Transmission of tuberculosis in the prison of Antananarivo (Madagascar)

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Abstract – The prevalence of tuberculosis in the Antananarivo prison is 16 times higher than that in the general population of Madagascar. We compared the clustering of Mycobacterium tuberculosis strains within and outside the prison and studied the transmission of strains in the prison. M. tuberculosis strains isolated in 1994 to 1995 from 146 prisoners and from 260 nonprisoner patients from Antananarivo were typed using the genetic markers IS6110 and direct repeat. We compared the strains isolated from prisoners and nonprisoners and found that the clustering rate was higher within (58.9%) than outside the prison (40%) suggesting that the transmission rate was higher in prison. Of the 146 incarcerated patients, 82 were grouped into 22 clusters. We checked for possible tuberculosis transmission between prisoners with identical strains by epidemiological investigation of the various prison clusters. We found that 9.5% of the incarcerated patients could have been sources of infection and that only 15.1% could have been infected in the prison. One hundred and twenty-seven prison patients were new cases. Epidemiological data suggested that 37% of them resulted from a reactivation of an old infection, due to poor living conditions or recent transmission from an index case outside the prison. © 2000 Éditions scientifiques et médicales Elsevier SAS

M. tuberculosis / prison / RFLP / IS6110 / Madagascar

1. Introduction

The annual incidence rate of tuberculosis (TB) in Madagascar has been estimated at 150 new pulmonary tuberculosis cases per 100 000 inhabitants [4]. Since 1991, the objectives of the National Tuberculosis Control Programme (NTCP) have been the detection and treatment of patients with pulmonary tuberculosis confirmed by microscopy throughout the country. The prevalence of HIV is still low in the total population (only 0.2% of the TB population from 1989 to 1994). Over this same period, all TB patients in the prison of Antananarivo were HIV-negative [2].

Several strain genotyping methods such as RFLP (restriction fragment length polymorphism) mapping, the use of genetic markers [16] and more recently, spoligotyping [9], are available to genetically characterise the various Mycobacterium tuberculosis strains. These methods have been used successfully to identify source cases during outbreaks, nosocomial infections, multidrug resistant TB outbreaks [1] and studies of TB transmission in high-risk groups (e.g. hospitals, prisons, hostels, etc.) [6, 7]. In the main prison of Antananarivo, the capital of Madagascar, the annual TB incidence rate, estimated from the number of TB cases notified and the number of new inmates, was 2 400 for 100 000 prisoners from 1990 to 1993 [3]. About 88.4% of these patients were new cases. This situation is similar to that in other countries, although several surveys of inmates have shown an association with HIV infection [5, 14]. As the
prevalence of HIV infection is still low, Antananarivo prison may be an ideal site for TB studies in HIV-negative patients.

In 1990, the NTCP started TB control in the prison with active detection and treatment of all TB cases. This measure resulted in a decrease in the number of pulmonary TB patients from 102 in 1991 to 79 in 1993 [3].

In this study, we evaluated the importance of TB transmission within the prison after 4 years of control, by the RFLP genotyping of M. tuberculosis strains with the IS6110 and DR genetic markers.

2. Study population and methods

2.1. Description of the central remand prison of Antananarivo

This prison has an official capacity of 850 inmates, but an average of about 2,800 individuals were daily incarcerated in seven blocks (A–G). Each block consisted of several rooms each about 100 m² in area, and housing about 50–70 inmates, with an open-air square used by the prisoners during the daytime. The size of the prison population fluctuated considerably (new entries, releases and transfers). As the exact number of prisoners over the study period was not available, for this study we referred to the prison population on December 31 1994 (table I). Thus it was difficult to determine the true incidence of TB in the prison. The incidence rate was then estimated as the percentage of new TB patients diagnosed among this population and in each block. Interactions between inmates and the outside population were frequent. About 800 inmates were working outside the prison during the daytime. On December 31 1994, 33 individuals were employed by the prison infirmary. Tonga Soa, a nongovernmental organisation, had a laboratory staff that realised the sputum smear microscopy for the diagnosis of TB in prisoners, and the ‘Aumônerie Catholique des Prisons’ was responsible for the treatment of these patients. After two-month treatment with four drugs (streptomycin, isoniazide, rifampicine, pyrazinamide) in the prison infirmary, the patients were transferred to the C block for a further 6 months of treatment with isoniazide and thiacetazone. Prisoners released during treatment were encouraged to continue their treatment at the civilian Amboditsiry health centre in Antananarivo.

