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Patterns and trends of leprosy in Mexico: 1989–2009

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Summary Data from the Mexican national leprosy control programme 1989–2009 are described and analysed. After initial increases associated with the introduction of MDT and the start of the global elimination initiative in the early 1990 s, both prevalence and incidence declined dramatically throughout most of the country. Reported prevalence fell below 1 per 10 000 in 1994 and has remained below that level ever since. There is considerable geographic heterogeneity, with highest case detection rates in western states bordering the Pacific and lowest in the south east. Reasons for these geographic differences are unclear. There is evidence of increases in average age of cases, and in proportions male and MB, as in several other populations with declining leprosy. There is some evidence of increasing leprosy in states bordering on Texas, USA, where *M. leprae* is known to be harboured in armadillos. The relevance of armadillos for leprosy in Mexico is unclear but a priority question.

Introduction

The introduction of short course multiple drug therapy (MDT) by the World Health Organization (WHO) in 1981 led to declines in reported leprosy prevalence across the world.[1] This success led the WHO in 1991 to call for the 'elimination of leprosy as a public health problem by 2000,' defined as the reduction in prevalence under 1 case per 10 000 of population.[2] Over the subsequent two decades prevalence continued to decline globally and WHO's target was reached in most endemic countries. Despite these declines, the disease persists in most countries of the world, and it is not clear that *Mycobacterium leprae*

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transmission has stopped completely in any country in recent years, with the possible exception of Japan.[3]

In the Americas MDT was implemented starting in 1985 but did not reach universal availability until 2001.[4] Prevalence in the region fell by 80% from 1992 to 1999, and all countries, with the exception of Brazil, claimed to achieve WHO's 'elimination' goal by 2005.[4] Little has been published on incidence trends for recent decades, but new case detection statistics, as reported to WHO, show evidence of continued transmission in most countries of the region.[5]

Mexico is the fifth largest and third most populous country in the Americas, and has long been endemic for leprosy. Its neighbours to the south (Guatemala and Belize) and to the north (USA) continue to report low numbers of new leprosy cases.[5] The circumstances in the USA are of particular interest in that there is recent evidence that *M. leprae* persists as a zoonosis among nine-banded armadillos in southern USA, and that the geographic range of this reservoir may be spreading.[6,7] The proximity of this zoonotic reservoir to Mexico makes it of particular interest for leprosy control and trends in the American region. This paper describes recent patterns and trends of leprosy in Mexico.

LEPROSY IN MEXICO: HISTORICAL REVIEW AND CONTROL INITIATIVES

The date of leprosy's arrival in Mexico is uncertain. It is generally believed that Spanish colonisation introduced *M. leprae* into the country in the 16th century. Historical reports of leprosy suggest four initial foci as sources of its spread throughout the country.[8] A central focus derived from the advance of Spanish colonisation from the eastern coast of Veracruz to the inside regions. The western and largest focus, associated with trade routes with Asia and the Philippines, might have been sustained by the immigration of Asian communities in the 16th and 17th centuries.[8–10] A third focus in the south-east peninsula of Yucatan was associated with trade routes with the Antilles. The fourth focus, in the north-east may be related to existing foci in southern USA, although this is unclear. Wherever and whenever the introductions took place, the disease spread throughout the country.

Though leprosy may have existed in Mexico since the 16th century, no surveillance or control took place, at a national level, until the 20th century.[8–9,11] It became a notifiable disease in 1921, and the first national census published in 1927 enumerated 1,450 leprosy patients.[8–9,11] Early efforts at leprosy control were based on confinement and isolation of cases. The introduction of dapsone in the 1940 s provided the first effective treatment for the disease and encouraged new control initiatives.

