

## **A study on transmission and a trial of chemoprophylaxis in contacts of leprosy patients: design, methodology and recruitment findings of COLEP**

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Accepted for publication 16 August 2004

*Summary* In this article, we describe the design, methodology and recruitment findings of the COLEP study. The objectives of this study were to determine the effectiveness of chemoprophylaxis with a single dose of rifampicin in the prevention of leprosy among close contacts of leprosy patients, and to find characteristics of contact groups most at risk to develop clinical leprosy. These characteristics should be usable by routine leprosy control programmes. COLEP consists of a cluster randomized, double-blind and placebo-controlled trial, a cohort study to determine risk factors characterizing the sub-groups most at risk within the total contact group of a patient, and a cohort study using a reference group from the general population to determine the prevalence and incidence of leprosy in the total population of the study area. The follow-up period will be 4 years. A coding system was developed describing the physical and genetic distance of the contact person to the patient. This study in Bangladesh includes 1037 newly diagnosed and previously untreated leprosy patients and their 21,867 contacts. The prevalence of leprosy among contacts was 7.3 per 1000. A total of 21,708 contacts without signs and symptoms of clinical leprosy are included in a trial of chemoprophylaxis with single dose rifampicin, and randomized at contact group level in treatment and placebo arms. The results of this large field trial will become available in the years to come.

## Introduction

The introduction of the relatively short multiple drug treatment regimens (MDT) for leprosy, an infection caused by *Mycobacterium leprae*, has resulted in a sharp decrease in the number of registered leprosy patients in the world.<sup>1,2</sup> Encouraged by this success, the World Health Organisation (WHO) adopted the goal of elimination of leprosy as a public health problem by the year 2000, defined as a worldwide prevalence of below 1/10,000. This was to be attained by early detection and treatment of patients. This goal was later extended to 2005.<sup>3</sup> However, the world-wide case detection rate is not decreasing, with the detection rate in 1998 being the highest since 1985.<sup>4</sup>

The apparent failure of MDT-based control to achieve declines in leprosy incidence calls for new strategies of leprosy control. High-risk groups for development of disease that may serve as sources of transmission should be included as a target population in new methods to be developed.

This prospective (sero-)epidemiological study on contact transmission and chemoprophylaxis in leprosy (COLEP) is designed to investigate the relative contributions of several risk factors and the possibilities of chemoprophylaxis to prevent leprosy in close contacts of leprosy patients. The hypothesis behind the study is that close contacts of leprosy patients may already have been infected by *M. leprae* by the time the patient is recognized and treatment started. By simultaneously treating these subclinical infections among contacts, it is hoped that development of clinical disease and further transmission in this group can be prevented.

The COLEP study has the following objectives:

- To determine the effectiveness of chemoprophylaxis by means of a single dose of rifampicin in preventing leprosy in close contacts.
- To determine the relative risk (as compared to the general population) of contacts of leprosy patients to develop leprosy and to study the contribution of spatial and genetic distance to the index case as risk factors.
- To determine the predictive value of anti-PGL-I antibody detection for the future development of leprosy.
- To determine the usefulness of monitoring the anti-PGL-I antibody levels as a way to measure the effectiveness of chemoprophylactic interventions.
- To determine the cost-effectiveness of chemoprophylaxis-based intervention among close contacts of leprosy patients.
- To determine the incidence and prevalence rates of leprosy in the study area.

In this paper, we describe the design, methodology and basic recruitment findings of COLEP.

## Materials and methods

### STUDY DESIGN

The COLEP study is divided into three sub-studies, each one supplementing the others (see also Tables 1 and 2):

**Table 1.** Summary of the COLEP trial and expected number of new patients

Reference group ( <i>n</i> = 20,000)	Trial group ( <i>n</i> = 20,000)	
IR = 0.25–1.0/1000 per year	IR = 1.0–2.0/1000 per year	Placebo
	Rifampicin	10,000
	10,000	10,000
4 years: 20–80 new cases	20–40 new cases*	40–80 new cases

\*The expected efficacy of intervention with rifampicin is 50%. It is therefore expected that the incidence rate in the group receiving rifampicin will decrease and that the number of new cases in this group will be lower as compared to the placebo group.