2.2. Patients

Between February 1994 and December 1995, 210 TB cases were reported in the prison, 146 of which were confirmed by culture. Pulmonary TB cases (P) were detected by sputum smear microscopy. Extrapulmonary TB patients (EP) were initially diagnosed on the basis of clinical symptoms and the diagnosis was then confirmed by culture or histological examination.

At least one clinical sample per patient (e.g. sputum, biopsy, pleural liquid) was sent for culture at the Pasteur Institute of Madagascar. Several specimens were obtained from a few patients. A total of 162 specimens obtained from 146 prisoners (105 P and 41 EP) tested positive by culture. All patients with a positive M. tuberculosis culture were included in the study.

We carried out a comparative study of strains isolated from prisoners and nonprisoners, using strains from consecutive patients diagnosed in the city of Antananarivo:

- from 471 new P patients diagnosed in the two main health centres of Antananarivo from August 1994 to December 1995, 130 P patients were randomly sampled and were representative of these two centres (which recruited 50% of the patients of the capital). These cases accounted for 20.7% of all new P cases reported in these centres over this period.
- 119 strains were from 119 EP patients and 11 strains were from 11 patients with both P and EP forms, recruited at the five main TB diagnostic centres of Antananarivo from May 1994 to July 1995.

2.3. RFLP genotyping method

Clinical samples were cultured for the isolation of mycobacteria on Lowenstein-Jensen medium. Bacterial DNA was extracted from colonies using the CTAB (N-cetyl,N,N,N-
trimethyl ammonium bromide) method [17]. Strains were genotyped using the standardised RFLP procedure [15]. Briefly, DNA was cut with the restriction enzyme PvuII (Pharmacia Biotech), subjected to electrophoresis in a 1% agarose gel, blotted onto a Hybond-N+ membrane (Amersham), and probed with the 807 bp PvuII–XhoI fragment of the IS6110 insertion sequence [13]. For strains with a single IS6110 copy, a second genetic marker was used. DNA was digested with AluI (Pharmacia Biotech) and probed with the 36-bp direct repeat (DR) probe [8]. All probes were labelled with horseradish peroxidase and were detected with the enhanced chemiluminescence system (ECL, Amersham) and autoradiography.

2.4. RFLP profile analysis

DNA profiles were compared using the Taxotron software (P.A.D. Grimont, Taxolab Software). The matching of profiles was confirmed by eye. A cluster was defined as a group of strains with identical DNA profiles or a group of patients with identical strains (‘clustered patients’).

2.5. Epidemiological investigations

To determine the eventual epidemiological relationships between patients, we investigated the following factors:

- the period of incarceration,
- the block and room of stay,
- the dates of entrance and TB diagnosis,
- the clinical TB form and the date of onset of the clinical symptoms when available,
- TB history of the patient (‘new case’, i.e. patient who had never been treated in the past or who had received less than 1 month treatment, a ‘recurrent case’, i.e. relapse case, treatment failure case or treatment interruption case according to WHO definitions [18]),
- known contact with other prisoner TB patients,
- when possible, whether members of their family had acquired TB in the past (and the date of the disease if known), or had a chronic cough.

Information was provided by the prison infirmary TB registers and/or by interviewing the prisoners.

Possible transmission from an index case to other prisoners was assessed by identifying the

<table>
<thead>
<tr>
<th>Block</th>
<th>Prison populationa</th>
<th>P patientsb</th>
<th>EP patientsb</th>
<th>No. total TB patients</th>
<th>Incidence rate</th>
<th>Patients included in the study</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>350</td>
<td>7</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>B</td>
<td>809</td>
<td>31</td>
<td>3</td>
<td>13</td>
<td>1</td>
<td>44</td>
</tr>
<tr>
<td>C</td>
<td>395</td>
<td>17</td>
<td>4</td>
<td>16</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td>D</td>
<td>199</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>E</td>
<td>63</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>F</td>
<td>733</td>
<td>36</td>
<td>3</td>
<td>32</td>
<td>0</td>
<td>68</td>
</tr>
<tr>
<td>G</td>
<td>300</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Subtotal</td>
<td>2 849</td>
<td>96</td>
<td>19</td>
<td>73</td>
<td>3</td>
<td>169</td>
</tr>
<tr>
<td>TongaSoa</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ex-prisoners</td>
<td>3</td>
<td>6</td>
<td>8</td>
<td>0</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>25</td>
<td>82</td>
<td>3</td>
<td>182</td>
<td>28</td>
</tr>
</tbody>
</table>

