Leprosy in Brazil: how can Brazil meet the World Health Organization's goal of leprosy control?

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ABSTRACT

Leprosy in Brazil: how can Brazil meet the World Health Organization's goal of leprosy control?

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Background: Leprosy causes a high social and economic cost on communities. Brazil has the second most cases of leprosy in the world. Brazil's incidence of leprosy decreased significantly with the start of multi drug therapy in 1981, but over the past ten years, the incidence has remained fairly fixed.

Objective: Brazil has not met the World Health Organization's leprosy goal for a prevalence of less than one patient per 10,000 inhabitants. The purpose of this literature review is to evaluate the progress of Brazil's leprosy control measures and highlight the areas in which Brazil can concentrate to meet this goal.

Methods: An online literature search was performed through the Ovid and PubMed databases describing leprosy in Brazil and management practices. Publications in Portuguese were translated into English.

Results: Several studies were found that identified various factors impeding the progress of Brazil toward its prevalence target. These general categories include: society and culture, stigma and isolation, vaccination and chemoprophylaxis, decentralization of resources and the leprosy control action, molecular tools, and relapses and non-adherence.

Conclusion: Leprosy continues to be a public health problem in Brazil and the incidence rates are not improving. The various factors impeding Brazil can be grouped into three main areas: prevention, diagnosis, and treatment. Optimizing resources in the ten clusters with the highest incidence rates will allow Brazil to reach its WHO prevalence goal.

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Table of Contents

List of Figures

Introduction

IMEP Experience:

One of the special opportunities within the UT Southwestern medical school curriculum is the Paris Exchange Program. When I began my education at UT Southwestern in 2011, I set a goal to participate in this program because it combines my passions for medicine, languages, and cultures. I was accepted to participate for the 2014-2015 school year and had an extremely positive experience. My six months in Paris were spent doing clinical rotations in dermatology and emergency medicine. My six months in developing countries were spent in Lima, Peru rotating in internal medicine and in Rio de Janeiro, Brazil working in a family and tropical medicine clinic. In Brazil I was exposed to patients with leprosy, or Hansen's disease. Diagnosing and treating these patients unveiled my own curiosity for this disease, which further motivated me to write my thesis on leprosy in Brazil.

FioCruz (Fundação Oswaldo Cruz):

Because of my interest in family medicine and desire to learn Portuguese, FioCruz was an ideal place to spend three of my six months in developing countries. FioCruz is located to the north of Rio de Janeiro in a favela, or shantytown, called Manguinhos. It is one of the most prestigious medical institutions in Brazil and all of Latin America. Here, they employ over 11,000 employees in a variety of areas including education, research, and clinical medicine, among many other things. FioCruz is one of the main referring centers for leprosy in the state of Rio de Janeiro. I spent every Tuesday of my rotation at the leprosy clinic, while my other days were spent in the family medicine clinic.

I knew very little about leprosy when I began my rotation. The few things I remembered were from studying for the Step One exam, i.e. like the two different immune responses. Also burned into my memory was a photo of a disfigured woman from the chronic, debilitating process of the disease. A couple of things stood out to me when I began my clinic work with leprosy patients. First was the subtle and unremarkable nature of the lesions. Second of all was the lack of use of masks. Despite knowing that the disease is transmitted via respiratory secretions, none of the staff protected themselves. Working alongside physicians, residents, and students, I learned firsthand the different ways leprosy is diagnosed, treated, and followed up. All in all, I developed a great appreciation for the amount of time and work that goes into caring for these patients.

History of Leprosy:

Leprosy, which originated in either Africa or Asia, has been documented for some 3000 years. The disease spread to Europe from India, carried by the troops of Alexander the Great in 300 BC [1]. It then arrived in Latin America from French, Spanish, and Portuguese settlers in the colonization period, and African slave traffic contributed to the dissemination of the disease throughout the Americas. The first cases in Brazil occurred in the 1600s in the city of Rio de Janeiro [1, 2]. In 1873, Norwegian physician Gerhard Armauer Hansen identified the leprosy bacillus, hence giving the disease the name, Hansen's disease. Stigmas and isolation have been the plague of the disease since its discovery [3]. Compulsory isolation has been the strategy over time to contain the disease, and only in the 20th century have treatments been introduced [1, 3].

