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Leprosy on Anjouan (Comoros): persistent hyper-endemicity despite decades of solid control efforts

EPCO HASKER*, ABDALLAH BACO**, ASSOUMANI YOUNOUSSA**, ABOUBACAR MZEMBABA**, SAVERIO GRILLONE**, TINE DEMEULENAERE***, GUIDO GROENEN****, PHILIP SUFFYS***** & BOUKE C. DE JONG*

**Institute of Tropical Medicine, Belgium*
***Leprosy and TB control program, Comoros*
****Damien Foundation, Belgium*
*****BELTA-TBnet, Belgium*
******Laboratory of Molecular Biology Applied to Mycobacteria, Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil*

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Summary

Introduction: Despite decades of solid leprosy control efforts, the disease remains highly endemic on the island of Anjouan, Comoros. Among a population of less than 400,000 over 300 new leprosy patients are diagnosed on average annually.

Methods: We analysed routine data for the period of 2000–2015 for trends in epidemiological parameters and clustering in time and space.

Results: Leprosy incidence remains high (7·4/10,000 per year, on average) with no indications of an imminent decrease. Increasing coverage of active case finding has led to increasing numbers of leprosy patients being detected over the past 8 years. The proportion of new patients presenting with visible deformities has consistently been low (2·4% on average). The proportion of children among new patients exceeds 30%, without any trend towards a decrease. At macro-level clusters in time and space were observed scattered across the island, without a clear pattern.

Discussion: The leprosy epidemic on Anjouan continues unabated despite the activities of a well-organised control programme. There appears to be a need to further scale up case finding efforts and organise them in a more systematic manner. Use of modern technology, such as Geographic Information Systems, could help to improve targeting of case finding efforts. Prophylactic treatment of contacts should be considered. Studying markers of infection such as anti PGL-1, and DNA finger printing of leprosy bacteria could provide insights in the patterns of transmission and could be useful in identifying those at higher risk of developing leprosy for prophylactic treatment.

Correspondence to: Epco Hasker, Instituut voor Tropische Geneeskunde Antwerpen, Antwerpen, Belgium

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Introduction

In 1991, Pattyn and Grillone published an article on leprosy in the Comoros, a group of islands in the Indian Ocean, reviewing data for the period 1981–1988.[1] The authors observed that on the main island, Grande Comore, leprosy had disappeared but that on the second largest island, Anjouan, the disease was still highly endemic. They concluded, however, that there were good reasons to expect a change on Anjouan. Proportions of patients with visible deformities (WHO Grade II) at time of diagnosis were low and information collected during 1987 and 1988 confirmed that both patients' and doctors' delays were short. Short diagnostic delays and the supportive role played by cured patients who referred people to be evaluated for leprosy to the specialised leprosy services, were cited as reasons for optimism. A good leprosy control programme had been in place since 1980, with support from the Damien Foundation in Belgium. However a quarter of a century later, leprosy endemicity on Anjouan remains as high as ever.

The 'Union des Comores' consists of three islands: Grande Comore, Anjouan and Mohéli with an estimated total population of approximately 800,000 people. The islands are located in the Indian Ocean, between the northern parts of Mozambique and Madagascar (Figure 1). The island of Anjouan has an estimated population of approximately 380,000.

The Comorian health system is organised as a district health system. At the district level there is a network of health centers, each covering a population ranging from 50,000 to over 100,000 inhabitants. Each island has a Regional Hospital. Several national programmes have been established to control priority diseases, including the National Programme to control