The National Leprosy Control Programme (NLCP) began in 1960.[4] It relied on active case finding (examination of household contacts), early treatment, social support, monitoring and surveillance, and was implemented 'vertically' through specialised hospitals and mobile units in high prevalence states. From 1960 to 1966, 8,275 new cases were registered, a considerable increase in case detection numbers compared to previous years.[9–12] The effectiveness of the programme declined in the following years, due to lack of political will and funding. In the 1980 s leprosy control was integrated into primary health care services and implemented by general practitioners and health workers at the community level.[9,11] The introduction of MDT and WHO's call to 'eliminate' leprosy as a public health problem in 1991 encouraged the NLCP to intensify its activities.[9] Active case finding and prompt treatment of cases, health education activities and promotion of health seeking behaviours, training of health care workers, strengthening of federal and district health

services, creation of partnerships with other institutions and ensuring political commitment and funding were among the measures implemented in the following years.[4] As a result, treatment coverage improved and prevalence dropped dramatically, reaching below the 1 per 10 000 threshold by 1994.[10]

This paper presents detailed data on newly reported leprosy cases in Mexico during the last two decades. Its aim is to elucidate trends and patterns of leprosy's incidence in Mexico from 1989 to 2009.

Materials and Methods

Materials

We carried out a retrospective study based on routine surveillance data on 4747 newly detected leprosy cases in Mexico from 1989 to 2009. As notification is compulsory, each time a leprosy case is diagnosed in the public or private health sector a notification form should be filled in and sent to the National Epidemiological Center or CENAVECE (Centro Nacional de Vigilancia Epidemiológica y Control de Enfermedades), where records are updated monthly. The data analysed here were obtained from several sources. Annual data on newly detected cases and registered prevalence were available for the years 1989 to 1996 in historical archives of the NLCP. Information on sex, age, classification, state of birth and of diagnosis was only available from 1996 to 2009. Data for the years 1996 to 2000 were transcribed from original notification forms, whereas data from 2000 onwards were extracted from the official electronic database. Because of these data constraints, detailed analyses are given for three time periods: 1996–2000; 2001–2005; 2006–2009.

The study was approved by the Ethics Committee of the London School of Hygiene and Tropical Medicine.

Methods

NEW CASE DETECTION AND PREVALENCE

Ascertainment of leprosy cases in Mexico is mainly passive, based on self-reporting to health providers. 'Active case search' activities accounted for 10–20% of the total new cases in our study period. In order to be registered, new cases of leprosy must meet clinical, bacillary and histopathological criteria specified in national guidelines and must not have received treatment before.

The new case detection number (NCDN) refers to the number of new cases diagnosed per annum, and the new case detection rate (NCDR) refers to the number of new cases detected per 100,000 of population per year. We calculated the NCDR for different time periods as the number of new cases reported, divided by the population at the middle of the time period, divided by the number of years in the time period (5, 5, or 4 for the periods 1996–2000, 2001–2005, and 2006–2009 respectively) and multiplied by 100,000.

Annual prevalence was defined as the number of cases on treatment plus those that have refused it at the end of each year (31 December), and prevalence rate corresponds to the

prevalence per 10 000 of population. Refusers are included in prevalence for 2 years. If they have not been persuaded to take the treatment by then, they are considered lost cases and excluded from prevalence.

CLASSIFICATION

Cases were classified as paucibacillary (PB) or multibacillary (MB) leprosy based on clinical criteria, slit skins smear and biopsy, and not on number of lesions as used in many countries in recent years. This is done by trained health workers in primary health care units. Recommended treatment durations are 24 months for MB and 6 months for PB cases, and have not changed during the period covered by this study.[13]

AGE

New cases were stratified into five age groups; 0–19, 20–39, 40–59, 60–79 and ≥ 80.

Age specific rates per 100,000 in different time periods were obtained by dividing the age specific detection numbers by the population for that age group at the middle year of the time period and by the number of years in the time period, and then multiplying by 100,000.

GEOGRAPHIC DISTRIBUTION

We calculated the annual reported incidence per state per time period, dividing the number of new cases by the population numbers of each state at the median point of the time period and dividing by the number of years in the time period per 100,000 of population.