Epidemiology:

Leprosy is endemic to tropical countries, especially developing nations. The number of leprosy cases worldwide has fallen significantly from the 1980s to 2012. The global prevalence has fallen from 12/10,000 in 1985 to slightly below 1/10,000 in 2002, and in 2012, there were 232,857 new cases of leprosy compared to the estimated 10 million infected patients in 1981[4, 5]. This huge decline is greatly attributed to the World Health Organization's (WHO) implementation of multi-drug treatment (MDT) in 1991 [1, 5]. The concern with Brazil is that the incidence has been fairly constant over the past 10 years. According to Figure 1 below, Brazil has the second highest rate of new cases, after India [4]. Considering India has approximately six times the population of Brazil, then per capita, Brazil has more new cases than India. As of 2011, Brazil had a prevalence of 1.54 per 10,000 inhabitants, with 33,955 new cases [1, 4]. This is well above the WHO's goal of 1 case per 10,000 inhabitants.

Country – Pays	Number of new cases reported – Nombre de nouveaux cas notifiés							
	2005	2006	2007	2008	2009	2010	2011*	2012
Bangladesh	7 882	6 280	5 357	5 249	5 239	3 848	3 970	3 688
Brazil – Brésil	38 410	44 436	39 125	38 914	37 610	34 894	33 955	33 303
China – Chine	1 658	1 506	1 526	1 614	1 597	1 324	1 144	1 206
Côte d'Ivoire	NR	976	1 204	998	884	NR	770	1 030
Democratic Republic of the Congo – République démocratique du Congo	10 369	8 257	8 820	6 114	5 062	5 049	3 949	3 607
Ethiopia – Éthiopie	4 698	4 092	4 187	4 170	4 417	4 430	NR	3 776
India – Inde	169 709	139 252	137 685	134 184	133 717	126 800	127 295	134 752
Indonesia – Indonésie	19 695	17 682	17 723	17 441	17 260	17 012	20 023	18 994
Madagascar	2 709	1 536	1 644	1 763	1 572	1 520	1 577	1 474
Myanmar	3 571	3 721	3 637	3 365	3 147	2 936	3 082	3 013
Nepal – Népal	6 150	4 235	4 436	4 708	4 394	3 118	3 184	3 492
Nigeria – Nigéria	5 024	3 544	4 665	4 899	4 219	3 913	3 623	3 805
Philippines	3 130	2 517	2 514	2 373	1 795	2 041	1 818	2 150
South Sudan – Soudan du Sud							1 799	1 801
Sri Lanka	1 924	1 993	2 024	1 979	1 875	2 027	2 178	2 191
United Republic of Tanzania – République-Unie de Tanzanie	4 237	3 450	3 105	3 276	2 654	2 349	2 288	2 528
Total (%)	**279 166 (93)**	**243 477 (92)**	**237 652 (92)**	**231 047 (93)**	**225 442 (92)**	**211 261 (92)**	**210 655 (93)**	**220 810 (95)**
Global total – Total global	**299 036**	**265 661**	**258 133**	**249 007**	**244 796**	**228 474**	**226 626**	**232 857**

* Updated data for 2011. – Données actualisées pour 2011.

Figure 1: Trends in the detection of leprosy in 16 countries. These 16 countries reported ≥1000 new cases during 2012. Each country's incidence is listed between 2005-2012 *[4].*

Etiology:

Mycobacterium leprae, the etiologic agent responsible for leprosy, was identified in 1873 by Norwegian physician Gerhard Armauer Hansen [1]. It primarily infects macrophages and Schwann cells. The bacteria have never been grown in artificial media and grow slowly with an optimum temperature of 27-30 degrees Celsius [1, 6-8]. Cole et al. sequenced the genome of M. leprae in 2001 [9]. It has been found that a maximum duration of seropositivity prior to diagnosis is 9 years, indicating the long incubation period prior to clinical diagnosis [10].

Clinical Presentation and Diagnosis:

Leprosy is often referred to as one of the great mimickers because of its varied clinical presentation, making diagnosis difficult. Cooler parts of the body are the most frequently affected organs including the skin and superficial peripheral nerves [5]. M. leprae can invade free nerve endings and/or invade peripheral nerve trunks causing neuritis. The neuritis can lead to a peripheral neuropathy consisting of sensory, motor, and/or autonomic dysfunction. This exists as a mononeuropathy or a multiple mononeuropathy. The most commonly affected nerves are: the facial and trigeminal nerves in the face; ulnar, median, and radial nerves in the upper extremities; and common fibular and posterior tibial nerves in the lower extremities [1, 11].

