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Koba, A; Ishii, N; Mori, S; Fine, PE (2009) The decline of leprosy in Japan: patterns and trends 1964-2008. Leprosy review, 80 (4). pp. 432-40. ISSN 0305-7518

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The decline of leprosy in Japan: patterns and trends 1964–2008

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Accepted for publication 27 November 2009

Summary

Objective Our purpose was to elucidate the patterns and trends of autochthonous leprosy in Japan from 1964 to 2008, to compare them with the findings from other studies of leprosy in decline, and to determine whether *M. leprae* transmission persists in Japan.

Design Data on registered leprosy cases in Japan in the period 1964–2008 were analysed with reference to trends in case detection, geographical distribution, age at diagnosis, sex, classification, family history and broad correlation with socio-economic conditions.

Results A consistent decline in leprosy case detection was observed in all areas of the country over the period 1964–2008. Highest incidence was consistently in Okinawa, the southernmost part of Japan. Autochthonous leprosy has not been reported in anyone born in Japan since 1980. Increasing average age and a shift towards lower latitudes were demonstrated throughout the period. There was an inverse association between regional measures of wealth and leprosy incidence.

Conclusions Leprosy has declined throughout the past century in Japan. Autochthonous transmission has probably stopped in mainland Japan, but may still occur at a low level in Okinawa, the country's southernmost region. Analyses of data on autochthonous cases revealed patterns similar to those reported in other countries with declining leprosy. Detailed comparisons between countries with very low leprosy incidence may help us to better understand the epidemiology of leprosy.

Introduction

Despite much discussion of leprosy elimination in recent years, the disease does not appear to have disappeared totally from any previously endemic countries in recent decades, though in many populations there have been dramatic declines in incidence. Several trends have been reported in settings with a declining incidence rate of leprosy. Observations of leprosy

trends in Norway, Portugal, China and USA have all shown increases in average age, in male-to-female sex ratio, and in proportion multibacillary among new cases.^{1–5} These patterns probably reflect an increase in the proportion of long incubation period cases as the disease disappears. Long incubation periods are associated more with multibacillary than with paucibacillary disease, and multibacillary disease is associated with males.^{1,6}

Japan is currently experiencing the final stage of endemic leprosy, with less than five new Japanese patients reported each year since 2003. However, leprosy was once a major public health problem in Japan, with a prevalence of about 70 per 100,000 population in 1900.⁷ Starting in 1907, hospitalisation of leprosy patients was the main control strategy, and this was mandatory by law from 1931 until the law was abolished in 1996. Overall leprosy incidence among the Japanese decreased constantly throughout the 20th century.

This report elucidates the patterns and trends of autochthonous leprosy in Japan from 1964 to 2008, and compares them with findings from other countries where leprosy has declined to very low levels.

Materials and Methods

MATERIALS

Although leprosy is not a legally notifiable disease in Japan, clinicians who see leprosy patients are encouraged to report them to the Leprosy Research Centre where data on leprosy patients are collected and reported on a regular basis. Data used for analyses in the present study are from multiple sources. Data on patients in the period 1964–1992 were derived from published literature⁷ and data on patients from 1993 onwards were based on case reports submitted to the Leprosy Research Centre (provided by NI). Both are considered to encompass nearly all cases of leprosy in Japan although the possibility of over- or under-diagnosis or cases not brought to medical attention cannot be completely excluded. The information available includes year of diagnosis, place (prefecture) of birth and of registration (1964–2008), age at diagnosis, sex and family history (1981–2008), and WHO classification (pauci/multibacillary) (1993–2008).

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

METHODS

The proportion of ‘foreign-born’ has increased greatly among newly registered leprosy patients in recent years in Japan, as observed in several other low-endemic countries.⁸ In the period 2001–2007, out of 73 new cases reported in Japan, 54 (74%) were foreign-born.⁹ In this report, all data and analyses were restricted to Japanese patients assumed to have contracted *M. leprae* infection within Japan. The study period was defined to cover 1964–2008 for the analysis by geographical distribution, 1981–2008 for analyses by age distribution, sex ratio and family history, and 1993–2008 for analyses by classification, as determined by data availability.

For analyses by geographical distribution, Japan was divided into eight regions: Hokkaido, Tohoku, Kanto, Chubu, Kinki, Chushikoku, Kyushu, Okinawa (Figure 1).

