



DAFTAR PUSTAKA

1. Pedoman Tata Laksana Sifilis Untuk Pengendalian Sifilis di Fasilitas Pelayanan Dasar. Kementerian Kesehatan Republik Indonesia. Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan. Jakarta: Kementerian Kesehatan RI. 2013.
2. Houston, Karen Vivien Lithgow, Kara Krista Osbak , Chris Richard Kenyon and Caroline E. Cameron, Houston et al. Functional insights from proteome-wide structural modeling of *Treponema pallidum* subspecies pallidum, the causative agent of syphilis Simon. BMC Structural Biology 2018; 18:7
3. Jose Victor Bampi, Maissa Estopa Correa, Graciela Mendoca, Silvana Beutinger, Simone Simionatto. Descriptive Analysis of Syphilis case reported in Mato Grosso do Sul, Brazil Identifies Failure in Treatment. Journal of Brazilian Society of Tropical Medicine. 2019. 52:20180026
4. Workowski Kimberly, Bolan Gail A. Sexually Transmitted Disease Treatment Guidelines. 2015. MMWR.2015;64 (3)
5. Susilawati, & Irawan, A. G. (2023). Manajemen Program Pencegahan Sifilis Dari Ibu Ke Anak. Zahra: Journal of Health and Medical Research, 3(3), 190–200
6. Suryani, Devi Putri dan Sibero, Amalia Hendra Tarigan. Syphilis. J MAJORITY. Volume 3 Nomor 7. 2014
7. Wiesman J, Lofy K, Terletter S, Goldoft MJ. A Monthly Bulletin on Epidemiology and Public Health Practice in Washington. Washington State Department of Health. J Epitrends. 2014;19(1):1-3
8. Clement, Meredith, Okeke,E. N. Lance , dan Hicks,Charles B. Treatment of Syphilis. A Systematic Review. JAMA November 12, 2014 Volume 312, Number 18
9. Brlek, P., Bulić, L., Bračić, M., Projić, P., Škaro, V., Shah, N., Shah, P., & Primorac, D. (2024). Implementing Whole Genome Sequencing (WGS) in Clinical Practice: Advantages, Challenges, and Future Perspectives. In Cells (Vol. 13, Issue 6). Multidisciplinary Digital Publishing Institute (MDPI). <https://doi.org/10.3390/cells13060504>



10. Costain, G., Cohn, R. D., Scherer, S. W., & Marshall, C. R. (2021). Genome sequencing as a diagnostic test. Canadian Medical Association Journal, 193(42), E1626–E1629. <https://doi.org/10.1503/cmaj.210549>
11. Van El, C. G., Cornel, M. C., Borry, P., Hastings, R. J., Fellmann, F., Hodgson, S. V., Howard, H. C., Cambon-Thomsen, A., Knoppers, B. M., Meijers-Heijboer, H., Scheffer, H., Tranebjaerg, L., Dondorp, W., & De Wert, G. M. W. R. (2013). Whole-genome sequencing in health care. European Journal of Human Genetics, 21(6), 580–584. <https://doi.org/10.1038/ejhg.2013.46>
12. Peeling, R. W., Mabey, D., Kamb, M. L., Chen, X., David, J., Benzaken, A. S., Street, K., Hepatitis, V., Union, P., & Hepatitis, V. (2018). HHS Public Access. Syphilis. Nat Rev Dis Primers., 3(17073), 1–48. <https://doi.org/10.1038/nrdp.2017.73.Syphilis>
13. Saputri BYA, Murtiastutik D. Studi Retrospektif: Sifilis Laten. Periodical of Dermatology and Venereology. 2019;3(1): 45-58
14. M Tampa, I Sarbu, C Matei, V Beneadan SR Georgescu. Brief History of Syphilis. J Med Life. 2014 Mar 15; 7(1): 4–10
15. James WD, Elston DM, Berger TG. Andrews' Diseases Of The Skin: Clinical Dermatology.12th Edition. Elsevier. 2016.
16. Katz AR, Johnson DW, Komeya AY, Thomas JE, Namiki TS, Kobayashi K. Case report: Dermatologically challenging syphilis presentation. International Journal of STD & AIDS. 2019. p. 1-3. DOI: 10.1177/095646241887636
17. Palmer, H. M., S. P. Higgins, A. J. Herring, and M. A. Kingston. 2003. Use of PCR in the diagnosis of early syphilis in the United Kingdom. Sex. Transm. Infect. 79:479–483.
18. Shields et al. A longitudinal evaluation of *Treponema pallidum* PCR testing in early syphilis. BMC Infectious Diseases 2012, 12:353
19. Koek, A. G. , Bruisten, S. M. , M. Dierdorp, A. P. van Dam dan K. Templeton. Specific and sensitive diagnosis of syphilis using a real-time PCR for *Treponema pallidum* Clin Microbiol Infect 2006; 12: 1233–1236
20. Ho, Emily L. dan Lukehar, Sheila A. Syphilis: using modern approaches to understand an old disease. J Clin Invest. 2011;121(12):4584–4592