There are many different methods to diagnose this disease. With the goal of simplifying the diagnostic process, the WHO created a scheme based on the number of skin lesions and the presence or absence of bacilli in slit-skin smears. If one to five skin lesions are identified and there is an absence of bacilli in slit-skin smears, this is classified as paucibacillary (PB). If there are more than 5 lesions and there is a presence of bacilli in slit-skin smears, this is classified as multibacillary (MB). This scheme is the basis of the current WHO treatment regimen [11].

Another system of classification, the Ridley-Jopling classification, has five levels of diagnosis based on the spectrum of cell-mediated response to the bacteria. On one end of the spectrum, the strongest immune response is the tuberculoid form (TT) with lesions characterized by epithelioid granulomas, lymphocytic Th1 type response, and few bacilli on slit-skin smears. Skin lesions in the (TT) form are generally few in number, characterized as erythematous plaques with defined borders, decreased sensitivity, and possibly alopecia

and/or anhydrosis over the lesion. On the other end of the spectrum, the weakest immune response is the lepromatous form (LL) with diffuse dermal lesions characterized by poorly differentiated young macrophages, lymphocytic Th2 type response, and heavy load of bacilli on slit-skin smears. Skin lesions in the (LL) form are generally multiple in number and symmetric, characterized variably as hypochromic, erythematous, or bright brownish spots with indefinite borders, and possible changes in sensation. As the disease progresses, the lesions infiltrate forming plaques and nodules. There are three more classifications in between the TT and LL forms of graded immune responses, called the borderline group. The clinical presentation varies within the borderline group because of varying degrees of immune response. The skin lesions can present more closely to the TT or LL form, depending on the immune response. The gold standard for diagnosis of leprosy, although not practical in most of the world, is a full thickness skin biopsy and observation of a granulomatous response and/or identification of acid-fast bacilli within nerves [1, 10-13].

To obtain a definite diagnosis, the clinical data is complemented with an evaluation of skin sensitivity and histamine or pilocarpine testing. In cases that are not as clear, the Mitsuda intradermal reaction (similar to a PPD test), slit-skin smear, and histopathology often make it possible to make a diagnosis. For cases with neural involvement, electroneuromyography and imaging tests are utilized. Serological, immunohistochemical, and molecular identification of M. leprae are ongoing areas of research that may someday make this diagnosis easier [14].

The host's immune system may react to M. leprae's antigens, causing either one of two types of reactions. Type I reactions are related to the cellular immune response again M. leprae's antigens and are characterized by lesions with edema, erythema, and

hyperesthesia. Type II reactions usually begin after treatment and are manifested as depositions of immune complexes formed between antibodies and substances released from the destroyed bacteria. The lesions are usually symmetric with nodules or target lesions and with systemic symptoms. Immunosuppressive medications like corticosteroids and thalidomide are prescribed to manage the two reactions [1].

Treatment:

Before the advent of effective antibiotics, preventing the spread of leprosy was the main focus. Compulsory isolation of patients in leper colonies started in Brazil in 1923 [1]. There was no effective treatment until 1942 with the development of sulfone. Sulfones, especially dapsone, were used as monotherapy until 1981. In 1981 the WHO recommended the use of multi-drug therapy (MDT) due to three main factors: drug resistance in monotherapy, effectiveness of rifampin, and to promote compliance and cost effectiveness [5, 14]. The MDT regimen was officially established in Brazil in 1993. For cases diagnosed as PB, the treatment consists of a daily, self-administered dose of 100 mg of dapsone along with six monthly, supervised doses of 600 mg of rifampicin and 100 mg of dapsone over a nine-month period. For MB cases, the treatment is 12 monthly, supervised doses over an 18-month period using the same drugs as the PB regimen, plus an additional daily, self-administered dose of 50 mg of clofazimine and a monthly, supervised dose of 300 mg of clofazimine. In the case of contraindications to these drugs, minocycline, fluoroquinolones, clarithromycin, rifapentine, linezolid, and fusidic acid are used. If reactions occur, MDT should continue and immunosuppressive medications like prednisone or thalidomide are prescribed [14].

Recent control strategy:

Leprosy affects millions of lives, has a high global incidence rate, and causes a significant social and economic toll on local communities [11]. Knowing this and with a general understanding of leprosy in place, how has the WHO been involved in controlling leprosy?

The WHO's biggest accomplishment in controlling leprosy was the introduction of MDT, a combination of dapsone, rifampin, and clofazimine, in 1981. With MDT, leprosy finally became curable [15]. In 1991, the WHO established a target for the elimination of leprosy at the country level at a prevalence of less than 1 patient per 10,000 inhabitants. This target was proposed because of the high efficacy of MDT and the global reduction in prevalence that ensued after its initiation. The WHO set the year 2000 as its target year. Brazil was one of the few countries that failed to reach this goal by 2000, or even today.

