# Leprosy in French Polynesia

D. Musso, C. Rovery, A. Loukil, V. Vialette, N.L. Nguyen

**Title:** Leprosy in French Polynesia

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**Authors and affiliations:** Didier Musso[1,2*], Clarisse Rovery[3], Ahmed Loukil[4], Véronique Vialette[1], Ngoc Lam Nguyen [5]

[1] Unit of Emerging Infectious Diseases, Institut Louis Malardé, Tahiti, Polynésie française

[2] Aix Marseille Univ, IRD, AP-HM, SSA, VITROME, IHU-Méditerranée Infection, Marseille, France

[3] Hôpital d'Uturoa, Tahiti, Polynésie française

[4] Aix Marseille Univ, MEPHI, IRD, IHU Méditerranée Infection, Marseille, France

[5] Infectious and Tropical Diseases Unit – Public Health Direction – Tahiti, Polynésie française

*** Corresponding author:**

Unit of Emerging Infectious Diseases, Institut Louis Malardé, PO Box 30, 98 713 Papeete, Tahiti, French Polynesia. Tel 689 40 416 470. Emails dmusso@ilm.pf dmusso12345@gmail.com

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## Abstract

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

## Introduction

Leprosy is a chronic bacterial disease caused by *Mycobacterium leprae* that predominantly affects skin and peripheral nerves. Leprosy is responsible for disabilities and deformities, associated with stigma. More than 200,000 new cases of leprosy are reported annually in the world with a slow decrease in the detection of new cases globally during the past decade [1.2].

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

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

We report a case of leprosy in FP diagnosed in 2018 and report data about epidemiology of leprosy in this country since early 20$^{th}$ century.

## Clinical case

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

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

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

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

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

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

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

## Microbial investigations

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

## Discussion

Leprosy was probably introduced in FP during past migrations from Asia, long before European migration, and the disease described as "*oovi*" in Tahitian language or "*koovi*" in Marquesian language [9]. The disease was subsequently described in the 18$^{th}$ century by

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

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

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

includes FP) the overall prevalence is below 1 per 10,000 population [6]. The higher prevalence of leprosy in North West Pacific is possibly due to its close location to South East Asia, the area in the word were ¾ of leprosy cases are reported [2].

Data about drug resistance and genetic diversity of *M. leprae* strains circulating in the Pacific and FP are scarce. Four French Polynesian strain genotyped using Single Nucleotide Polymorphism (SNP) belonged to SNP genotype 3, however the 4 SNP types have been isolated in New Caledonia [16]. FISH has been reported to successfully detect *Mycobacterium leprae* in paraffin-embedded tissue sections from skin biopsy sample [17]. In this case, FISH allowed to detect and visualize *Mycobacterium leprae* bacilli directly on skin smears and nasal mucosa smears offering an additional method for leprosy diagnosis.

With less than 10 cases per year in the past decade, leprosy became a rare disease in FP and new physicians are not trained to detect early clinical signs of leprosy. Consequently leprosy can remain undetected or misdiagnosed, as illustrated by this case report. It highlights the need to maintain leprosy surveillance, to have specialists and general health care staff trained to detect and report cases, as timely diagnosis and proper implementation of treatment will prevent development of nerve damages, disabilities, and reduce the disease burden of leprosy [1,3].

**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 Microsystèmes, Nanterre, France) for Ziehl-Neelsen-positive mycobacteria (right panels). FISH=fluorescence *in situ* hybridization. DAPI=4, 6-diamidino-2-phenylindole.

