https://doi.org/10.25208/vdv15827

Check for updates

Determination of molecular types and resistance to macrolides in *Treponema pallidum* isolates isolated in the Russian Federation

© Olga A. Obraztsova*, Kseniya M. Lagun, Georgii L. Katunin, Marina V. Shpilevaya, Nikita Yu. Nosov

State Research Center of Dermatovenereology and Cosmetology, Moscow, Russia

Background. The number of syphilis cases in the Russian Federation increased significantly in 2022. Control of heterogeneity of *Treponema pallidum* subtypes is important to monitor the emergence and spread of antibiotic-resistant strains

Aims. To determine molecular subtypes and resistance to macrolides in *T. pallidum* isolates isolated in the Russian Federation in 2022.

Methods. We analyzed DNA isolated from 49 samples of clinical material obtained from patients from dermatovenerological treatment and prevention facilities in three federal districts (CFD, SFD, SCFD) of the Russian Federation in 2022 with diagnoses of primary syphilis and secondary syphilis. *T. pallidum* DNA isolation and confirmation of the presence of genetic material were performed according to the existing algorithms. To search for genetic determinants of resistance to macrolides, a fragment of the 23S rRNA gene was analyzed. Primary decoding of nucleotide sequences was performed in Sequencing Analysis 5.3.1. Mega 11 program was used to align the analyzed fragments of target genes to *T. pallidum* reference sequences.

Results. In 2022, three subtypes of *T. pallidum* were identified in the territory of the represented federal districts of the Russian Federation: 14d/f, 14d/g, 14d/d with continued dominance of subtype 14d/f. The macrolide-resistant subtype 14d/d was identified in two federal districts, which is new for the Russian Federation.

Conclusions. The population of *T. pallidum* continues to expand in the Russian Federation, including the emergence of azithromycin-resistant strains. The data obtained confirm the need for continuous monitoring of circulating strains and may facilitate understanding of their geographic distribution.

Keywords: ***Treponema pallidum*; macrolides; mutation A2058G; subtype**

Conflict of interest: the authors declare that there are no obvious and potential conflicts of interest associated with the publication of this article.

Funding source: the manuscript was prepared and published at the expense of funding at the place of work of the authors.

For citation: Obraztsova OA, Lagun KM, Katunin GL, Shpilevaya MV, Nosov NYu. Determination of molecular types and resistance to macrolides in *Treponema pallidum* isolates isolated in the Russian Federation. Vestnik Dermatologii i Venerologii. 2024;100(2):52–58. doi: https://doi.org/10.25208/vdv15827

https://doi.org/10.25208/vdv15827

Определение молекулярных типов и резистентности к макролидам у изолятов *Treponema pallidum*, выделенных на территории Российской Федерации

© Образцова О.А.*, Лагун К.М., Катунин Г.Л., Шпилевая М.В., Носов Н.Ю.

Государственный научный центр дерматовенерологии и косметологии, Москва, Россия

Обоснование. В 2022 г в Российской Федерации значительно выросло количество случаев заболевания сифилисом. Контроль гетерогенности субтипов *Treponema pallidum* важен для надзора за появлением и распространением антибиотикорезистентных штаммов.
Цель исследования. Определить молекулярные субтипы и устойчивость к макролидам у изолятов *T. pallidum*, выделенных на территории Российской Федерации в 2022 г.
Методы. Анализировали ДНК, выделенную из 49 образцов клинического материала, полученного в 2022 г. от пациентов лечебно-профилактических учреждений дерматовенерологического профиля с диагнозами «первичный сифилис» и «вторичный сифилис», находящихся в трех федеральных округах Российской Федерации (Центральном, Сибирском и Северо-Кавказском). Выделение ДНК *T. pallidum* и подтверждение присутствия генетического материала проводили в соответствии с существующими алгоритмами. Для поиска генетических детерминант резистентности к макролидам анализировали фрагмент гена *23S рРНК*. Первичную расшифровку нуклеотидных последовательностей проводили в программе Sequencing Analysis 5.3.1. Для выравнивания анализируемых фрагментов целевых генов на референсные сиквенсы *T. pallidum* использовали программу Mega 11.
Результаты. В 2022 г. на территории представленных федеральных округов Российской Федерации идентифицированы три субтипа *T. pallidum* — 14d/f, 14d/g, 14d/d с продолжающимся доминированием субтипа 14d/f. В двух федеральных округах определен новый для Российской Федерации устойчивый к макролидам субтип 14d/d.
Заключение. На территории Российской Федерации продолжается расширение популяции *T. pallidum*, в том числе за счет появления азитромицин-устойчивых штаммов. Полученные данные подтверждают необходимость непрерывного мониторинга циркулирующих штаммов и могут облегчить понимание их географического распространения.

