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LETTER TO THE EDITOR

Trypanosoma cruzi: THE SUPPOSED REMOVAL OF THE USE OF THE XENODIAGNOSIS AND BLOOD CULTURE

São Paulo, February 16, 2012

Dear Sir

In 2009 the centenary of the unveiling of animal and human infections by *Trypanosoma cruzi* took place. Thus the disease known as "Chagas' disease" emerged, and it received numerous evaluations under different aspects. The studies were conducted in Brazil and in other countries, even some outside Latin America. These studies were able to back up parasitological, epidemiological and clinical matters amongst others, as well as activities regarding prevention and transmission, for example. However, at the time mentioned it was noted that we lacked information about three major issues: an effective inference regarding pathogenicity; the absence of a foolproof serological test to establish the diagnosis, considering its sensitivity and specificity; and the fact that there is no specific treatment that has great effectiveness and which is satisfactorily tolerated.

Research has continued to make progress and recently a method capable of revealing the presence of the parasite became available. I refer to the polymerase chain reaction (PCR), which is based on molecular biology, and now useful in the context of Chagas' disease, being valuable in the recognition of causes of several disorders.

The PCR motivated enthusiasm and has influenced researchers to consider not using the traditional procedures commonly used in the diagnosis, among them, the xenodiagnosis and blood culture for evidencing *T. cruzi*. It happens to be the case, however, that these decisions require caution, without the influence of personal preferences and they must take into account a set of facts and the experience of those who have a broad vision about the disease, so that decisions like this are based on facts already well documented. In other words, one should avoid drastic resolutions that do not fit in the fullness of what is known concerning the matter.

I believe that relevant comments will help find valuable elements that may help to make a satisfactory positioning on the matter. It certainly won't be complete, but it may serve the purpose. I will quote certain facts.

The acute phase of Chagas disease is the one in which T. *cruzi* is found in the peripheral blood, as shown by laboratory tests known as direct methods, such as the examination of fresh or stained slides, the search for the parasite in the leukocyte concentrate and the use of concentration processes like QBC (Quantitative Buffy Coat - QBC). IgM positive results for *T. cruzi* cooperate without appearing in the current methods as explained above. The parasitemia found in these tests usually lasts four to eight weeks, excluding exceptions. Thus, the PCR does not delimit this step and I cannot seem to justify a change to the traditional methods, so far satisfactory.

Currently, immunosuppression is a situation that has become more common due to the influence of various diseases or procedures. Treatments that provide immunosuppression are undoubtedly prescribed with significant frequency. Therefore, people infected with *T. cruzi* and compromised by such immune deficiency, are likely to reactivate their parasitemia, which is documented by the finding of the parasite in blood, cerebrospinal fluid or even tissues. The PCR does not participate in the recognition of this complication, because it's generally positive in those hosting the parasite, at any point of the disease.

It is important to note that reactivation is not the same as the acute phase. It is not a regression, a return to the acute phase or a relapse. In reactivation, the IgM tests are negative.

A particularity is the heart transplantation in patients with Chagas' disease which no longer benefit from conventional therapeutic measures. As a result of immunosuppression, reactivation can occur, usually as a cause of the drug therapy that did not cure the infection. There is a constant demand of conduct designed to find out as soon as possible what is the problem. We also aim to achieve a less intense immunosuppression over time.

The reactivation is characterized by parasitological determinations and the PCR does not help in this matter: it should always be noted that the transplant recipient is infected with *T. cruzi*.

In surveys of various types, to obtain new drugs, the assessment of results requires the use of techniques that reveal whether the infection has healed or not. The participation of *T. cruzi* is investigated, using serological tests as well. If the PCR can be used in this form of research, is not yet known. My aim is that the investigations will show that it evolves to negativity when the parasitemia is cleared.

To acquire scientific information on the trypanosomiasis, among other actions, the parasite is often required. The information is related to grouping, epidemiological interpretation, virulence marking, correlating results with the severity of disease and, almost as a curiosity, the use of triatominae

insects for the selection of drugs. Included here are only a few achievements and undoubtedly there are quite a few others. The PCR for now has no important role in this area.

These considerations are the result of my personal experiences regarding Chagas´ disease, mainly involving epidemiological, clinical, laboratory, therapeutic and preventive activities. They are genuine and I believe perhaps that they do not serve to change, rejecting consecrated tests like xenodiagnosis and blood culture. PCR should generate longer observations and, in this way, its spectrum of uses will be well-defined in the future. Among other investigations, I suggest checking if the results become negative after the parasitological cure and if a quantitative test will be able to gather new interpretations about the damage caused by the disease.

A major obstacle today is the impossibility of being able to count extensively on the PCR. The implementation requires expensive equipment and well-prepared laboratory staff. This is impossible in the short term in Brazil and Latin America.

Common-sense, recognition of the value of previously acquired knowledge and the use of new subsidies will avoid misunderstandings.

Vicente AMATO NETO
Laboratório de Investigação Médica/Parasitologia do
Hospital das Clínicas, da Universidade de São Paulo
Laboratório de Parasitologia do
Instituto de Medicina Tropical de São Paulo/USP
Av. Dr. Enéas de Carvalho Aguiar 470
05403-000 São Paulo, SP, Brasil
E-mail: amatonet@usp.br