1. A single-centre, cluster randomized, double-blind, placebo-controlled trial. There are two treatment groups, one receiving a single standardized dose of rifampicin, the other a placebo. The development of clinical leprosy within these groups will be assessed at 2-year intervals for a period of 4 years by independent (blinded) assessors.
2. These two treatment groups will also be used in a prospective cohort study investigating the predictive value of the presence of anti-PGL-I antibodies for the development of leprosy, and to determine to which extent physical and genetic (kinship) distance to the primary case are risk factors for the development of leprosy.
3. A population-based reference group is formed to determine the prevalence and incidence of leprosy in the general population and to calculate the relative risks of different categories of contacts of leprosy patients to develop the disease.

The Bangladesh Medical Committee granted ethical clearance.

**Table 2.** Time frame of COLEP trial

Year/activity	Trial group		Reference group
	Rifampicin	Placebo	
2002–2003			
Intake	Physical examination, serology ( <i>n</i> = 10,000)	Physical examination, serology ( <i>n</i> = 10,000)	Physical examination ( <i>n</i> = 20,000), serology ( <i>n</i> = 2200)
Early analysis			
2004–2005			
1st follow-up	Physical examination, serology	Physical examination, serology	Physical examination, serology
Mid-term analysis			
2006–2007			
2nd follow-up	Physical examination, serology New cases (estimated): 20–40*	Physical examination, serology New cases (estimated): 40–80	Physical examination, serology New cases (estimated): 20–80
2007–2008			
Final analysis			

\*The expected efficacy of intervention with rifampicin is 50%. It is therefore expected that the incidence rate in the group receiving rifampicin will decrease and that the number of new cases in this group will be lower as compared to the placebo group.

## POWER CALCULATIONS

*Power calculation for the first sub-study (trial group)*

In this power calculation, heterogeneity in the chance of close contacts to develop clinical symptoms of leprosy was taken into account, but no major effect on the numbers needed was found. Given an incidence rate (IR) of 2 per 1000 per year, with a 50% reduction through intervention ( $\alpha = 0.05$  two-sided, power = 0.80), a total of about 12,000 contacts will be necessary. With an IR of 1 per 1000 per year, this number increases to just over 20,000. This means that about 10,000 contacts in each treatment group is sufficient to detect reliably an expected efficacy of intervention of 50%, even taking into account an expected 10–20% loss to follow-up of contacts.

*Power calculation for the second sub-study (serology)*

It is assumed that 10% of contacts are seropositive. According to calculations based on a rate of 9:1 for unexposed (seronegative) versus exposed (seropositive), a leprosy incidence of 1 per 1000 per year in the seronegative group ( $\alpha = 0.05$  two-sided; power = 0.80), 10,000 contacts will be sufficient to demonstrate a relative risk of 3 for the development of leprosy in the seropositive group compared with the seronegative group.

Regarding the usefulness of detection of PGL-I antibodies to monitor the effectiveness of chemoprophylactic interventions in preventing leprosy, the power calculations are as follows: based on an initial seropositivity of 10% in contacts at the time of the prophylactic treatment ( $\alpha = 0.05$  two-sided; power = 0.80), a decrease of 3% in seropositivity in the intervention group as compared to the placebo group (e.g. 7% versus 10%) after a period of 4 years can be determined in a random sample of 2000 contacts in each group.