21. Deshpande dan Joshi, Mohini. Polymerase chain reaction: methods, principles and application. IJBR 1 [5] [2010]81-97
22. Grange dkk. Evaluation of a PCR Test for Detection of *Treponema pallidum* in Swabs and Blood. J Clin Microbiol. 2012 Mar; 50(3): 546–552.
23. Klausner. The Great Imitator Revealed: Syphilis. Topics in Antiviral Medicine. 2019;27(2): 71-74
24. Pedoman Nasional Penanganan Infeksi Menular Seksual. Kementerian Kesehatan Republik Indonesia. Jakarta: Kementerian Kesehatan RI. 2015.
25. Zenilman JM. Syphilis. Fitzpatrick Dermatology. 9th Edition. 3143-3168.
26. Zhang, R. L., Wang, Q. Q., Zheng, Z. J., Liang, G. J., Yang, L. J., Yang, L. G., Pei, D. N., & Lin, S. C. (2019). Relationship between the High Frequency of 23S rRNA Point Mutations in *Treponema pallidum* and Low Serological Response Rate to Azithromycin Treatment in China. International Journal of Dermatology and Venereology, 2(1), 6–14. <https://doi.org/10.3760/cma.j.issn.2096-5540.2019.01.00>
27. Chaudhry, S., Akinlusi, I., Shi, T., & Cervantes, J. (2023). Secondary Syphilis: Pathophysiology, Clinical Manifestations, and Diagnostic Testing. Venereology, 2(2), 65–75. <https://doi.org/10.3390/venereology2020006>
28. WHO Guidelines For The Treatment of *Treponema pallidum* (syphilis). World Health Organization. 2016.
29. Mathew A. Beale, Michael Marks, Sharon K. Sahi, Lauren C. Tantalo, Achyuta V. Nori, Patrick French, Sheila A. Lukehart, Christina M. Marra & Nicholas R. Thomson Genomic epidemiology of syphilis reveals independent emergence of macrolide resistance across multiple circulating lineages. Nature Communication. 2019; 10:3255
30. Ambrose, Charles T., "Pre-Antibiotic Therapy of Syphilis" Microbiology, Immunology, and Molecular Genetics Faculty Publications. 2016: 83
31. Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient



- antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005;365:579–587.
32. Kenyon C, Buyze J, Wi T. Antimicrobial consumption and susceptibility of *Neisseria gonorrhoeae*: a global ecological analysis. *Frontiers in Medicine*. (In Press).
33. Baquero F. Evolving resistance patterns of *Streptococcus pneumoniae*: a link with long-acting macrolide consumption? *J Chemother* 1999;11:35–43.
34. Magpantay G, Cardile AP, Madar CS, Hsue G and Belnap C: Antibiotic desensitization therapy in secondary syphilis and Listeria infection: Case reports and review of desensitization therapy. *Hawaii Med J* 70: 266-268, 2011.
35. Furtado, J.M. et al. (2022) 'Ocular syphilis', *Survey of Ophthalmology*, 67(2), pp. 440–462. Available at:
<https://doi.org/10.1016/j.survophthal.2021.06.003>.
36. Kahn RH, Moseley KE, Johnson G and Farley TA: Potential for community-based screening, treatment, and antibiotic prophylaxis for syphilis prevention. *Sex Transm Dis* 27: 188-192, 2000.
37. Hook EW III, Behets F, Van Damme K, Ravelomanana N, Leone P, Sena AC, Martin D, Langley C, McNeil L and Wolff M: A phase III equivalence trial of azithromycin versus benzathine penicillin for treatment of early syphilis. *J Infect Dis* 201: 1729-1735, 2010.
38. Read P, Jeoffreys N, Tagg K, Guy RJ, Gilbert GL and Donovan B: Azithromycin-resistant syphilis-causing strains in Sydney, Australia: Prevalence and risk factors. *J Clin Microbiol* 52: 2776-2781, 2014.
39. Castro R, Prieto E, Aguas MJ, Manata MJ, Botas J and Pereira FM: Molecular subtyping of *Treponema pallidum* subsp. *pallidum* in lisbon, portugal. *J Clin Microbiol* 47: 2510-2512, 2009.