a On December 31 1994. b P = pulmonary TB; EP = extrapulmonary TB. c For one patient in block G, TB history was not known. d Laboratory technicians. e Ex-prisoners treated at Amboditsiry health centre. f For three P patients from whom we obtained clinical samples, the block was not mentioned in the TB register of the prison, but they were included in this study.
patients in each cluster and analysing all epidemiological data. We assumed that only patients with pulmonary TB were contagious and that they could have transmitted TB only to prisoners in the same block. For the clustered prisoners with no evident relationship with prisoners in the same cluster and the same block, the following data were analysed: eventual contacts with other TB patients in the other prison blocks or previous contacts with patients in the city, history of TB, and the presence of the cluster in the city. The same analysis was performed for the patients who did not cluster in the prison.

3. Results

3.1. Characteristics of TB patients in the prison

Table I shows the number of TB cases detected in the prison in 1994 and 1995 and their distribution in the various blocks. The incidence rate calculated among the prison population was 5.9% (table I). One hundred and ninety-one TB cases were detected among the inmates (169 of which were new cases and 22 were recurrent cases). Seventeen cases were detected among ex-prisoners (11 of which were new cases and six recurrent cases), and two new cases were detected among the laboratory staff. The highest proportions of new TB cases were observed in the C and F blocks. One hundred and twenty-five patients were pulmonary TB cases and 85 were extrapulmonary cases. All but four patients were male. All patients were HIV-negative. Their mean age was 33 years (17-67) which was not significantly different from that of the total inmate population, 31 years (17-76) [3]. One hundred and forty-six patients were included in this study; 127 were new cases (123 prisoners, two ex-prisoners, two laboratory technicians) and 18 were recurrent cases; for one patient TB history was not known.

3.2. M. tuberculosis strains isolated from prisoners

Of the 210 TB cases identified during the study period, 146 tested positive by culture. A total of 162 M. tuberculosis strains were isolated because several strains were isolated from different clinical specimens for 13 patients: 115 from 105 P patients (88 new cases) and 47 strains from 41 EP patients (39 new cases). These 105 P and 41 EP patients accounted for 84.8% of the P cases and 47% of the EP cases identified in 1994–1995.

3.3. Genotyping of the prison M. tuberculosis strains

We obtained 81 different IS6110 RFLP profiles from the 162 M. tuberculosis strains. If several strains were isolated from the same patient, identical IS6110 profiles were observed for all strains.

Sixty (41.1%) of the 146 patients testing positive by culture had strains with unique IS6110 RFLP patterns and 86 (58.9%) could be assigned to 21 clusters of 2–11 patients with identical IS6110 patterns strains (figure 1A). Two of these clusters contained strains with only one copy of IS6110: cluster no. 20 (seven patients) and cluster no. 21 (11 patients). As these single IS6110 copy strains were frequent (12% of the patients), we genotyped 17 of them using the DR marker (one strain was not typed due to technical problems and was thus excluded from the final analysis). Three of these 17 patients had unique DR profiles and 14 were assigned to three DR clusters: one cluster with two patients, one with three patients and one with nine patients (figure 1B). All the isolates with one IS6110 copy were identified as M. tuberculosis.

Based on IS6110 and DR patterns, the prisoners with TB could be divided into two groups: one with 63 ‘nonclustered patients’ (i.e. with strains with a unique genotype) and the other with 82 clustered patients with a strain identical to that of at least one other patient. These 82 patients were classified into 22 clusters each containing 2–11 patients.

3.4. Comparison of clustered and nonclustered patients in the prison

We compared the characteristics of clustered and nonclustered patients in the prison (table II). Mean population ages, proportions of new cases,
clinical TB forms and time incarcerated before diagnosis did not differ significantly between the two groups.

There were 1–18 copies of IS6110 in the clustered group and 1–26 in the nonclustered group. Strains with 1, 8, 12 or 13 copies seemed to be more frequent in the clustered group, whereas copy number tended to be high in the nonclustered group (data not shown).

There was no significant difference between new and recurrent patients (table III). For the 127 new cases, clustered and nonclustered patients had similar characteristics. In the recurrent patients, however, there was a significant difference between the clustered and the nonclustered group in the mean time between incarceration and diagnosis ($P < 0.05$ according to the Kruskal-Wallis test).

