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1 **Title:** Leprosy in French Polynesia

2

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1 **Title:** Leprosy in French Polynesia

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3

4 **Abstract**

5 Leprosy is a neglected endemic infectious disease in the Pacific region. In French Polynesia,
6 leprosy is not any longer a public health problem at the national level, defined by the World
7 health Organization as a prevalence rate below 1 case per 10,000 population. However, even
8 if its incidence has dramatically declined in French Polynesia in the last decades, leprosy is
9 still endemic at low level. Here we present a case of leprosy of a 34-year-old man from
10 French Polynesia diagnosed in 2018. Clinical and microbiological examinations including
11 fluorescence *in situ* hybridization, led to the diagnosis of a multibacillary leprosy and a
12 multidrug therapy was initiated. There is a need to maintain leprosy surveillance, and trained
13 medical staff for the detection and treatment of new cases.

14 **Introduction**

15 Leprosy is a chronic bacterial disease caused by *Mycobacterium leprae* that predominantly
16 affects skin and peripheral nerves. Leprosy is responsible for disabilities and deformities,
17 associated with stigma. More than 200,000 new cases of leprosy are reported annually in the
18 world with a slow decrease in the detection of new cases globally during the past decade
19 [1,2].

20 The goal of eliminating leprosy as a public health problem at the national level was defined
21 by the World health Organization (WHO) in 1991 as a prevalence rate below 1 case per
22 10,000 population [1-3]. The goal of WHO for 2020 is to have 0 new child diagnosed with
23 grade-2 leprosy (visible damage/deformity or disability), less than 1 newly diagnosed leprosy
24 patient with grade-2 leprosy per million population and no countries with legislation that
25 allows discrimination against people with leprosy [4].

26 French Polynesia (FP), is a remote French overseas Territory located in the South Pacific.
27 French Polynesian population is about 280,000 inhabitants distributed in 72 inhabited Islands
28 grouped in 5 archipelagoes. FP belongs to the 22 Pacific Islands Countries and Territories.
29 Leprosy is endemic in the Pacific region, including FP and is considered as a neglected
30 disease in the region with an incidence stable in the past decade [1,3,5,6].

31 We report a case of leprosy in FP diagnosed in 2018 and report data about epidemiology of
32 leprosy in this country since early 20th century.

33

34 **Clinical case**

35 A 34-year-old man living in Raiatea Island, French Polynesia, was admitted in September
36 2018. The patient has no underlying disease and no known contact with people suffering
37 leprosy.

38 Clinical signs appeared in mid-2016, at examination he had erythematous plaques (improperly
39 classified as urticarial plaques) on trunk and arms, hand and feet edema with dyschromic
40 plaques, and asthenia. At this time he was treated for toxocarosis because a serology for
41 *Toxocara canis* was positive.

42 Clinical examination at admission in September 2018 (Figure 1) yielded: leonine facies,
43 bilateral conjunctivitis, loss of end eyebrows, feet and hands edema, nodules in different part
44 of the body (hypochromic and hyperchromic), small nodules on extremities and earlobes, loss
45 of feeling on feet, enlarged nerves on ankles, small inguinal and axillary adenopathies (< 1
46 centimeter), hypertrophy of mammary glands, nasal congestion with nose bleeding after
47 sample collection, and asthenia. Cardiac and pulmonary examination detected no
48 abnormalities. Hepatic enzymes, urea, creatinine, and thyroid laboratory markers results were
49 in the normal range.

50 This patient had two of the three WHO diagnosis criteria for leprosy: thickened or enlarge
51 peripheral nerve with loss of sensation and/or weakness of the muscles supplied by the nerve,
52 and presence of acid-fast bacilli in a slit-skin smear [1]. This case was classified as a
53 multibacillary leprosy according to the clinical WHO classification (more than five skin
54 lesions or more than one nerve trunk involvement or with bacilli in a skin smear), and grade 1
55 disability (loss of sensation but not yet visible damage, deformability of disability [1]).