We classified states as 'low' (LS), 'intermediate' (IS), or 'high' (HS) in terms of case detection on the basis of whether their case detection rates were $< 0{\cdot}09$, $0{\cdot}09–0{\cdot}8$ or $> 0{\cdot}8$ per 100,000 of population, respectively over the years 1996 to 2009. We further differentiated the 'intermediate' states crudely as 'increasing' (IIS) and 'decreasing' (DIS) patterns of NCDR over time, simply by whether the NCDR was higher or lower in the last compared to the first time period.

Results

NATIONAL STATISTICS

After an initial slight increase from 1989 to 1991 there was a dramatic decline in registered prevalence, from 1992 to 1995, from 17 020 to 6,032 respectively (Figure 1).

Prevalence declined steadily since 1995, to 555 in 2009. The prevalence rate fell under the one per 10 000 threshold in 1994, and remained under this value for all subsequent years.

Starting in 1989 when 235 new cases were reported, NCDN doubled to 518 in 1992, reaching its highest number in 1994 when 570 new cases were registered. There has been a gradual if irregular decline in NCDN and NCDR since 1995 (Figure 2).

Throughout the study period, males have always predominated over females, with proportions that ranged between 57·1% and 61·8% of newly registered cases. There was a predominance of MB disease throughout the years under consideration, increasing from 58·9% of new cases in 1998 to 78·3% in 2009. The proportion of MB has been consistently higher in males than in females, with odds ratios ranging from 2·1 to 2·4.

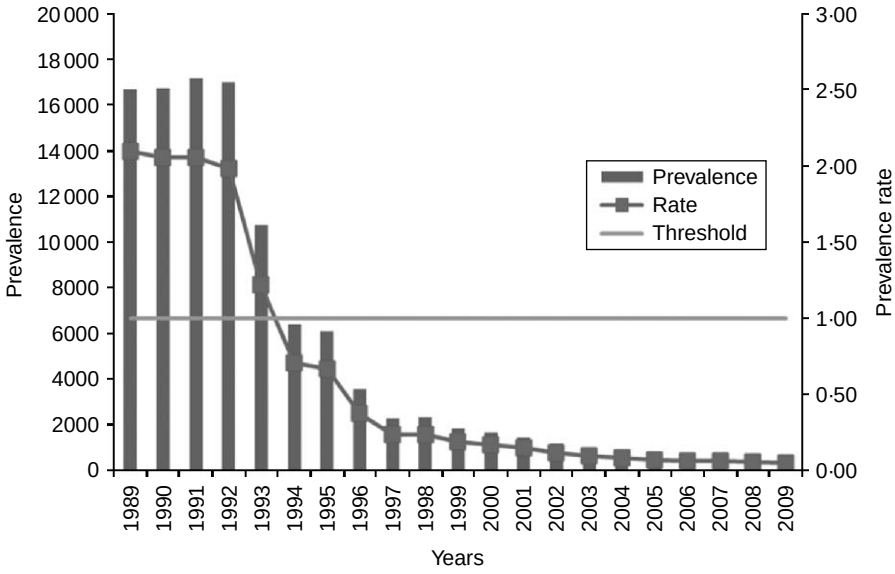

Figure 1. Registered prevalence of leprosy and rate (per 10 000 of population) per year in México. 1989–2009. Threshold is the 1 per 10 000 defined as 'elimination as a public health problem' by WHO.

With regard to age, the pattern was similar in each time period, with rates increasing to a peak in the 60–79 age group, followed by a decline in the oldest age group (Figure 3).

Leprosy is increasingly uncommon among the young in Mexico, with 183, 88 and 36 cases among individuals less than 20 years old in the 1996–2000, 2001–2005 and 2006–2009 periods respectively. The comparable figures were 578, 419 and 343 for individuals 60–79