3.5. Comparison of the $M$. tuberculosis strains isolated from prisoners and nonprisoners

It is generally accepted that clustering is indicative of recent infection with rapid progression to disease [12] and may reflect a high transmission rate. We evaluated whether the rate of TB transmission was higher within than outside the prison by comparing the clustering of the strains. Isolates from 260 nonprisoner patients (130 P, 11 patients with both P and EP forms, and 119 EP) recruited from several health centres in Antananarivo during the study period were typed with the IS6110 marker. We observed
178 IS6110 profiles among these 260 isolates: 156 strains (60%) had unique patterns and 104 strains (40%) were classified into 22 clusters each containing 2–31 identical strains. Forty-five strains

### Table II. Characteristics of the clustered and the nonclustered prisoner groups.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study population</th>
<th>Clustered patients</th>
<th>Nonclustered patients</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>146(^b)</td>
<td>82</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>32.8 years (17–67)</td>
<td>33.1 years (17–67)</td>
<td>32.4 years (17–60)</td>
<td>0.68</td>
</tr>
<tr>
<td>Clinical forms:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>104 (71.7%)</td>
<td>58 (70.7%)</td>
<td>46 (73%)</td>
<td>0.86</td>
</tr>
<tr>
<td>EP</td>
<td>41 (28.3%)</td>
<td>24 (29.3%)</td>
<td>17 (27%)</td>
<td></td>
</tr>
<tr>
<td>TB history:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>new cases</td>
<td>127 (87%)</td>
<td>72 (88%)</td>
<td>55 (87.3%)</td>
<td>0.46</td>
</tr>
<tr>
<td>failure</td>
<td>2 (1.4%)</td>
<td>2 (2.4%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>relapse</td>
<td>5 (3.4%)</td>
<td>3 (3.6%)</td>
<td>2 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>interruption of treatment</td>
<td>11 (7.5%)</td>
<td>4 (4.8%)</td>
<td>6 (9.5%)</td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>1 (0.7%)</td>
<td>1 (1.2%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mean time incarcerated before TB diagnosis</td>
<td>507.2 days</td>
<td>510.4 days (among 79 patients)</td>
<td>515.6 days (among 58 patients)</td>
<td>0.85</td>
</tr>
<tr>
<td>Time incarcerated before TB diagnosis:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>37 (25.4%)</td>
<td>19 (23.2%)</td>
<td>17 (27%)</td>
<td>0.61</td>
</tr>
<tr>
<td>6–12 months</td>
<td>40 (27.4%)</td>
<td>22 (26.8%)</td>
<td>18 (28.5%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>61 (41.8%)</td>
<td>38 (46.3%)</td>
<td>23 (36.5%)</td>
<td></td>
</tr>
<tr>
<td>unknown</td>
<td>8 (5.5%)</td>
<td>3 (3.7%)</td>
<td>5 (8%)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) According to the Kruskal-Wallis test.

\(^b\) Including one P patient (interruption of treatment) with a strain with one IS6110 copy but for whom the DR pattern was not established, and thus could not be classified into any group.

### Table III. Characteristics of new and recurrent cases\(^a\).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>New cases ((n = 127))</th>
<th>Recurrent cases ((n = 17))(^b)</th>
<th>P value(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>72</td>
<td>9</td>
<td>8</td>
</tr>
<tr>
<td>Mean age</td>
<td>32.6 years (33 years)</td>
<td>34.1 years (35 years)</td>
<td>33 years</td>
</tr>
<tr>
<td>Clinical forms:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td>49</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>EP</td>
<td>23</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>Mean time incarcerated before TB diagnosis</td>
<td>37.3 months</td>
<td>80.8 months</td>
<td>0.2</td>
</tr>
<tr>
<td>Time incarcerated before TB diagnosis:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>19</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>6–12 months</td>
<td>19</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 12 months</td>
<td>32</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>unknown</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) TB history was not known for one patient who was thus excluded from this analysis.

\(^b\) One of the 18 recurrent patients, with a strain with one copy of IS6110 which was not typed with the DR marker, was excluded from this analysis.

\(^c\) Comparison between the new and recurrent cases according to the Kruskal-Wallis test.
had a single copy of IS6110 and gave five profiles differing in the position of the hybridising IS6110 band: two clusters of one strain, one of 31, one of seven, and one cluster containing five M. bovis strains (IS6110 band located at 1.8 kb). These latter strains were isolated from three P and two EP nonprisoner patients. Twenty-seven of the strains with a single copy of IS6110 were typed with the DR marker and were classified into 16 DR clusters each containing one to four strains.

