



## Necrológico/Obituary

### Joaquim Romeu Cançado

(★ 1913 †2011)

This eminent Full Professor of Internal Medicine and pioneer in specific treatment for Chagas disease has been considered one of the more important figures in the recent history of American trypanosomiasis. Very early on, Carlos Chagas and other elder eminent researchers, such as Villela, Mazza, Dias, Romaña, Botafogo, Muniz and Pakchanian, worked with dedication to face the challenge of developing a specific treatment; however, their results were consistently discouraging. A wide variety of drugs and treatment schedules were tested and all were repeatedly ineffective. Thus, until the 1960s, the treatment of human Chagas disease (HCD) was understood as an almost unmentionable and unattainable subject. At that time, Cançado became more and more preoccupied with the high prevalence of chronic HCD in the hospitals of Belo Horizonte and with the continuous detection of acute cases in Minas Gerais, both situations induced very strong motivation concerning the disclosure of this disease, its specific treatment and medical management. Simultaneously, another emblematic name in Chagas Disease research, Zigman Brener, was implementing a brilliant study in experimental chemotherapy, showing the effectiveness of certain nitroimidazole compounds in acute and chronic infected mice.

The first trials in human cases were conducted in Argentina (Cerisola, Rowhder, Bocca Tourres) and Brazil (Ferreira, Rassi, Cançado), with optimistic results reported primarily in acute cases. Nevertheless, Cançado insisted on treating chronic patients, because of their major epidemiological importance in all endemic regions. Treating dozens of patients with Brener's long-term proposal/protocol, its effectiveness in resolving acute disease and an as important suppressive action in chronic individuals (determined by serial xenodiagnosis) were unquestionably proven, leaving the ongoing problem of cure assessment in chronic individuals in whom conventional serology continued to be positive for several years. Some of Cançado's important scientific characteristics were his deep sense of logic and a tremendous patience to explore all the aspects and possibilities of his ideas. The action of nifurtimox and benznidazole against various strains of *Trypanosoma cruzi* had been established for both blood and tissue forms, but the persistence of conventional antibodies in chronic treated patients remained a reason for the scientist's discouragement, since it indicated therapeutic failure. During this period, Cançado had always been very resolute and restrictive: the only accepted cure marker for him was total and permanent serology conversion from positive to negative results. The permanence of positive results following treatment could only be explained by drug failure or by the long-term persistence of prior formed antibodies. Both possibilities were considered by Cançado, for whom serial negative results of xenodiagnosis at least indicated an important suppression of the parasite. Some years later, Sonia Andrade and others studied this problem in dogs, verifying that memory in spleen dendritic cells could explain the permanence of antibodies for long periods in the absence of living parasites. By treating several chronic patients over many years, Cançado developed a very complete protocol, including considering the clinical profile, different treatment schedules, the behavior of serology and xenodiagnosis. Thus, he was able to confirm and emphasize the immediate and consistent suppression of parasitism and the maintenance of serological titers in chronic treated individuals, which occasionally led to treatment failure, revealed by late positive xenodiagnosis. His cases continued to be reviewed for many years, some of them (8-10%) achieving negative conventional serology after 15 years of follow-up. More recently, using Krettli's technique of complement-mediated lysis, it was possible to verify that the cure rate could reach 20 or 25%, which was also endorsed by Anis Rassi while following his patients for more than 30 years.

It is important to remember that very few researchers maintained their interest in HCD treatment between 1960 and 1990 and Romeu Cançado was certainly one of the principal names among them. His work was extremely important in terms of protocol design, treatment strategies, side effects management and epidemiology. In the very disastrous affair concerning the possibility of a higher occurrence of lymphatic cancer among benznidazole-treated individuals, Cançado was one of the researchers who strongly rejected the hypothesis, based on the long-term follow up he had conducted of a large sample of treated patients. He was also very rigid in analyzing numerous publications dedicated to HCD treatment, often finding serious problems in protocol design and data interpretation. For instance, he never accepted the conclusion of cure when the laboratory parameters were restricted to parasitological data (xenodiagnosis, hemoculture).

Fighting almost his entire professional life against Chagas disease, Cançado was also distinguished as an important mold of physicians and researchers dedicated to this subject, in Brazil and abroad. In particular, he organized two remarkable international courses concerning HCD in Belo Horizonte, Brazil, in two crucial moments of scientific recognition of this disease. Leading an international team of important collaborators, Cançado drew on these courses to edit two memorable and comprehensive books, which have been of enormous importance among physicians and researchers in all Latin America: *Chagas Disease* (1968) and *Chagas Cardiopathy* (1984). In parallel, Cançado created a nongovernmental foundation, the *Fundação Carlos Chagas*, in order to provide funding for research, publications and meetings concerning HCD. Together with Aluizio Prata and other colleagues, he was also the founder of the important International Meeting on Applied Research in Chagas Disease (1984), as well as being its first coordinator. In the same spirit, Cançado always accepted invitations to participate gratuitously in different congresses and meetings on HCD, for instance, collaborating with Pilar Aderette in her *Programa de Salud Humana*, organizing courses of HCD management & control in Argentina, Paraguay and Brazil.

From a humanistic standpoint, Cançado was also an extraordinary figure. An excellent professional, he always paid a great attention to his patients, listening to their stories thoroughly and treating them with tenderness and deep respect. He married Mrs Ana Cançado and raised three beautiful daughters with her, all of whom became scientific collaborators in his work. During his life, Cançado received a great deal of honor, numerous merit medals and academic titles. Extremely modest and detached, he used to simply say "thank you", smiling tenderly on such occasions. He was Emerit Professor of the University of Minas Gerais and was a member of the Minas Gerais Academy of Medicine.

Cançado worked intensively until 2010, always studying and researching on HCD. Today, all the scientific technicians involved with this disease are pinning their hopes and agendas on treating the millions of individuals infected by Chagas. And, of course, Romeu Cançado remains involved in this task, due to his scientific example and unforgettable personality.



**João Carlos Pinto Dias**

Centro de Pesquisas René Rachou, Belo Horizonte, MG

**José Rodrigues Coura**

Fundação Oswaldo Cruz, Rio de Janeiro, RJ