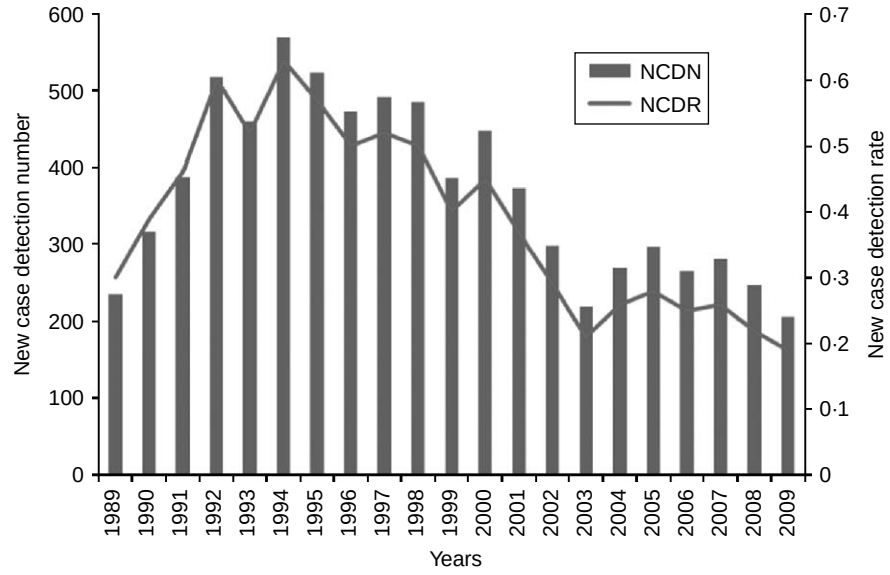

Figure 2. Number of annual new registered cases (NCDN) and new case detection rates per 100,000 of population (NCDR) in México over time. 1989–2009.

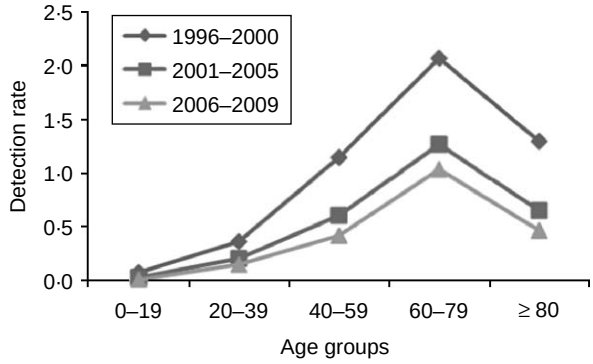

Figure 3. New case detection rates (per 100,000) stratified by age group and year group.

years, and 51, 37 and 26 for individuals over age 80. The case detection numbers thus fell by 80% for ages below 20, but by only 41% for individuals over age 60.

ANALYSES BY STATE

Mexico's 32 states are shown in the map in Figure 4, with shading representing their low, intermediate or high prevalence status. The high prevalence states are all on the west coast, the low states are clustered in the south-east, and the intermediate states mainly in the north.

Table 1 shows a breakdown of the new cases by sex, classification and time period separately for states classified as with low, intermediate or high leprosy prevalence. There is a predominance of males over females in each state group in all time periods. In all state groups the proportions of males increased slightly from the 1996–2000 to 2001–2005 year group and then declined to the 2006–2009 year group.