Interestingly, the fall in prevalence did not correspond with a fall in incidence, implying the transmission of M. leprae was a continuing problem [16]. Untreated MB patients are probably the most important source of transmission. Household contacts of MB patients have a five to ten fold greater risk of developing leprosy than the general population. However, in new patients no history of close contact with leprosy patients is often established [17]. Since M. leprae cannot be cultured in vitro, it is very difficult to assess exposure, onset of infection, and progression of the disease [12].

Currently, Brazil tracks three main epidemiological indicators: rate of new cases, rate of new cases in children younger than 15 years old, and cases of grade 2 disability. The number of new cases in children helps to localize highly endemic areas of active infection. New cases in children have decreased from 4,181 cases in 2003 to 2,420 cases in 2011. Tracking cases of grade 2 disabilities, defined as disability or deformity in the eyes, hands,

or feet at the time of diagnosis, suggests late diagnosis, which is used to measure quality of services. In 2011, there were 2,165 new cases of grade 2-disability [1].

MATERIALS AND METHODS:

The Ovid and PubMed databases were searched in English and Portuguese using search words that included: Brazil, leprosy, Hansen's disease, prevention and control, diagnosis, therapy, drug therapy, vaccination, and community health agent. The complete list of articles and the references for the relevant articles were reviewed. Articles in Portuguese were translated into English.

RESULTS:

Society and Culture:

Similar to other infectious and endemic diseases, social and cultural factors affecting general health play a role in leprosy. The following articles illustrate the relationship between poverty and leprosy. In a study from Pará, Brazil, Barreto et al. looked at starvation and found an association between complete days with no meals and increased rates of leprosy. This group also found that over half of the patients shared a bed [11, 18]. Another study from Rao and John found undernutrition to be more common in leprosy patients [11, 19]. Kerr-Pontes et al. in their study from Ceará, Brazil found that patients with leprosy have less frequent changing of bed linens, more frequent hunting practices, and more frequent bathing in open water like rivers and lakes [11, 20]. Higher rates of leprosy have been reported in certain states of Brazil where consumption of armadillo meat is a common practice, although it is not certain that transmission actually occurs [11]. Migration patterns have also been studied, and Murto et al. in a study from the state of

Maranhão found higher rates of leprosy among people who migrated between states in the past 5 years [11, 21].

Stigma and Isolation

Societal stigma and forced isolation is another area of study. Historically, policies of segregation and isolation were the norm. There are currently still 33 of these types of communities in Brazil, which house mainly people affected by leprosy and their family members. Even former patients live in these communities because of disabilities secondary to leprosy and stigmas from outside these communities. Confining oneself and family members to these communities can lead to delays in diagnosis and treatment [11, 22]. In 2005 in a workshop in one of these communities, residents noted that many factors need to be addressed including: limited health care access, limited rehabilitation services, poor sanitation, building decay, lack of employment opportunities, and mental health issues [11, 23].

Spatial distributions of leprosy identify isolated communities. In 2007, Penna et al. identified 10 clusters of high incidence rates in Brazil (see Figure 2 below). This data comprised 173 of 5,000 municipalities, 10% of Brazil's population, and 53.5% of all new cases reported. The leprosy case detection rate for the clusters was 6.68 per 10,000 inhabitants, compared to 1.23 per 10,000 for the area outside the clusters. These areas were given top priority in terms of surveillance and treatment [16, 24].

