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Geographic Determinants of Leprosy in Karonga District, Northern Malawi

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Sterne J A C (London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK), Pönnighaus J M, Fine P E M and Malema S S. Geographic determinants of leprosy in Karonga District, Northern Malawi. *International Journal of Epidemiology* 1995; **24:** 1211–1222.

Background. Geographical differences in leprosy risk are not understood, but may provide clues about the natural history of the disease. We report an analysis of the geographical distribution of leprosy in Karonga District, a rural area of Northern Malawi, between 1979 and 1989.

Methods. Cohort study of the incidence of leprosy based on two total population surveys. Area of residence was determined using aerial photographs, which allowed identification of households, as well as location of roads, rivers and the lake shore.

Results. Incidence rates were between two and three times higher in the north compared to the south of the district, and lowest in the semi-urban district capital. The most obvious environmental difference between these regions is the north's higher rainfall and more fertile soil. There was no overall association between leprosy incidence and population density, although highest rates were observed in the least densely populated areas. Looking at the entire district, incidence rates increased with increasing distance from a main road, but declined with increasing distance from a river or from the shore of Lake Malawi. The negative association with proximity to rivers may reflect the larger number of rivers in the north of the district. Apparent differences in incidence rates between groups speaking different languages reflected confounding by area of residence.

Conclusions. There is a marked variation, not explained by socioeconomic or cultural factors, in the incidence of leprosy within Karonga District. Our results are consistent with a theme in the literature associating the environment, particularly proximity to water, with leprosy.

Keywords: leprosy, ecological study, geographical distribution, environment

Peculiarities in the geographical distribution of leprosy have long been recognized, but are still not understood. Though once endemic as far north as the Arctic Circle, the disease disappeared progressively from northern Europe and North America over recent centuries and is now restricted to warmer parts of the globe. Even within endemic regions, leprosy is not uniformly distributed. Observations of local clustering have led to hypotheses that the geographical distribution of leprosy is determined by genetic factors, by patterns of social contact and/or by environmental factors such as elevation, humidity, rainfall, or temperature.[1,2]

Associations with water are a recurrent theme in the literature, from folklore that leprosy is somehow related to fish,[3] to evidence of broad associations between leprosy and rainfall in Africa,[4] to detailed studies showing higher leprosy risks along the coastal areas of Norway compared to inland populations.[5] The association with water or humidity has been linked to evidence that *Mycobacterium leprae* survives longer outside the body in humid than in dry atmospheres.[6]

Evidence that *M. leprae* may be transmitted by 'intimate contact', or by the respiratory route from nasal lesions of multibacillary patients, has led to analogies with tuberculosis, and expectations that leprosy might be associated with crowded environments.[7] Alternatively, there are indications that leprosy is more common in rural than in urban settings.[8] This may be due to conditions favouring persistence of the organism, and therefore transmission, or to immunological interactions between leprosy and other mycobacterial infections (*M. tuberculosis* or non-tuberculous mycobacteria) which are in turn associated with certain environmental characteristics. It has also been suggested that exposure to various 'environmental mycobacteria' may contribute to the substantial geographic variation in the efficacy of BCG against both leprosy and tuberculosis.[9,10]

Interpretation of the geographical distribution of leprosy is particularly difficult because so many of the

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potentially relevant environmental and socioeconomic factors are associated with one another. Thus climatic, social and economic factors are inevitably linked and their analysis requires detailed data relating to the several factors together. We report here an analysis of the geographic distribution of leprosy based on extensive data collected in the LEPRA Evaluation Project (LEP), a total population study of the incidence of leprosy in Karonga District, a rural area of Northern Malawi, over the years 1979–1989.

SUBJECTS AND METHODS

Karonga District is bordered by Lake Malawi to the east, the escarpment of the Central African Plateau (which rises to over 2500 m) to the west, the Songwe river (which forms the border with Tanzania) to the north and by Rumphi District and the Henga valley to the south. The climate tends to be warm and wet from December to April, cool and dry from May to September and hot and dry from September to December. The main crops are maize, rice, cassava, bananas and cotton. The majority of the population live scattered along the lake shore and along the foothills of the Central African Plateau, though several thousand people live in relatively crowded conditions in and around Karonga, the district capital.

The data analysed here were derived during the course of two total population surveys, called 'LEP-1' (1979–1984) and 'LEP-2' (1986–1989). The second survey served to identify incident leprosy cases which had arisen since LEP-1, and as the recruitment phase of a vaccine trial.[11] The methods of these surveys have been described in detail elsewhere.[12,13] Fieldwork was carried out by teams which moved across the district. Examinations were performed by trained paramedical workers, and all individuals with lesions considered suspicious of leprosy were reviewed by a medical officer (usually JMP). Details of the processing of biopsies and the derivation of diagnostic certainty of leprosy for each suspect have been described previously.[14,15] In this study we restrict analyses to incident cases with the greatest diagnostic certainty ('narrow' group[15]).