The percentage of patients clustered for the IS6110 marker in new TB cases was higher (P < 0.01) for prisoners (58.9%) than for nonprisoners (40%). Furthermore, when excluding from the analysis the patients with one IS6110 copy strain (17 strains from new prison patients and 45 from nonprisoners), the percentage of clustered patients was still higher for the prisoners (45.6%) than for the nonprisoners (28.3%), suggesting a higher rate of transmission within the prison.

When considering all the 406 prison and nonprison isolates, 238 IS6110 profiles were found: 199 strains had a unique IS6110 profile and 207 strains (51%) were assigned to 39 IS6110 clusters (figure 2) of 2–38 patients. Ten clusters (23 strains) contained exclusively prison isolates and nine clusters (27 strains) exclusively nonprison isolates. We found 20 clusters (158 strains) that were common to prison and nonprison isolates. These corresponded to 51.2% of the clusters and to 8.4% (20/238) of the IS6110 profiles.

3.6. Epidemiological analysis of the prison clusters

We investigated whether transmission of M. tuberculosis occurred within the prison and tried to identify possible source cases, by carrying out an epidemiological analysis of the 22 prison clusters (82 clustered prisoners).

We first investigated whether patients of the same cluster were living in the same block. This was the case in only 12 clusters, corresponding to a total of 45 patients (including one interruption of treatment and two relapse cases). We then analysed these cases to try to identify possible sources. Several patients may have infected other patients in the same block. However, for some clusters, it was difficult to identify with certainty the index case, and some patients were probably infected outside the prison because they were diagnosed just after their incarceration or entered the prison when the supposed source of infection was already being treated.

The available data for these 45 patients show that 36 were either sources of infection (14 patients, including one interruption of treatment) or patients infected in the prison (22 patients). Of the 22 patients suspected to have been infected in prison, there was one new patient in block A, four new patients in B, four in C and 12 in F. These patients accounted for 9, 14.8, 15.4 and 24.5%, respectively, of the new patients in these blocks. Another patient suspected to have been infected in prison was a relapse case, in block A. We were unable to determine whether this was a case of reinfection or of reactivation of a latent infection.

Among the other 46 clustered patients without any evident epidemiological relationship, 16 patients were in eight clusters exclusively found in the prison:

- four cases of treatment interruption for whom actual TB was probably a reactivation of the old infection,
- one relapse case who was a released prisoner (after 5 years of incarceration),
- one treatment failure case,
- eight new cases who entered the prison after February 1994, and thus could have been already infected before their incarceration,
- and two new cases incarcerated before February 1994, who thus could have been infected in the prison before the study period.

One relapse case (a prisoner released in 1992) and 27 new patients in prison were in clusters also found in nonprison patients. Twelve of them were incarcerated before the beginning of this study, so it was difficult to determine where they have been infected. The 15 others entered the prison after February 1994. One patient from the Tonga Soa laboratory staff was diagnosed in February 1995. He was in cluster no. 20b, that
**Figure 2.** IS6110 clusters among prison and nonprison patients. On the left of the figure, the number of the IS6110 clusters previously reported in figure 1 are in bold. The number of patients in clusters is given on the right of the figure. The clusters with both prison and nonprison isolates are in italics.
contained two other prisoners diagnosed respectively in April 1994 and November 1995, but his isolate also clustered with nonprison isolates, so we cannot determine whether he was infected in the laboratory. For one patient, the history of TB was unknown.

In summary, 23 new patients (eight in prison clusters exclusively, and 15 who clustered with nonprison patients) could have involved reactivation of infection acquired before incarceration.

3.7. Analysis of the nonclustered prisoners

Among the 63 nonclustered prisoners (tables II and III), eight had a previous history of TB: six cases of treatment interruption (one entered the prison before February 1994, and five during the study period), and two relapse cases. For the two relapse cases, they did not cluster with patients in Antananarivo and they were incarcerated for more than 4 years, so they could have been reinfected in the prison.

Fifty-five nonclustered prisoners were new cases. Nine prisoners had isolates which clustered with nonprison isolates: one released prisoner, and five prisoners who entered the prison during the study period, could have been infected in the city; for three patients incarcerated before February 1994 (one declared having contact with another TB patient in prison in 1993), we could not reach a conclusion.