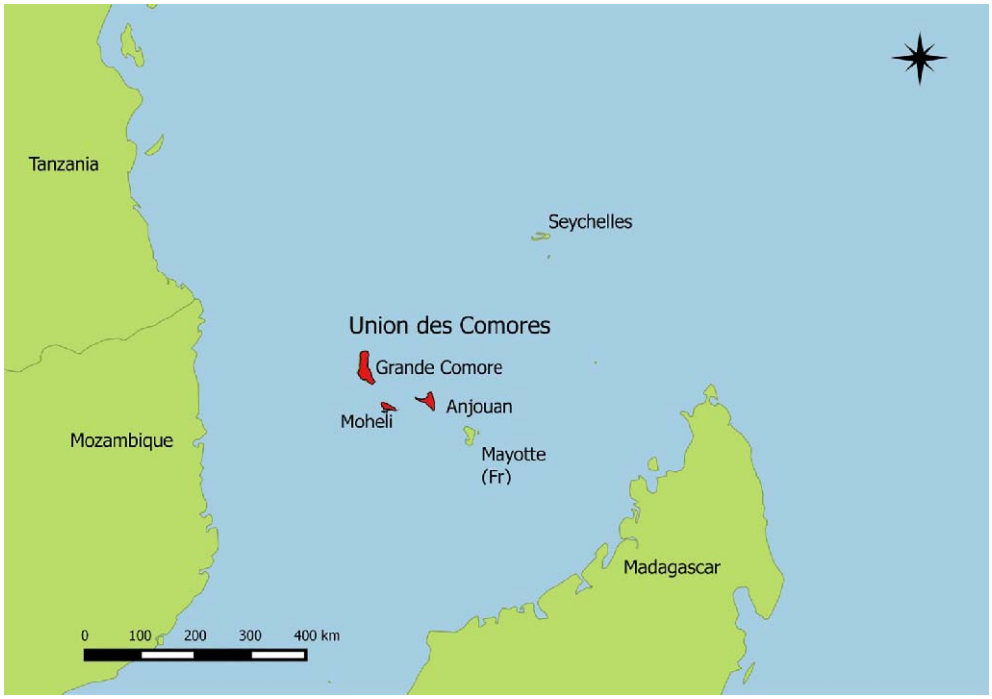

Figure 1. The 'Union des Comores' and surrounding countries and territories (source: DIVA-GIS, http://www.diva-gis.org/Data).

Tuberculosis and Leprosy, NTLP, which includes the Leprosy Control Programme (LCP). The LCP is integrated within the general health services at all levels, including the district level.

In 2002 a single large scale leprosy elimination campaign (LEC) took place, followed by several smaller so-called 'mini campaigns' from 2008 onwards. During such campaigns LCP teams have gone to high incidence villages and invited the population for screening for skin conditions. This has led to a major increase in annual case detection of leprosy which has been sustained since 2008. Another approach that has been stepped up is the examination of contacts, in which all those residing in the same household as a new leprosy patient are screened.

To search for clues on the reasons for the continuing high endemicity of leprosy on Anjouan and to identify potential solutions, we conducted an analysis of routine data for the period 2000–2015. In particular, we tried to detect trends in epidemiological and programme indicators, and clusters of leprosy cases in time and space.

Methods

We extracted data at the individual patient level for the period of 2000–2015 from the existing LCP database. For the purpose of exploring trends in incidence and clustering, data were regrouped by village/town and by year. All newly detected patients were allocated to 94 locations (villages/towns). For each location, geographic coordinates and estimated population sizes by year were obtained. For each location and each year, we determined the total number of leprosy patients. The dataset thus consisted of 1504 records, i.e. 94 villages times 16 years. Using this dataset we conducted a Poisson regression using Stata IC 14·1 for Windows, with year as explanatory variable, the log of population (by village and year) as offset, and count of patients (by village and year) as outcome to explore for trends in incidence rate ratios. We considered the entire period (2000–2015) as well as the period since the start of regular active case finding (2008–2015).

The same dataset was used to run a retrospective space-time analysis using a Poisson model in SaTScan v9.4.2. The software selects all possible clusters in space and time and calculates incidence rate ratios using as reference the overall incidence rate outside the cluster.[2] The maximum spatial cluster size was set to 25% of the population and the maximum temporal cluster size was set to 90%, the maximum allowed by the software. Thus we identified clusters of leprosy cases in space and time.

To explore trends in proportions we looked at annual cohorts of registered leprosy patients. We calculated proportions of relapses and other re-admissions. Among newly diagnosed leprosy patients, we explored proportions of multibacillary cases (MB), proportions of children (defined as age below 15 years at time of diagnosis) and proportions of patients with visible deformities (WHO Grade II) at time of diagnosis.[3] For exploring trends in proportions we calculated Chi square for trend using Stata IC 14·1 for Windows.