56 A multidrug therapy for multibacillary leprosy was initiated with rifampicin 600 mg per day,
57 clofazimine 100 mg per day and dapsone 100 mg per day, slightly different from the WHO
58 recommendations [1]. This therapeutic regimen is used by French Polynesian leprologists for
59 many years.

60 Written consent was obtained from the patient for reporting this case.

61 Incidence rate of leprosy in FP from 1967 to 2017 is reported in Figure 2.

62

63 **Microbial investigations**

64 Ziehl-Neelsen-stained skin smears from the earlobes and nasal mucosa yielded numerous acid
65 fast bacilli with a bacterial index 5 (100-1,000 bacilli in every field at magnification 100X)
66 and intra and extra cellular *globi* (clumps of bacilli in capsular material). Histopathological
67 examination of skin lesion showed a nonspecific inflammatory infiltrate with predominance
68 of histiocytes, with numerous acid fast bacilli after Ziehl-Neelsen staining (Figure 3).
69 Diagnosis was confirmed by the specific detection of *Mycobacterium leprae* in nasal mucosa
70 and skin smears by combining fluorescence *in situ* hybridization (FISH) and Ziehl-Neelsen
71 staining using a modified protocol already tested on mycobacteria [7, 8]. Briefly, smear slides
72 were fixed in 4% paraformaldehyde and covered with 10 mg/mL lysozyme then 10 µg/mL
73 proteinase K (respectively at 37°C for 30 min and 37°C for five min). Slides were incubated
74 overnight with a 10-µL suspension containing the specific probe targeting the *Mycobacterium*
75 *leprae rpoB* gene (Alexa 555-GCCAGAGCAAGACAGACGTT-3'). After washing steps,
76 smears were stained with Ziehl-Neelsen staining (Kit Quick-TB, RAL DIAGNOSTICS,
77 Martillac, France) and mounted with ProLong Diamond antifade (Fisher Scientific, Illkirch,
78 France) containing 4, 6-diamidino-2-phenylindole. Microscopic observation was performed
79 using the 100X objective lens of Leica DMI 6000 fluorescence microscope (Leica
80 Microsystems, Nanterre, France). FISH and Ziehl-Neelsen-staining combination yielded
81 specific detection of *Mycobacterium leprae* as red fluorescent and Ziehl-Neelsen-positive
82 bacilli (Figure 4).

83

84 **Discussion**

85 Leprosy was probably introduced in FP during past migrations from Asia, long before
86 European migration, and the disease described as “*oovi*” in Tahitian language or “*koovi*” in
87 Marquesian language [9]. The disease was subsequently described in the 18th century by

88 explorers. The last introductions probably occurred by Chinese immigrants in the Marquesas
89 archipelago in the 19th century. From the 19th century, patients suffering leprosy were isolated
90 in leper colonies. The first leper colonies were in Tahiti (the main FP island) and Marquesas
91 in 1914, the last one located in Tahiti was closed in 1976 [6,9]. In FP, notification of leprosy
92 cases has been systematic since 1902 and leprosy was a mandatory reporting communicable
93 disease since 1911. Up to 1946, diagnosis was based on clinical examination only. Lepromin
94 skin test, search for acid-fast bacilli and biopsy for pathological examination were available
95 from 1946 [10]. Dapsone monotherapy was implemented in 1952 and multidrug therapy
96 including rifampicin in 1982. Case detection rate of leprosy in FP decreased from 50 per
97 100,000 population in 1902 to 25 per 100,000 in 1946 to 8 per 100,000 in 1991, to 1.8 per
98 100,000 population in 2017 with an average annual rate of decrease of 2% between 1902 and
99 1991 [10]. Introduction of multidrug therapy contributed to the decline of leprosy in FP but it
100 is difficult to evaluate the respective contribution of multidrug therapy, economic
101 improvement of the country and natural decline of leprosy [11].

102 The prevalence of leprosy in FP is under the rate of 1 case per 10,000 population since 1991
103 and is stable since then with a mean prevalence of 0.44 per 10,000 population and a mean
104 incidence of 1.6 cases per 100,000 population from 2000 to 2017 [6].