Ключевые слова: ***Treponema pallidum*; макролиды; мутация A2058G; субтип**

Конфликт интересов: авторы данной статьи подтвердили отсутствие конфликта интересов, о котором необходимо сообщить.

Источник финансирования: рукопись подготовлена и опубликована за счет финансирования по месту работы авторов.

Для цитирования: Образцова О.А., Лагун К.М., Катунин Г.Л., Шпилевая М.В., Носов Н.Ю. Определение молекулярных типов и резистентности к макролидам у изолятов *Treponema pallidum*, выделенных на территории Российской Федерации. Вестник дерматологии и венерологии. 2024;100(2):52–58. doi: https://doi.org/10.25208/vdv15827

Background

Syphilis caused by *Treponema pallidum* subspecies *pallidum (T. pallidum*) is a systemic sexually transmitted infectious disease. According to official state statistical surveillance, the incidence rate of all the syphilis forms in the Russian Federation in 2019 was 15.0 cases per 100,000 population; in 2020, 10.5; in 2021, 14.5; and in 2022, 18.9 cases. Hence, a significant increase in the incidence of syphilis was observed throughout the country in 2021–2022 [1].

Molecular typing is an important tool for determining the diversity and antibiotic resistance of circulating *T. pallidum* isolates. In 1998, the US Centers for Disease Control and Prevention (CDC) first introduced a typing scheme based on determining the number of 60-bp repeats in the *arp* (acidic repeat protein) gene and sequence differences in the *tprII* subfamily genes [2], which was subsequently supplemented by sequencing of the *tp0548* gene region [3]. Results of molecular genetic typing of an individual clinical isolate are presented using triple digital and alphabetic designation (e.g., 14a/a) characterizing the variants of the *arp*, *tprII* and *tp0548* genes found in it.

According to research results, the *T. pallidum* subtypes endemic to the Russian Federation belong to the Street Strain-14 (SS14) line [4], which holds a leading position in the world [5, 6]. Eight molecular subtypes of *T. pallidum* have been identified in the Russian Federation in 2014–2021: 14d/f, 14d/g, 14b/f, 14c/f, 14i/f, 9d/f, 14b/g, and 14e/f, with stable dominance of subtype 14d/f [7].

In accordance with Russian clinical guidelines, penicillins are first-line medications for treating syphilis [8]. However, despite their proven effectiveness, treatment of syphilitic infection with these drugs is limited by the possible development of allergic reactions [9–11]. In the 1990s, azithromycin, a macrolide antibiotic that was initially considered to be a convenient alternative to the therapeutic option benzathine benzylpenicillin G, started to be used to treat patients with early forms of syphilis.

Azithromycin is easy to use, requires no invasive procedures, has few side effects and can be used in accelerated partner therapy for syphilis [12]. In 1993–2003, azithromycin was included in the list of reserve drugs for treating early syphilis in the Russian Federation in cases when patients are intolerant to penicillin and other reserve drugs, doxycycline and cephalosporin [13–15]. Because of the increasing resistance of *T. pallidum* to macrolides [16, 17], azithromycin was removed from the subsequent Russian syphilis treatment guidelines. Some foreign guidelines, in particular the US Centers for Disease Control and Prevention (CDC), currently include this antibiotic as a second-line drug for treating early forms of syphilis [18].