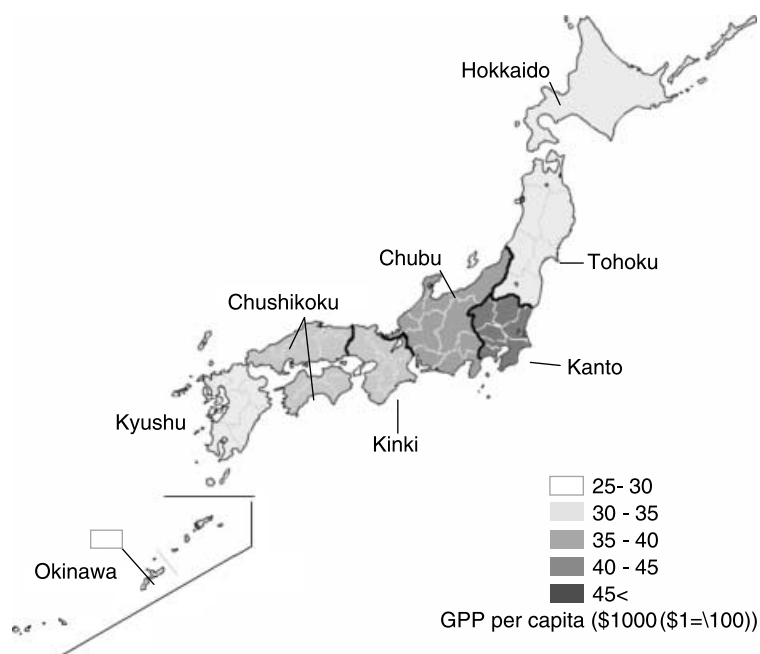


Figure 1. Japan, showing its eight regions, with shading to show Gross Prefectural Product per capita in 2006. Note shading for Okinawa in inset rectangle.

As the patterns appeared to differ between Okinawa, the southernmost part, and the rest of Japan, referred to as mainland Japan, the analyses were conducted separately for these regions, where appropriate.

Unless otherwise specified, 'incidence' in the present study refers to case detection rate per 100,000 population per year. Annual incidence within each region was calculated as the number of new cases per decade divided by the population within each region at the median point of the decade, divided by 10 (or by five for the period 2004–2008) to give an average per annum incidence rate.

For the analysis by age, the 28-year study period was split in half and the patterns by age at diagnosis were compared between the former and latter 14 years. Because birth decade but not exact age at diagnosis was available for cases reported 1981–1992, the ages at diagnosis of these cases were estimated on the assumption that individuals were born in the central year of their birth decade.

Sex ratio is expressed as ratio of males-to-females.

The simplified WHO system – i.e. paucibacillary vs. multibacillary – was used for the analysis by classification.

Results

OVERALL INCIDENCE

Table 1 shows the number of newly registered autochthonous leprosy patients during each decade and the annual incidence rate per 100,000 population in the whole country.

Table 1. Overall annual incidence (case detection) numbers and rates of autochthonous leprosy in Japan, 1964–2008

Period	No. of patients	Annual incidence*
1964–1973	1661	0.16
1974–1983	572	0.05
1984–1993	222	0.02
1994–2003	59	0.005
2004–2008	9	0.0007

* Per 100,000 population.

From 1964 through to 1973, annual incidence of leprosy was greater than 0.1 per 100,000. A continuous decline was observed throughout the following years until it became less than 0.001 per 100,000 in the period 2004–2008.

GEOGRAPHIC DISTRIBUTION

Table 2 and Figure 2 show the trend in annual incidence rate of leprosy in different regions of Japan.

There is a clear inverse correlation with latitude. Throughout the study period, the highest incidence was observed in Okinawa region, which consists of an archipelago in the southernmost part of Japan. During 1964–1973, the annual incidence in Okinawa exceeded 10 per 100,000, while that of the six northern regions was below 0.1 per 100,000. There have been no autochthonous cases recognised in the northern region of Hokkaido since 1987. The region with the highest incidence during 2004–2008 was still Okinawa, although the annual incidence had fallen from 11.2 to 0.07 per 100,000 over the 40 years since 1964.

AGE DISTRIBUTION

The numbers and relative frequency of newly registered patients are shown by age groups in Figures 3A and 3B.