105 Even if data are lacking from some remotes Pacific Islands, leprosy is endemic in the region
106 [12-15]. The overall prevalence of leprosy in the Pacific Islands Countries and Territories in
107 2010 was 1.64 per 10,000 population, then the threshold of 1 per 10,000 population was not
108 yet achieved [3]. But disparities exist within the Pacific areas. Federated States of Micronesia,
109 Marshall Islands and Kiribati failed to reach leprosy elimination with a prevalence over 10
110 cases per 100,000 population; in Nauru and Palau the annual prevalence range from 1 to 10
111 cases per 10,000 population [3]. These Pacific Islands Countries and Territories are located in
112 North West Pacific. If we consider the East Pacific Islands Countries and Territories (that

113 includes FP) the overall prevalence is below 1 per 10,000 population [6]. The higher
114 prevalence of leprosy in North West Pacific is possibly due to its close location to South East
115 Asia, the area in the world where ¾ of leprosy cases are reported [2].
116 Data about drug resistance and genetic diversity of *M. leprae* strains circulating in the Pacific
117 and FP are scarce. Four French Polynesian strain genotyped using Single Nucleotide
118 Polymorphism (SNP) belonged to SNP genotype 3, however the 4 SNP types have been
119 isolated in New Caledonia [16]. FISH has been reported to successfully detect *Mycobacterium*
120 *leprae* in paraffin-embedded tissue sections from skin biopsy sample [17]. In this case, FISH
121 allowed to detect and visualize *Mycobacterium leprae* bacilli directly on skin smears and
122 nasal mucosa smears offering an additional method for leprosy diagnosis.
123 With less than 10 cases per year in the past decade, leprosy became a rare disease in FP and
124 new physicians are not trained to detect early clinical signs of leprosy. Consequently leprosy
125 can remain undetected or misdiagnosed, as illustrated by this case report. It highlights the
126 need to maintain leprosy surveillance, to have specialists and general health care staff trained
127 to detect and report cases, as timely diagnosis and proper implementation of treatment will
128 prevent development of nerve damages, disabilities, and reduce the disease burden of leprosy
129 [1,3].

130

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133

134 **Figure 1:** Leprosy in a 34 years old French Polynesian man

135

136 **Figure 2:** Incidence rate of leprosy in French Polynesia (cases per 10,000 population) from

137 1967 to 2017.

138

139 **Figure 3:** Smears showing numerous acid fast bacilli with intra and extra cellular *globi*

140

141 **Figure 4:** Microscopic images of smears from nasal mucosa (A) and skin biopsy (B)

142 combining FISH with DAPI and Ziehl-Neelsen staining. Image acquisition was performed for

143 the same microscopic field using a Hamamatsu Orca AG camera (Hamamatsu Photonics,

144 Herrsching-am-Ammersee, Germany) to visualize FISH-positive mycobacteria (left panels)

145 and using a DFC425C Digital Microscope Camera (Leica Microsystems, Nanterre, France)

146 for Ziehl-Neelsen-positive mycobacteria (right panels). FISH=fluorescence *in situ*

147 hybridization. DAPI=4, 6-diamidino-2-phenylindole.

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Figure 1: Leprosy in a 34 years old French Polynesian man