*Power calculation for the third sub-study (reference group)*

Based on an expected IR over a 4-year period of 1.25–5.0 per 1000 population, a representative sample size with 95% confidence level of 20,000 is sufficient when subjects are spread evenly in the population. However, as leprosy is a clustered disease, the reference group will be divided into 20 clusters of 1000 people from the general population in the study area, thus slightly reducing the level of confidence. The clusters will be sampled from the 13 subdistricts of the two districts involved, on the basis of size of the respective populations in the subdistricts. At least one cluster is allocated to each subdistrict, in order to ensure an even geographical distribution. The distribution within the subdistricts is determined at random from lists of villages and unions (larger unit than villages).<sup>5</sup>

## STUDY POPULATION

The study will be performed among the population of the districts of Nilphamari and Rangpur in north-west Bangladesh, within the well-developed vertical leprosy control programme of the Danish Bangladesh Leprosy Mission (DBLM). For practical reasons, the upazilla (subdistrict) of Pargacha has been excluded, as the leprosy control programme there is already integrated into the government health programme. The population of these two districts totals around 4,000,000 (according to the 1991 census), and the number of new leprosy patients among this population during the period 1995–2000 was approximately 1800 per year. The population is

mainly rural, but within the two districts there are four main towns: Rangpur, Saidpur, Kaunia and Nilphamari. In Saidpur and Rangpur there are sizeable Bihari populations, which are ethnically and socially different from the local Bangladeshi population.

#### CONSENT PROCEDURE

All eligible subjects (patients, contacts and reference group) will be informed verbally about the study and invited to participate. Written consent is required in the case of blood sampling or taking of prophylaxis. Consent is requested from each adult. For children, consent from a guardian is needed.

#### STUDY SUBJECTS

##### *Patients*

Around 1000 consecutive leprosy patients will be enrolled.

The diagnosis of leprosy is generally carried out according to the DBLM guidelines, which follow those of the national leprosy control programme.<sup>6</sup> However, in the DBLM field programme, a single leprosy lesion with satellites is regarded as single-lesion PB, which is not according to the national guidelines. In order not to interfere with the normal routine programme, this policy has not been changed. All leprosy cases included in the study are confirmed by a medical officer, and this confirmation is written on the patient card.

Exclusion criteria for patients are as follows:

- Any patient who refuses examination of contacts.
- Any patient who suffers from the pure neural form of leprosy.
- Any patient who resides only temporarily in the study area.
- Any new patient found during contact examination of the index case.
- Any new patient living less than six houses (or less than 100m) away from a patient already included in the study.
- First and second degree relatives of a patient already included in the study.

##### *Contacts*

For the 1000 consecutive new leprosy patients, contact groups will be formed consisting of around 20 persons for each patient. Thus the total number of contacts will be around 20,000.

All close contacts of the 1000 consecutive new leprosy patients who are recruited for the study will be considered for inclusion. A contact group consists of around 20 individuals. The following categories of contacts have been distinguished:

- Those living in the same house (household members).
- Those living in a house on the same compound, sharing the same kitchen.
- Direct neighbours (first neighbours).
- Close business or social contacts, including relatives. In order to be included into this category, one has to be in contact with the patient at least 5 days a week and during at least 4 h/day.
- Neighbours of direct neighbours (second neighbours).

A coding system has been developed to distinguish between several levels of contact. Two parameters were considered: physical and genetic distance to the patient. For physical distance, six categories were defined, based on the local housing situation:

- Those living under the same roof *and* using the same kitchen (KR).
- Those living under a separate roof, but using the same kitchen (K).
- Those living under the same roof, but not using the same kitchen (R).
- Next-door neighbours (N1).
- Neighbours of the neighbours (N2).
- Social contacts (business contacts, colleagues who stay in the same room at least 4 h a day for 5 days a week) (S).

For the genetic distance, seven categories are defined in which C, P, B and O represent genetic relationships. The others are not genetically related to the patient: spouse (M), child (C), parent (P), sibling (B), other relative (O), relative-in-law (CL, PL, BL or OL), non-relative (N).

All contacts are coded according to both types of contact; thus a child-in-law, living next door but using the same kitchen would be coded K and CL. General details of all contacts such as age, gender and presence of a Bacillus Calmette–Guérin (BCG) vaccination scar are recorded, as well as any exclusion criteria, when applicable. All data are entered on a contact registration card.