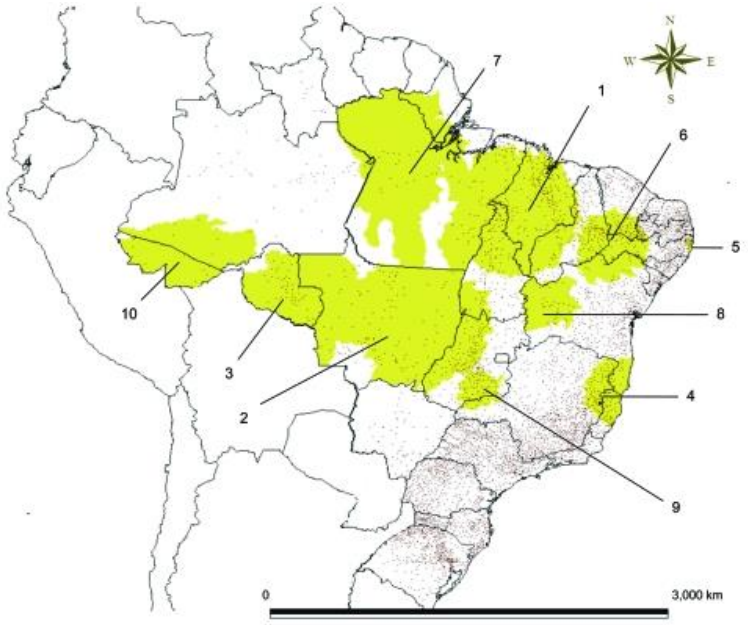

Figure 2: Ten clusters of leprosy in Brazil. The regions shaded in yellow represent the highest incidence of leprosy in Brazil between 2005 to 2007. *[24].*

Another spatial distribution was done in the city of São José do Rio Preto by Cury et al. Between 1998 and 2007, they found that clusters of high leprosy occurrence were associated with areas of the lowest socioeconomic level. They also found that locations where ill people live lack healthcare services [25].

Vaccination and chemoprophylaxis

The Bacillus Calmette-Guérin (BCG) vaccine has been recommended for the prevention of leprosy in Brazil since the 1970s. Even though the BCG vaccine has historically been used to prevent tuberculosis, it is well known that it provides protection against leprosy. In 1991, the Brazilian Ministry of Health recommended all household contacts of leprosy patients who had no BCG scar or only one BCG scar to receive the vaccine; if the household contact had two BCG scars, then no further vaccination was recommended [14, 26]. Düppre et al. designed an observational study with 1161 leprosy

patients and their 5680 contacts at the FioCruz Leprosy Outpatient Clinic between 1987 and 2006 to assess the effectiveness of this vaccine on household contacts. Their findings revealed an effectiveness in reducing the disease on contacts after the index case diagnosis with a protection of 56% [26]. Similar figures in a meta-analysis of trials of the BCG vaccines performed by Zodpey show a protection of 43% [27, 28].

Development of a better vaccine than the BCG vaccine has been attempted. In India, the Mycobacterium W vaccine was launched in 1998 for public use. It was an adjunct to chemotherapy. Sharma et al. treated 156 MB leprosy patients with MDT and administered the Mycobacterium W vaccine and compared this to 145 similar leprosy patients who received a placebo injection with MDT. The patients given the Mycobacterium W vaccine were found to expedite bacterial clearance, accelerate clinical regression of lesions, significantly shorten the period of release from treatment, induce a fall in the bacterial index (BI), and show histopathological upgrading. The main issue with the vaccine was the higher incidence of type 1 reactions [5, 29, 30].

The use of chemoprophylaxis in contacts, especially in phenolic glycolipid-1 (PGL-1) seropositive and Mitsuda negative individuals, seems to help in the prevention of new cases but is a questionable measure that requires short and accessible therapeutic regimens. A meta-analysis performed by Revelz et al. found that rifampin (single dose of 300 to 600 mg), dapsone (50 or 100 mg once or twice a week for 2 years), or acedapsone (an intramuscular injection of 225 mg every 10 weeks for 7 months) are superior to placebo in reducing the incidence of leprosy in contacts of new disease cases [14, 31].

Schuring et al. found an immunoprophylactic effect was observed when the BCG

vaccine was combined with rifampin in the prophylactic treatment of close contacts. Individually, BCG (given at infancy) and rifampin protected against leprosy respectively at 57% and 58%, but combined raised the protective effect to 80% [14, 32].

Politically: decentralization and leprosy control action

Brazil has a unique structure in place to care for the underserved, called the family health care team (FhCT). The team consists of nurses, doctors, community health agents (CHAs), as well as other positions (see Figure 3 below). CHAs are integral to the team; they go door to door in neighborhoods and identify health concerns, provide general health information, follow up on treatments, and relay this information to nurses and doctors. This system is built as a triaging process that directs the nurses and doctors to see patients that need the most urgent care. This system created in 1991 has been crucial in the improvement of Brazil's national health indicators [33].