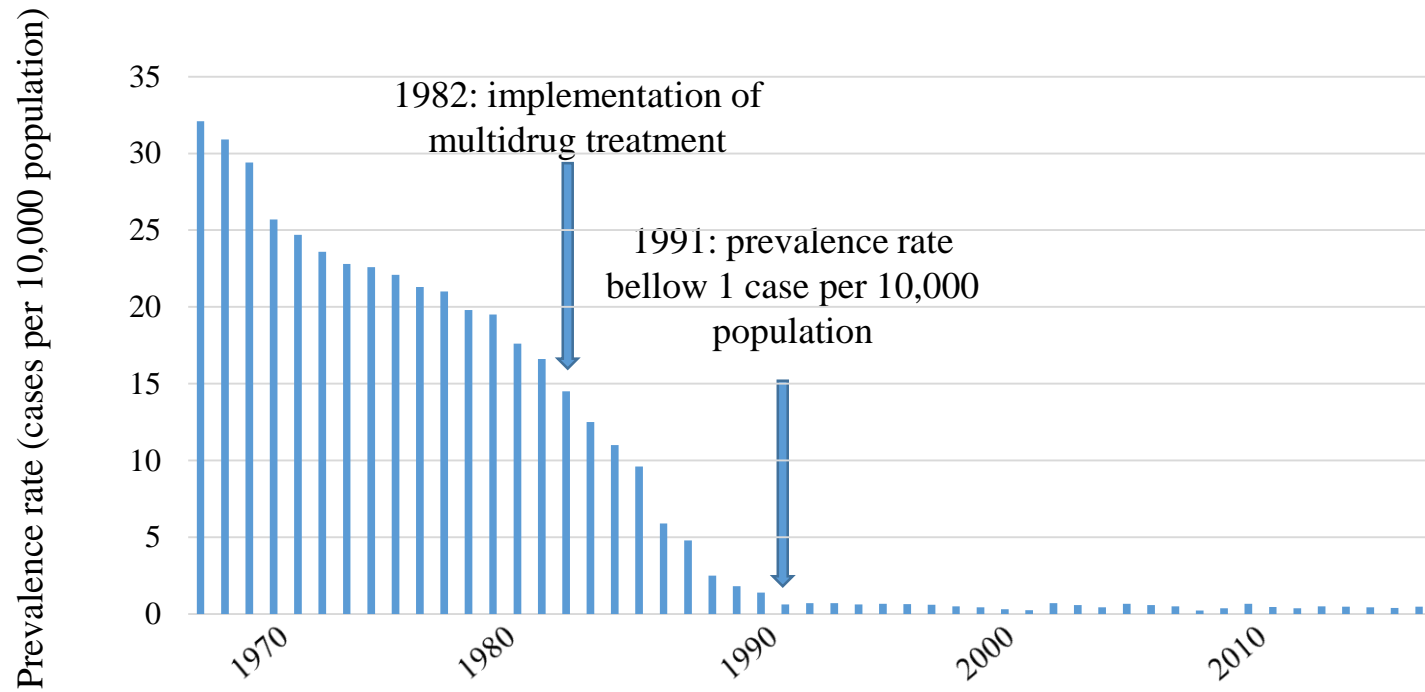


Figure 2: Incidence rate of leprosy in French Polynesia (cases per 10,000 population) from 1967 to 2017.

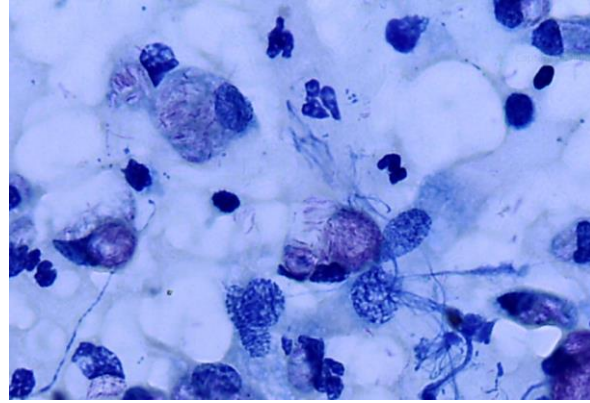
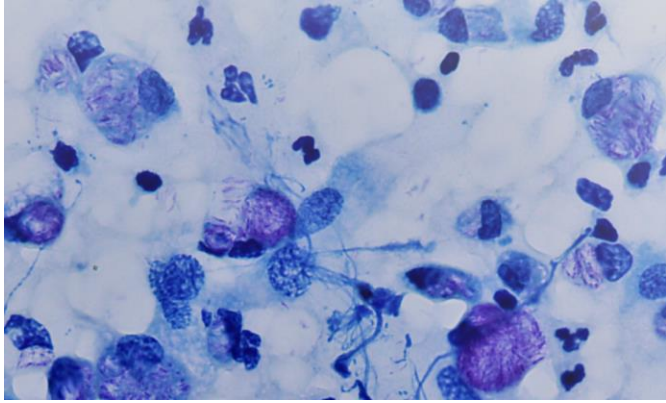


