic disease are of late onset; Chagas (1916) had suggested that this form of disease could be a sequelae of acute meningoencephalitis. The cases here referred of digestive and nervous form of congenital Chagas' disease occurring during or soon after the acute phase confirm the observations of other authors that the lesions responsible for these forms of disease occur very early in the course of infection.

There are geographical differences in the frequency of congenital Chagas' transmission. In Table I, we can see that the prevalence of transmission is greater in Santa Cruz de la Sierra – Bolivia (Azougue, personnel communication) than in Bahia – Brazil (Bittencourt et al., 1972; Bittencourt, 1984). These differences are much higher if we consider that Azougue did not include stillbirths and did not eliminate seronegative mothers in their study. The incidence of Chagas' disease transmission is also lower in Bahia than in some areas of Argentina (Bittencourt, 1984). Various authors elsewhere in Brazil have failed to identify cases of congenital Chagas' disease: they examined few cases and applied different methods for detection (Oliveira, 1958; Barcellos, 1960; Passos, 1960; Lopes et al., 1967; Carvalheiro, Favero & Duarte,

TABLE I

Incidence of congenital Chagas' disease in two endemic areas

	Weight ⩽2.000g	Weight >2.000g
Among newborns and stillbirths of chagasic mothers (Salvador, Bahia)	10,5%	1,6%
Among newborns of unselected mothers (Santa Cruz de la Sierra, Bolivia)	14,8%	4%



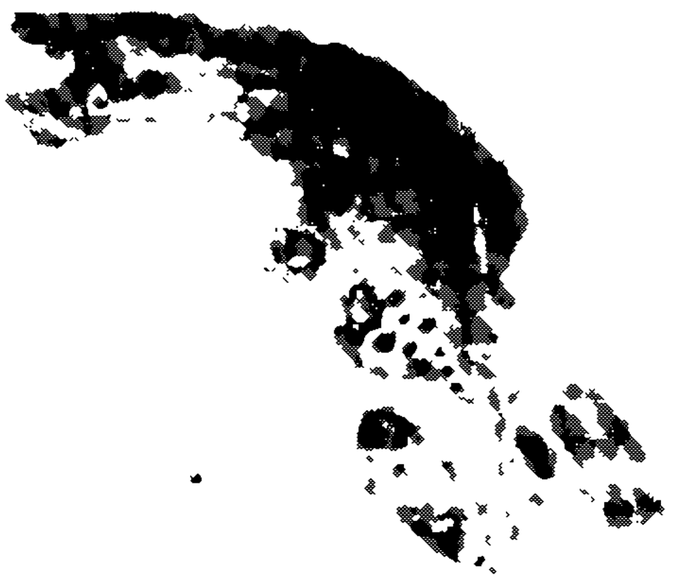


Fig. 4 – Lung. An inflammatory infiltrate of mononuclear cells in the interalveolar septae and a parasitized cell protruding in the alveolar lumen are seen. H & E, x 400. Fig. 5 – Umbilical cord. See amastigotes within the amnionic epithelium. H & E, x 1000. Fig. 6 – The radiological aspect of the megaesophagus.

1974; Trindade et al., 1981). Dias (1979), working in a previously endemic area (Bambuí – Minas Gerais) where vector-mediated transmission had stopped for several years, found no cases of infection in 300 children of chagasic mothers. This finding is representative but does not exclude the possibility of *T. cruzi* transmission with intrauterine deaths. Recently, in Brasília, Medina (1983) found among newborns of chagasic mothers a rate of transmission of 1%; these mothers are provenient of different states of Brazil, including Bahia, though this percentual can not be used for comparative studies. There may be regional differences in the frequency of congenital Chagas' disease in Brazil but this subject can only be clarified if incidence studies of congenital transmission are done using similar methods of detection. The majority of the incidence studies include only full-term newborns; if the severity of congenital infection varies in different states of Brazil, it is possible that in some areas the congenital transmission causes mainly prematurity and intrauterine deaths; in this way, positive cases can only be detected if a more extensive evaluation is done, including all products of gestation. Furthermore, it has been observed that the severity of congenital chagasic infection is higher in Bahia than in Cordoba – Argentina, where the infected cases are in general asymptomatic newborns (Moya – personnel communication).

Congenital Chagas' disease is an important problem in Public Health, at least, in the state of Bahia since: 1 – There is nearly one case of congenital infection per each 1.000 births; 2 – The infected conceptuses may present early severe forms of disease. Besides, as I have already said, in other areas of South America the frequency of chagasic congenital infection is higher than in the state of Bahia.

A prevalence study of Chagas' disease made in Salvador, Bahia, among pregnant women of low socio-economic status indicated a prevalence rate of infection of 8,5%; fifty-eight per cent of these women were born in rural areas of the state of Bahia. Besides, it was observed that the prevalence rate of infection among these women was higher (10,8%) than among the women born in Salvador (1,7%) (Bittencourt, 1984). Therefore a serologic examination for Chagas' disease in the mothers originally from rural areas would be advisable during the prenatal period. Otherwise, all the products of conception of these mothers should be examined. A good method for detection of disease in the newborns is the direct blood examina-

tion with the microhematocrit technique because it is simple, cheap, gives immediate results and does not require venipuncture, so it can be done easily even in newborns with very low birth weight (Bittencourt, 1984).

As we cannot identify mothers who will transmit, nor are the side effects of Nifurtimox (Bayer, 2502) and Benzonidazol (Ro-1051) on the fetus known, hence, no drug prophylaxis has been attempted in seropositive pregnant women. On the other hand, these drugs probably did not change the evolution of the disease in the indeterminate and chronic phases. Only in acute maternal disease is treatment indicated because the early administration of these drugs can improve the course of maternal disease. However the potencial harm of the treatment to the fetus should be discussed with the mother.

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