Both in the Okinawa region and on mainland Japan, there was a substantial rise over time in the average age at diagnosis. In the period 1981–1994, the average ages at diagnosis in Okinawa and in mainland Japan were 50.8 and 61.3 years of age respectively, increasing to 58.5 and 71.5 years of age in the period 1995–2008.

Table 2. Annual incidence (case detection) rates of autochthonous leprosy per 100,000 in Japan, 1964–2008, by region. Regions are ordered north (left) to south (right). See Figure 1

Period	Hokkaido	Tohoku	Kanto	Chubu	Kinki	Chushikoku	Kyushu	Okinawa
1964–1973	0.006	0.041	0.018	0.058	0.045	0.062	0.208	11.19
1974–1983	0.000	0.016	0.005	0.013	0.011	0.017	0.062	3.53
1984–1993	0.000	0.007	0.002	0.004	0.006	0.016	0.023	1.13
1994–2003	0.000	0.002	0.001	0.001	0.001	0.003	0.005	0.27
2004–2008	0.000	0.000	0.000	0.000	0.001	0.002	0.003	0.07

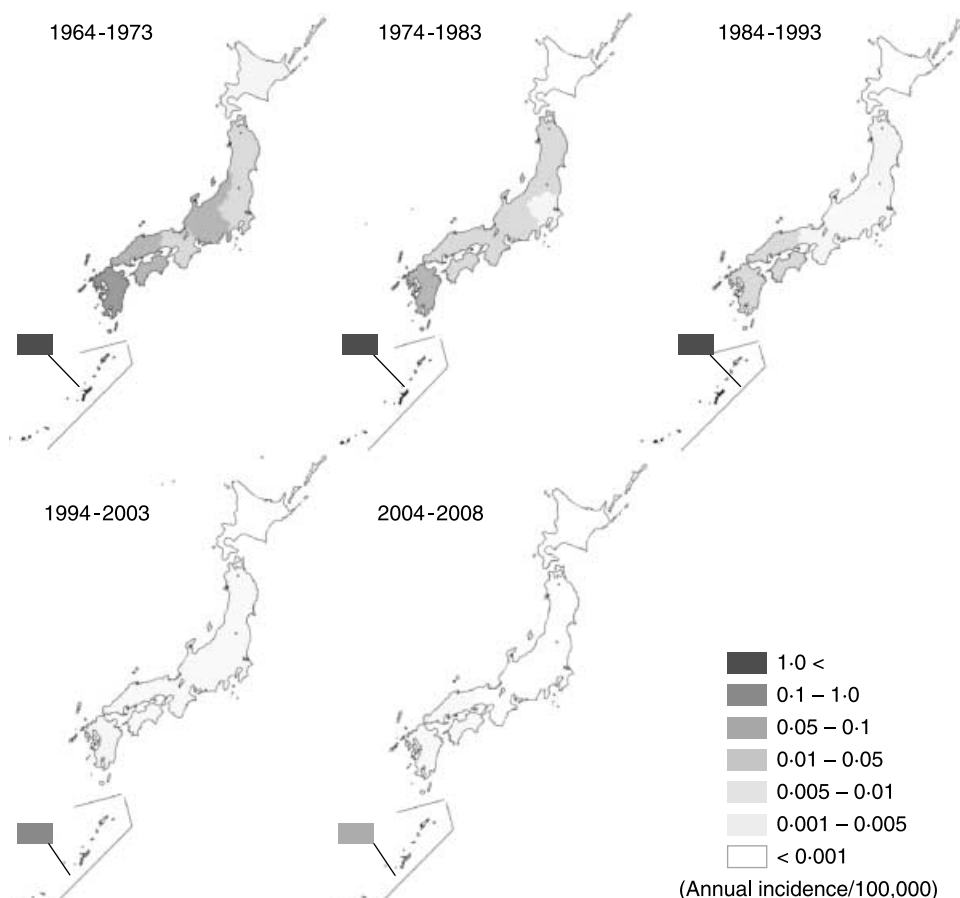


Figure 2. Annual incidence rates of leprosy in Japan by region and over time. Note shading for Okinawa in inset rectangle.