Ethics

All data used were routine data, already available at the LCP. After data extraction, all personal identifiers were removed. When describing trends we aggregated data by year, and

for our analysis of clustering we used data at village level. The study was approved by the institutional review board of the Institute of Tropical Medicine, Antwerp, Belgium.

Results

Altogether over the 16-year period, 3,828 leprosy patients were reported, of whom 44 were relapses and five were returns after being lost-to-follow-up. The remaining 3,779 were all new patients, resulting in an average annual incidence of 7·4/10,000. Out of 94 towns or villages, 83 reported at least one leprosy patient over the study period. The highest incidence observed in a single calendar year at the town/village level was 1·8%. An overview of the main findings appears in Table 1.

As becomes evident in Figure 2 as well, there was substantial fluctuation in reported annual incidence. There were major increases in 2002, when a first LEC took place, and from 2008 onwards when smaller but sustained mini campaigns began to be implemented.

The Poisson regression model revealed a statistically significant trend towards increase, IRR 1·05, 95% CI 1·04–1·06, when the entire period is considered. However, when considering only the period since 2008, there appears to be a mild decrease (IRR 0·96, 95% CI 0·94–0·98).

Of all 3,779 new leprosy patients registered, 1,429 (37·8%) were MB, 1251 (33·1%) were children and 91 (2·4%) presented with visible deformities at time of diagnosis. Figure 3 below shows the trends over time.

The child proportion has been consistently high over the 16-year period (30–40%, chi square for trend analysis shows a *P*-value of 0·47, i.e. no statistically significant trend towards increase or decrease). The disability Grade II proportion has been consistently low with no apparent trend, the *P*-value of the chi square for trend is 0·46. The MB proportion appears to have increased over the period, in particular since 2008. For both periods combined, as well

Table 1. Overview of main epidemiological data and programme indicators

Year	Estimated population size	New Leprosy cases	Annual incidence per 10,000	Multi-bacillary proportion	Child proportion	Disability Grade II proportion
2000	259,001	91	3·5	33·0%	29·7%	0·0%
2001	265,888	147	5·5	23·8%	36·1%	0·7%
2002	272,957	286	10·5	22·4%	31·1%	0·4%
2003	280,218	101	3·6	29·7%	38·6%	5·9%
2004	287,672	129	4·5	27·9%	34·9%	3·1%
2005	295,328	120	4·1	22·5%	42·0%	3·3%
2006	303,199	120	4·0	35·0%	33·6%	4·2%
2007	311,275	108	3·5	40·7%	38·3%	7·4%
2008	319,573	333	10·4	29·7%	33·0%	3·6%
2009	328,092	292	8·9	30·5%	33·2%	2·1%
2010	336,842	325	9·7	39·1%	26·8%	2·5%
2011	345,830	439	12·7	35·3%	38·0%	0·9%
2012	355,061	342	9·6	44·7%	30·4%	1·8%
2013	364,544	412	11·3	52·2%	27·7%	2·2%
2014	374,286	253	6·8	55·3%	32·4%	2·4%
2015	384,282	281	7·3	50·9%	37·4%	3·9%
Overall		3,779		37·8%	33·1%	2·4%

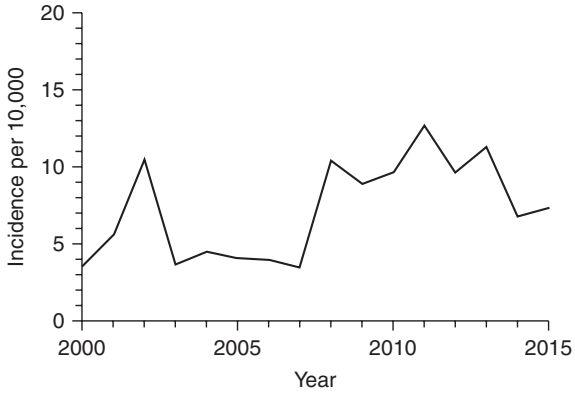

Figure 2. Leprosy incidence on Anjouan (Comoros), 2000–2015.

as for the period since 2008, the *P*-value of chi square for trend is $<0{\cdot}0001$. The slope for the period from 2008 to 2015 is 0·039 as opposed to 0·020 for the entire period.