40. Heroldova-Dvorakova M and Votava M: Molecular detection and subtyping of *Treponema pallidum* subsp. *Pallidum* in clinical specimens. Epidemiol Mikrobiol Imunol 55: 105-111, 2006 (In Czech).
41. Pandori MW, Gordones C, Castro L, Engelman J, Siedner M, Lukehart S and Klausner J: Detection of azithromycin resistance in *Treponema pallidum* by real-time PCR. Antimicrob Agents Chemother 51: 3425-3430, 2007.
42. Katz KA and Klausner JD: Azithromycin resistance in *Treponema pallidum*. Curr Opin Infect Dis 21: 83-91, 2008.
43. Chen XS, Yin YP, Wei WH, Wang HC, Peng RR, Zheng HP, Zhang JP, Zhu BY, Liu QZ and Huang SJ: High prevalence of azithromycin resistance to *Treponema pallidum* in geographically different areas in China. Clin Microbiol Infect 19: 975-979, 2013.
44. Kubanova AA, Melekhina LE, Kubanov AA, Bog- danova EV. Syphilis incidence in Russian Federation in 2004–2013 [Zabolevaemost' sifilisom v Rossijskoj Federacii za period 2004–2013 gg]. Vestn Dermatol Venerol 2014;5:24–31. [In Russian].
45. Netesov SV, Conrad J. Emerging infectious diseases in Russia, 1990–1999. Emerg Infect Dis 2001;7:1–5.
46. Syrneva TA, Obukhov AP, Surganova VI, Kuular UC. The main epidemiological regularities of syphilis spreading in Tuva Republic [Osnovnye epidemio- logicheskie zakonomernosti rasprostraneniya sifilisa v Respublike Tyva]. Klinitceskaia Dermatologija i Ven- erologiia 2009;3:35–7. [In Russian].
44. [No authors listed] Sexually transmitted diseases: summary of 2015 CDC Treatment Guidelines. J Miss State Med Assoc 2015; 56: 372–375.



45. Whiting, C., Schwartzman, G. and Khachemoune, A. (2023) 'Syphilis in Dermatology: Recognition and Management', *American Journal of Clinical Dermatology*, 24(2), pp. 287–297. Available at: <https://doi.org/10.1007/s40257-022-00755-3>.
46. Bond, S. M., & Blain, M. L. M. (2021). Diagnosis and Treatment of Secondary Syphilis in Women. *Journal of Midwifery and Women's Health*, 66(3), 372–379. <https://doi.org/10.1111/jmwh.13241>
47. 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. *N Engl J Med* 2004; 351: 154–158.
48. Šmajš D, Paštěková L, Grillová L. Macrolide Resistance in the syphilis spirochete, *Treponema pallidum* ssp. pallidum: can we also expect macrolide-resistant yaws strains? *Am J Trop Med Hyg* 2015; 93: 678–683.
49. Janier, M. et al. (2021) '2020 European guideline on the management of syphilis', *Journal of the European Academy of Dermatology and Venereology*, 35(3), pp. 574–588. Available at: <https://doi.org/10.1111/jdv.16946>.
50. Theel, E.S., Katz, S.S. and Pillay, A. (2020) 'Molecular and Direct Detection Tests for *Treponema pallidum* Subspecies pallidum: A Review of the Literature, 1964-2017', *Clinical Infectious Diseases*, 71(Suppl 1), pp. S4–S12. Available at: <https://doi.org/10.1093/cid/ciaa176>.
51. Ren, M., Dashwood, T. and Walmsley, S. (2021) 'The Intersection of HIV and Syphilis: Update on the Key Considerations in Testing and Management', *Current HIV/AIDS Reports*, 18(4), pp. 280–288. Available at: <https://doi.org/10.1007/s11904-021-00564-z>.