SEX RATIO

A slight increase in male-to-female sex ratio was observed from 1.47 in 1964–1980 to 1.54 in 1985–1994 and to 1.57 in 1996–2008 (Table 3).

When looking at sex ratio separately for Okinawa and mainland Japan in the period 1981–2008, the male-to-female sex ratio increased from 1.56 in the first half of the period to 2.18 in the latter half of the period in Okinawa, whereas it decreased from 1.51 to 1.00 in mainland Japan. Given the small numbers this difference was not statistically significant.

CLASSIFICATION

In the period 1993–2008, 58% of newly registered leprosy cases in Okinawa and 81% of newly registered cases in mainland Japan were multibacillary. The average age at diagnosis of Okinawan multibacillary cases was 61.7 years and that of mainland Japan was 76.0 years, whereas for paucibacillary cases they were 51.9 years and 59.5 years respectively.

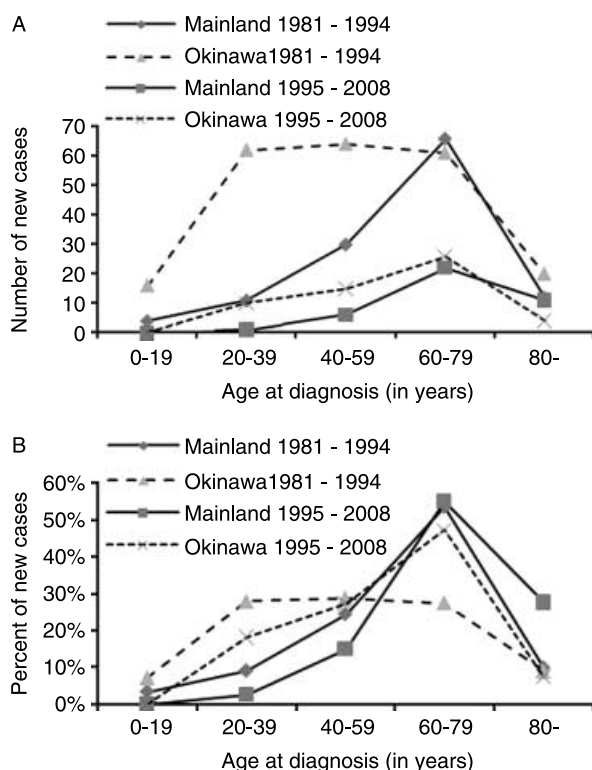


Figure 3. The numbers (A) and relative frequencies (B) of autochthonous leprosy cases by age, in mainland Japan and Okinawa, in the periods 1981–1994 and 1995–2008.

FAMILY HISTORY

Cases with a record of positive family history accounted for 24%, 22% and 11% in the period of 1964–1983, 1981–1994 and 1995–2008, respectively.

SOCIO-ECONOMIC FACTORS

There was no recorded marker among the data for socio-economic status of the cases such as occupation or income. On a regional scale, Okinawa had the lowest Gross Prefectural Product (GPP) of all 47 prefectures in Japan (2006) (Figure 1).

Discussion

Over the period 1964–2008, there was a continuous downward trend in reported autochthonous cases of leprosy in Japan. The decline appears to have started earlier, or to have been much more rapid, in northern compared to southern Japan. The epidemiological pattern in Okinawa, the southernmost part of Japan consisting of 49 inhabited islands and numerous uninhabited islets, has been quite different from that in the rest of Japan. Prominent among the differences is the age distribution of cases, with consistently older average ages at

Table 3. Male to female sex ratios and their 95% confidence interval (CI)

Period	_@	Total	Male	Female	Sex ratio* (95%CI)
1964–1980	Total	1185	705	480	1.47 (1.31, 1.65)
1981–1994	Okinawa	223	136	87	1.56 (1.20, 2.07)
	Mainland	123	74	49	1.51 (1.06, 2.21)
1995–2008	Total	346	210	136	1.54 (1.25, 1.93)
	Okinawa	35	24	11	2.18 (1.14, 5.23)
	Mainland	24	12	12	1.00 (0.43, 2.33)
_@	Total	59	36	23	1.57 (0.94, 2.77)

* Male-to-female sex ratio.