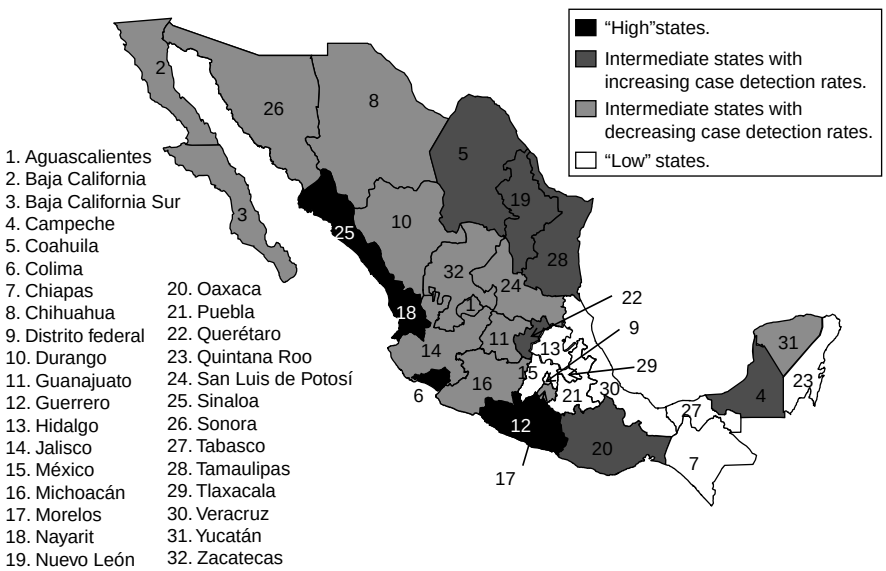

Figure 4. 'High', 'Low', 'Intermediate increasing' and 'Intermediate decreasing' states.

Table 1. Proportion and number of multibacillary (MB) leprosy cases among males (M) and females (F) in 'high', 'intermediate' and 'low states' over time

		HS		IS		LS	
Year Groups	Sex	MB (%)	Total	MB (%)	Total	MB (%)	Total
1996–2000	M	403 (*63*)	637	509 (*76*)	666	40 (*89*)	45
	F	207 (*45*)	460	257 (*61*)	422	22 (*76*)	29
2001–2005	M	297 (*80*)	371	377 (*78*)	485	27 (*93*)	29
	F	129 (*55*)	235	188 (*66*)	286	9 (*69*)	13
2006–2009	M	194 (*85*)	227	279 (*81*)	345	17 (*68*)	25
	F	107 (*64*)	166	149 (*69*)	215	9 (*69*)	13

Several broad trends are evident concerning classification: higher proportions of MB among males compared to females, increase in the proportion of MB among both males and females over time, and higher proportion of MB among both males and females in 'low' states compared to 'high' states. The only exception is among males in the 'low' states in the last time period.

The age patterns were broadly similar in the low, intermediate and high states, with peak rates in the 60–79 age group. Examination of individual case histories by age was revealing. Only two cases under 19 years old were diagnosed in LS throughout our study period. They were diagnosed at 15 and 18 years of age in Puebla and Veracruz in 1996 and 2006 respectively. The more recent one was born in a HS (Sinaloa) and had a history of household contact with leprosy. The place of birth of the other case was unknown. Both were males, with MB disease. In the 2006–2009 period only seven cases under 39 years old were registered in all the low states. Two were born in a HS (Sinaloa) and one in an IS (Michoacán). Of these seven cases, five were PB and two were MB. All of them were males and all but one had histories of household contact with known leprosy cases. Only one of these cases was identified through active case detection.

Figure 4 shows the intermediate level states, according to whether their case detection rates increased or decreased over the period of this study. Six states were classified as increasing. Three of the six were in the northeast of the country, contiguous to the USA.

Discussion

The prevalence of leprosy in Mexico has declined dramatically during the past 20 years. The decline was especially great from 1992 to 1994, shortly after the introduction of MDT (which was introduced into six states in 1990, and nationally by the end of 1991). The coverage (proportion of cases on short course MDT regimens) increased from 36% to 77% from 1991 to 1995.[14] The rapid decline in prevalence reflects cleaning of the registers (discharging cases no longer in need of treatment) which began in 1989 as well as discharge of accumulated prevalent cases after completion of their MDT regimens. After 1995, newly detected case numbers more closely balanced the numbers of cases released from MDT, producing a steady declining trend in prevalence rate.

It is recognised that reported prevalence is not a sensitive indicator of transmission. It is dependent on case ascertainment and duration of treatment, and might not include PB cases

diagnosed early in the year, let alone cases self-healed prior to diagnosis. In addition there is typically a delay of several years between infection and clinical disease manifestation. For these reasons, it is preferable to emphasize incidence or case detection in evaluating leprosy trends.[15,16]

The NCDR is not an exact measure of incidence, as it relies on self-reporting of cases and depends upon case finding measures. Inevitably, some cases will remain undetected, not reporting to health services due to stigma or lack of access. The observed trend in NCDRs over time in Mexico is complex. The initial rise, to 1994, is likely to reflect increased case finding activity associated with the introduction of MDT and the WHO elimination initiative. An appreciable proportion of the cases detected prior to 1994 may have been 'backlog' prevalent cases, which had arisen in previous years but had not been detected.