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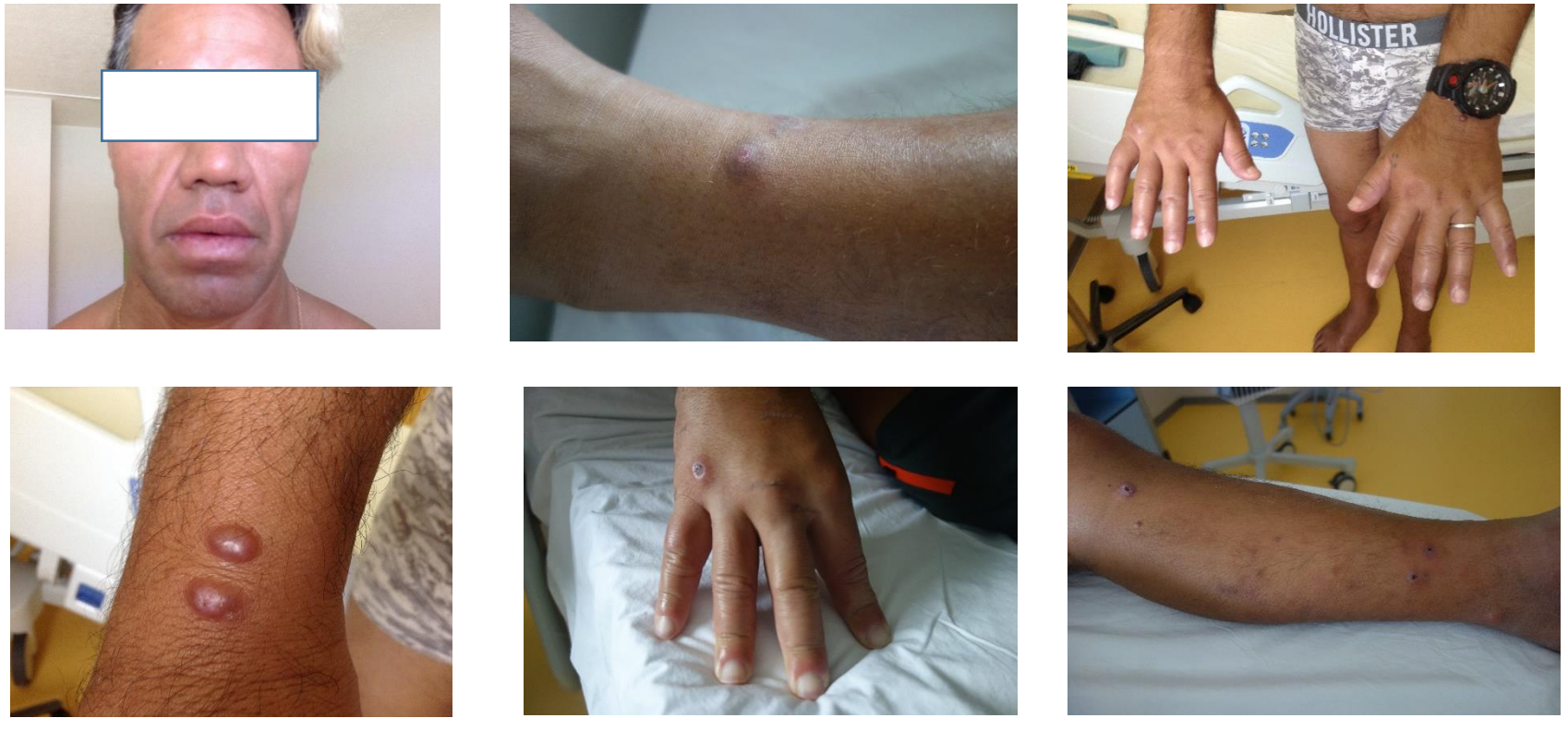