Position	Male/female ratio	Monthly salary	Total system cost
Physician: n = 35 (10.4%)	34/1	R$ 4500 (US$ 2054)	R$ 157 500 (35.9%)
University-educated nurse: n = 35 (10.4%)	1/34	R$ 2100 (US$ 958)	R$ 73 500 (16.8%)
Auxiliary nurse: n = 35 (10.4%)	2/33	R$ 800 (US$ 365)	R$ 28 000 (6.4%)
Dentist: n = 17 (5.1%)	1/16	R$ 4000 (US$ 1826)	R$ 68 000 (15.5%)
Dental assistant: n = 17 (5.1%)	1/16	R$ 800 (US$ 365)	R$ 13 600 (3.1%)
CHA: n = 196 (58.6%)	12/184	R$ 500 (US$ 228)	R$ 98 000 (22.3%)
Total = 325 (100%)	51/284		R$ 438 600 (100%)

Conversion: 1US$ = R$2.19 (R = Brazilian Real currency; commercial rate on 28 November 2006).

Figure 3: Composition of the family health strategy team. There are six positions that make up each FhCT *[33].*

In 2000 Brazil integrated the leprosy control action (LCA) into the family health care team [34]. Historically, the LCA was delivered through centralized programs using referral centers for diagnosis and treatment, but since the family health care team has incorporated

the LCA, a decentralization of diagnosis and treatment is taking place, and patients are increasingly cared for in their homes [35].

Skin and neurological examinations of household contacts for new leprosy patients are one of the main goals of the LCA. Unfortunately, in many states in Brazil skin examinations of household contacts are not occurring at an acceptable rate. The good news is that since the initiation of the LCA, a statistically significant increase in the number of cases detected by contact examinations has occurred [34]. Moura et al. visited 258 residences and examined 719 household and neighbor contacts in the city of Mossoró. Of these, 62 without prior history were suspected to have leprosy. Fifteen people were confirmed with the diagnosis, giving 2.4 cases per 100 examinations of household and neighbor contacts. Six people were household and nine were neighbor contacts, with no difference in the rate of new cases in household (2.9/100) or neighbor (2.1/100) contacts ($p = 0.555$) [36].

Fuzikawa et al. studied 435 new cases of leprosy in the city of Betim and examined the pre-and post-decentralization process of the LCA into the FhCT. They found three main conclusions from their study: earlier diagnoses and treatments occurred after 2001 compared to before (see Figure 4 below), fewer cases of diagnoses with deformities, and more patients diagnosed and treated closer to their homes after decentralization. These conclusions were attributed to improved access of care with health services closer to the homes of patients [35].

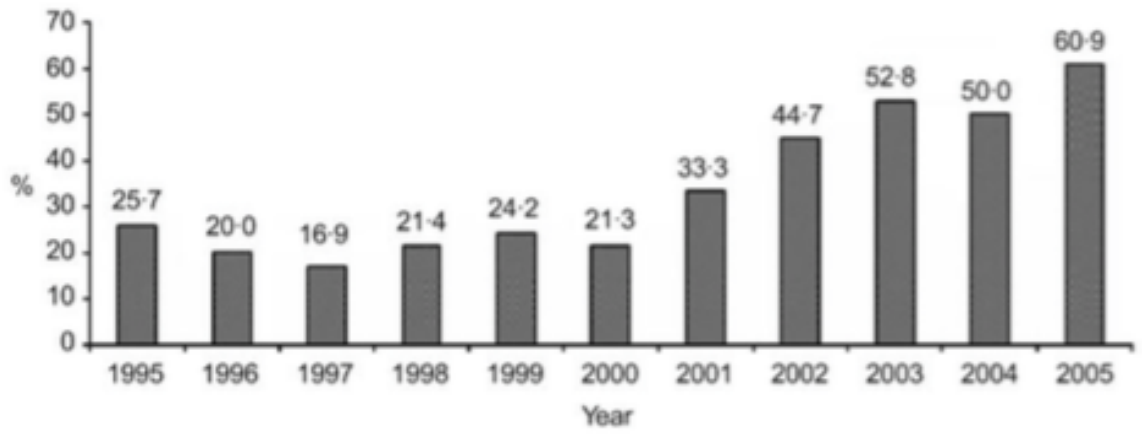

Figure 4: New leprosy cases closer to patients' homes. The percentage of new leprosy cases increased from 2000 to 20001 when the LCA was incorporated into the FhCT in the city of Belim, Minais Gerais [35].

Molecular tools

Molecular and immunologic tests for leprosy have been studied and used in research but not used clinically. The Polymerase Chain Reaction (PCR) technique makes possible the detection and quantification of specific RNA or DNA sequences of organisms. Among all nucleic acid markers of M. leprae in the literature according to Goulart and Goulart, the RLEP3, 85-B and 16S rRNA sequences are the only three that have presented significant results [10]. Donoghue et al. focused on the RLEP3 sequence, which is repeated 28 times in the M. leprae genome. Its primers were tested against the sensitivity of primers targeting the previously established 18- and 36-kDa genomic sequences. The authors concluded that the RLEP primer set was 10 and 1,000 times more sensitive than the 18- and 36-kDa sets, respectively [10, 37].