A close association was shown to exist between macrolide resistance and the A2058G and A2059G mutations in the 23S rRNA of *T. pallidum* [19–21]. A feature of *T. pallidum* is that laboratory testing of its antibiotic sensitivity cannot be performed because of the nonculturability of the syphilis causative agent, which necessitates the use of molecular genetic research methods that allow one to comprehensively study the genetic determinants of resistance. Over the period between 2014 and 2021, three subtypes carrying the A2058G mutation associated with azithromycin resistance have been identified in the Russian Federation: 14d/g, 14b/g and 14b/f [7, 22].

The objective of this study is to analyze the molecular types and resistance to macrolides in *T. pallidum* isolates designated in the Russian Federation in 2022.

Methods

In 2022, 49 *T. pallidum* isolates were obtained from patients of dermatovenereological healthcare institutions in three federal districts of the Russian Federation: 24, from the Siberian Federal District; 23, from the Central Federal District, and two, from the North Caucasian Federal District. The diagnosis of syphilis was made based on clinical data and laboratory tests, including rapid plasma reagin (RPR) test, passive hemagglutination (PHA) test, and enzyme-linked immunosorbent assay (ELISA) [23].

Among syphilis patients from whom clinical isolates (separate from erosive and ulcerative elements) containing *Treponema pallidum* were derived, there were 35 males and 14 females aged 16–76 years. The patients were distributed as follows according to their diagnosis: 14 patients were diagnosed with primary syphilis (A51.1 according to ICD-10); 34 patients, with secondary syphilis (A.51.3); and one patient, with syphilis of other localizations (A51.2).

DNA was extracted from clinical samples using a Proba-NK set of reagents (DNA-Technology, Russia) according to the manufacturer's instructions. The presence of genetic material of *T. pallidum* in clinical samples was confirmed by PCR with primers for the species-specific polA gene encoding DNA polymerase I of this microorganism (Table 1) [24].

Molecular typing of the samples with confirmed presence of *T. pallidum* genetic material was conducted following the algorithm recommended by the Centers for Disease Control and Prevention (CDC) in Druid Hills, Atlanta, Georgia. The procedure and assessment of the method results were described previously [25]. Amplification of *T. pallidum* genes was performed using specific primers [24] on a DNA amplification T100 Thermal Cycler (Bio-Rad, USA). After the first amplification stage, the PCR product was purified using the QIAquick PCR Purification Kit (Qiagen, Germany). The purified PCR product was utilized for the second amplification stage using labeled terminating nucleotides from the Big Dye Terminator v. 3.1 Cycle Sequencing Kit (Applied Biosystems, USA). Precipitated PCR products were used for sequencing a variable fragment of the 23S rRNA gene on a 3130 Genetic Analyzer (Applied Biosystems, USA) with the 3130 Data Collection software v. 3.0 [7]. Primary nucleotide sequence decoding was performed using the Sequencing Analysis 5.3.1 software. The analyzed fragments of the target genes were aligned to the reference sequences of *T. pallidum* using the Mega 5 software.

Results

In 49 clinical samples, the presence of *T. pallidum* DNA was confirmed using PCR with primers targeting the polA gene. Molecular typing of isolates based on the arp, tpr, and *tp0548* genes allowed one to identify the complete molecular subtype of each isolate. One variant of the arp gene (variant 14) and *tprII* gene (variant d) and three variants of the *tp0548* gene (variants d, f, and g) were detected. Therefore, three molecular subtypes were identified in the analyzed population: 14d/f (32 strains, 65%), 14d/d (10 strains, 20%), and 14d/g (7 strains, 15%); the 14d/d subtype was detected for the first time (Figure 1).

