

## Chagas Disease: Parasticide Treatment and Healing Criteria

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The lesions that characterize the Chagas disease – mainly the cardiomyopathy – may be due to different processes. (1-4) The immune-pathogenic processes have been recognized as having significant responsibility. (5, 6) Nevertheless, there is no doubt that parasitism by *T. cruzi* is the basic etiological agent. With no infection, the disease would not manifest. However, it should be accepted that the reverse situation, with a treatment, may not be valid. Beyond this question mark, there is enough information about experimental infection, as well as about human parasites, that shows those undergoing treatment with parasticide drugs have different evolutivity from those who do not undergo treatment. Even so, the main medical concern is still the therapeutic assessment. Particularly, the improvement of the systems to evidence the efficacy of the parasticide actions. Basically, the **capacity** and the **promptness** to confirm that the parasitism tends to deplete or disappear.

The lack of relevant clinical signs in most infected patients during long periods of parasitosis determined a biological and conceptual domain in defining a therapeutic cure. There have been limitations in demonstrating the parasite eradication by methods that directly expose it as live agent (xenodiagnosis), or its presence as genetic material (PCR).

For various decades, it has been resorted to the detection and titration of specific antibodies against *T. cruzi*, as indicator of posttherapeutic evolutivity. This approach has been successful in patients recently infected, especially among children, whose treatment with benznidazol results in total serum negativization in less than two years since the treatment was started. On the other hand, it has been observed among the long-standing infected patients that the tendency to the serum titration fall or to its negativization is very slow and can last decades. This issue has left medicine helpless to measure the therapeutic effectiveness **promptly**. This issue generated great interest in finding immunologic evidences of seric antibodies or cell-mediated responses that tend to extinguish faster.

The results provided in the research study by Bertocchi et al. (7) are suscribed in the course of the studies to find out one or more indicators of healing evolutivity. It should be pointed out that in the pharmacotherapy of the so-called infection-immune diseases (long latent periods with no clinical signs), the evolutivity demonstrated through biological or sero-

logical methods has been the main stimulus to persevere in pharmacology research. Without a system to measure evolutivities, the medical interest in the problem tends to disappear. This issue is highly relevant and commits us to give value to all the information that earlier evidences the fall of immunological reactivity. This is valid provided the effect cannot be attributed to the immunosuppressant effects of the drugs.

In other pathologies, the posttherapeutic evolutivity, of syphilis, for example, was assessed mainly by a **non-specific** serologic test, as is the case of cardioplin tests. If medicine had attempted to use monitoring based on specific serologic tests to detect antibodies against the *treponema* (FTA-ABS, or any other), it would have encountered the same dilemma we have today regarding the therapy of the *T. cruzi* infection. The specific antibodies against *treponemas* persist for decades in individuals who have been considered cured according to the cardioplin tests. The success of this criterium was corroborated by the tendency for the syphilitic tertiarism to disappear in those patients treated during the latent period of syphilis.

In view of the above, we point out that our main concern when searching for systems or methods to indicate the therapeutic effectiveness should be to find answers with accelerated dynamics –even when they are not specific– because, after all, there is no major stimulus for physicians that the **improvement** or the **worsening** of what we recognize as the evolution of the disease. It is precisely for this issue that the search for evolutivity indicators should not exclude clinical signs. This is particularly valid for the diagnostic imaging, as may result from the non-invasive angio-coronography (multi-slice CT).

The above mentioned would be relevant as a result of two convergent evidences. Various authors have pointed out the coronary flow involvement present in chagasic patients, and the association of the chagasic myocardopathy with a significant endothelial dysfunction, (8-10) which is manifested with paradoxical vasomotion (stricture effect, instead of dilation effect) when an acetylcholine infusion in the coronary arteries is performed. Similar effects can be found in assessments with cold tests and radioisotopic perfusion measurement.

Together with what was stated above, it is worth mentioning that we, as well as other authors, have

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accumulated clear evidence that 30-35% of patients infected with *T. cruzi* show significant amount of antibodies against muscarinic receptors with **agonist** properties, of the acetylcholine type, in the circulation. (11-14) It might be considered that these patients are permanently subject to the acetylcholine infusion, together with the potential ischemias resulting from the paradoxical vasoconstriction. The vasoconstriction measurement or the flow reduction in the coronary system may result in a highly dynamic system for the evolutive control of heart disease in patients with *T. cruzi*.

The findings of the study carried out by Bertocchi et al. (7) add information about evolutivity criteria based on immunological answers mediated by cells that are potentially more precocious to disappear than the serologic-type cells. These criteria lead to the idea that there could be more precociousness in the negativization of this type of responses compared to the immune-serum responses.

In Chagas disease, we should emphasize the clinical perception of evolutivity, and search for dynamic indicators of improvement, mainly in cardiac-type conditions, even more than the parasitologic healing criteria. Though successful, these criteria can be rather inconsistent with respect to the clinical evolutivity.

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