**Figure 1:** Leprosy in a 34 years old French Polynesian man

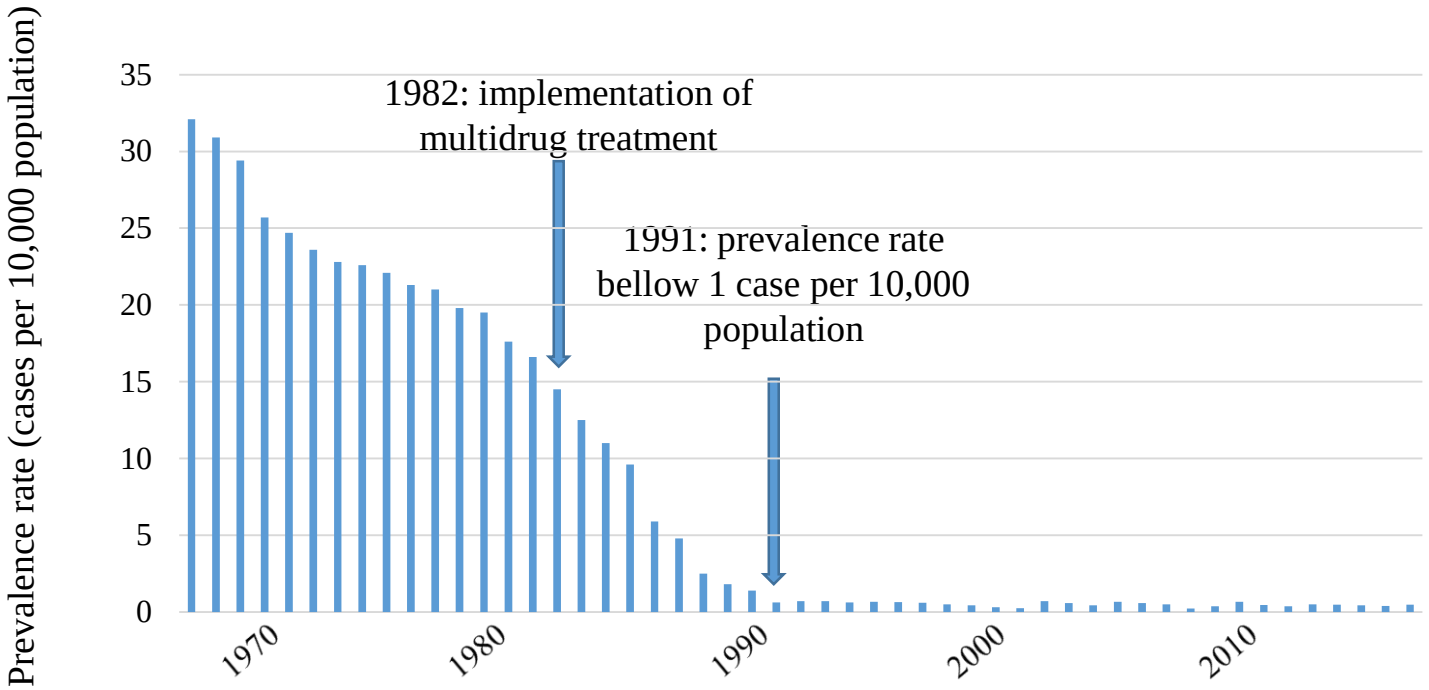



**Figure 2:** Incidence rate of leprosy in French Polynesia (cases per 10,000 population) from 1967 to 2017.

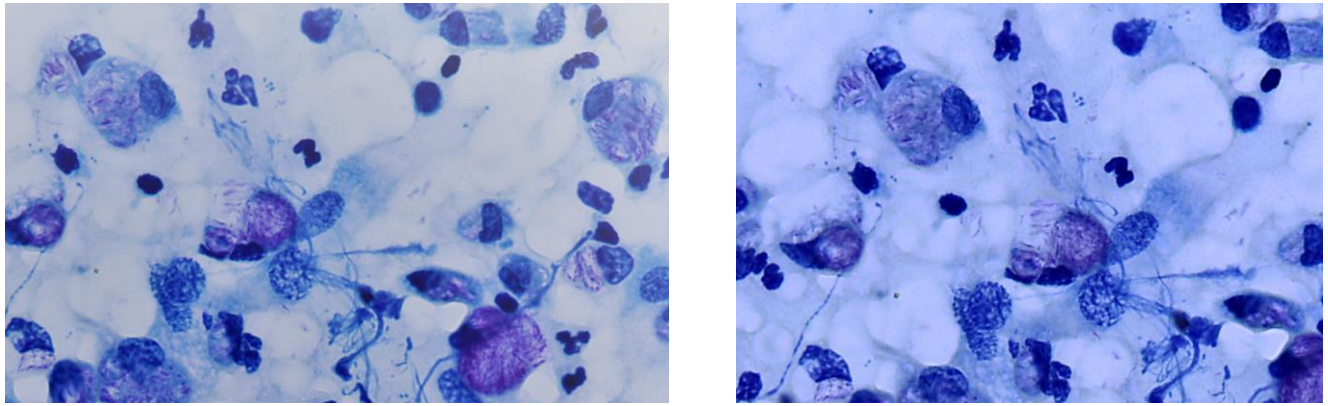