The A2058G transition, with a proven role in providing high-level resistance to macrolide antibiotics, was associated

Table 1. Primer sequences used for amplification of *T. pallidum* target genes
Таблица 1. Последовательности праймеров, использованных для амплификации целевых генов *T. pallidum*

Gene	Primer name	Nucleotide sequence
arp	ARP-1	5'-ATCTTTGCCGTCCCGTGTGC-3'
	ARP-2	5'-CCGAGTGGGATGGCTGCTTC-3'
tprII	A-1	5'-ACTGGCTCTGCCACACTTGA-3'
	B-2	5'-CTACCAGGAGAGGGTGACGC-3'
	IP-6	5'-CAGGTTTTGCCGTTAAGC-3'
	IP-7	5'-AATCAAGGGAGAATACCGTC-3'
tp0548	tp0548 sense	5'-GGTCCCTATGATATCGTGTTCG-3'
	tp0548 antisense	5'-GTCATGGATCTGCGAGTGG-3'
23 S	23 Sf	5'-GTCTCCCACCTATACTACACAT -3'
	23 Sr	5'-GGAGAGGTTCGTGGTAACACA -3'

Type of the *tp0548* gene	Nucleotide sequence																																		
d	c	-	-	-	a	g	g	g	t	c	c	a	g	t	g	g	t	t	c	c	g	a	c	a	g	t	g	a	t	g	g	c	a	a	g	c
f	c	t	g	g	a	g	g	g	t	c	c	a	g	t	g	g	t	t	g	c	a	g	c	g	a	t	a	a	t	g	g	c	a	a	c	c
g	c	e	a	g	a	g	a	g	t	c	c	a	g	t	g	g	t	t	g	c	a	g	c	g	a	t	a	a	t	g	g	c	a	a	c	c

Fig. 1. Nucleotide sequence variants in the *tp0548* gene of *T. pallidum*
Рис. 1. Варианты нуклеотидных последовательностей в гене *tp0548 T. pallidum*

with 14d/d and 14d/g subtypes (a total of 17 strains, 35%). Table 2 shows the distribution of isolates by federal districts.

Discussion

Because *Treponema pallidum* is a non-culturable pathogen that does not grow on culture media, antibiotic resistance of this microorganism is studied using molecular genetic methods by determining the known and potential genetic determinants of resistance. Of particular interest is the search for determinants of *T. pallidum* resistance to broad-spectrum antibacterial drugs used as an alternative treatment regimen in cases of penicillin intolerance, which is observed in 8–12% of the population. Two mutations identified in the 23S rRNA gene are mentioned in the literature. The first mutation, A2058G, confers resistance to macrolides with a 14-membered (erythromycin, roxithromycin, clarithromycin) and 15-membered (azithromycin) lactone ring in *T. pallidum*. The second mutation, A2059G, confers resistance to 14-, 15-, and 16-membered macrolides (spiramycin and tylosin). A limitation of the current study is that clinical manifestations of the identified resistance cannot be investigated since azithromycin is excluded from federal clinical recommendations for managing syphilis. However, the data on macrolide resistance based on the conducted molecular typing of clinical isolates allowed one to analyze the Russian population of *T. pallidum*.

Table 2. Distribution of *T. pallidum* subtypes by federal districts
Таблица 2. Распределение субтипов *T. pallidum* по федеральным округам

Federal District	Territorial entity of the Russian Federation	Number of isolates for each subtype		
		14d/f	14d/g*	14d/d*
North Caucasian	Stavropol	—	—	2
Siberian	Kyzyl	24	—	—
Central	Moscow	8	6	8
	Kaluga Oblast	—	1	—

*Subtypes containing a macrolide resistance mutation.
*Субтипы, содержащие мутацию устойчивости к макролидам.