52. Newman L, Rowley J, Vander Hoorn S, Wijesooriya NS, Unemo M, Low N, et al. Global estimates of the prevalence and incidence of four curable sexually transmitted infections in 2012 based on systematic review and global reporting. *PloS One* 2015; 10: e0143304
53. Shah, A.C.T. (2019) 'Serological Tests for Syphilis', *The Lancet*, 249(6461), pp. 923–924. Available at: [https://doi.org/10.1016/S0140-6736\(47\)91386-X](https://doi.org/10.1016/S0140-6736(47)91386-X).
54. Nonaka L, Connell SR, Taylor DE. 16S rRNA mutations that confer tetracycline resistance in *Helicobacter pylori* decrease drug binding in *Escherichia coli* ribosomes. *J Bacteriol* 2005; 187: 3708–3712.
55. Dadashzadeh K, Milani M, Rahmati M, Akbarzadeh A. Real time PCR detection of 16S rRNA novel mutations associated with *Helicobacter pylori* tetracycline resistance in Iran. *Asian Pac J Cancer Prev* 2014; 15: 8883–8886.
56. Bicillin L-A (penicillin benzathine) package insert. New York, NY: Pfizer Inc; 2019 Apr
57. Gartlan WA, Reti K. Benzathine Penicillin. [Updated 2019 Sep 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK507723>
58. Centers for Disease Control and Prevention. 2015 sexually transmitted diseases treatment guidelines: syphilis during pregnancy. 2015. Available from: <https://www.cdc.gov/std/tg2015/syphilis-pregnancy.htm>
59. Prescribers' Digital Reference. Penicillin G benzathine – drug summary. 2019. Available from: <https://www.pdr.net/drug-summary/Bicillin-L-A-penicillin-G-benzathine-283#11>
60. National Center for Biotechnology Information. PubChem Database. Benzathine penicillin G, CID=15232, <https://pubchem.ncbi.nlm.nih.gov/compound/Benzathine-penicillin-G>



61. Waluyo . L. 2004. Mikrobiologi Umum. Malang : Penerbit Universitas Muhammadiyah Press.
62. Lullmann H, et al. 2000. Color Atlas of Pharmacology. 2nd ed. Georg Thieme Verlag: Stuttgart.
63. Eliopoulos, G. M. (2002). Mechanisms of Resistance to Macrolides and Lincosamides: Nature of the Resistance Elements and Their Clinical Implications. *Clinical Infectious Disease*, 34:482-492
64. Mazzei, T., Mini, E., Noovelli, A., dan Periti, P. (1993). Chemistry and Mode of Action of Macrolides. *Journal of Antimicrobial Chemotherapy* 31 Suppl. C: 1-9
65. 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: 1236–1244.
66. Šmajš D, Paštěková L, Grillová L. Macrolide Resistance in the syphilis spirochete, *Treponema pallidum* ssp. *pallidum*: can we also expect macrolide-resistant yaws strains? *Am J Trop Med Hyg* 2015; 93: 678–683.
67. A2058G Prevalence Workgroup. Prevalence of the 23S rRNA A2058G point mutation and molecular subtypes in *Treponema pallidum* in the United States, 2007 to 2009. *Sex Transm Dis* 2012; 39: 794–798.
68. Nonaka L, Connell SR, Taylor DE. 16S rRNA mutations that confer tetracycline resistance in *Helicobacter pylori* decrease drug binding in *Escherichia coli* ribosomes. *J Bacteriol* 2005; 187: 3708–3712.
69. Ross JI, Eady EA, Cove JH, Cunliffe WJ. 16S rRNA mutation associated with tetracycline resistance in a grampositive bacterium. *Antimicrob Agents Chemother* 1998; 42: 1702–1705.



70. Dadashzadeh K, Milani M, Rahmati M, Akbarzadeh A. RealAdvances in dermatology and venereology ActaDV Acta Dermato-Venereologica ActaDV *Resistance of Treponema pallidum strains to macrolides and doxycycline 5/5* Acta Derm Venereol 2020 time PCR detection of 16S rRNA novel mutations associated with Helicobacter pylori tetracycline resistance in Iran. Asian Pac J Cancer Prev 2014; 15: 8883–8886.
71. Gerrits MM, de Zoete MR, Arents NLA, Kuipers EJ, Kusters JG. 16S rRNA mutation-mediated tetracycline resistance in Helicobacter pylori. Antimicrob Agents Chemother 2002; 46: 2996–3000.
72. Xiao Y, Liu S, Liu Z, Xie Y, Jiang C, Xu M, et al. Molecular subtyping and surveillance of resistance genes in *Treponema pallidum* DNA from patients with secondary and latent syphilis in hunan, China. Sex Transm Dis 2016; 43: 310–316.
73. Wu B-R, Liu W-C, Wu P-Y, Su Y-C, Yang S-P, Hung C-C, et al. Surveillance study of *Treponema pallidum* harbouring tetracycline resistance mutations in patients with syphilis. Int J Antimicrob Agents 2014; 44: 370–372.
74. Giacani L, Ciccarese G, Puga-Salazar C, Dal Conte I, Colli L, Cusini M, et al. Enhanced molecular typing of *Treponema pallidum* subspecies *pallidum* strains from 4 Italian hospitals shows geographical differences in strain type heterogeneity, widespread resistance to macrolides, and lack of mutations associated with doxycycline resistance. Sex Transm Dis 2018; 45: 237–242.
75. Fernández-Naval C, Arando M, Espasa M, Antón A, Fernández- Huerta M, Silgado A, et al. Enhanced molecular typing and macrolide and tetracycline-resistance mutations of *Treponema pallidum* in Barcelona. Future Microbiol 2019; 14: 1099–1108.