Incidence rates of leprosy are based on individuals who were examined at least twice, with an interval of at least 30 days between examinations, and for whom the medical officer did not suspect leprosy at their initial examination. Individuals whose initial records indicated a hypopigmented spot or blemish at the site of a future leprosy lesion were excluded.[16] The follow-up period continued until the first of (a) an examination at which leprosy was suspected, (b) receipt of a vaccine during LEP-2, or (c) the last recorded examination prior to 1 January 1990.[16]

The main dwelling of each household was identified on aerial photographs (taken in 1978).[12] A location number was given to each household in terms of geographic coordinates within a grid system specially designed for the project and drawn on the photographs by cartographers at the Malawi Department of Surveys. The scale of the maps was 1:10 000, so that grid lines drawn 10 cm apart defined 1 km squares (although distances were distorted in the hills due to variations in distance between the land and the aircraft camera).

Interviewers carried these maps when they first visited households, in order to arrange a suitable date for the team to interview and examine all members of the household. A pin was stuck into the map identifying the location of the main dwelling and the distances to the nearest north-south and east-west grid lines were measured. Occasionally it proved difficult to identify an isolated household whose roof provided little contrast with the surrounding countryside. The majority of dwellings could be located to within 10 m.

For the purposes of the present study, the location of each individual was taken as that of his/her household during the first survey. Unusual 'households', such as traditional healer camps, or the local prison, whose residents are likely to change frequently, were excluded. Only individuals who were household members, renters, or employed workers or their relatives were included in the study. For individuals who were seen on more than one occasion, the location was taken for the household in which they were first identified.

The same rules were used to derive the household of individuals examined during the second survey. For individuals who were recorded as members of eligible households in both surveys, the distance between their households in the first and second surveys was calculated.

The routes of the main rivers and roads in the district, together with the lake shore, were coded manually from the aerial photographs. There are several perennial rivers, namely (from north to south) the Songwe (with several tributaries), Rufilya, North Rukuru, Nyungwe, Wovwe, Chonanga and Hara. Other rivers flow intermittently during the rainy season. The main road runs from the south to Karonga, the district capital and then north to Kaporo. There is also a road from Karonga to Mpata and on towards Chitipa district. A map of the district, showing these features is presented as Figure 1.

There is considerable variation in climate across the district. Mean annual rainfall ranges from >2400 mm in the north to <800 mm in the south.[17] Mean temperature decreases as altitude increases towards the

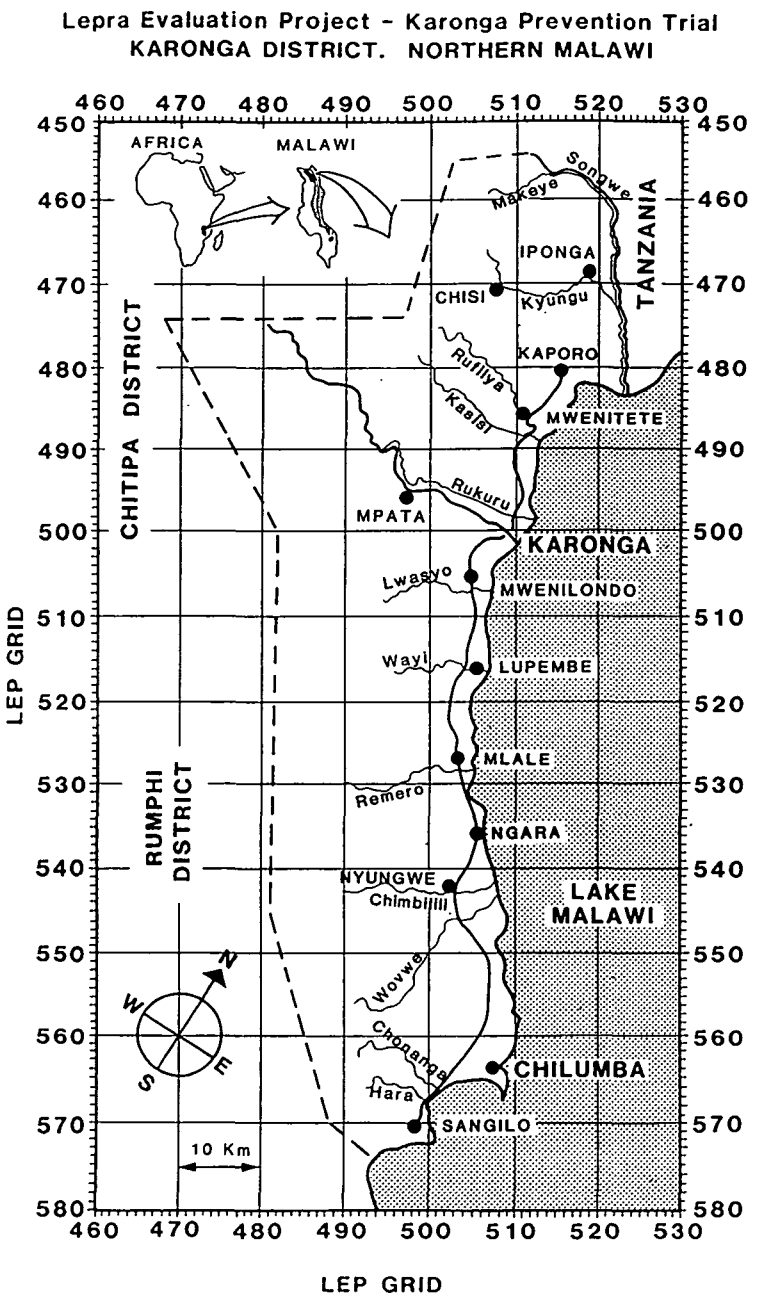

FIGURE 1 *Map of Karonga District, showing location within Malawi and names of major towns, villages and rivers*