Figure 3: Smears showing numerous acid fast bacilli with intra and extra cellular *globi*

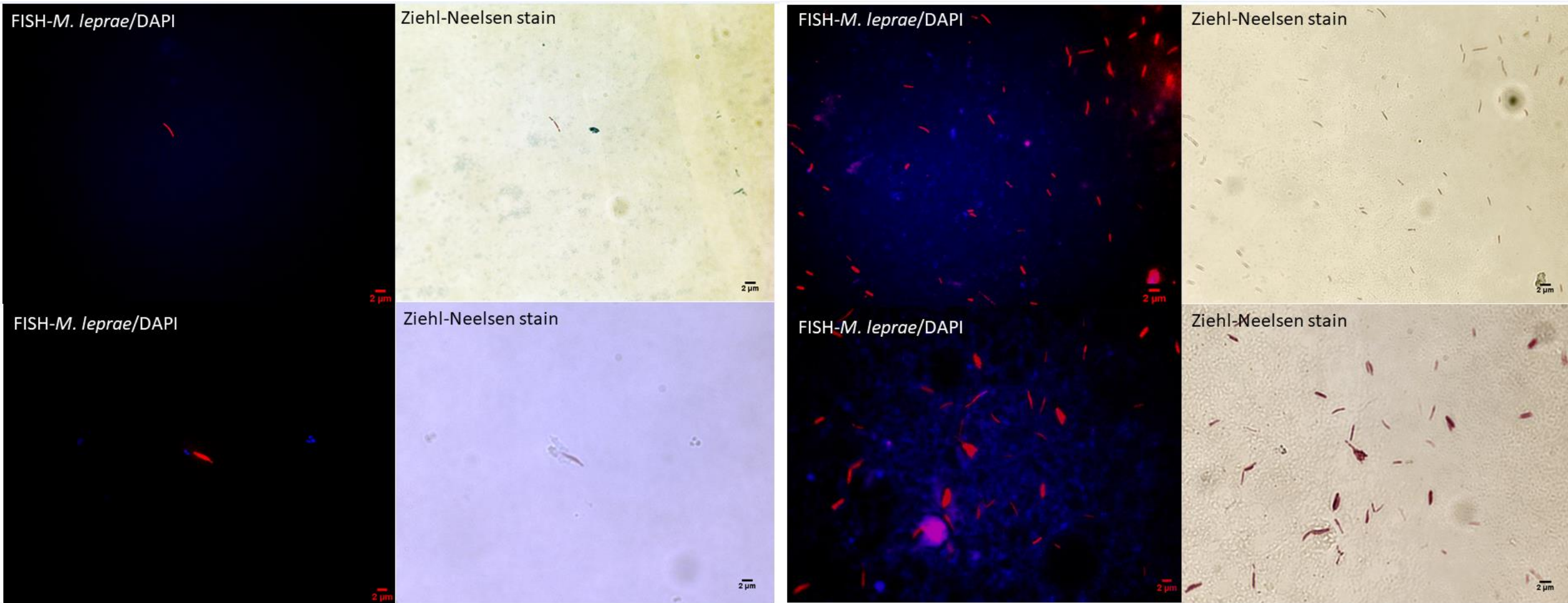


Figure 4: Microscopic images of smears from nasal mucosa (A) and skin biopsy (B) combining FISH with DAPI and Ziehl-Neelsen staining. Image acquisition was performed for the same microscopic field using a Hamamatsu Orca AG camera (Hamamatsu Photonics, Herrsching-am-Ammersee, Germany) to visualize FISH-positive mycobacteria (left panels) and using a DFC425C Digital Microscope Camera (Leica Microsystems, Nanterre, France) for Ziehl-Neelsen-positive mycobacteria (right panels). FISH=fluorescence *in situ* hybridization. DAPI=4, 6-diamidino-2-phenylindole.

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