In 2022, three subtypes of *T. pallidum* were identified in the represented federal districts. It is worth noting the ongoing dominance of the endemic subtype 14d/f in Russia, which remains sensitive to macrolides. The macrolide-resistant subtype 14d/g was previously detected in the Siberian and Central Federal Districts. In 2022, a new macrolide-resistant subtype 14d/d emerged in the Central (predominantly) and North Caucasian Federal Districts. This particular subtype of *T. pallidum* has never been predominant in any country but is among the most common ones in Argentina, also being occasionally found in the Czech Republic, France, and Australia. Isolates of this subtype with the A2058G macrolide resistance mutation have been identified in Brazil.

These findings indicate the continuous expansion of the *T. pallidum* population in Russia, including the emergence of azithromycin-resistant strains. Thus, in 2013, *T. pallidum* isolates carrying the A2058G mutation associated with azithromycin resistance belonged to subtypes 14d/g and 14b/f; in 2016, to subtype 14b/g; and in 2022, to subtype 14d/d. Additionally, isolates 14b/g and 14e/f without the macrolide resistance mutation were identified in the Siberian Federal District in 2016 and 2017. According to the Federal State Statistics Service, in 2022, in Moscow, there were twice as many new syphilis cases diagnosed compared to the previous year. A rise in migration flows is one of the reasons for the increase in the incidence rate. A less obvious reason could be the uncontrolled use of antibiotics, which may mask the symptoms of the disease.

Ethical review

Based on our research, patients are not involved, and there is no intervention in the course of treatment. The study exclusively uses biomaterial specimens from individuals in the Russian Federation. The information obtained does not allow either direct or indirect identification of patients and cannot lead to any risks of criminal or civil responsibility for patients, nor jeopardize their financial status, employment, or reputation.

Conclusion

The results of molecular typing of clinical isolates of *T. pallidum* conducted in 2022 confirmed the existing trend: in 2022, the molecular type 14d/f dominated among the samples of *T. pallidum* circulating in the Russian Federation, while other subtypes were less common; all the samples with the subtype g of the tp 0548 gene carried the dominant A2058G macrolide resistance marker.

Since Russia is considered a geographic region with low prevalence of macrolide resistance, the emergence of isolates carrying markers of resistance to azithromycin can be attributed to cross-border transmission associated with labor migration or tourism from a specific geographic region. Therefore, continuous monitoring of the Russian population of *T. pallidum* can facilitate understanding the geographical distribution of the infection and antibiotic resistance of *T. pallidum* strains.