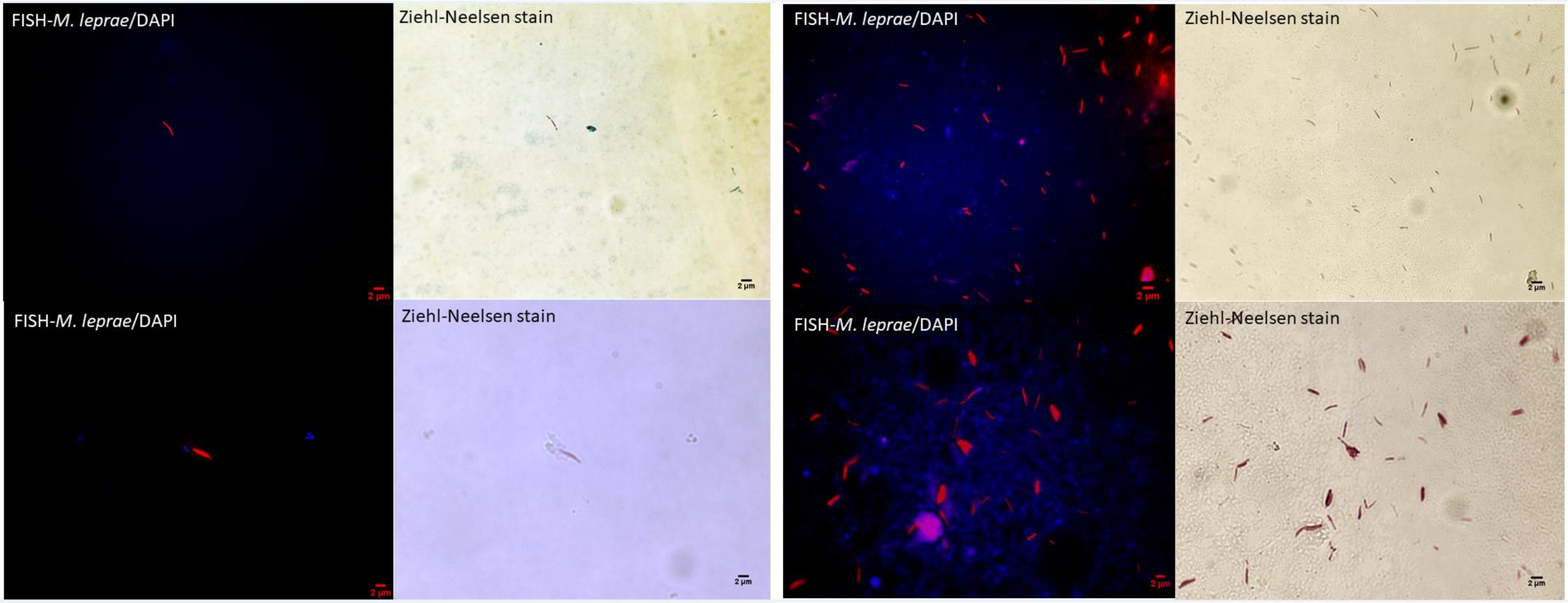


**Figure 3:** Smears showing numerous acid fast bacilli with intra and extra cellular *globi*

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