After 1994, the NCDR shows a slow decline, due to a combination of the exhaustion of backlog cases and a true decline in incidence. Operational factors may also have played a role in this decline. The abrupt fall in 1999 may have been influenced by changes of NLCP coordinators and their teams in every state in that year. This meant a temporary disturbance in the running of the NLCP as mentioned in several evaluation reports.[4] From 2000 to 2003 the NCDR declined and from 2004 it has remained more stable. In 2002 a new quality surveillance plan was introduced,[4] improving the quality of assistance and reporting services, but its effects are not obvious in the national data.

The earliest accurate data to show declining case detection rates came from Norway, which had a national register of leprosy cases from 1850 to 1950.[17] Similar trends have since been described in several other countries. Despite the differences between studies in methods and analysis, findings from study areas with declining case detection rates show common trends which suggest general epidemiological patterns. A shift towards older age groups in onset of disease, and an increase in multibacillary cases and in male predominance, are common findings in countries with declining leprosy, and may be extrapolated to other populations.[18]

FACTORS AFFECTING AGE SPECIFIC NCDR

There was a *relative* increase in the proportion of cases in older age groups, in Mexico, up to 80 years, in all time periods, with the highest rates in the 60–79 age group as shown in Figure 3. This age pattern in new cases is consistent with what has been found in other studies in low incidence settings with declining leprosy. It is also consistent with the increase of MB cases associated with longer incubation periods.[19] The increasing proportion of older cases can mean either that these individuals were infected later in life or that, if infected earlier, had long incubation periods. Both mechanisms can be involved.[18] It may be that older cases are more likely to report to health facilities than younger cases, increasing the possibility of detecting leprosy among them, but we have no direct evidence to support it.

The NCDR in children provides an indicator of recent transmission in the community. When transmission declines successive cohorts of children have less and less exposure to infection, resulting in fewer new cases. Our findings are consistent with this. The NCDR declined to very low levels in the youngest groups over our study period. We are not aware of changes in the case finding practices which could explain this pattern, and thus it probably reflects declining transmission.

We note a predominance of males over females among leprosy cases in Mexico, consistent with the general male excess in leprosy disease in most populations reported in

literature.[19] It might be interpreted as males having a higher susceptibility either to infection or to disease once being infected, but differences in sex ratios in low incidence settings can also be influenced by bias in case ascertainment. Social stigma may be a cause of low self-reporting of females in some settings and difficulties in proper examination of female patients can also reduce ascertainment among them. In addition, some sociological patterns can contribute to true differences in incidence between males and females. In certain societies female confinement to the house, or to certain employments or activities, may lessen their risk of exposure, while males tend to circulate more in the community and thus have more chance to have contact with infectious sources. The extent to which these various factors might be applicable to Mexico is unclear.

Concerning classification, the proportion of MB cases has been found to increase in several populations concomitant with declining incidence.[18] Despite an initial decline from 1996 to 1998 (perhaps associated with active case finding activities) the proportion of MB cases has shown an increasing trend over time in Mexico.

If MDT affects the transmission of infection it should reduce the NCDR of PB cases first because of their shorter incubation periods. Although our findings with reference to classification could be the result of MDT and decline in transmission we lack figures from earlier years to see whether the number and proportion of PB was already declining since or prior to the introduction of MDT.

Some authors have speculated that as transmission decreases only the most susceptible individuals become infected in the community at large (perhaps males), and develop MB leprosy due to their relatively low resistance.[20] It is difficult to distinguish such a mechanism from an increase in MB attributable to declining transmission and a consequent increase in long incubation period cases over time.

