EDITORIAL

CONGENITAL CHAGAS IN NEONATES OF ASYMPTOMATIC MOTHERS NEED FOR STANDARDIZED EARLY DIAGNOSIS

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Chagas disease is a life-threatening, chronic parasitic disease caused by the protozoan Trypanosoma cruzi [1,2].
Around of 28 millions of people I know find in risk of acquire it. It is endemic in twenty-one countries; the number of people affected it is of 8 millions Y I know produce 41,200 new annual cases and 12,500 deaths. Regarding the congenital disease, it can be estimated that, in America, there are 2 million women of reproductive age infected by T. cruzi , of which that between 4 and 8% would transmit the condition to the fetus via the transplacental route and, consequently, 15,000 children with Chagas disease will be born annually congenital [3,4].
Due to the increase in immigration from America to the rest of the world, the disease of Chagas he has past of be a endemic in America Latin a a illness global (FIG. 1).

It is transmitted to humans primarily through the feces or urine of insects. triatomines (vector pathway). But T. cruzi can also be transmitted [5,6]:

1) consuming food contaminated by the parasite through contact with feces or urine of triatomines or marsupials (causes foodborne outbreaks with morbidity more severe and higher mortality);
2) by transfusion of blood or blood products from infected donors;
3) by transmission from the infected mother to her child during pregnancy or childbirth;
4) by transplantation of organs from an infected person, and
5) due to laboratory accidents.
In Argentina, it has been estimated that, for each case of vectorial Chagas, there would be 10 cases of Congenital Chagas [7]. The risk of vertical transmission varies according to the strain of T. cruzi , the
Maternal parasitaemia , placental lesions, geographic region, and susceptibility genetics for infestation.
The importance of early detection at the time of birth allows for early treatment of this parasitosis and -consequently- its cure. If it is not detected early, the child will

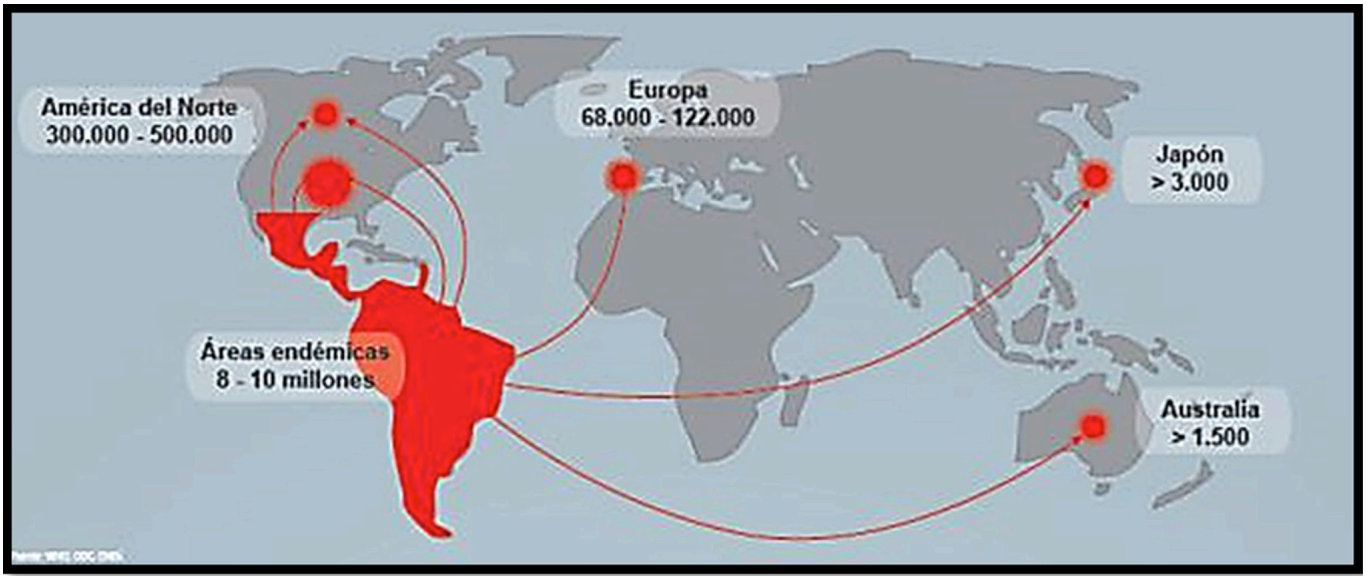

FIG. 1: CHAGAS DISEASE WORLDWIDE (taken from planeta_futuro /1464024832_881388.html)