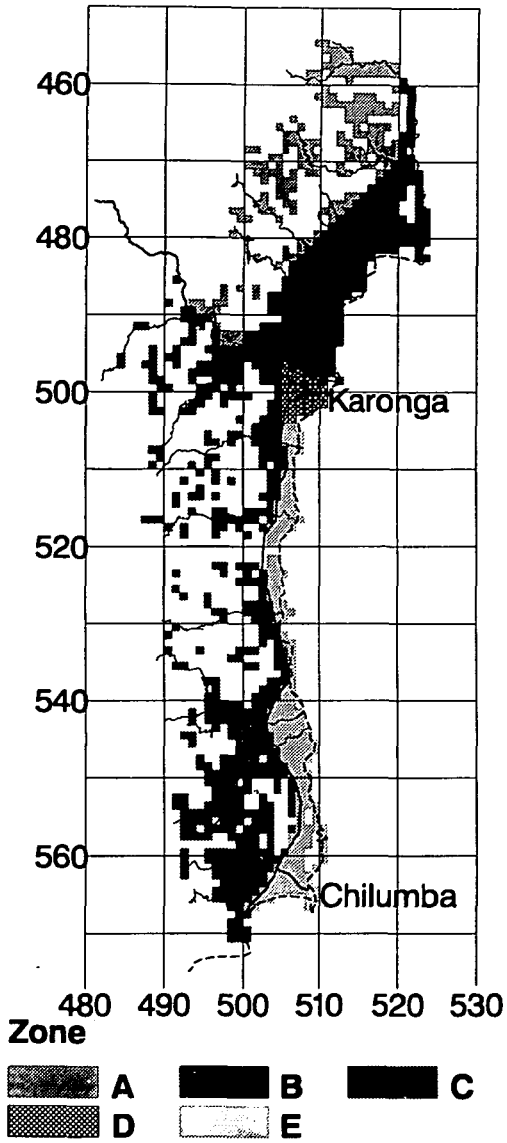

FIGURE 2 *Ecological zones within Karonga District as used in the analysis. Roads are denoted by thick continuous lines, rivers by thin continuous lines and the lake shore by a thick dashed line*

Central African Plateau, to the west. These climatic differences result in clear differences in mean normalized difference vegetation indices derived from remote sensing by satellites (FAO-ARTEMIS NOAA AVHRR Image Bank, Africa 1981–1991, FAO-Remote Sensing Centre, Via delle Terme di Caracalla, 00100 Rome, Italy). Five ecological 'zones' were defined on the basis of general ecological features. These represent the northern hills (zone A), the northern lake shore (zone B), the southern hills (zone C), the semi-urban area around the district capital (zone D) and the southern lake shore (zone E). Figure 2 shows the zone distribution of each square km in which at least one person in the incidence analysis was first examined, together with the rivers (thin continuous lines), roads (thick continuous lines) and lake shore (thick dotted line).

Zone A is a hilly area with several small streams which flow into the Makeye or Kyungu or reach the Songwe directly. Many households in this region grow two crops per year by irrigating patches of land along the streams. The area is cool enough to grow beans (which is unusual in the rest of Karonga District). Zone B comprises plains along the lake and the lower Songwe river. These plains are swampy during the rainy season so rice can be grown abundantly. In many places the soil retains enough moisture into the dry season for people to grow a second crop, in particular maize, groundnuts or tomatoes. Zone C is the area between the tar road south of Karonga and the steep escarpment to the west. Apart from two irrigation schemes (at Wovwe and Hara) the area tends to be dry and sandy with rainfall frequently below the amount required for a satisfactory crop (of maize). The area to the east of the tar road (zone E) is similar to C but less hilly, with easier access to the lake so that many people supplement their diet or income by fishing. Zone D is Karonga Town, with low density housing areas for wealthy businessmen and senior civil servants, and high density housing for the remainder of the population.

Different ethnic groups within the district can be distinguished on the basis of the first language of the household. The main group (around half the population) speak Kyangonde, and live mainly between Mlale and the Tanzanian border in the north. Tradition has it that they migrated from the north around the 17th century under their high-priest or king, the Kyungu. Three-quarters of the remaining population speak Tumbuka. They tend to live in the south of the District, but have also formed several villages in the north. They originate from the Henga valley in Rumphi district, to the south-west. A significant proportion of individuals in the north of the district and around the Wovwe and Hara irrigation projects speak languages of neighbouring districts, from where they or their forebears came. A variety of other languages are spoken, for example in the households of civil servants who have been posted to the district.

Data were checked and coded at project headquarters and entered on computers for ultimate analysis in London. Analyses reported here were carried out on an IBM RS/6000 using SAS, EGRET and STATA software.