diagnosis in mainland Japan compared to Okinawa. The peak age group of Okinawan patients in 1964 was teenagers, accounting for nearly 40% of all cases,¹⁰ so the trend of increasing age is rapid in Okinawa. Another interesting difference was seen in the pattern of classification. In mainland Japan, multibacillary cases accounted for 81% in the period 1993–2008, whereas in Okinawa only 58% of cases were multibacillary in the same period. Considering increasing age and dominance of multibacillary cases as markers of leprosy in decline, it appears that Okinawa is several decades behind the rest of Japan in terms of leprosy's disappearance. There has been a continued fall in incidence in Okinawa since the turn of this century, with less than five new cases occurring each year. An increase in average age has repeatedly been observed in association with falling incidence of leprosy.^{1–5} It is likely that this reflects an increase in the proportion of cases with longer incubation periods, and is consistent with the increase in the proportion multibacillary among newly diagnosed cases. Evidence for continued *M. leprae* transmission may also be inferred from the years of birth of recently diagnosed patients. Since 1993, there have been six new patients who were born during the 1970s in Okinawa. In contrast, on mainland Japan, all new patients diagnosed since 1993 were born before 1940, with three exceptions: one born in the 1970 who had close relatives in Okinawa, and two from neighbouring Kyushu, born in the 1940s and 1950s. Precise dating of infection transmission is not possible, because of the long incubation period of clinical leprosy, but these findings suggest that the transmission of *M. leprae* ceased in mainland Japan several decades ago, whereas it continued to more recent times and might still be going on, though at a very low level, in Okinawa.

There was some evidence for an increase in proportion among male cases in Okinawa though not for the small number of cases in the mainland. This is at least consistent with observations elsewhere, where the trend has been associated with increases in multibacillary disease, for which males appear to have a predilection.^{1,6}

Our data on family contacts are probably not complete. Reports from European countries suggest that family contacts may play an increasingly important role as a transmission route as leprosy disappears from a population. In both Norway and the UK, the last autochthonous cases were children of known leprosy cases.^{11,12} In Japan, the last autochthonous case in Hokkaido, the northernmost island of Japan, reported in 1987 was a brother of a leprosy patient.¹³ These episodes at least suggest that domestic transmission might play a crucial role in communities with extremely low risk of infection.

Okinawa has had the highest incidence of leprosy in all of Japan since the first national survey in 1900. In mainland Japan, a continuous decline of prevalence started

before 1900, whereas leprosy prevalence in Okinawa did not turn downward until after the Second World War.¹⁰ There are several possible explanations for the delay of improvement in Okinawa. In mainland Japan, five public leprosaria were established in 1909. In contrast, due to strong protest from the residents, there was no leprosarium to serve the Okinawan population until 1938. Thus patients remained in the community without effective treatment approximately 30 years longer in Okinawa than in mainland Japan.¹⁰ Saikawa investigated the association between leprosy incidence and socio-economic factors such as GNP, personal expenditure on housing and number of people per household in Okinawa and Taiwan, and concluded that improvement in socio-economic conditions has made a great contribution to reducing leprosy in the community.¹⁴ We show data on the average personal income in 2006 based on Gross Prefectural Product (GPP) within eight regions of the country. Although GPP is not a direct measure of wealth at individual level, as it includes corporate income, it reflects wealth level at a regional level and is likely to correlate with standards of hygiene and sanitation. Comparing Figure 1 with Figure 2, we see that Okinawa, with the highest leprosy incidence had the lowest in GPP per capita of the eight regions; and the Kanto-area, the wealthiest part of the country, was most successful in reducing the incidence relatively early compared with adjacent regions. Both of these observations are consistent with an association between leprosy incidence and socio-economic circumstances, as has been observed in many countries.⁶

Our data suggest that the decline in leprosy incidence started earliest in the northern part of Japan. This is consistent with patterns seen elsewhere in the northern hemisphere. Autochthonous cases were reported widely in northern Europe a century ago, but are now reported only in Southern Europe, around the Mediterranean. This decline is likely to reflect a combination of socio-economic and ecological factors.

We have analysed Japanese leprosy data from 1964–2008 and observed trends that are similar to those in other countries with declining incidence, such as increase in age and in proportion of males among cases, and a shift towards lower latitudes. The similarity in patterns between different countries with declining leprosy indicates that they reflect fundamental properties of the natural history of this disease. Detailed comparisons between such countries help us to better understand the epidemiology of leprosy.

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