Reply of the authors of the Continuing Medical Education article to Dr. Jaison Barreto and Dr. Laila Laguiche

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We appreciate your interest and comments regarding our Continuing Medical Education article (*Leprosy: current situation, clinical and laboratory aspects, treatment history and perspective of the uniform multidrug therapy for all patients. An. Bras.Dermatol. 2017; 92 (6): 761-73*. doi: 10. 1590/abd 1806-4841.20176724), authored by a group of experts who have been working with this disease for decades.

We do not express a personal opinion. We published science with solid substantiation. In this case in particular, what we did was update mainly the aspects related to treatment evolution and current perspectives. Physiopathogenesis, bacilloscopy and other classical subjects are widely known by all; they are mentioned in articles and available in textbooks of Hansen's disease.

Everything that we wrote was based on the experience acquired over the past 38 years by the research group, whose members were pioneers in some important actions for the control of Hansen's disease: they were the first to identify drug resistance through the inoculation in mouse footpad[1]; the first to commence/implement Multidrug Therapy in the 1980s, as recommended by WHO, initially to treat/prevent drug resistance[2]; last year, the first ones to prove with the sequencing of the whole genome of *M.leprae,* that Hansen's disease patients can be reinfected[3]. Over time, we researched and followed all changes relative to the duration and evaluation of new drugs for the chemotherapeutic treatment of Hansen's disease.

The "*Independent study to determine the efficacy of the 6-dose Uniform MDT (U-MDT) scheme for patients with Hansen's disease*", financed by CNPq, was designed by the Center of Tropical Medicine of the Universidade de Brasília in collaboration with the following national and international institutions: Royal Tropical Institute (Netherlands); London School of Hygiene and Tropical Medicine; École Polytechnique Fédéral de Lausanne/EPFL (Switzerland); Centro de Saúde Dona Libânia (Fortaleza), Fundação Instituto Alfredo da Matta (Manaus), Universidade Federal Fluminense, Universidade Federal de Goiás, Instituto Lauro de Souza Lima (Bauru, SP), Universidade Federal de Minas Gerais, Universidade Federal do Ceará and Fundação Oswaldo Cruz.

In this controlled, randomized clinical trial, approximately 900 patients were diagnosed, treated and followed along 11 years, obtaining relevant data that were published and are therefore available in the world literature, such as:

(1) There was no statistically significant difference between the groups treated with 6 or 12 months in relation to frequency of Hansen's disease reactions among multibacillary patients;

(2) There was no statistically significant difference between the groups treated with 6 or 12 months in relation to reduction of the bacterial index;

(3) Introduction of clofazimine did not have a negative impact on PB patients;

(4) There was no statistically significant difference between the groups treated with 6 or 12 months in relation to progression of physical disability;

(5) The recurrence/reinfection rate in 10 years was similar among the groups, and completely acceptable for the implementation in primary health care;

(6) Also important, the study broke the paradigm of the lack of reinfection in Hansen's disease, confirmed by the complete genome sequencing of *M. leprae*. This finding confirms that susceptible patients, even when adequately treated, can become infected.[4-13]

In the implementation of the study, all tests recommended for the research were performed in series such as FBC, biochemistry, bacilloscopy, histopathology, serology. Follow up was performed according to the good practices of research. The techniques for analysis of epidemiology and statistics were the most sophisticated available in current scientific knowledge.

This project was overseen by an External Committee, made by internationally known experts like Celina Maria Turchi, Euzenir Sarno, Maria Leide Wand-del-Rey de Oliveira, Paulo Roberto Lima Machado, Sinésio Talhari, Ji Bahong; Pannikar V, and Diana Lockwood.

The study was recorded in ClinicalTrials.gov. All steps of research development, as well as results/conclusions were published (15 scientific articles) in indexed journals. In addition, two master's theses and seven PhD theses directly related to the development of the research were defended. Dozens of presentations of the different steps of the study were made in national Epidemiology, Dermatology, Infectology and Tropical Medicine scientific congresses and in the world congresses of Hansenology in Hyderabad, India, in Salvador, Brazil, in Brussels and Beijing. Everything the group produced is available in the *Lattes* platform.[14]

Moreover, we highlight that with the quality of the Biobank created with the samples collected for the research, which was put together under strict international parameters, this study will generate other manuscripts and will continue building masters and doctors.

The main conclusion of this investigation is very important for the patients. It is possible to reduce the treatment of Hansen's disease to 6 months, without the need to classify them into clinical forms, similarly to what occurs with tuberculosis.

As you can see, Dr. Jaison, the CME article is based in the collective experience of a group that brings together expertise in basic, clinical and epidemiological research, acquired over many years of work, having particularly on this subject, been through many peer reviews. Additionally, we should emphasize that everything that is written was published and is available on *Pubmed.* Besides these publications, other three studies in Bangladesh, India and China reported their results supporting the findings of the Brazilian clinical trial, which is differentiated for being randomized with a control group.[15-17]

We should of course respect everyone's personal opinions. However, these opinions should be expressed in scientific journals,

based on other studies, to go against the publications one disagrees with.

Dr. Laila, as a demonstration of interest to your written declaration, we visited your *Curriculum Lattes*. We only found small case reports and no important investigational study that could enrich our article or rebut our data. You see, science is made with research, as demonstrated in this study with 853 patients assigned to the clinical trial. Therefore, our publication is based on concrete data and we believe it has the appropriate level for Continuing Medical Education, focusing on dozens of residents and dermatologists that see few patients with Hansen's disease, a disease that is so neglected in our country.

Finallly, if what worries you is a new treatment, it is precisely this new treatment favoring the patients that encourages us. There are 17 scientific articles published on the theme, cited below. In case there are any authored by you, or known to you, that are consistent and demonstrate the opposite of what we state, please, submit them to peer review for publication.

Yours sincerely,

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