To examine the effects of geographical factors on leprosy incidence, the district was divided into square km defined according to the grid shown on Figure 1. As age, sex and BCG scar status are known to be major risk factors for leprosy in this population,[16,18] the expected number of incident leprosy cases in each square km was calculated by multiplying the person-years in each age-sex-BCG specific stratum in the square by the corresponding leprosy incidence rate for the whole population. Dividing the observed by the expected number of cases gives an indirectly standardized rate ratio. To examine whether socioeconomic factors influence the geographic distribution of leprosy incidence, the expected number of cases in each square km was recalculated using strata defined also by duration of schooling and quality of housing, which have also been shown to be associated with leprosy incidence.[19]

Population density was derived by calculating the number of people seen in each square km during the first survey. The location of each individual was defined as that of the household in which he or she was first seen as a member (in preference to presence as a visitor, renter or employee). The minimum distance of each square km from the roads, rivers and lake shore (as shown on Figure 2) was calculated as follows. If (for instance) there was a road within the square km then the distance of the square from a road was 0 km. The distance of each other square km from a road was the distance from the centre of the square to the centre of the closest of the 0 km squares. Distances were grouped for ranges in which only small numbers of individuals lived.

To examine the association between population density and leprosy incidence, and the variation in incidence according to distance from roads, rivers, and the lake shore, we used Poisson regression, using the expected number of cases in each square km as the rate multiplier. Likelihood ratio (heterogeneity) tests were derived for the null hypothesis of no effect. Analyses were repeated after excluding individuals whose household in the second survey was more than 2 km from that in the first survey, and then separately for the north and south of the district. To examine whether geographical differences in leprosy incidence have a cultural or genetic origin, Poisson regression was also used to compare incidence rates in different language groups, controlling for the variation between ecological zones.

RESULTS

Of more than 110 000 individuals examined in LEP-1 and considered at that time to have no evidence of leprosy, 83 438 were later re-examined. Out of 80 477 who fit the eligibility criteria for the present study, 332 were later diagnosed as incident cases of leprosy with the highest level of diagnostic certainty.[15,16] Average follow-up time was approximately 5 years, giving 423 762 total person-years at risk.

TABLE 1 *Distance between first and second survey households for 79 542 individuals examined in an acceptable household in the second survey*

Distance (km)	Frequency	%
<1[a]	57 286	72.0
1–2[a]	6365	8.0
2–3	2602	3.3
3–4	1692	2.1
4–5	1040	1.3
5–10	3241	4.1
10–20	2970	3.7
20–50	2691	3.4
>50	1655	2.1
Totals	79 542	100.0

[a] 'Non-migrating' individuals.

In all, 79 542 individuals were examined in acceptable households in the second survey. Table 1 shows the distance between the first and second survey households for these individuals: 80% were recorded as still living within 2 km of their original household. These individuals were defined as 'non-migrating'. There were 255 incident cases of leprosy among these non-migrating individuals.

There were 1174 square km with at least one person at risk of incident leprosy. Figure 3 is a map of the geographic distribution of indirectly standardized leprosy incidence rate ratios in these squares. The shading is grouped to give approximately equal numbers of squares in each non-zero category (a rate ratio of 0 means that there were no incident leprosy cases in that square km). Although the use of standardized rate ratios corrects for population size in each area, it should be noted that large standardized rate ratios can occur when there is only a single case in a square where the expected number of cases was low because the population was small. The map thus attracts visual attention to such areas. Accepting this proviso, the map gives an overall impression of a north-south gradient of leprosy incidence, with greatest incidence in the area north of Karonga. There may also be an impression of higher leprosy incidence near to the rivers.

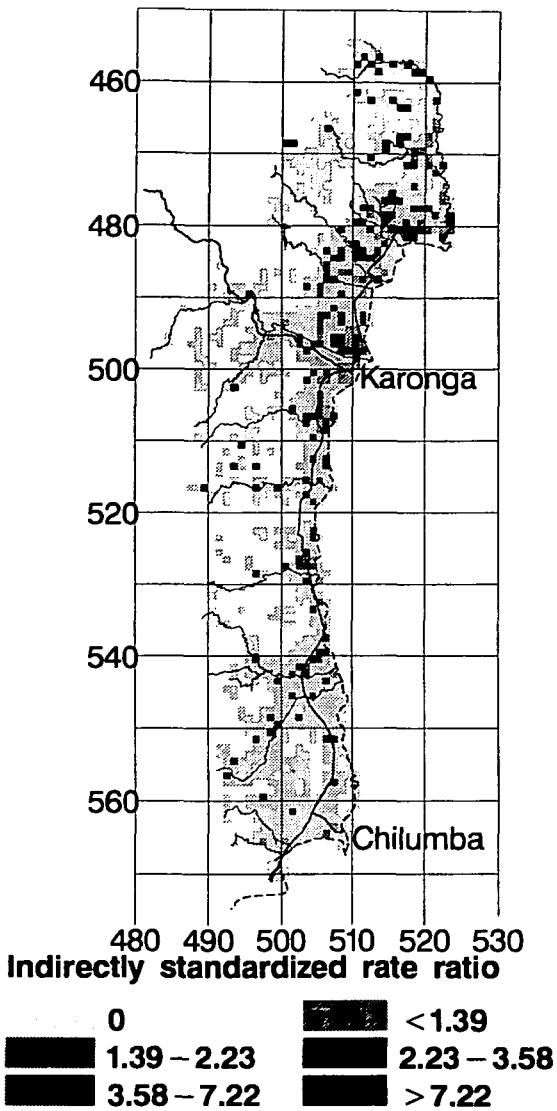

FIGURE 3 *Indirectly standardized (by age, sex and BCG scar) leprosy incidence rate ratios in each square km. Darkest squares have the highest incidence of leprosy*