Another molecular tool is immunologic testing. Duthie et al. studied patients from Venezuela and Brazil who were diagnosed according to the Ridley-Jopling diagnosis scale, and their immune responses were noted with the magnitude of anti-PGL-1 IgM response

and anti-leprosy IRDI diagnostic-1 (anti-LID-1) IgG response. The median antibody response for anti-PGL-1 IgM was highest in the LL patients and continued to reduce as the clinical form lessens. In these analyses, using a threshold of ELISA index above 1.1, 97.7% of LL patients, 96.4% of BL patients, and 76.9% of BB patients were positive for anti-LID-1 responses, with 90.9%, 85.7%, and 38.5%, respectively, having ELISA indices above 5. They also looked at antibody levels before and after treatment and found significant reductions after treatment (see figure 5 below) [38].

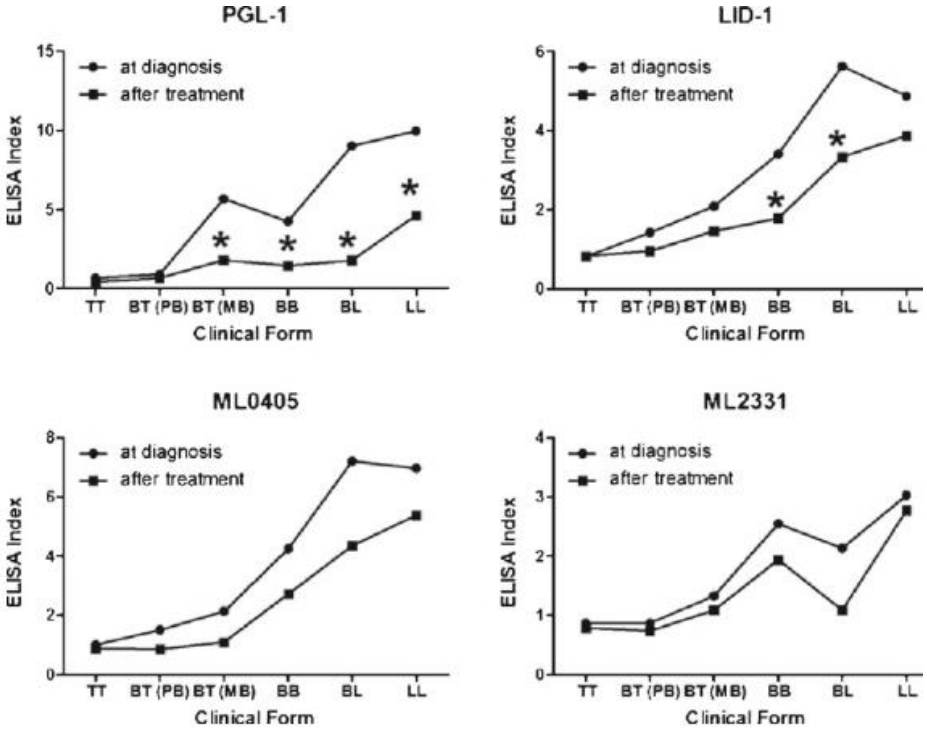

Figure 5: Antigen-specific antibody responses. For each antigen-specific antibody response, there are reduced antibody levels after treatment than at diagnosis. [38]

Relapses and non-adherence

Relapses and non-adherence are associated with a multitude of factors. Ferreira et al. studied patients from the state of Mato Grosso and found the following to be factors

associated with relapses: renting, wooden housing, living with more than five people, using public transportation, alcoholism, and irregular treatments [39].

Relapses also happen due to interruption in treatments because of side effects. Deps et al. found that out of 194 patients treated with the MDT protocol, side effects due to at least one drug were found in 45% of the patients [15]. Drug resistance can also lead to relapse. Drug resistance has been reported and the mechanism elucidated for dapsone, rifampin, and oflaxacin [10]. One report showed that 19% of 265 M. leprae isolates from biopsied samples of patients were resistant to various concentrations of dapsone, rifampin, or clofazimine and 6.23% were resistant to more than one drug in the mouse footpad susceptibility assay [12, 40]. Also, many investigators have identified multi-drug resistant strains of M. leprae [12].

