



Multicenter Surveillance of Prevalence of the 23S rRNA A2058G Point Mutation and Molecular Subtypes in *Treponema pallidum* in Taiwan, 2009 to 2013

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Abstract

Background: *Treponema pallidum* that exhibits A2058G or A2059G mutation on 23S ribosomal RNA (rRNA) is increasingly reported worldwide, which has been reported to cause treatment failures in patients receiving azithromycin for syphilis. Genotyping of *T. pallidum* strains sequentially isolated from patients with recurrent syphilis using the enhanced genotyping methodology is rarely performed.

Methods: Between September 2009 and August 2013, we prospectively collected clinical specimens from patients who presented with syphilis for genotyping that examined the number of 60-bp repeats in the acidic repeat protein (*arp*) gene, *T. pallidum* repeat (*tpr*) polymorphism, and *tp0548* gene and for detection of A2058G and A2059G point mutations of 23S rRNA gene using restriction fragment-length polymorphism.

Results: During the 4-year study period, we collected 658 clinical specimens from 375 patients with syphilis. *T. pallidum* DNA was identified from 45.2% (n=298) of the specimens that were collected from 216 (57.6%) patients; and 268 (40.7%) specimens tested positive for 23S rRNA gene were examined for macrolide resistance. Two isolates (0.7%) had A2058G mutation on 23S rRNA gene from two HIV-infected individuals. A total of 14 strains of *T. pallidum* were identified, with 14f/f (57.5%) and 14b/c (10.0%) being the two most predominant strains. Forty patients presenting with recurrent syphilis had *T. pallidum* DNA identified from the initial and second episodes, with five cases demonstrating strain discrepancies. One patient had two strains identified from different clinical specimens collected in the same episode.

Conclusions: We found that genotype 14f/f was the most common *T. pallidum* strain in this multicenter surveillance study of syphilis in Taiwan, where the prevalence of *T. pallidum* that exhibited A2058G or A2059G mutation on 23S rRNA gene remained low. Different genotypes of *T. pallidum* can be identified in patients with recurrent episodes of syphilis.

Introduction

1. A high prevalence of macrolide-resistant *T. pallidum* has been increasingly reported in several developed and developing countries, which makes surveillance of *T. pallidum* with macrolide resistance mutation an integral part of syphilis control program.
2. Genotyping of *T. pallidum* using enhanced molecular typing methods may make the monitoring of epidemiology of *T. pallidum* infection possible in different geographic regions.

Methods

1. Subjects: patients with syphilis
2. Study design: multicenter, surveillance study
3. Study site: 8 hospitals around Taiwan
4. Clinical specimens (swabs of chancres, blood, CSF, or vitreal fluid) collected for PCR assays that was used to amplify a 377-bp fragment of *T. pallidum pol I* gene
5. Presence of A2058G and A2059G mutations were detected by amplification of 23s ribosomal (rRNA) gene of *T. pallidum* DNA, followed by testing with the use of restriction fragment-length polymorphism
6. Strain typing was performed based on CDC methodology that targeted two loci: the number of 60 bp repeats in the acidic repeat protein (*arp*) gene and restriction fragment-length polymorphism patterns of *T. pallidum* repeat (*tpr*) genes subfamily II genes (*tprE*, *tprG* and *tprJ*), combined with a sequence of a short region in *tp0548* gene (131-215 bp).

Figure 1. Study flow

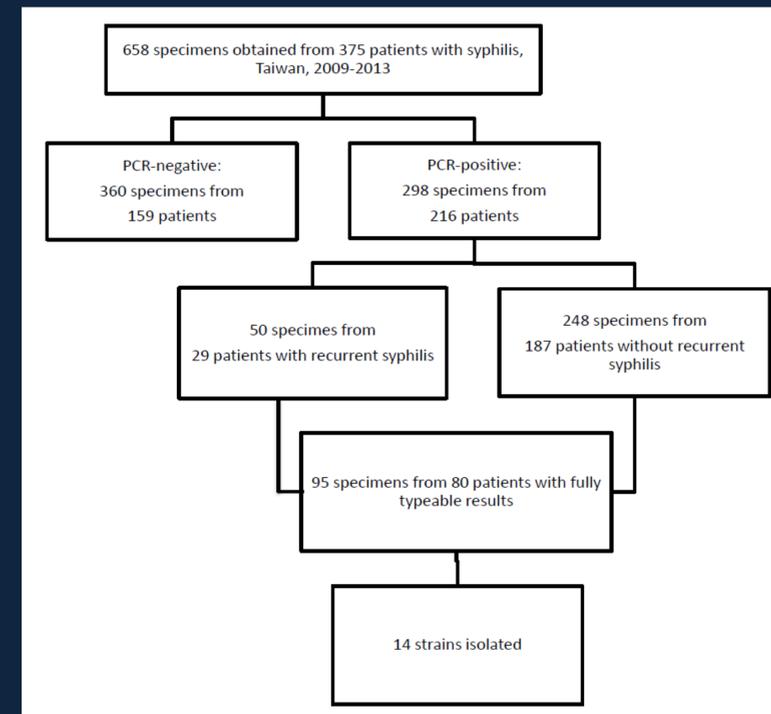


Figure 2. Distribution of genotypes of the *T. pallidum* strains identified between September 2009 and August 2013



Figure 2. Prevalence of *T. pallidum* harboring A2058G, 2009-2013

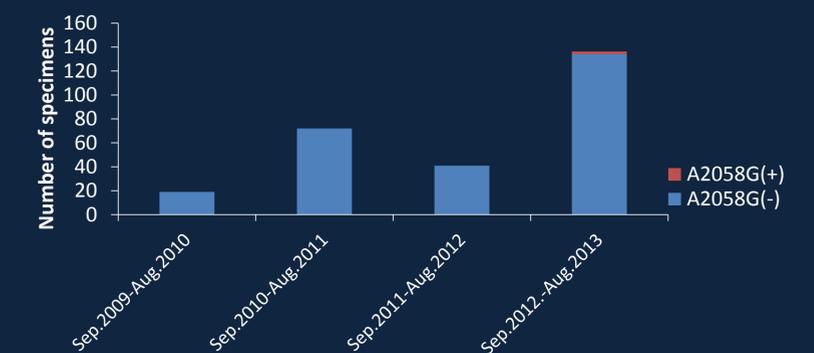


Table. Characteristics of the 40 patients with recurrent episodes of syphilis

	1 st episode	2 nd episode
Age, median (range), years	29 (22-28)	31 (23-48)
MSM, n (%)		
RPR titer, median (range), log ₂	6 (3-9)	7 (2-10)
Primary syphilis	12 (30.0)	11 (27.5)
Secondary	16 (40.0)	8 (20.0)
Primary and secondary	3 (7.5)	2 (5.0)
Early latent	8 (20.0)	18 (45.0)
Fully typing, n (%)	14 (35.0)	6 (15.0)
Strain distribution ^d	14f/f (n=9), 14k/f (3), 14a/f (2), 14f/c (1), /f (5), k/a, 14 /f, j/f, f/f, c/f, a/c, /c, /f (1 for each)	14f/f (n=4), 13f/f (1), 10b/a (1), /f (5), /a (2), f/f, b/c, a/f, /c (1 for each)

Conclusions

1. Genotype 14f/f remains the predominant stain of *T. pallidum* in Taiwan.
2. The prevalence of *T. pallidum* with macrolide resistance mutations remains low in Taiwan.
3. Different genotypes of *T. pallidum* can be identified in patients with recurrent episodes of syphilis.