Table 2 shows numbers of cases and person-years at risk (pyar) in each zone, with rate ratios of incident leprosy for zones B, C, D and E compared to zone A. These rate ratios are presented first controlling for the effects of age, sex and BCG, second after controlling additionally for the effects of duration of schooling and quality of housing and third after restricting the analysis to non-migrating individuals. Leprosy incidence was highest in zone A, intermediate in zone B and lowest in zones C, D and E. Although the differences were reduced slightly by controlling for schooling and housing, they remained highly statistically significant.

The distribution of population density is shown in Figure 4. The areas of greatest population density have the darkest shading: for example in Chilumba and Karonga, the two major towns in the district. Table 3 shows leprosy cases and pyar, with incidence rate ratios, in square km of decreasing population density, compared to square km with the highest population density. Estimates are shown first after controlling for the effects of age, sex and BCG, second after controlling additionally for the effects of schooling, housing and the other geographic variables (distance from roads, rivers and the lake shore), and third after restricting the analysis to non-migrating individuals. Although rates were higher in the least densely populated areas, there was no convincing evidence of an overall association with population density. On this basis, population density was ignored in subsequent analyses.

Tables 4, 5 and 6 show leprosy cases, pyar, and incidence rate ratios, in square km at increasing distances from roads, rivers and the lake shore. Estimates are shown after controlling for the effects of age, sex and BCG, after controlling additionally for the effects of schooling, housing and the other two geographic variables and after restricting the analysis to non-migrating individuals.

Looking at the entire district, leprosy incidence rates rose with increasing distance from roads: the association remained highly statistically significant after controlling for other variables (Table 4). In contrast, leprosy incidence rates fell with increasing distance from rivers (Table 5). The effect of increasing distance from the lake shore was less clear (Table 6). Although rates rose when controlled only for age, sex and BCG, they rose and then fell at larger distances after controlling for other variables. The observed associations between leprosy incidence and distance from roads or the lake shore did not change markedly when analyses were restricted to non-migrating individuals; however the apparent effect of distance from a river was increased.

Table 7 shows the effects of distance from roads, rivers and the lake shore, separately for zones A and B (north, high incidence) and zones C, D and E (south, low incidence). The effects appear to differ between the zones. The effect of distance from a road is evident in the north, but not the south. The generally moist nature of zones A and B meant that no square km was more than 5 km from a river. Although incidence rates were lower away from, than along, rivers in both the north

TABLE 2 *Leprosy cases and person-years at risk (pyar) in each zone, with estimated rate ratios for zones B to E compared to zone A*

Zone	Cases/pyar	Controlling for age, sex and BCG			Controlling additionally for schooling and housing			Restricting additionally to non-migrating individuals		
		Rate ratio	95% CI		Rate ratio	95% CI		Rate ratio	95% CI	
A	42/22 103	1			1			1		
B	175/176 625	0.60	0.43	0.83	0.65	0.46	0.91	0.69	0.47	1.01
C	52/106 798	0.27	0.18	0.40	0.31	0.20	0.46	0.34	0.21	0.53
D	19/39 558	0.27	0.16	0.46	0.31	0.18	0.53	0.27	0.14	0.52
E	44/78 673	0.31	0.20	0.48	0.37	0.24	0.57	0.36	0.22	0.59
		LRS[a] = 63.4 (4 d.f., $P < 0.001$)			LRS = 51.7 (4 d.f., $P < 0.001$)			LRS = 41.8 (4 d.f., $P < 0.001$)		

[a] Likelihood ratio statistic.

and the south, the patterns seemed less convincing, particularly in the north, than when the entire district was considered. The tendency for lowest incidence rates at greatest distance from the lake was present in both north and south, but was statistically significant only in the north.

The number of individuals whose language was recorded was 80 225, of whom 312 developed leprosy. Table 8 shows incidence rates and rate ratios for the different language groups. While there were substantial differences after controlling for age, sex and BCG scar status these disappeared almost completely after controlling additionally for ecological zone.

DISCUSSION

Geographic patterns of an infectious disease may reflect environmental factors which directly facilitate transmission of infection, or progression to disease, or the acquisition of protective immunity to either of these. Alternatively, they may reflect non-environmental factors such as socioeconomic conditions, behaviour, or nutritional status, each of which may vary within and between populations and thereby produce geographic variation in disease patterns.

