Transactions of the Royal Society of Tropical Medicine and Hygiene (2008) **102**, 631–638

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Effectiveness of BCG vaccination among leprosy contacts: a cohort study

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Received 17 July 2007; received in revised form 7 April 2008; accepted 8 April 2008
Available online 2 June 2008

KEYWORDS
Leprosy;
BCG;
Vaccines;
Effectiveness;
Contact tracing;
Brazil

Summary The study assessed the effectiveness of BCG vaccination against leprosy among the contacts of 1161 leprosy patients at the FIOCRUZ Leprosy Outpatient Clinic, RJ, Brazil, from June 1987 to December 2006. Following National Leprosy Program guidelines, the clinic has administered one-to-two doses to all healthy contacts since 1991. Among the 5680 contacts, 304 (5.4%) already had leprosy. Of the 5376 eligible healthy contacts, 3536 were vaccinated, 30 of whom were excluded due to previous or current tuberculosis, or HIV. In 18 years of follow up, 122 (2.15%) incident cases were diagnosed (58 vaccinated and 64 not), 28 occurring in the first year of follow up (21 vaccinated, 16 with no scar). The protection conferred by BCG was 56% and was not substantially affected by previous BCG vaccination (50% with a scar and 59% without). The risk of tuberculoid leprosy during the initial months was high among those vaccinated with no scar. However, it had substantially declined by the first year and in the following years, when the protection rate in this group reached 80%. Since Brazil is endemic for leprosy and the detection rate is not declining satisfactorily, vaccinating all contacts could be an effective means of substantially reducing the incidence of leprosy.

1. Introduction

According to the WHO (2006), in 2005, leprosy prevalence worldwide was 227 427 cases and the new-case detection rate showed a sharp annual decline, falling by over 110 000 cases (27%) in comparison to 2004. In Brazil, however, a country endemic for leprosy that has experienced only

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0035-9203/$ – see front matter
doi:10.1016/j.trstmh.2008.04.015

gradual annual declines, the total number of new cases in 2005 was 51 738, with a detection rate of 2.09/10 000 (Ministério da Saúde, 2007).

The WHO Strategic Plan for the Elimination of Leprosy 2000—2005 supported a variety of national programs throughout the world for the purpose of intensifying early detection efforts and treatment of all known leprosy cases with effective multidrug therapy (MDT) and carrying out leprosy control procedures consisting of passive case detection, treatment, prevention of disability and rehabilitation (WHO, 2000).

In an attempt to halt the spread of leprosy, the BCG vaccine has been recommended as a preventive measure against leprosy in Brazil since the early 1970s. These recommendations were extended in 1991 (Ministério da Saúde, 1991). Although the primary purpose of the BCG vaccine has historically been to prevent tuberculosis (TB), it is well established that a single dose of BCG confers significant protection against leprosy, ranging anywhere from 20 to 80% (Abel et al., 1990; Fine et al., 1999; Zodpey et al., 2005). Multiple doses of BCG have been reported to confer even further protection (Bertolli et al., 1997; Convit et al., 1993).

The Brazilian Ministry of Health (BMH) therefore recommends that all household contacts of leprosy patients be given BCG vaccine. Since 1991, the BMH has additionally advised that two doses of i.d. BCG be administered to both current household contacts and those whose index cases were diagnosed within the previous 5 years. The vaccine is administered irrespective of TB or leprosy skin test results. If the contact never received BCG, or if this information is doubtful, he/she is to receive two BCG doses at a 6-month interval. If he/she has already received one dose of BCG, a single dose is given (Ministério da Saúde, 1991). Neonatal i.d. BCG vaccination of the Brazilian population has been successfully administered to prevent TB, reaching coverage rates of at least 90% across the country. From 1994 (Ministério da Saúde, 1994) until its suspension in 2006 (Ministério da Saúde, 2006), a second BCG dose was also recommended for schoolchildren aged 6—14 years to combat severe forms of TB.

Two cohort studies (Cunha et al., 2004; Matos et al., 1999) and two case-control studies (Lombardi et al., 1995; Rodrigues et al., 1992) carried out in Brazil confirmed that the neonatal BCG routinely administered to prevent TB does have an important and often overlooked impact on the occurrence and transmission of leprosy. In these studies, the majority of the population received BCG vaccine soon after birth, and thus prior to becoming contacts.

The only similar vaccine study performed outside Brazil is a trial conducted in Venezuela by Convit et al. (1992), in which the study population received BCG as part of a TB control program, i.e. probably before these individuals had become contacts. These same individuals were later revaccinated as part of a leprosy program. At that time, the Venezuelan leprosy control policy consisted of repeated lepromin testing of contacts (i.d. injection of about 10 million killed leprosy bacilli) and repeated BCG vaccination of those that tested negative. Their findings showed that the risk of contracting leprosy was lowest among contacts with two or more BCG scars.

The Venezuelan study served as a model for recommending two doses of BCG for leprosy contacts as an important measure toward reducing the incidence of leprosy among contacts in Brazil. As stated above, the measure took effect in 1991 but no evaluation of the results has yet been made. The objective of the present study was, therefore, to evaluate the protective effect of the BCG vaccine in leprosy contacts subsequent to index case diagnosis, in accordance with BMH guidelines.

2. Materials and methods

2.1. Study design

This was an observational study involving 1161 leprosy patients and their contacts examined between June 1987 and December 2006 at the Leprosy Outpatient Clinic National Reference Center located at the Oswaldo Cruz Foundation in Rio de Janeiro, RJ, Brazil. Recruitment of participants continued throughout the entire June 1987—December 2005 period and follow up ended in December 2006.

All the individuals resided in the State of Rio de Janeiro, in which the leprosy prevalence rate in 2006 was 0.97/10 000 and the new-case detection rate was 1.42/10 000 individuals (Ministério da Saúde, 2007).

2.2. Contact identification

Individuals diagnosed with leprosy were first interviewed by a social worker to obtain their personal data, after which the initial signs and symptoms of the disease were described. The individuals were then requested to inform their family members and household contacts of the urgent necessity of their being examined at the leprosy outpatient clinic for possible disease. An experienced clinical dermatologist examined all of the contacts to detect any leprosy lesions as well as the typical neonatal BCG scar. Contacts suspected of having leprosy were submitted to bacteriological, histopathological and immunological examinations and classified according to the Ridley and Jopling scale (Ridley and Jopling, 1966) as: borderline-borderline (BB), borderline-lepromatous (BL), lepromatous-lepromatous (LL), borderline-tuberculoid (BT), tuberculoid-tuberculoid (TT), or indeterminate leprosy (IL). They were also grouped according to their bacillary index (BI) as either multibacillary (MB positive BI) or paucibacillary (PB negative BI).

Whenever a MB leprosy case was detected among the contacts of a PB patient, this MB individual was considered an index case. Household and non-household contacts were examined and enrolled in the study no later than 12 months after their index cases commenced MDT. The dermatologists responsible for these patients and their contacts remained the same throughout the 15-year study period.

A household contact was defined as an individual who had either lived in the same or an adjacent dwelling during the 5-year period before index case detection. In addition, non-household contacts were also examined and defined as those who, while not meeting any of the criteria for household contacts, had had occasional contact as neighbours and/or relatives, as indicated by the index case.