carry the parasite in a chronic form, thus increasing the risk of morbidity and mortality.
For this reason, screening at birth is key to the health of the individual, as well as to reducing future public health costs.
The majority of pregnant women with Chagas are pregnant during the indeterminate stage or chronic infestation, with few or no clinical manifestations. They have also been described cases with acute disease, although this is not always synonymous with fetal infection.
Vertical transmission of T. cruzi cannot be prevented, but diagnosis and treatment timely treatment of congenital infection reaches cures close to 100%. CONICET researchers [8] performed DNA analysis of blood samples from 217 children born to mothers with Chagas infection. Of these, 101 children had congenital infection, and 116 did not. The researchers focused on a group of genes that are expressed in the placenta. In two Of the genes examined, ADM-12 and MMP-2, modifying a base alters the propensity for congenital transmission of Chagas. In the ADM-12 gene, located on chromosome 10 and with more than 370,000 bases, the change from adenine to guanidine at the rs11244787 site appears to increase the risk of vertical transmission. In contrast, the mutation of cytosine to thymidine in that same site, would protect against infestation.
microhematocrit technique for Optical Microscopy is the most used method for the diagnosis of the infestation. congenital [9,10]. Routine serodiagnosis that detects IgG against T. cruzi is only useful after the child is 6 months old, while recombinant LAMP and PCR are excellent alternatives for immediate use, at birth [11] .
The search for congenital infestation in children of women with confirmed Chagas or without it, and its follow-up up to one year of life, it is essential to achieve the detection and treatment early of new cases. Loss of follow-up of potential cases of congenital Chagas it is alarmingly high [12].
This emphasizes the need to optimize diagnostic techniques at the time of birth.

SUGGESTIONS FOR LABORATORY DIAGNOSIS

When choosing a diagnostic tool, it is important to take into account:
A) the phase of the disease, and
B) the scope and limitations of the method to be used.
Thus, the newborn is in the acute phase and the mother is in the chronic phase [13]. The acute phase is characterized by a parasitemia not always detectable at birth, but only two or more months later. In turn, after one year of life, the parasitaemia usually decreases below the limits of detection, so the diagnosis is made by determining anti-T. cruzi .
With regard to the methods available, at the Institute Malbrán, it is worth mentioning:
1) Optical Microscopy;
2) PCR;
3) LAMP;
4) Chemiluminescence;
5) recombinant ELISA; and
6) indirect hemagglutination.
It should be noted that only the first three are applicable to the newborn; the rest are used in older children and adults.
At least two tests must be carried out. to increase diagnostic accuracy [14,15].

The detection of live parasites in the umbilical cord collides with the possibility that they are maternal and not necessarily neonatal. For this reason, said parasites should preferably be sought in the venous blood of the NB [16].
Parasitological techniques by light microscopy concentrate the parasites by centrifugation in capillary tubes (microhematocrit test) or in tubes Eppendorf (“ microstrout ” method) [17]. If the test based on Optical Microscopy is negative at birth, it should be repeated at one month of age in cases of children of mothers with Chagas , when usually observe the parasitaemia peak . All of the above delays diagnosis and increases desertion. In effect, these tests require – on the part of the time-effectors, processing of the sample within 24 hours, trained laboratory personnel and quality controls, all these factors that can influence the results and, on the part of the mothers, that there be no desertion. Other tests have been proposed, but require equipment with biological protection and they are not used routinely for the diagnosis of congenital cases [18].
Molecular methods are another approach for early detection of infestations [19]. Loop-mediated isothermal amplification (LAMP) it is an alternative of very high sensitivity and specificity, low cost, does not require equipment sophisticated (because it is optionally turbidimetric or colorimetric), and it can be done at birth, thus constituting a valid option [20]. Recently, ANMAT has approved a method based on the isothermal molecular amplification of a fragment of genetic material from T. Cruzi in a sample of whole blood in dried droplets or purified DNA (performable at the time of birth), which would be choice, to be able to generalize [21].
Histological examination of the placenta or molecular detection of T. cruzi DNA in tissues of the placenta, has low sensitivity and specificity, and placental involvement -as stated above- does not correlate with fetal compromise [22].
Serologic tests for infants should also be performed on their mothers.
Detection of antibodies against T. cruzi in infants older than 10 months (i.e., missing and to passively transferred maternal antibodies) indicates an infestation congenital