The SaTScan analysis identified eight clusters of which six were statistically significant, all with *P*-values $\leq 0{\cdot}0015$. One large cluster consisted of 11 villages, the others of only one or two villages. Relative risks comparing incidence inside the cluster to incidence outside ranged from 2·5 to 9·2. Details on the six clusters that were statistically significant are shown in Figure 4 and Table 2.

Out of 3,779 cases reported over the period, 1,951 (51·6%) were part of a cluster. The 17 villages (out of 94) that were part of a cluster generally had above average population sizes, with a median of 3,636 inhabitants per village in 2015, as compared to 2,338 per village for the island as a whole. Out of 11 villages with a population above 10,000, five were part of a cluster, as opposed to only one out of 19 small villages with populations below 1,000.

As can be seen from the map and from Table 2, clusters were spread rather evenly across the island. Over the study period all the regions of the island had at least one cluster. Two clusters had started in 2001, the others after 2006; two clusters were still active in 2015. In 2015 five out of six clusters (all except cluster six) still reported incidence levels of above one per 1,000 population (1·0–9·9 per 1,000), whereas outside the clusters the incidence was 0·35 per 1,000. In cluster six on the south side of the island there had been no cases prior

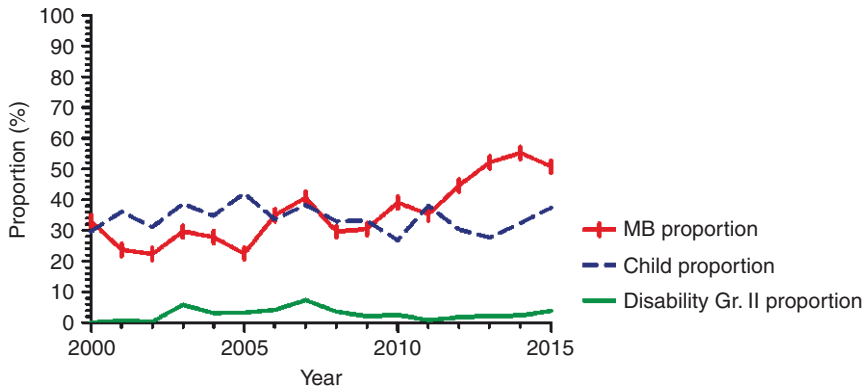

Figure 3. MB, child and disability Grade II proportions over time.