Leprosy incidence is more than twice as high in the north, compared to the south of Karonga District. The most obvious environmental difference between these regions is the north's higher rainfall and more fertile soil. In the north, rates in zone B are markedly lower than zone A: the major differences between these areas are the lower temperature and greater elevation in zone A, which is also more remote. In the south, rates are similar between zones C and E, with slightly lower rates in the semi-urban area around the District capital. Although there were differences in incidence rates between language groups, these disappeared after controlling for ecological zone. This suggests that the geographical variation in leprosy incidence rates is explained by environmental, rather than cultural or genetic factors.

There was no clear evidence for an association between leprosy incidence and population density. It should be remembered that Karonga District is predominantly rural—the total population of zone D, which contains the district capital, was just over 12 000. Thus we are not able to compare rural with truly 'urban' areas; but in the context of this rural area, and with the exception of apparently high rates among the small number of individuals living in the least densely populated areas, we have found little evidence that the difference between sparsely and more densely populated areas is of importance for leprosy incidence.

The variation in leprosy incidence between zones was not explained by socioeconomic status as measured by duration of schooling and quality of housing, both of which have been shown to be related to leprosy incidence.[19] Differences in incidence between zones were slightly reduced after controlling for the effects of these variables (Table 2), but were still highly statistically significant.

Differences in socioeconomic status must be considered as an explanation for our finding of lowest incidence rates nearer main roads. However, there is still a clear association after controlling for the effects of schooling and housing. Given that living near a road is likely to lead to generally better living conditions, there is likely to be residual confounding between socioeconomic status and distance from a road even after controlling for the effects of schooling and housing. However the increase in leprosy incidence with increasing distance from a road is also consistent with the

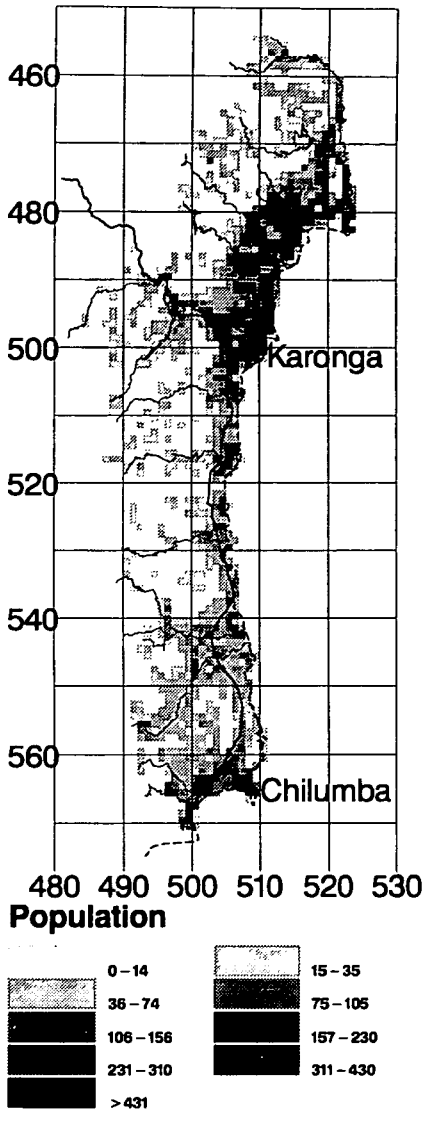

FIGURE 4 *Population density. Darkest squares have the highest population density*

hypothesis that easier access to health care leads to a reduction in leprosy incidence.

Our results are consistent with an association between water in the environment and leprosy incidence. The observed decrease in incidence with increasing distance from a river is increased after analyses are restricted to individuals who did not move their residence more than 2 km between the two surveys. To explain the results, one must consider how the environment might vary with increasing distance from a river, and how this might affect transmission of *M. leprae* or progression to clinical disease. Possible explanations include humidity-dependent survival of *M. leprae* outside the human host (either following secretion from the noses of infected individuals[20,21] or from an environmental source[22]), or humidity-dependent environmental mycobacteria, exposure to which can influence the human immune response to *M. leprae*. Another possibility (though perhaps less plausible) is that water in the environment encourages transmission from non-human sources of *M. leprae*[23] or via arthropods such as mosquitoes.[24] Again, we cannot exclude residual confounding by socioeconomic status, which tended to increase with increasing distance from a river.

Associations with geographic factors were less clear when examined separately in the north and the south than for the district as a whole. Almost all individuals living more than 5 km from a river lived in zones C and E (Table 7). Reduced numbers of cases in subgroup analyses inevitably mean that effects will be estimated less accurately, and that standard errors will increase. More importantly, the observed tendency for leprosy incidence to decrease with increasing distance from rivers (Table 3) is partly a function of the fact that incidence is greater in the north, where individuals live closer to rivers. This highlights the difficulty in excluding alternative explanations for associations observed in ecological studies such as this: given the general north-south divide in leprosy incidence one will inevitably observe an association with any ecological variable whose distribution differs between north and south. On the other hand, the larger numbers of rivers in the north may partly explain the higher incidence of leprosy there.