Exclusion criteria for contacts are as follows:

- Any person who refuses informed consent.
- Any woman indicating that she is pregnant.
- Any person currently on TB or leprosy treatment.
- Any person below 5 years of age.
- Any person known to suffer from liver disease or jaundice.
- Any person residing temporarily in the area.
- Any person suffering from leprosy at the initial survey (these patients will be referred to the clinic for leprosy treatment.)
- Any person who is a contact of another (COLEP) patient and is already enrolled in the contact group of the other patient.

### *Reference group*

The reference group (sub-study 3) consists of clusters of inhabitants from 20 selected areas. All people living in the area who are present during the survey and willing to participate are included, until the number of 1000 per cluster has been reached.

### DRUGS AND PLACEBO ADMINISTRATION

The capsules containing either 150 mg rifampicin or placebo were manufactured by Aventis Bangladesh in Dhaka. Independent quality control of the drugs has shown that the quality conforms the requirements of the University Hospital Groningen (The Netherlands). The capsules are the same as used for regular rifampicin production, and thus the name rifampicin is printed on them, regardless of whether it actually contains rifampicin or placebo.

The factory packs the capsules in containers of 120 pieces each, being 30 (maximum number of contacts)  $\times$  4 (maximum dosage per contact). One coded container containing either rifampicin or placebo is issued for the complete contact group of one patient. The randomization is done in Rotterdam and the coding of the containers is done in Dhaka by members of the research team from The Netherlands. The codes are kept under lock and key at the Department of Public Health in Rotterdam.

As soon as the prophylaxis is administered to all the eligible contacts of one patient, the container is returned for central storage. The number of unused capsules left in the containers is checked at random. Destruction of the remaining capsules is obligatory to ensure that no placebo medicine labelled rifampicin will find its way into the community. This is done centrally in Nilphamari by incineration.

#### CHEMOPROPHYLAXIS REGIME

A single dose of rifampicin or a placebo is given to all included contacts. The rifampicin comes in capsules of 150 mg and the dosage is the same as recommended in the guidelines of the national leprosy control programme of Bangladesh and DBLM (Table 3).<sup>6</sup> According to body weight and age, 2–4 capsules are taken by the contact under direct supervision of a DBLM staff member. All the contacts of one patient receive medication from the same container.

Other possible chemoprophylactic regimes as well as the risk of the development of resistance against rifampicin by *M. leprae* or *M. tuberculosis* were considered. Expert opinion made clear that an additional positive effect could not be expected from other regimes and that the risk of development of resistance after a single dose of rifampicin is remote.<sup>7</sup>

#### SEROLOGY

Finger prick blood samples are collected from all patients and contacts and from one in every nine persons from the reference group. All samples are collected on Schleicher & Schuell blotting paper GB 002, dried and stored at  $-20^{\circ}\text{C}$  until transport to the Netherlands. In addition, finger prick blood from all patients is immediately tested in the field using the ML Flow test, a newly developed lateral flow test that is capable of detecting anti-*M. leprae* IgM antibodies.<sup>8</sup>

At KIT Biomedical Research, an ELISA for the detection of anti-*M. leprae* IgM antibodies is performed according to established procedures.<sup>9</sup> The antigen used is NT-P-BSA, a semi-synthetic analogue containing the *M. leprae*-specific trisaccharide moiety of phenolic glycolipid-I.

**Table 3.** Dosage of rifampicin according to age and body weight

Age/weight	Dose of chemoprophylaxis
Adult > 35 kg	600 mg
Adult < 35 kg	450 mg
Child 10–14 years	450 mg
Child 5–9 years	300 mg

