Surveillance Of Leprosy Drug Resistance. Responsibility Beyond The Network.

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In 2009, the World Health Organization (WHO) established the World Sentinel Surveillance Network for Drug Resistance for Leprosy, after careful discussions on the topic with experts during two workshops held in India (2006) and Vietnam (2008)[1]. Currently, India, Brazil, Colombia, Paraguay, Sri Lanka, Madagascar, Vietnam, China, Bangladesh, Congo, Chad, Indonesia, Iran, Mozambique, Myanmar, Philippines, Morocco, Tanzania, Yemen and some Western countries from Africa represented by the respective reference laboratories are the participating countries. Brazil's expertise in primary care for patients with suspected leprosy drug resistance played an important role in building the global network, generating data that corroborates significantly in the preparation of WHO recommendations on resistance to multidrug therapy for leprosy.

To standardize technical and operational procedures, a guide for leprosy resistance surveillance was published[2], and the quality control protocol was established between participating countries and reference laboratories. In Brazil, there was training in DNA sequencing for the technical staff of the laboratories involved in carrying out the tests in the country, allowing all laboratories to use the same WHO's framework.

At the last World Network meeting held in Nepal in 2016, the protocols and results obtained by the various national programs were discussed. At this meeting, two main products were generated, the publication of data on resistance (2009-2015) from all countries participating in the network in the Clinical Microbiology and Infection (submitted), orchestrated by WHO, and the revision of the guideline for resistance surveillance[1]. Still, as a result of this meeting, the WHO made recommendations that met the efforts of institutions in Brazil, already engaged in the surveillance of drug resistance for leprosy, in various services in the country, working with the available tools.

Among the recommendations, criteria for the selection of patients for resistance testing were redefined, with the guidance being to test all cases of relapse and 10% of new leprosy diagnosed cases per year. In Brazil, in addition to following the WHO's recommendations, all cases of therapeutic failure will also be tested[3].

In order to implement the Leprosy Drug Resistance Surveillance Network by the Ministry of Health at the end of 2018[4], several tasks were undertaken: meetings and training for professionals organized by the National, State and

Municipal Leprosy Control Programs,; strengthening the laboratories network for complementary exams; establishing the flow for transporting samples in the country, taking advantage of the existing infrastructure for other diseases; implementation of a online system to facilitate the collection and management of clinical, epidemiological and laboratory data from patients selected for resistance surveillance.

Finally, laboratories with installed capacity were designated to meet the country's demand for resistance testing by genomic DNA sequencing.

The 30 years of experience of Instituto Lauro de Souza Lima in drug susceptibility testing, has shown that most cases of resistance detected are in leprosy patients who have relapsed one or more times. This leads us to think that relapses would play an important role in maintaining the infection, with the possibility of transmitting resistant mutant strains, especially in areas of high endemicity.

However, our experience in detecting resistance among newly diagnosed leprosy cases is still poor. Despite of that, in a former colony area in Brazil, we have shown evidences of transmission of resistant strains within the studied population[5]. Will the same happen to patients with therapeutic failure coming from our routine services? Are they responsible for maintaining the endemic? And if the maintenance of disease activity is related to resistance, what will be the treatment regimen for these patients?

The conclusion we reached, with the few results obtained during the implementation of the resistance surveillance network in Brazil, is that even though MDT is effective to kill M. leprae in most cases, there is still much to be studied. However, the pathway was paved. We will continue to train professionals to diagnose relapses, manage therapeutic failures, structure the network of laboratories and implement new tools, encourage contact assessment in drug resistant cases, in addition to seeking for alternative drugs.

The proposed workflow for the resistance surveillance network will certainly allow us to generate and expand the much-needed knowledge of post-discharge events in leprosy.

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