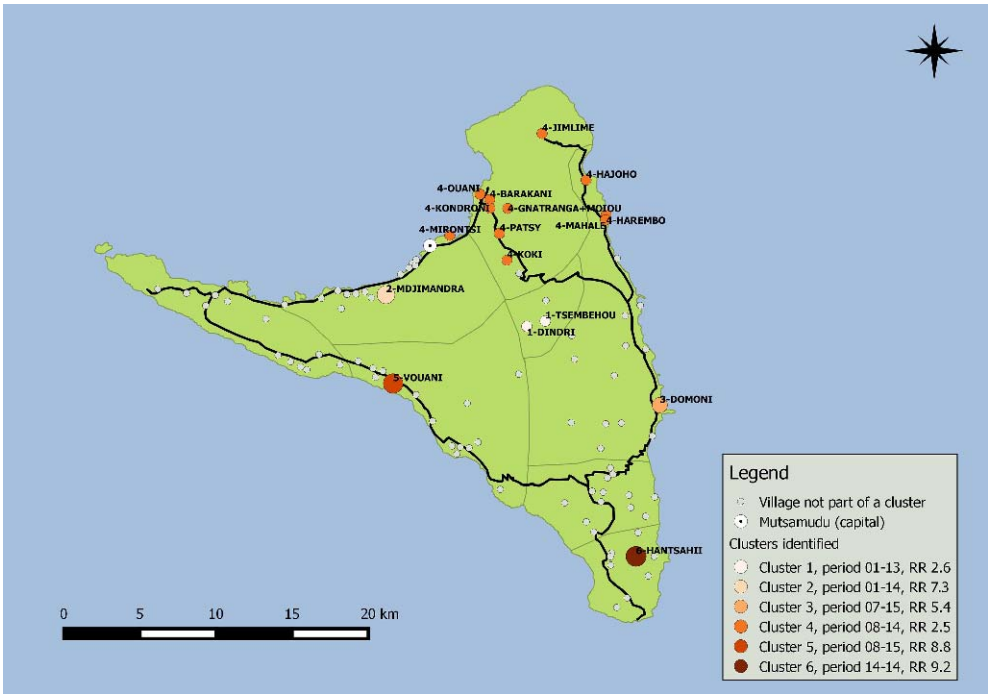

Figure 4. SaTScan analysis of Anjouan leprosy incidence 2000–2015 (size of dots used to indicate clusters on map is proportional to risk ratio).

to 2013, with a sudden increase in 2014 when 11 cases were reported in a population of 1,376. This cluster was preceded by a more gradual increase in incidence in two neighbouring villages starting in 2010 – these were the two non-significant clusters identified in the SaTScan analysis. By 2015 in the three villages combined, incidence was down again to 0·63/1,000 (four cases on a total population of 6,310).

Discussion

Our analysis of routine leprosy data from the island of Anjouan from 2000 through to 2015 reveals that, despite the presence of a well-functioning leprosy control programme, the annual

Table 2. Overview of statistically significant clusters identified in SaTScan analysis

Cluster	Period	Population	Total no. of cases	RR	p-value	District (region)
1	2001–2013	18,738	432	2·6	<0·0001	Tsembehou (Center)
2	2001–2014	2,576	187	7·3	<0·0001	Mutsamudu (West)
3	2007–2015	12,961	462	5·4	<0·0001	Domoni (East)
4	2008–2014	54,531	692	2·5	<0·0001	Ouani (North)
5	2008–2015	3,000	167	8·8	<0·0001	Pomoni (West)
6	2014	1,376	11	9·2	0·0015	Mramani (South)
All		93,182	1,951			

incidence remains very high with little indication of an imminent decrease. Over the 16-year period, the average annual case notification rate has been 7·4 per 10,000 population. Diagnostic delays appear to be minimal, as over the years on average 2·4% of patients had visible deformities at time of diagnosis, without a noticeable trend towards increase or decrease.

Since 2008 active case finding activities have been stepped up and this has led to a major increase in numbers of cases detected. At the same time there has been some increase in the proportion of patients diagnosed with MB leprosy, which could be a first indication of an epidemic approaching its final phase. The average incubation time of MB leprosy is assumed to be 10 years, versus 3·5 years for PB.[4] Thus if transmission ceases, MB cases will continue to arise for a longer period, whereas PB cases will disappear earlier. This notion of reduced transmission is however contradicted by the fact that over the years one third of leprosy patients diagnosed have been children, indicative of recent transmission, and that there is no noticeable trend towards a decrease in the proportion of child cases.[5]

The SaTScan analysis revealed clusters of leprosy patients spread all over the island and over different periods of time. There is no clear pattern of incidence shifting from one side of the island to another, nor are there places with a consistently much higher incidence over the 16-year period. Smaller villages appear to be less affected but this may just be due to such villages being less likely to be targeted for active screening.

The main trend that does become apparent from this analysis is a major increase in case notification rates whenever active case finding was intensified. This happened during the LEC in 2002 and on a more continuous basis since active case finding activities were increased