#### MONITORING INTAKE AND FOLLOW-UP

After a patient is diagnosed, patient details are recorded such as type of leprosy, duration of symptoms, bacillary index (BI) etc. MDT is started according to the national guidelines. Intake of single-lesion PB (SLPB) patients will be stopped when 400 such patients have been included; the same will apply to the group of other PB patients (PB2-5, with two to five skin lesions on physical examination). This will ensure an intake of at least 200 MB patients. After the patient has received his second dose of MDT, the contact survey is performed. In this way, the chance of re-infection of the contacts by the patient is kept low. During the contact survey, a check for signs and symptoms of leprosy is done. If leprosy is diagnosed, this is recorded and the newly found patient is referred to the clinic for appropriate treatment. This particular contact is then excluded from the trial. All other members of the contact group are asked for a blood sample, which is collected on filter paper for ELISA testing. The results of these tests will not be made available, neither to the contact nor to the field worker, until the study is completed. All field data are recorded on paper initially and entered in a computer database afterwards. The prophylaxis is taken under direct supervision. Follow-up examinations will be carried out after 2 and 4 years.

For the reference group, mass surveys are done in the selected areas. All subjects are checked for signs and symptoms of leprosy and one in every nine subjects is asked for a blood sample. Details are recorded and follow-up examinations will be performed after 2 and 4 years (see Table 1).

#### OUTCOME MEASURES

The primary outcome measure is the number of new leprosy patients emerging from the contact groups. The proportions between the rifampicin and the placebo group will be compared at 2-year intervals. Analysis will be carried out in order to define special groups at risk. The results of the serological tests will also be compiled and analysed. The number of leprosy patients found in the reference group will be used to calculate the prevalence rate (at intake) and the incidence rate (during follow-up) in the general population, allowing for calculation of relative risks among the contacts. A cost-effectiveness study will be part of the analysis.

#### DATA HANDLING AND ANALYSIS

A separate database has been designed, which is a modification of the database already in use at DBLM. Data are entered in the field during clinic visits and contact/reference group surveys, onto specially designed data sheets. These data are sent to Nilphamari, where they are entered into the database. All paper forms are scanned and filed on hard disk and CD. The paper copies of the data will be retained for a minimum of 2 years after the COLEP study has been completed. An electronic copy of the database is sent to the department of Public Health of Erasmus MC in the Netherlands on a monthly basis. Modern back-up facilities are available at Nilphamari as well. Protection of privacy of patients in the database will be according to Erasmus MC standards. Quality checks on all aspects of the data collection and entry are performed regularly, and feedback on the results is given to the field staff, laboratory personnel and the data entry assistant.

The blood samples on filter paper are sent for ELISA testing to KIT in Amsterdam. The results of these tests will be entered into the database at KIT and an electronic copy is

sent regularly to the central database in Rotterdam. The analysis of the data will be done in The Netherlands at Erasmus MC in Rotterdam and KIT in Amsterdam using appropriate statistical methods.

## Results

### PILOT PHASE

In the preparatory phase of the study, a 2-month pilot phase was included, which was evaluated before the official start of the study. Evaluation was carried out on the aspects of participation, reasons for exclusion and the practical application of the definitions used in the protocol. The main difficulty in defining contacts was the relative code: parents, spouses, children, brothers and sisters were no problem, but the child of a brother-in-law was sometimes coded as CL (child-in-law) and the difference between O (other relative) and OL (other relative-in-law) was not always clear to the field staff. The distance code was generally filled in correctly, but the difference between N(ighbour)1 and N2 was sometimes vague, as the real situation often differed from the standard lay-out provided. In general, however, it was clear that N1 contacts lived closer by than N2 contacts. By the high number of S (social) contacts and by the housing situation described, it was suspected that many of these S contacts were in fact neighbours of N2 contacts, who did not meet the criteria for the S category. This was indeed the case and special attention was given to correct this, although it remained a weak point during the intake phase.