76. Montaño MA, Dombrowski JC, Dasgupta S, Golden MR, Duerr A, Manhart LE, et al. Changes in sexual behavior and STI diagnoses among MSM initiating PrEP in a clinic setting. *AIDS Behav* 2019; 23: 548–555.
77. [No authors listed] Sexually transmitted diseases: summary of 2015 CDC Treatment Guidelines. *J Miss State Med Assoc* 2015; 56: 372–375.
78. Molina J-M, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. *Lancet Infect Dis* 2018; 18: 308–317.
79. Molina J-M, Charreau I, Chidiac C, Pialoux G, Cua E, Delaugerre C, et al. Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial. *Lancet Infect Dis* 2018; 18: 308–317.
80. Edmondson, D.G., Wormser, G.P., Norris, S.J., 2020. *In Vitro Susceptibility of *Treponema pallidum* subsp. *pallidum* to Doxycycline.* *Antimicrob Agents Chemother* 64, e00979-20.
<https://doi.org/10.1128/AAC.00979-20>
81. Gultom, D.A., Rosana, Y., Efendi, I., Indriatmi, W., Yasmon, A., 2017. Detection and identification of azithromycin resistance mutations on *Treponema pallidum* 23S rRNA gene by nested multiplex polymerase chain reaction. *Med J Indones* 26, 90–6.
<https://doi.org/10.13181/mji.v26i2.1543>
82. Jin, Q., Zhang, J., Xia, J., Qin, J., Zhou, X., 2023. Epidemiological analysis of syphilis surveillance among entry-exit population at Shanghai Port, China from 2014 to 2022. *Arch Public Health* 81, 157.
<https://doi.org/10.1186/s13690-023-01176-2>



83. Kawi, N.H., Sihotang, E., Nisa, T., Hui, B., Causer, L.M., Januraga, P.P., Ronoatmodjo, S., 2019. Incidence and risk factors for syphilis infection among men who have sex with men: A cohort study from an urban sexual health clinic in Jakarta, Indonesia. *International Journal of STD and AIDS*, 33(12), 1065-1072. <https://doi.org/10.1177/09564624221125079>
84. Kojima, N., Klausner, J.D., 2018. An Update on the Global Epidemiology of Syphilis. *Curr Epidemiol Rep* 5, 24–38. <https://doi.org/10.1007/s40471-018-0138-z>
85. Kong, F.Y.S., Kenyon, C., Unemo, M., 2023. Important considerations regarding the widespread use of doxycycline chemoprophylaxis against sexually transmitted infections. *Journal of Antimicrobial Chemotherapy* 1–8.
86. Kusumawaty, M., Djawad, K., Nasrum Massi, M., Adam, A.M., Wahab, S., Bahar, B., 2019. Sero-epidemiology and risk factors of syphilis in Makassar, Indonesia. *Serbian Journal of Dermatology and Venereology* 11, 43–49. <https://doi.org/10.2478/sjdv-2019-0006>
87. Li, Y., Li, J., Hu, W., Luo, H., Zhou, J., Li, C., Chen, C., 2018. Gene subtype analysis of *Treponema pallidum* for drug resistance to azithromycin. *EXPERIMENTAL AND THERAPEUTIC MEDICINE*.
88. Liu, D., He, S.-M., Zhu, X.-Z., Liu, L.-L., Lin, L.-R., Niu, J.-J., Yang, T.-A., 2021. Molecular Characterization Based on MLST and ECDC Typing Schemes and Antibiotic Resistance Analyses of *Treponema pallidum* subsp. *pallidum* in Xiamen, China. *Front. Cell. Infect. Microbiol.* 10, 618747. <https://doi.org/10.3389/fcimb.2020.618747>