References/Литература

1. Единая межведомственная информационно-статистическая система (ЕМИСС). [Edinaya mezhvedomstvennaya informacionno-statisticheskaya sistema (EMISS). (In Russ.)] URL: https://fedstat.ru/indicator/41709 (accessed: 20.09.2023).
2. Pillay A, Liu H, Chen CY, Holloway B, Sturm AW, Steiner B, et al. Molecular subtyping of Treponema pallidum subspecies pallidum. Sex Transm Dis. 1998;25(8):408–414. doi: 10.1097/00007435-199809000-00004
3. Marra CM, Sahi SK, Tantalo LC, Godornes C, Reid T, Behets F, et al. Enhanced molecular typing of Treponema pallidum: geographical distribution of strain types and association with neurosyphilis. J Infect Dis. 2010;202(9):1380–1388. doi: 10.1086/656533
4. Образцова О.А., Алейникова К.А., Обухов А.П., Кубанов А.А., Дерябин Д.Г. Генетические детерминанты резистентности к антимикробным препаратам и их распространенность у различных молекулярных субтипов *Treponema pallidum subsp. pallidum.* Клиническая микробиология и антимикробная химиотерапия. 2018;20(3):217–221. [Obraztsova OA, Aleynikova KA, Obukhov AP, Kubanov AA, Deryabin DG. Genetic antimicrobial resistance determinants and their prevalence in molecular subtypes of *Treponema pallidum* subsp. pallidum. Clinical microbiology and antimicrobial chemotherapy. 2018;20(3):217–221. (In Russ.)] doi: 10.36488/cmac.2018.3.216-221
5. Stamm LV. Global challenge of antibiotic-resistant *Treponema pallidum*. Antimicrob Agents Chemother. 2010;54(2):583–589. doi: 10.1128/AAC.01095-09
6. Matejková P, Strouhal M, Smajs D, Norris SJ, Palzkill T, Petrosino JF, et al. Complete genome sequence of Treponema pallidum ssp. pallidum strain SS14 determined with oligonucleotide arrays. BMC Microbiol. 2008;8:76. doi: 10.1186/1471-2180-8-76
7. Образцова О.А., Шпилевая М.В., Катунин Г.Л., Обухов А.П., Шагабиева Ю.З., Соломка В.С. Распространенность мутации A2058G в гене 23S рРНК, определяющей устойчивость к макролидным антибиотикам в российской популяции *Treponema pallidum.* Клиническая микробиология и антимикробная химиотерапия. 2022;24(4):369–374. [Obraztsova OA, Shpilevaya MV, Katunin GL, Obukhov AP, Shagabieva YuZ, Solomka VS. Prevalence of the A2058G mutation in 23S rRNA gene, which determines *Treponema pallidum* macrolide resistance in Russian population. Clinical microbiology and antimicrobial chemotherapy. 2022;24(4):369–374. (In Russ.)] doi: 10.36488/cmac.2022.4.369-374
8. Сифилис: Клинические рекомендации РФ. М.; 2020. [Sifilis: Klinicheskie rekomendacii RF. Moscow; 2020. (In Russ.)]
9. Macy E, Poon K-YT. Self-reported antibiotic allergy incidence and prevalence: age and sex effects. Am J Med. 2009;122(8):778.e1–778.e7. doi: 10.1016/j.amjmed.2009.01.034
10. Albin S, Agarwal S. Prevalence and characteristics of reported penicillin allergy in an urban outpatient adult population. Allergy Asthma Proc. 2014;35(6):489–494. doi: 10.2500/aap.2014.35.3791
11. Arando M, Fernandez-Naval C, Mota-Foix M, Alvarez A, Armegol P, Barberá MJ, et al. The Jarisch-Herxheimer reaction in syphilis: could molecular typing help to understand it better? J Eur Acad Dermatol Venereol. 2018;32(10):1791–1795. doi: 10.1111/jdv.15078
12. Riedner G, Rusizoka M, Todd J, Maboko L, Hoelscher M, Mmbando D, et al. Single-dose azithromycin versus penicillin G benzathine for the treatment of early syphilis. N Engl J Med. 2005;353(12):1236–1244. doi: 10.1056/NEJMoa044284
13. Лечение и профилактика сифилиса: Методические рекомендации. М.: Минздрав России; 1993. 31 с. [Lechenie i profilaktika sifilisa: Metodicheskie rekomendacii. Moscow: Minzdrav Rossii; 1993. 31 s. (In Russ.)]
14. Лечение и профилактика сифилиса: Методические указания № 98/273. М.: Минздрав России; 1999. 20 с. [Lechenie i profilaktika

sifilisa: Metodicheskie ukazaniya No. 98/273. Moscow: Minzdrav Rossii; 1999. 20 s. (In Russ.)]

15. Приказ Минздрава России от 25.07.2003 № 327 «Об утверждении протокола ведения больных «Сифилис». [Prikaz Minzdrava Rossii ot 25.07.2003 No. 327 "Ob utverzhdenii protokola vedeniya bol'nyh "Sifilis". (In Russ.)] URL: https://base.garant.ru/4179725/

16. Centers for Disease Control and Prevention. Brief report: azithromycin treatment failures in syphilis infections — San Francisco, California, 2002–2003. MMWR Morb Wkly Rep. 2004;53(9):97–198.