After controlling for other variables, there is some evidence for a decrease in leprosy incidence at greatest distance from the lake shore, although incidence rates were higher between 1 and 3 km from the lake shore compared to 0 km from the lake shore. If similar associations with leprosy incidence were observed for distance from rivers and from the lake shore, this might imply that the association was due to ease of access to water. The more consistent trend with distance from a river than from the lake shore leads us to hypothesize that it is the nature of the soil or crops, rather than access to water *per se* which underlies the association. The amount of water used by a household, and the standard of hygiene of the household, should be equally affected by proximity to the lake shore. An environmental, rather than behavioural, explanation for this association may also be supported by the less clear association between incidence and distance from a river in the north: we hypothesize that distance from rivers

TABLE 3 *Leprosy cases and person-years at risk (pyar) by population density in square km of residence, with estimated rate ratios for the effect of population density on leprosy incidence (compared to square km containing more than 430 people)*

		Controlling for age, sex and BCG			Controlling additionally for schooling, housing and other geographic variables			Restricting additionally to non-migrating individuals		
Number of individuals	Cases/pyar	Rate ratio	95% CI		Rate ratio	95% CI		Rate ratio	95% CI	
>430	29/49 326	1			1			1		
311–430	38/50 199	1.32	0.81	2.13	1.18	0.71	1.94	1.35	0.79	2.31
231–310	50/59 123	1.42	0.90	2.24	1.23	0.76	1.97	1.18	0.70	1.99
157–230	74/90 937	1.34	0.87	2.06	1.11	0.70	1.75	1.08	0.66	1.79
106–156	42/58 871	1.16	0.72	1.86	1.02	0.62	1.67	0.94	0.54	1.62
75–105	36/40 938	1.41	0.86	2.30	1.20	0.71	2.02	0.95	0.51	1.74
36–74	32/48 389	1.03	0.62	1.71	0.86	0.50	1.47	0.87	0.48	1.58
15–35	18/19 309	1.41	0.78	2.54	1.05	0.56	2.00	0.82	0.36	1.86
1–14	13/6656	2.88	1.49	5.53	1.85	0.91	3.76	2.57	1.20	5.52
		LRS = 11.7 (8 d.f., $P = 0.16$)			LRS = 6.6 (8 d.f., $P = 0.58$)			LRS = 11.1 (8 d.f., $P = 0.20$)		

TABLE 4 *Leprosy cases and person-years at risk (pyar) by distance from main roads, with estimated rate ratios for the effect of distance from roads compared to square km containing roads*

		Controlling for age, sex and BCG			Controlling additionally for schooling, housing and other geographic variables			Restricting additionally to non-migrating individuals		
Distance (km)	Cases/pyar	Rate ratio	95% CI		Rate ratio	95% CI		Rate ratio	95% CI	
0	40/87 014	1			1			1		
1	92/36 097	1.47	1.01	2.14	1.33	0.91	1.95	1.23	0.81	1.88
2	63/63 125	2.20	1.48	3.27	1.97	1.30	2.97	1.71	1.07	2.73
3	25/32 045	1.73	1.05	2.85	1.82	1.06	3.12	1.97	1.08	3.56
4–5	34/40 654	1.82	1.16	2.88	1.87	1.07	3.24	1.91	1.03	3.56
6–10	35/40 215	1.91	1.21	3.00	2.16	1.26	3.70	1.91	1.05	3.49
>10	43/24 608	3.58	2.32	5.50	7.06	2.98	16.7	6.51	2.40	17.7
		LRS = 38.8 (6 d.f., $P < 0.001$)			LRS = 30.4 (6 d.f., $P < 0.001$)			LRS = 21.0 (6 d.f., $P = 0.002$)		

TABLE 5 *Leprosy cases and person-years at risk (pyar) by distance from a river, with estimated rate ratios for the effect of distance from a river compared to square km containing a river*

		Controlling for age, sex and BCG			Controlling additionally for schooling, housing and other geographic variables			Restricting additionally to non-migrating individuals		
Distance (km)	Cases/pyar	Rate ratio	95% CI		Rate ratio	95% CI		Rate ratio	95% CI	
0	111/117 581	1			1			1		
1	119/140 641	0.90	0.70	1.17	0.97	0.74	1.27	0.85	0.63	1.15
2	54/75 390	0.76	0.55	1.05	0.80	0.57	1.12	0.68	0.42	1.01
3	23/36 079	0.65	0.42	1.02	0.73	0.46	1.15	0.63	0.38	1.08
4	14/20 669	0.69	0.39	1.20	0.81	0.46	1.42	0.70	0.36	1.35
5	9/12 550	0.74	0.38	1.46	0.77	0.39	1.55	0.75	0.34	1.65
6	1/5894	0.18	0.02	1.27	0.26	0.04	1.85	0.09[a]	0.01[a]	0.67[a]
≥7	1/14 953	0.07	0.01	0.49	0.11	0.02	0.81			
		LRS = 28.5 (7 d.f., $P < 0.001$)			LRS = 15.2 (7 d.f., $P = 0.03$)			LRS = 16.1 (6 d.f., $P = 0.01$)		

[a] Rate ratio for individuals living ≥6 km from a river (no cases living >6 km from a river).