### RECRUITMENT FINDINGS: PATIENTS AND CONTACTS

Contacts of 1037 newly diagnosed leprosy patients were included in the study. Distribution of age, sex and classification of these patients are given in Table 4. A total of 28,083 contacts were registered, of whom 6216 were excluded for various reasons (see Table 5). Although the experimental nature of the study was explained clearly, motivation among the contact population to participate in the study was high, resulting in relatively few refusals (1.2%). The remaining 21,867 contacts were examined for leprosy, of which 159 were confirmed to have previously undiagnosed leprosy. These newly found patients commenced MDT and were excluded from the trial. In total, 21,708 contacts were finally included in the trial. With 159 newly diagnosed leprosy patients, the intake survey revealed a prevalence of

**Table 4.** Distribution of age, sex and classification of newly detected leprosy patients

Age	Male				Female				Total
	SLPB	PB2-5	MB	Total	SLPB	PB2-5	MB	Total	
5-9	3	5	1	9	2	6	2	10	19
10-14	21	22	12	55	20	19	6	45	100
15-19	37	39	23	99	26	16	5	47	146
20-29	60	43	38	141	33	21	12	66	207
30-39	47	40	39	126	32	27	8	67	193
40-49	32	39	66	137	33	19	14	66	203
50 and older	38	26	52	116	16	20	17	53	169
Total	238	214	231	683	162	128	64	354	1037

**Table 5.** Reasons for exclusion in contact population

	<i>N</i>	<i>n</i>	%
Total number of contacts enumerated	28,083		100
<i>Reason for exclusion</i>			
Refusal of informed consent		338	1.2
Under 5 years of age		2964	10.6
Absent		2217	7.9
Temporary resident		131	0.5
Pregnancy		438	1.6
Liver disease or jaundice		51	0.2
Current TB or leprosy treatment		42	0.1
Contact of other COLEP patient		4	0
Not recorded		18	0.1
Suspected leprosy		16	0.1
Total excluded from contact examination		6216	22.1
Total included for contact examination	21,867		77.9
Confirmed new leprosy		159	0.6
Total excluded from trial		6375	22.7
Number of contacts included in trial	21,708		77.3

7.3 per 1000 among contacts (Table 6). The prevalence was higher among contacts of paucibacillary index patients with two to five patches and multibacillary index patients, compared with single lesion paucibacillary index cases.

## Discussion

Although in general passive case detection has been regarded as the most appropriate method for early case-finding, in many settings where awareness, motivation, and diagnostic procedures were regarded as inadequate, active case finding methods have been developed and implemented to find hidden leprosy cases. From this, it became clear that leprosy control programmes face the problem of many leprosy cases remaining undetected. Transmission that took place before the case finding will result in many more new cases in future, years after the completion of these campaigns and most likely also years after the elimination goal

**Table 6.** New cases of leprosy detected on examination of close contacts

Type of leprosy of patient (index)	No. patients	No. contacts included	No. of contacts with leprosy	Prevalence per 1000 contacts	95% CI
Single skin lesion (one patch) paucibacillary	400	8835	49	5.5	4.1–7.3
Two to five patches paucibacillary	342	7013	62	8.8	6.8–11.3
Multibacillary	295	6019	48	8.0	5.9–10.6
Total	1037	21,867	159	7.3	6.2–8.5

as defined by WHO has been reached. Mathematical modelling suggests that it may not be easy to achieve rapid declines in leprosy transmission solely through intensified case finding in combination with MDT treatment.<sup>10,11</sup> It will therefore remain important for leprosy control programmes to detect new patients as early as possible and to do so in an effective and sustainable manner.

With the integration of leprosy control activities into the general health service, and the limited resources available, less efforts in active case finding in general populations may be expected. As leprosy disease becomes less frequent (and thus less well-known), detection delays may also increase, with possible negative consequences for both disability and transmission, since many of the undetected patients may serve as a continuous source of infection.