17. Mitchell SJ, Engelman J, Kent CK, Lukehart S, Godornes C, Klausner JD. Azithromycin resistant syphilis infection: San Francisco, California, 2000–2004. Clin Infect Dis. 2006;42(3):337–345. doi: 10.1086/498899

18. Sexually Transmitted Infections Treatment Guidelines, CDC. MMWR Recomm Rep. 2021;70(4):1–187. doi: 10.15585/mmwr.rr7004a1

19. Lukehart SA, Godornes C, Molini BJ, Sonnett P, Hopkins S, Mulcahy F, et al. Macrolide resistance in Treponema pallidum in the United States and Ireland. New Engl J Med. 2004;351(2):154–158. doi: 10.1056/NEJMoa040216

20. Molini BJ, Tantalo LC, Sahi SK, Rodriguez VI, Brandt SL, Fernandez MC, et al. Macrolide Resistance in Treponema pallidum Correlates With 23S rDNA Mutations in Recently Isolated Clinical Strains. Sex Transm Dis. 2016;43(9):579–583. doi: 10.1097/olq.0000000000000486

21. Пушков А.А., Савостьянова К.В., Никитин А.Г. Краткие рекомендации по подготовке рукописей, содержащих информацию о результатах молекулярно-генетических исследований. Вопросы современной педиатрии. 2018;17(5):364–366. [Pushkov AA, Savostyanov KV, Nikitin AG. Brief Guidelines on Preparation of Manuscripts Containing Information on the Results of Molecular Genetic Research. Current Pediatrics. 2018;17(5):364–366. (In Russ.)] doi: 10.15690/vsp.v17i5.1951

22. Khairullin R, Vorobyev D, Obukhov A, Kuular U-H, Kubanova A, Kubanov A, et al. Syphilis epidemiology in 1994–2013, molecular epidemiological strain typing and determination of macrolide resistance in Treponema pallidum in 2013–2014 in Tuva Republic, Russia. APMIS. 2016;124(7):595–602. doi: 10.1111/apm.12541

23. Приказ Минздрава России от 26.03.2001 № 87 «О совершенствовании серологической диагностики сифилиса». Приложение № 1 «Постановка отборочных и диагностических тестов на сифилис». [Prikaz Minzdrava Rossii ot 26.03.2001 No. 87 "O sovershenstvovanii serologicheskoj diagnostiki sifilisa". Prilozhenie No. 1 "Postanovka otborochnyh i diagnosticheskih testov na sifilis". (In Russ.)] URL: https://docs.cntd.ru/document/901788110

24. Liu H, Rodes B, Chen CY, Steiner B. New tests for syphilis: rational design of a PCR method for detection of Treponema pallidum in clinical specimens using unique regions of the DNA polymerase I gene. J Clin Microbiol. 2001;39(5):1941–1946. doi: 10.1128/JCM.39.5.1941-1946.2001

25. Кубанов А.А., Воробьев Д.В., Обухов А.П., Образцова О.А., Дерябин Д.Г. Молекулярная эпидемиология *Treponema pallidum* в приграничном регионе Российской Федерации (Республика Тыва). Молекулярная генетика, микробиология и вирусология. 2017;35(1):26–30. [Kubanov AA, Vorob'ev DV, Obukhov AP, Obraztsova OA, Deryabin DG. Molecular epidemiology of *Treponema pallidum* in border region of Russian Federation (Tuva Republic). Molecular Genetics, Microbiology and Virology. 2017;35(1):26–30. (In Russ.)] doi: 10.18821/0208-0613-2017-35-1-26-30

26. Vaulet LG, Grillova L, Mikalova L, Casco R, Fermepin MR, Pando MA, et al. Molecular typing of Treponema pallidum isolates from Buenos Aires, Argentina: Frequent Nichols-like isolates and low levels of macrolide resistance. PLoS One. 2017;12(2):e0172905. doi: 10.1371/journal.pone.0172905

27. Grange PA, Allix-Beguec C, Chanal J, Benhaddou N, Gerhardt P, Morini J-P, et al. Molecular Subtyping of Treponema pallidum in Paris, France. Sex Transm Dis. 2013;40(8):641–644. doi: 10.1097/OLQ.0000000000000006