In Mexico the highest NCDRs have been found among states located on the west coast. States located along the west coast historically accounted for most of the cases registered in the first national census in 1927.[11,21] Furthermore, data from the beginnings of the NLCP showed similar findings in the 1960 s.[21] Some authors have suggested this may be a consequence of an historic endemic focus derived from trade routes with Philippines, that brought new cases into the area.[8–11] We are aware that this might not be enough to justify its sustained presence, and influences of the environment, control measures and case reporting in the area should also be considered. This western area has always been a priority for the NLCP. Intensification of case finding measures and a high index of suspicion among health workers and population might have helped sustain high case detection numbers compared to other areas. Despite having the highest NCDRs over time, the high case detection states have all shown a significant decline in NCDR throughout our study period. Findings in age, sex and type among new cases also support a declining incidence trend.

Low case detection states (LS) were found in the central-south and south west of the country. A predominance of males, MB disease and older average age were found according to what would be expected associated with their low incidence. Exceptional findings of a decrease of MB and male proportions in the last time period should not be over interpreted considering the small numbers of cases in those years. Of the two cases under 19 years of age found in LS one of them was born in Sinaloa a ‘high’ state, and from seven cases under age 39 detected in LS in the last period of time, two were born in Sinaloa. This would suggest that a substantial proportion of young cases in the low case-detection states have been infected elsewhere, giving a misleading impression of transmission in the ‘low’ states. The apparent low proportion of MB among these patients is based on small numbers. They all had a history

of household contact with leprosy, which is consistent with the evidence suggesting that domestic transmission plays an increasing role in settings with declining incidence.[19] The low numbers of young patients in these states suggest very low transmission, although case detection of young cases could be influenced by low case finding measures and low awareness in the population and among health workers in the area, added to the diagnostic difficulties of cases in these age groups. To assess this, the NLCP introduced special guidelines for LS in 2004 to monitor the interruption of transmission in these areas.

IS were classified by their NCDR trends into 'increasing' (IIS) and 'decreasing' (IDS) states. Although this classification is crude, being based upon small numbers rather than statistical significance, it is interesting to note clustering of IIS in the north east part of the country bordering with the state of Texas in USA. It may be relevant that Texas is a leprosy endemic focus[22] and that there is good evidence that some of the leprosy in Texas is attributable to transmission of *M. leprae* from nine-banded armadillos.[6] This species of armadillo is widespread in Mexico, but there are no convincing data on whether Mexican armadillos harbour *M. leprae*. Further studies will need to address the role of this animal reservoir and the possibility of increasing NCDR in some Mexican states.[6,7]

The epidemiology of leprosy is known to differ significantly among different geographic regions.[3,17,20] Clustering of cases seems to be particularly obvious in areas of low prevalence.[19] It is not always clear to what extent the geographic distribution of cases is a reflection of particular environmental characteristics, differences in populations or different case finding activities between areas. Genetic and cultural differences have also been suggested as having some influence on population susceptibility and there is evidence in the literature that leprosy is more frequent in rural than urban areas.[17,19–20] We are unable to explain leprosy's geographic distribution in Mexico on the basis of the data available in this study. Further studies on individual cases and environmental conditions surrounding them will be needed to clarify these issues.

Conclusions and Recommendations

Leprosy has declined substantially in Mexico in recent decades, and the decline continues. Control measures carried out by the NLCP have doubtless played an important role in this decline. Improvements in socioeconomic conditions, and BCG vaccination (widely used in Mexico since the 1970 s, with reported coverage in infants over 67% since 1990 and over 98% since 2000), should also be considered, though their relative contributions to leprosy's decline are difficult to assess.[23]

Several of our findings suggest issues which deserve further investigations. Among these is the dramatic heterogeneity in leprosy between different areas of Mexico. The extent to which this may be attributable to historical, environmental, socio-economic or other factors remains unclear. Analyses of data including detailed socio-economic information, rural versus urban location, and histories of family contacts may provide valuable insights. The potential role of the armadillo in leprosy in Mexico raises particular issues. There is good evidence that *M. leprae* infection is spreading in the armadillo population in southern USA, and that it may be responsible for an increasing number of autochthonous cases.[6,7] Whether this is true in Mexico, and if so the geographic extent of armadillo-related zoonotic infections is unclear but it is an issue which the Mexican programme should monitor.

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