Mass surveys to actively detect new patients are not cost-effective and are therefore not routinely applied in leprosy control programmes. Many programmes have restricted active case finding to household contacts of newly detected leprosy patients, since this group has an increased risk of disease.<sup>12</sup> However, the majority of the incident cases originate from the pool of people in the population without known household contact.<sup>13</sup> A recent study showed that contact with a leprosy patient is nevertheless the major determinant in incident leprosy, whereby the type of contact is not limited to household relationships, but also includes neighbour and social relationships.<sup>14</sup> This concept shows similarities with the 'stone-in-the-pond' principle describing tuberculosis transmission in concentric circles around a patient.<sup>15</sup> In principle, this concept could be translated into a valuable and sustainable tool for leprosy control programmes and elimination campaigns by focussing case detection, prophylactic intervention and health promotion activities not only on household contacts but also on at least neighbours of leprosy cases. Such a strategy especially becomes feasible in circumstances with reduced caseload because high-risk groups become 'manageable' in size (and distinguishable from the general population). Furthermore, this concept concurs with the view that under such circumstances an outbreak approach of leprosy control is needed, whereby contacts of the index case are examined.

Apart from undetected or hidden leprosy patients, other major sources of ongoing transmission are likely to be those who are infected subclinically with *M. leprae*; especially for persons incubating multibacillary disease this is easily conceivable. There is increasing evidence from nasal PCR studies that sub-clinical transmission may exist and that those infected may go through a transient period of nasal excretion.<sup>16</sup> This indicates, as was previously already shown by sero-epidemiological studies, that leprosy is a highly infective disease and transmitted relatively easily in endemic areas.<sup>17,18</sup> Household contacts, neighbours, and social contacts have a higher chance to contract the disease. Whether this is mainly the result of closer contacts to the index case of the infection, similar genetic and immunological background, environmental factors, or a combination of all, is not yet resolved.<sup>12</sup> By using standardized contact definitions in the COLEP study, relative risks for developing leprosy can be calculated for several categories of contacts.

The fact that MDT control has so far failed to accelerate declines in leprosy incidence necessitates re-thinking of how to control leprosy.<sup>19,20</sup> It is likely that high-risk groups (for development of disease and as source of transmission) should be included as target population for the measures to be taken in order to maximize the impact of control measures. In the absence of a vaccine, one rational intervention strategy would be prophylactic treatment of high risk groups, since it has the potential to greatly reduce the force of infection in the community, as was already expressed by the expert panels during the International Leprosy

Congress in China and at other meetings since.<sup>21,22</sup> It is well documented that dapsone has a chemoprophylactic effect.<sup>23,24</sup> Now, with modern powerful short-course antibiotic combination therapies at hand, the next logical step in this area is to study the feasibility (costs versus effect) of chemoprophylaxis with rifampicin as an intervention strategy alternative to an only-patient-based MDT control of leprosy.

After several years of extensive investigation, it has become apparent that serology with PGL-I is useful for detection of contacts at high risk of developing disease. Furthermore, it has been suggested that seroprevalence in school children is an indicator of the leprosy endemicity in an area and could thus be valuable as an indicator of transmission.<sup>25</sup> The simple lateral flow assay for the detection of antibodies to PGL-I, which is now available, promises to be useful under field conditions.<sup>8</sup>

In 2000, the official registered prevalence of leprosy in the study area (Nilphamari and Rangpur districts) was 2.63 per 10,000 population and the new case detection rate 4.33 per 10,000. In Bangladesh as a whole, the official figures in that year were 0.82 per 10,000 and 1.17 per 10,000 respectively.<sup>26</sup> The intake survey for the COLEP study revealed a prevalence of 7.3 per 1000 among contacts. The COLEP study was designed to answer several urgent questions related to contact transmission, risk factors for contracting leprosy, and the possibility of preventing leprosy by means of chemoprophylaxis. Included in COLEP are 1037 newly diagnosed leprosy patients and 21,708 close contacts. These contacts are included in a trial of chemoprophylaxis with single dose rifampicin, and are randomized at contact group level in treatment and placebo arms. The results of this large field trial will become available in the years to come.

## Acknowledgements

We gratefully acknowledge the American Leprosy Missions and The Leprosy Mission International for financial support of the COLEP study. We also acknowledge with gratitude the advice and scientific support of the Study Advisory Group of the COLEP study, consisting of Dr W. H. van Brakel, Dr P. Klatser, Dr P. R. Saunderson, Professor W. C. S. Smith, and Dr S. G. Withington.

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