For the 46 other new patients, their isolates did not cluster with any nonprison strains. One was a released prisoner. Twenty-three patients entered the prison before February 1994 and for all of them, delay time between incarceration and TB diagnosis was over 6 months. It is therefore difficult to determine whether it was a reactivation or an infection. Nineteen patients entered the prison during the study period; as no patients with the same strains was found in the prison during this period it is more likely that they were infected before their incarceration. One patient, an EP TB case, was a technician of the Tonga Soa laboratory where he was working since 1991. His isolate did not cluster with any other prison or nonprison strain of the study period. So it is not possible to determine whether it was a laboratory contamination. For two new patients, no epidemiological information was available.

In summary, among nonclustered prisoners, reactivation of mistreated infection or an infection acquired outside the prison was more probable for the six patients who interrupted treatment and for 24 new cases.

4. Discussion

We investigated TB transmission in a prison in Madagascar. Unlike most of the surveys of inmates in other countries [5, 14], this study was conducted in a country with a very low prevalence of HIV infection. In a previous study [3], because movements in the prison of Antananarivo were very difficult to evaluate, the prevalence of TB was estimated considering that 454 TB cases were registered between June 1990 and December 1993, while 19 214 new entries were recorded. This corresponded to an observed prevalence of 2.4%, which was much higher than in the city. To determine whether the high incidence of TB in the prison of Antananarivo was due to a greater risk of infection inside than outside the prison, we characterised the M. tuberculosis strains circulating in the prison by the RFLP method using two genetic markers, IS6110 and DR. Genotyping classified 145 TB patients in the prison into two groups: 82 clustered patients and 63 nonclustered patients.

We evaluated the extent of TB transmission in prison by comparing the clustering of M. tuberculosis strains for patients inside and outside the prison. The proportion of clustered patients among new cases was significantly higher for prisoners (58.9%) than for nonprisoners (40%), suggesting that the transmission rate was higher within the prison than in the general population. When analysing the prison and nonprison isolates together, 207 strains (51%) were assigned to 39 IS6110 clusters. Ten clusters were found in strains from prisoners. Twenty clusters were common to the prison and the city, suggesting active circulation of strains between the prison and the outside, or a reactivation of old infections acquired outside. We also noted the pres-
ence of a cluster with *M. bovis* strains. All were isolated from nonprisoners. Thus, despite the presence of bovine TB in Madagascar [11], we did not reveal any circulation of *M. bovis* strains in the prison. This may be due to the low prevalence (about 1%) of *M. bovis* in human TB ([10], this study). We investigated whether *M. tuberculosis* infection was acquired in prison by assuming that transmission was possible only within a block and that only pulmonary patients were contagious. We found that *M. tuberculosis* strains may have circulated among 36 patients (24.7% of the included patients (36/146)) of whom 14 (9.5% of the study population) were the source of infection for the other 22 prisoners (15.1% of the study population). Nevertheless, for each patient, infection outside the prison before incarceration could not be excluded. Concerning the other 46 clustered patients, our data suggested that for 23 new patients, infection was more likely to have been acquired before incarceration. Of the 63 nonclustered prisoners, eight were recurring cases and 55 were new cases, of which 24 might be reactivation of old infection due to the difficult living conditions in the prison. There is no published data concerning intake of calories among prison versus nonprison TB patients. However, the diet improved significantly in prison between the time of this study and 1997: the food ratio increased from 8 kg of rice/year/prisoner to 28 kg of rice/year/prisoner. This resulted in a decrease of the TB annual incidence from 119 cases in 1995 to 52 cases in 1997, 30 in 1998 and 21 in 1999 (detected mainly among new entrants) and the drop in the global mortality rate among the prisoners from 6% to < 1% (M. Clouzeau and J. Rabehaja, personal communication). This observation lends strong support to the impact of malnutrition in the emergence of TB.

In conclusion, this study showed that 15.1% of the patients in prison were likely to have acquired TB infection in prison during the study period. Of the 127 new TB cases, 47 (37%) were probably contaminated by index cases outside the prison. For all the other patients, no clear epidemiological relationship could be established. They could, however, have been infected before February 1994 by patients not included in the study. As the prevalence of TB in Madagascar is very high, it is likely that most of the prisoners were already infected when entering the jail. The use of additional polymorphic gene markers from *M. tuberculosis* genome analysis may be of greater value for typing the strains more precisely. Finally, this work shows the huge difficulty of carrying out surveys within prisons in developing countries.

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