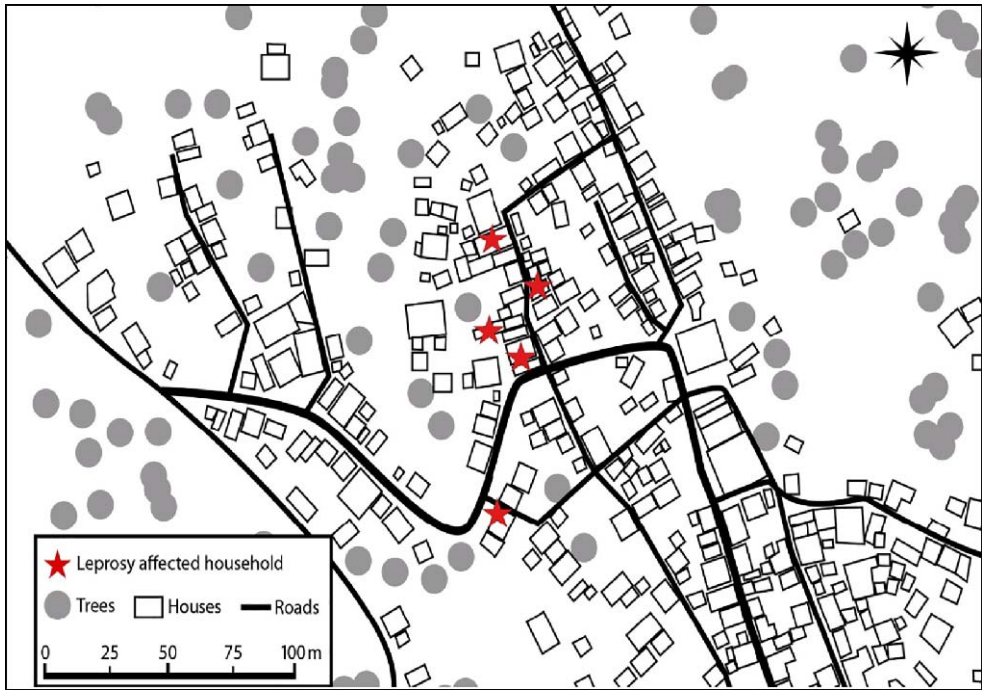

Figure 5. Mapping of recent leprosy cases (2014–2015).

from 2008 onwards. Patients are detected early and the LCP is able to provide adequate treatment, reflected in very low proportions of relapses and readmissions among patients detected (1·1% and 0·1% respectively). Given the consistently high case notification rates, further expanding the scope of active case finding campaigns will likely be worthwhile. This would also be in line with the objective of: 'Promoting early case detection through active case-finding (e.g. campaigns) in areas of higher endemicity and contact management', formulated in the Global Leprosy Strategy 2016–2020 of WHO.[6] More exact mapping of leprosy cases within their villages could help identifying local clusters where it might be worthwhile examining not only the household members but also those living in neighbouring households. One such approach could be through an application in Open Data Kit (ODK) that can be used on any smartphone to map leprosy patients and document their contacts.[7] The app allows recording of data on each household member but also GPS coordinates of the households that can then be plotted on a digitized Google Earth image using Quantum GIS (QGIS).[8] Both ODK and QGIS are freeware. The result of a pilot screening in one Comorian village is shown in Figure 5. Please note that for privacy reasons in this manuscript we converted the actual Google Earth image into a drawing and will not disclose the name of the village. Such preliminary results are promising and the concentration of incident cases within the mapped locations is intriguing.

This demonstration illustrates that mapping every new leprosy case is feasible and would allow for a more targeted active screening approach. Identifying the distribution patterns of incident leprosy could also inform a decision on whether and how to implement prophylactic treatment, and monitor its impact – another strategy that has proven successful in an island setting.[9]

Finally, operational research using modern technologies such as anti-phenolic glycolipid-1 (PGL-1) serology and DNA-fingerprinting may be able to provide important clues on the reasons for the high incidence rates observed. Anti-PGL-1 can be used as a marker of infection on the MB side of the spectrum and would therefore specifically identify the more infectious individuals, whether symptomatic or asymptomatic.[10,11,12] This can be of use when deciding on whom to provide with prophylactic treatment. DNA-fingerprinting can be used to establish chains of transmission.[13,14] A pilot study has been initiated. Findings on Anjouan will almost certainly have implications in other settings as well.

In conclusion, leprosy on Anjouan is not yet under control but scaling up the current active case finding approach with the help of new technologies has the potential to provide important insight to solve the problem. At the same time, the unique epidemiological situation on the island offers an opportunity to study patterns of transmission and how novel technologies may impact these; findings of such studies will have implications beyond the specific setting of Anjouan.

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