(when previous vector transmission and blood transfusions have been ruled out) blood), but has lost enormous therapeutic time [23]. Likewise, as already stated, evaluating children only at 10 months of age increases the risk of loss to follow-up.

Other tests, such as trypomastigotes excreted/secreted IgM antigens or acute phase scavenged antigens (SAPA) ELISA IgG (which detects SAPA within first 3 months of infection), are not available for mass use, and require long-term evaluation to guarantee their usefulness [24].

In short, strategies that facilitate diagnosis as early as possible should be evaluated and implemented. possible, taking into account the frequent lack of attendance of mothers to visits from follow-up to health centers.

Therapies to treat Chagas are relatively effective in the acute phase of the disease. disease and in childhood cases; increasing the chance of healing, the more diagnosis is early [25-27].

Most of the techniques for the detection of T. cruzi DNA have a sensitivity analytics of a hundredth to one thousandth of a parasite and a detection level of 1 parasite/ml of blood [28]. Minor parasitemias are only detectable when analyzed larger volumes of 5 ml of blood. Parasitemias in congenital infection are among 6 and 55,000 parasites/ml.

Techniques for immediate use at birth (PCR; LAMP) are undeniably useful due to their simplicity and diagnostic speed (10 to 60 min) [29].

IMPLICATIONS, AND ITS COMPARISON WITH THE FEI:

An epidemiological comparison with the Hypothyroidism Screening Program is outlined. Congenital and Phenylketonuria, later transformed into Law 26,279. With successive additions, this analysis allows early detection of the following diseases:

Congenital hypothyroidism

Its incidence ranges between one in 2,500/6,000 live births.

Phenylketonuria

The incidence is 1/10,000 births among Caucasians.

Congenital adrenal hyperplasia

It has an incidence of 1 in 10,000/18,000 people.

Cystic fibrosis

Its incidence varies from 1 in 3,000/8,000 live births.

Galactosemia

The incidence is estimated at 1/40,000-1/60,000 in Western countries.

Biotinidase deficiency

The prevalence is estimated at 1/61,000.

Law 26,279 establishes the system for the detection and subsequent treatment of pathologies in the newborn in a mandatory way in all public establishments of state management or social security and private, but also includes in this obligation the study of Chagas.

Indeed, always according to the Law, the Red Eye Reflex must be investigated (to rule out glaucoma, retinoblastoma , retinal abnormalities, systemic diseases with ocular manifestations and high refractive errors), Syphilis and Chagas [30].

But -in our environment, and in reality- the correct eye fundus examination requires the Specialist assistance; and both syphilis and Chagas are only investigated when there is data confirmed or presumptive maternal deaths, with which the existing law is not fully complied with.

CONCLUSIONS:

We consider There is an urgent need to incorporate early diagnostic screening and mandatory for CHAGAS, in all newborns, even in the absence of symptoms suspects of the binomial mother/son and without previous diagnosis of the mother, based on the basis that 15,000 newborns infected during pregnancy are registered and that this parasitaemia has treatment with effective cure. In short, that Law 26,281 not only exists (it has just now been regulated) but that it is complied with, with the methodology of greater sensitivity, specificity, and economic accessibility, and not limited to children born to mothers with a previously confirmed diagnosis, since that -in our extensive experience throughout Argentina- is not the common currency in these cases.

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