89. Lu, H., Li, K., Gong, W., Yan, L., Gu, X., Chai, Z., Guan, Z., Zhou, P., 2015. High frequency of the 23S rRNA A2058G mutation of *Treponema pallidum* in Shanghai is associated with a current strategy for the treatment of syphilis. Emerging Microbes & Infections 4, 1–4. <https://doi.org/10.1038/emi.2015.10>
90. Noda, A.A., Matos, N., Blanco, O., Rodríguez, I., Stamm, L.V., 2016. First Report of the 23S rRNA Gene A2058G Point Mutation Associated With Macrolide Resistance in *Treponema pallidum* From Syphilis Patients in Cuba. Sexually Transmitted Diseases 43, 332–334. <https://doi.org/10.1097/OLQ.0000000000000440>
91. Orbe-Orihuela, Y.C., Sánchez-Alemán, M.Á., Hernández-Pliego, A., Medina-García, C.V., Vergara-Ortega, D.N., 2022. Syphilis as Re-Emerging Disease, Antibiotic Resistance, and Vulnerable Population: Global Systematic Review and Meta-Analysis. Pathogens 11, 1546. <https://doi.org/10.3390/pathogens11121546>
92. Peyriere, H., Makinson, A., Marchandin, H., Reynes, J., 2018. Doxycycline in the management of sexually transmitted infections. Journal of Antimicrobial Chemotherapy 73, 553–563.
93. Rosana, Y., Yasmon, A., Indriatmi, W., Effendi, I., Kusumawati, R.L., Rowawi, R., Sudigdoadi, S., Pradini, G.W., Wiraguna, A.A.G.P., Puspawati, N.M.D., Kusumawaty, M., Massi, M.N., 2022. Detection of A2058G and A2059G on the 23S rRNA Gene by Multiplex Nested PCR to Identify *Treponema pallidum* Resistance to Azithromycin in Indonesia. Jpn J Infect Dis 75, 355–360. <https://doi.org/10.7883/yoken.JJID.2021.738>



94. Sanchez, A., Mayslich, C., Malet, I., Grange, P., Janier, M., Saule, J., Martinet, P., Robert, J., Moulene, D., Truchetet, F., Pinault, A., Vermersch-Langlin, A., Benhaddou, N., Chanal, J., Dupin, N., 2020. Surveillance of Antibiotic Resistance Genes in *Treponema pallidum* Subspecies Pallidum from Patients with Early Syphilis in France. *Acta Derm Venereol* 100, adv00221. <https://doi.org/10.2340/00015555-3589>
95. Stahlman, S., Plant, A., Javanbakht, M., Cross, J., Montoya, J.A., Bolan, R., Kerndt, P.R., 2015. Acceptable Interventions to Reduce Syphilis Transmission Among High-Risk Men Who Have Sex With Men in Los Angeles. *Am J Public Health* 105, e88–e94. <https://doi.org/10.2105/AJPH.2014.302412>
96. Stamm, L.V., 2021. Hope for new antibiotics for syphilis treatment. *EBioMedicine* 66, 103320. <https://doi.org/10.1016/j.ebiom.2021.103320>
97. Tantalo, L.C., Lieberman, N.A.P., Pérez-Mañá, C., Suñer, C., Vall Mayans, M., Ubals, M., González-Beiras, C., Rodríguez-Gascón, A., Canut, A., González-Candelas, F., Mueller, J., Tapia, K., Greninger, A.L., Giacani, L., Mitjà, O., 2023. Antimicrobial susceptibility of *Treponema pallidum* subspecies pallidum: an in-vitro study. *The Lancet Microbe* S2666524723002197. [https://doi.org/10.1016/S2666-5247\(23\)00219-7](https://doi.org/10.1016/S2666-5247(23)00219-7)
98. Tao, Y.-T., Gao, T.-Y., Li, H.-Y., Ma, Y.-T., Li, H.-J., Xian-Yu, C.-Y., Deng, N.-J., Zhang, C., 2023. Global, regional, and national trends of syphilis from 1990 to 2019: the 2019 global burden of disease study. *BMC Public Health* 23, 754. <https://doi.org/10.1186/s12889-023-15510-4>