28. Read P, Tagg KA, Jeoffreys N, Guy RJ, Gilbert GL, Donovan B. Treponema pallidum Strain Types and Association with Macrolide Resistance in Sydney, Australia: New TP0548 Gene Types Identified. J Clin Microbiol. 2016;54(8):2172–2174. doi: 10.1128/JCM.00959-16

29. Sato NS, Morais FR, Polisel JO, Belda W, Fagundes LJ. Molecular typing and detection of macrolide resistence in treponema pallidum dna from patients with primary syphilis in São Paulo, Brazil. Sex Transm Infect. 2017;93(Suppl2):A1–A272. doi: 10.1136/sextrans-2017-053264.151

Authors' participation: all authors are responsible for the content and integrity of the entire article. Conducting molecular biological research — Olga A. Obraztsova, Kseniya M. Lagun; obtaining samples of clinical material — Georgii L. Katunin; analysis and interpretation of data — Marina V. Shpilevaya; editing — Nikita Yu. Nosov.

Участие авторов: все авторы несут ответственность за содержание и целостность всей статьи. Проведение молекулярно-биологических исследований — О.А. Образцова, К.М. Лагун; получение образцов клинического материала — Г.Л. Катунин; анализ и интерпретация данных — М.В. Шпилевая; редактирование — Н.Ю. Носов.

Information about the authors

***Olga A. Obraztsova** — Cand. Sci. (Biol.); address: 3 blbg 6 Korolenko street, 107076 Moscow, Russia; ORCID: https://orcid.org/0000-0002-5728-2139; eLibrary SPIN: 8243-2537; e-mail: valeeva19@gmail.com

Kseniya M. Lagun — ORCID: https://orcid.org/0009-0004-9700-2455; eLibrary SPIN: 4770-8904; e-mail: xobanaa@mail.ru

Georgii L. Katunin — MD, Cand. Sci. (Med.); ORCID: https://orcid.org/0000-0003-0599-6305; eLibrary SPIN:1 598-8595; e-mail: g.katunin@rambler.ru

Marina V. Shpilevaya — Cand. Sci. (Biol.); ORCID: https://orcid.org/0000-0002-9957-4009; eLibrary SPIN: 6600-3311; e-mail: aniram1970@list.ru

Nikita Yu. Nosov — Cand. Sci. (Biol.); ORCID: https://orcid.org/0000-0002-3967-8359; eLibrary SPIN: 8806-8539; e-mail: nnosov@cnikvi.ru

Информация об авторах

***Образцова Ольга Анатольевна** — к.б.н.; адрес: Россия, 107076, Москва, ул. Короленко, д. 3, стр. 6; ORCID: https://orcid.org/0000-0002-5728-2139; eLibrary SPIN: 8243-2537; e-mail: valeeva19@gmail.com
Лагун Ксения Михайловна — ORCID: https://orcid.org/0009-0004-9700-2455; eLibrary SPIN: 4770-8904; e-mail: xobanaa@mail.ru
Катунин Георгий Леонидович — к.м.н.; ORCID: https://orcid.org/0000-0003-0599-6305; eLibrary SPIN: 1598-8595; e-mail: g.katunin@rambler.ru
Шпилевая Марина Валентиновна — к.б.н.; ORCID: https://orcid.org/0000-0002-9957-4009; eLibrary SPIN: 6600-3311; e-mail: aniram1970@list.ru
Носов Никита Юрьевич — к.б.н.; ORCID: https://orcid.org/0000-0002-3967-8359; eLibrary SPIN: 8806-8539; e-mail: nnosov@cnikvi.ru

Submitted: 26.09.2023
Accepted: 09.04.2024
Published online: 17.04.2024

Статья поступила в редакцию: 26.09.2023
Принята к публикации: 09.04.2024
Опубликована онлайн: 17.04.2024