Two studies from Bakirtzeit and Barrata report the following factors as determinants of non-adherence to treatment of leprosy: doctor-patient relationship, lack of bonding between them, patients' feeling of powerlessness over their health, lack of education, receiving a supervised dose every 28 days, and major side effects of the treatments [41, 42].

DISCUSSION:

The results reveal many different areas in which Brazil can improve its current leprosy situation. As to be expected, the effects of poverty like undernutrition, crowded living conditions, and insanitation are associated with increased rates of leprosy. Knowing that M. leprae uses armadillos as a reservoir, attempts could be made to limit the consumption as a food source.

Continuing to identify isolated leprosy communities and mapping clusters of high incidence rates across Brazil should direct the placement of resources and time. A more humanized model is the goal for leprosy, with more widespread efforts to reduce stigma and improve public awareness of the signs and symptoms, promote social reintegration, and improve quality of life [43]. Research needs to continue to discover why these communities still exist, if they are truly due to forced isolation or perceived societal stigma, and what can be done to break down these barriers [11, 23].

Ensuring vaccination and chemoprophylaxis of household contacts, especially in the endemic areas of Brazil, can serve a vital role [11, 23]. The Mycobacterium W vaccine is a promising alternative to the BCG vaccine, but its side effects prevent this as standard of care. Much more information is needed to make vaccines more efficacious and a practical alternative to prevent leprosy. In order to develop new vaccines, areas like genomic information on M. leprae, identification of more antigens, gene cloning, and tools for recombinant protein expression are needed [14].

Employing a quicker and more accurate diagnosis will help Brazil reach the WHO goal. Moura et al. showed that detection rates between household contacts and neighbors were not significant. This suggests that contact examination should be extended to neighboring homes, especially those who live close to a multibacillary case. The family health care team since its integration with the leprosy control action is serving an important role in identifying new cases [36]. These teams must increase the rate of skin examinations of household contacts of leprosy.

New diagnostic tools are currently available but not yet used clinically, some of which include: serological tests with the PGL-1 and protein antigens, immunohistochemical

reaction with antibodies for BCG, PGL-1, and LID-1, and also PCR at different genomic targets of M. leprae. Further research in molecular markers for M. leprae, developing sensitive lab tests for asymptomatic patients or those with few symptoms, and to predict disease expression among exposed individuals will all contribute to providing an earlier diagnosis and treatment, which are key in breaking the transmission cycle [14]. The PCR technique will hopefully become the gold standard laboratory test for leprosy diagnosis, like it is for so many other diseases. Among all nucleic acid markers in the literature, three of them present significant results: RLEP3, 85-B and 16S rRNA [10].

Improvements in treatments with less relapses will help Brazil reach its WHO goal. Duthie et al. showed that IgG antibody levels could be used as an auxiliary tool to help diagnose, assess treatment efficacy, and assess disease relapse. The data and clinical information from their study indicate that positive responses to these proteins are indicative of active leprosy and that responses may disappear upon successful treatment. Directly observed treatment (DOT) to prevent relapses in tuberculosis patients is the model of care for that disease. Similarly, Brazil can employ more of this type of therapy in the homes of patients using the family health care team. Educating patients about the disease, its long-term effects, and the treatment regimen is shown to prevent relapses [39]. Alternative medications exist for each component of the MDT regimen. Creating observational studies to determine the efficacy of each drug would demonstrate the best treatment combination.

Conclusion:

An improvement in a variety of factors can help Brazil meet the WHO's leprosy goal for a prevalence of less than one patient per 10,000 inhabitants. These various factors can be organized into three main groups: prevention, diagnosis, and treatment.

For Brazil to meet its goal, the author of this thesis favors targeting resources and time toward the ten clusters with the highest incidence rates. These resources and time include the following: 1) mandatory vaccination and providing optional chemoprophylaxis of household and neighboring contacts, 2) increasing the presence of the FhCT, 3) improving the rate of skin examinations of household and neighboring contacts performed by the FhCT, 4) providing more directly observed treatment (DOT) in patients' homes, and 5) educating patients and the contacts about the disease and appropriately treating it. Increased research on leprosy is also a top priority, but this will take a more international and collaborative approach.

With the World Cup in 2014 and the Olympics approaching, Brazil is increasingly in the international spotlight with often much criticism. Decreasing the burden from widely treatable diseases like leprosy will elevate Brazil on the international stage. Brazil owes it to its people to meet this higher standard of medical care.

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