99. Thurlow, C.M., Joseph, S.J., Ganova-Raeva, L., Katz, S.S., Pereira, L., Chen, C., Debra, A., Vilfort, K., Workowski, K., Cohen, S.E., Reno, H., Sun, Y., Burroughs, M., Sheth, M., Chi, K.-H., Danavall, D., Philip, S.S., Cao, W., Kersh, E.N., Pillay, A., 2022. Selective Whole-Genome Amplification as a Tool to Enrich Specimens with Low *Treponema pallidum* Genomic DNA Copies for Whole-Genome Sequencing. *mSphere* 7, e00009-22. <https://doi.org/10.1128/msphere.00009-22>
100. Tsuboi, M., Evans, J., Davies, E.P., Rowley, J., Korenromp, E.L., Clayton, T., Taylor, M.M., Mabey, D., Chico, R.M., 2021. Prevalence of syphilis among men who have sex with men: a global systematic review and meta-analysis from 2000–20. *The Lancet Global Health* 9, e1110–e1118. [https://doi.org/10.1016/S2214-109X\(21\)00221-7](https://doi.org/10.1016/S2214-109X(21)00221-7)
101. Venter, J.M.E., Müller, E.E., Mahlangu, M.P., Kularatne, R.S., 2021. *Treponema pallidum* Macrolide Resistance and Molecular Epidemiology in Southern Africa, 2008 to 2018. *J Clin Microbiol* 59, e02385-20. <https://doi.org/10.1128/JCM.02385-20>
102. Wang, X., Abiliz, P., Deng, S., 2023. Molecular Characteristics of Macrolide Resistance in *Treponema pallidum* from Patients with Latent Syphilis in Xinjiang, China. *IDR* Volume 16, 1231–1236. <https://doi.org/10.2147/IDR.S400068>
103. Workowski, K. A., Bachmann, L. H., Chan, P. A., Johnston, C. M., Muzny, C. A., Park, I., Reno, H., Zenilman, J. M., & Bolan, G. A. (2021). *Sexually Transmitted Infections Treatment Guidelines, 2021*. 70(4).



104. Wu, B.-R., Yang, C.-J., Tsai, M.-S., Lee, K.-Y., Lee, N.-Y., Huang, W.-C., Wu, H., Lee, C.-H., Chen, T.-C., Ko, W.-C., Lin, H.-H., Lu, P.-L., Chen, Y.-H., Liu, W.-C., Yang, S.-P., Wu, P.-Y., Su, Y.-C., Hung, C.-C., Chang, S.-Y., 2014. Multicentre surveillance of prevalence of the 23S rRNA A2058G and A2059G point mutations and molecular subtypes of *Treponema pallidum* in Taiwan, 2009–2013. Clinical Microbiology and Infection 20, 802–807. <https://doi.org/10.1111/1469-0691.12529>
105. Xiao, Y., Liu, S., Liu, Z., Xie, Y., Jiang, C., Xu, M., Zhao, F., Zeng, T., Yu, J., & Wu, Y. (2016). Molecular Subtyping and Surveillance of Resistance Genes In *Treponema pallidum* DNA From Patients With Secondary and Latent Syphilis in Hunan, China. Sexually Transmitted Diseases, 43(5), 310–316. <https://doi.org/10.1097/OLQ.0000000000000445>
106. Zhang, R.-L., et al, 2019. Relationship between the high frequency of 23S rRNA point mutations in *Treponema pallidum* and low serological response rate to azithromycin treatment in China. International Journal of Dermatology and Venereology 2, 6–14.
107. Wu, B.-R., Liu, W.-C., Wu, P.-Y., Su, Y.-C., Yang, S.-P., Hung, C.-C., Chang, S.-Y., 2014. Surveillance study of *Treponema pallidum* harbouring tetracycline resistance mutations in patients with syphilis. International Journal of Antimicrobial Agents 44, 370–372.
108. Noda, A.A., Rodríguez, I., Grillová, L., Bosshard, P.P., Lienhard, R., 2019. Accuracy of PCR and serological testing for the diagnosis of primary syphilis: Both tests are necessary. Int J STD AIDS 30, 1087–1094. <https://doi.org/10.1177/0956462419859764>
109. Zhou, C., Zhang, X., Zhang, W., Duan, J., Zhao, F., 2019. PCR detection for syphilis diagnosis: Status and prospects. Clinical Laboratory Analysis 33, e22890. <https://doi.org/10.1002/jcla.22890>