TABLE 6 *Leprosy cases and person-years at risk (pyar) by distance from the lake shore, with estimated rate ratios for the effect of distance from the lake shore compared to square km containing lake shore*

		Controlling for age, sex and BCG		Controlling additionally for schooling, housing and other geographic variables		Restricting additionally to non-migrating individuals	
Distance (km)	Cases/pyar	Rate ratio	95% CI	Rate ratio	95% CI	Rate ratio	95% CI
0	16/33 851	1		1		1	
1	61/84 504	1.54	0.89 2.67	1.25	0.71 2.19	1.33	0.68 2.60
2	68/78 736	1.92	1.11 3.30	1.51	0.93 2.80	1.85	0.96 3.56
3	33/39 879	1.77	0.98 3.22	1.19	0.65 2.17	1.08	0.52 2.25
4	24/34 145	1.54	0.82 2.90	0.90	0.47 1.72	0.94	0.44 2.01
5	21/32 440	1.41	0.74 2.70	0.76	0.38 1.52	0.81	0.36 1.82
6–7	34/41 259	1.76	0.97 3.19	0.87	0.45 1.68	0.78	0.35 1.73
8–12	30/43 739	1.42	0.78 2.61	0.64	0.33 1.26	0.68	0.31 1.49
>12	45/35 204	2.53	1.43 4.48	0.44	0.17 1.10	0.43	0.14 1.28
		LRS = 15.3 (8 d.f., $P = 0.05$)		LRS = 21.6 (8 d.f., $P = 0.006$)		LRS = 21.5 (8 d.f., $P = 0.006$)	

TABLE 7 *Estimated rate ratios for the effect of geographic variables, controlling for age, sex, BCG, schooling, housing and other geographic variables, among individuals who did not migrate, separately for different areas of the district*

		North (zones A and B)			South (zones C, D and E)		
Geographic variable	Distance (km)	Rate ratio	95% CI		Rate ratio	95% CI	
Distance from road	1	1.27	0.66	2.43	1.18	0.67	2.08
	2	2.13	1.04	4.36	1.08	0.51	2.31
	3	3.16	1.31	7.57	0.87	0.28	2.71
	4–5	2.50	1.00	6.26	0.97	0.26	3.54
	6–10	1.51	0.68	3.34	1.90	0.57	6.38
	>10	20.8	2.18	198.3	2.14	0.36	12.7
		LRS = 17.9 (6 d.f., $P = 0.007$)			LRS = 2.0 (6 d.f., $P = 0.92$)		
Distance from river	1	0.76	0.53	1.10	0.99	0.56	1.75
	2	0.56	0.34	0.94	0.77	0.38	1.56
	3	0.46	0.22	0.96	0.94	0.41	2.13
	4	0.82	0.39	1.74	0.37	0.08	1.61
	5	0.86[a]	0.26[a]	2.78[a]	0.90	0.30	2.70
	≥6				0.12	0.02	0.94
		LRS = 8.2 (5 d.f., $P = 0.15$)			LRS = 10.2 (6 d.f., $P = 0.12$)		
Distance from lake shore	1	2.09	0.73	6.04	0.81	0.33	1.96
	2	2.03	0.71	5.78	1.23	0.51	2.96
	3	1.15	0.37	3.50	0.52	0.15	1.79
	4	0.81	0.25	2.64	0.70	0.21	2.26
	5	0.58	0.17	2.01	0.72	0.20	2.58
	6–7	0.61	0.18	2.09	0.84	0.25	2.80
	8–12	0.78	0.23	2.58	0.66	0.19	2.22
	>12	0.13	0.01	1.45	0.38	0.08	1.93
		LRS = 24.7 (8 d.f., $P = 0.002$)			LRS = 5.6 (8 d.f., $P = 0.69$)		

[a] Rate ratio for individuals living ≥5 km from a river (no cases living >5 km from a river).

TABLE 8 *Leprosy cases and person-years at risk (pyar) by language group, with estimated rate ratios compared to Tumbuka speakers*

Language group	Cases/pyar	Controlling for age, sex and BCG			Controlling additionally for ecological zone		
		Rate ratio	95% CI		Rate ratio	95% CI	
Tumbuka	80/128 638	1			1		
Kyangonde	167/191 475	1.44	1.10	1.88	0.999	0.747	1.34
Neighbouring Districts	62/47 436	2.12	1.52	2.95	1.07	0.720	1.58
Others	3/3919	1.29	0.408	4.10	1.15	0.361	3.65
		LRS = 19.5 (3 d.f., $P < 0.001$)			LRS = 0.2 (3 d.f., $P = 0.98$)		

matters less in the moist north than the dry south, where the change in the environment is much greater as distance from a river increases.

These results provide evidence that environmental, as well as socioeconomic factors are of importance in the aetiology of mycobacterial diseases. The evidence for higher risks associated with the more fertile northern part of Karonga District, and with close proximity to rivers, is consistent with a tradition in the literature associating leprosy with water. Such evidence is consistent with an important role for the environment in supporting viable *M. leprae*, or for exposure to environmental mycobacteria in determining natural immunity to the infection. The observation of lower risks along roads is consistent with much evidence that socioeconomic development is inimical to leprosy, though precisely what the relevant socioeconomic factors may be remains obscure. A better understanding of the aetiology of mycobacterial diseases may assist in control efforts. Further clarification of the role of environmental mycobacteria in imparting protective immunity against these diseases may assist in the search for improved vaccines against them.

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