110. Peyriere, H., Makinson, A., Marchandin, H., Reynes, J., 2017. Doxycycline in the management of sexually transmitted infections. *Journal of Antimicrobial Chemotherapy*. <https://doi.org/10.1093/jac/dkx420>
111. Li, J., Zheng, H.-Y., 2014. Early syphilis: serological treatment response to doxycycline/tetracycline versus benzathine penicillin. *J Infect Dev Ctries* 8, 228–232. <https://doi.org/10.3855/jidc.3013>
112. Goig, G.A., Blanco, S., Garcia-Basteiro, A.L., Comas, I., 2020. Contaminant DNA in bacterial sequencing experiments is a major source of false genetic variability. *BMC Biol* 18, 24. <https://doi.org/10.1186/s12915-020-0748-z>
113. Hwang, K.-B., Lee, I.-H., Li, H., Won, D.-G., Hernandez-Ferrer, C., Negron, J.A., Kong, S.W., 2019. Comparative analysis of whole-genome sequencing pipelines to minimize false negative findings. *Sci Rep* 9, 3219. <https://doi.org/10.1038/s41598-019-39108-2>
114. Thurlow, C.M., Joseph, S.J., Ganova-Raeva, L., Katz, S.S., Pereira, L., Chen, C., Debra, A., Vilfort, K., Workowski, K., Cohen, S.E., Reno, H., Sun, Y., Burroughs, M., Sheth, M., Chi, K.-H., Danavall, D., Philip, S.S., Cao, W., Kersh, E.N., Pillay, A., 2022. Selective Whole-Genome Amplification as a Tool to Enrich Specimens with Low *Treponema pallidum* Genomic DNA Copies for Whole-Genome Sequencing. *mSphere* 7, e00009-22. <https://doi.org/10.1128/msphere.00009-22>
115. Goldfeder, R.L., Priest, J.R., Zook, J.M., Grove, M.E., Waggett, D., Wheeler, M.T., Salit, M., Ashley, E.A., 2016. Medical implications of technical accuracy in genome sequencing. *Genome Med* 8, 24. <https://doi.org/10.1186/s13073-016-0269-0>



116. Chen, W., Šmajš, D., Hu, Y., Ke, W., Pospišilová, P., Hawley, K.L., Caimano, M.J., Radolf, J.D., Sena, A., Tucker, J.D., Yang, B., Juliano, J.J., Zheng, H., Parr, J.B., 2021. Analysis of *Treponema pallidum* Strains From China Using Improved Methods for Whole-Genome Sequencing From Primary Syphilis Chancres. *The Journal of Infectious Diseases* 223, 848–853. <https://doi.org/10.1093/infdis/jiaa449>
117. Nishiki, S., Lee, K., Kanai, M., Nakayama, S., Ohnishi, M., 2021. Phylogenetic and genetic characterization of *Treponema pallidum* strains from syphilis patients in Japan by whole-genome sequence analysis from global perspectives. *Sci Rep* 11, 3154. <https://doi.org/10.1038/s41598-021-82337-7>
118. Firth A, Prathapan P. European Journal of Medicinal Chemistry Azithromycin : The First Broad-spectrum Therapeutic. *Eur J Med Chem [Internet]*. 2020;207:112739.
119. Cohen, M. K., Muntner, P., Kent, C. K., King, P. H., Gottardy, A. J., Leahy, M. A., Spriggs, S. R., Velarde, A., Yang, T., Starr, T. M., Yang, M., Jones, T. F., Boulton, M. L., Brooks, C., Caine, V. A., Fielding, J. E., Fleming, D. W., Halperin, W. E., Mullen, J., ... Johnson, L. (2024). Morbidity and Mortality Weekly Report Centers for Disease Control and Prevention Recommendations and Reports Centers for Disease Control and Prevention MMWR Editorial and Production Staff (Serials) MMWR Editorial Board CONTENTS. In *Recommendations and Reports* (Vol. 73).
120. Wang Y, Sibaii F, Lee K, J. Gill M, L. Hatch J. NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice. 1. medRxiv. 2021;1(165):1–13.



121. Su JR, Pillay A, Hook EW, Ghanem KG, Wong W, Jackson D, et al. Prevalence of the 23S rRNA A2058G point mutation and molecular subtypes in *Treponema pallidum* in the United States, 2007 to 2009. *Sex Transm Dis.* 2012;39(10):794–8.
122. Morando, N., Vrbová, E., Melgar, A., Rabinovich, R. D., Šmajc, D., & Pando, M. A. (2022). High frequency of Nichols-like strains and increased levels of macrolide resistance in *Treponema pallidum* in clinical samples from Buenos Aires, Argentina. *Scientific Reports*, 12(1), 16339. <https://doi.org/10.1038/s41598-022-20410-5>