

Chlamydia test-of-cure in pregnancy

Jessie Pettit MD Carol Howe MD MLS Joshua Freeman MD

Clinical Inquiries question

What is the optimal interval between treatment and test-of-cure (TOC) in pregnant women with *Chlamydia trachomatis* (CT)?

Evidence-based answer

The optimal interval between treatment and TOC in pregnant women with CT is 3 to 4 weeks (strength of recommendation C: several small prospective and retrospective cohort studies; a high-quality nonsystematic review; and a consensus guideline). Testing before 3 weeks might give false-positive results, while waiting longer than 4 weeks might delay detecting new infections or result in treatment failure.

Evidence summary

The Centers for Disease Control and Prevention recommends an interval between treatment and TOC based on a few small studies, which used either azithromycin or doxycycline in standard treatment regimens. Only 2 studies included pregnant women: a 2015 feasibility study and a 2017 prospective cohort study. The feasibility study of self-collected vaginal nucleic acid amplification tests (NAATs) for antenatal CT screening noted a TOC rate of 86% at 3 or more weeks after treatment (n=52).¹ The prospective cohort study, which included pregnant women (n=36) and nonpregnant women (n=36), followed the participants' self-collected weekly vaginal swabs after treatment, stopping once the NAAT results were negative. Twenty days after treatment, 94% of pregnant participants and 96% of nonpregnant participants had negative CT NAAT results. All NAAT results were negative 29 days after treatment (n=47).² Both of these studies used APTIMA second-generation NAATs, which use target-capture, transcription-mediated amplification, and hybridization protection assay. Additionally, a 2014 retrospective analysis in nonpregnant adolescents analyzed polymerase chain reaction (PCR) vaginal swab results after treatment: 21 days after treatment, 89% of women had negative test results for CT (109 of 123), consistent with the 3-week cure rates in the aforementioned studies using APTIMA.³

A 1993 prospective study followed 20 women for 5 months after CT treatment; all participants had negative cell culture and PCR findings 4 weeks after treatment.⁴ A 1998 prospective study followed adolescents after treatment: 15 days after therapy, all urine test results (PCR and ligase chain reaction) were negative; however, the final analysis only included 8 participants.⁵ In a 2011 prospective study, results of APTIMA vaginal swabs collected at 4 time points over a 2-week period were positive in 21%


of participants 14 days after treatment (13 of 61 samples). No samples were collected after 14 days. Based on the percentage of women with negative APTIMA results at the 4 time points, a multiple linear regression analysis was used to predict 100% clearance at 17 days.⁶ The authors posited that positive APTIMA results 14 days after treatment were likely due to the presence of CT ribosomal RNA in nonviable organisms, although serologic subtyping of CT was not performed.

The findings in one prospective cohort study challenge the strategy of a 1-time TOC 3 to 4 weeks after treatment. Forty-six women and 6 men were treated and followed at 6 time points over 8 weeks. Forty-two percent of participants had positive test results for at least 1 vaginal or anorectal sample (transcription-mediated amplification and PCR) taken after 3 weeks, suggesting that a single TOC might miss treatment failure or reinfection, though there was no serologic subtyping of CT to differentiate between these possibilities.⁷

Recommendations from others

The Centers for Disease Control and Prevention's 2015 "Sexually Transmitted Diseases Treatment Guidelines" state that pregnant women who have positive test results for CT should have a TOC with an NAAT 3 to 4 weeks after treatment.⁸ A 2013 advisory group for the 2015 guidelines reviewed the available literature in addition to 2 less robust studies. Given the small size of these studies and considerable heterogeneity in study design, the advisory group concluded that the precise timing of CT clearance is unclear and continued to recommend an interval of 3 to 4 weeks between treatment and TOC in pregnancy.⁹

Editor's take-away

This high-risk group, patients recently diagnosed with CT, needs retesting because of possible treatment failure and risk of reinfection. The evidence also shows that early retesting—before 3 weeks—can yield false-positive results. Large randomized controlled trials are needed to support the conclusion to retest for CT 3 to 4 weeks after treatment. 

Dr Freeman is Clinical Professor and **Dr Pettit** is Associate Professor in the Department of Family and Community Medicine at the University of Arizona in Tucson. **Dr Howe** is a librarian in the Health Sciences Library at the University of Arizona.

Competing interests

None declared

Correspondence

Dr Joshua Freeman; e-mail jfreeman3@gmail.com

References

1. Cabeza J, Garcia PJ, Segura E, Garcia P, Escudero F, La Rosa S, et al. Feasibility of *Chlamydia trachomatis* screening and treatment in pregnant women in Lima, Peru: a prospective study in two large urban hospitals. *Sex Transm Infect* 2015;91(1):7-10. Epub 2014 Aug 8.

2. Lazenby GB, Korte JE, Tillman S, Brown FK, Soper DE. A recommendation for timing of repeat *Chlamydia trachomatis* test following infection and treatment in pregnant and nonpregnant women. *Int J STD AIDS* 2017;28(9):902-9.
3. Williams JA, Ofner S, Batteiger BE, Fortenberry JD, Van Der Pol B. Duration of polymerase chain reaction-detectable DNA after treatment of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis* infections in women. *Sex Transm Dis* 2014;41(3):215-19.
4. Workowski KA, Lampe MF, Wong KG, Watts MB, Stamm WE. Long-term eradication of *Chlamydia trachomatis* genital infection after antimicrobial therapy. Evidence against persistent infection. *JAMA* 1993;270(17):2071-5.
5. Gaydos CA, Crotchfelt KA, Howell MR, Kralian S, Hauptman P, Quinn TC. Molecular amplification assays to detect chlamydial infections in urine specimens from high school female students and to monitor the persistence of chlamydial DNA after therapy. *J Infect Dis* 1998;177(2):417-24.
6. Renault CA, Israelski DM, Levy V, Fujikawa BK, Kellogg TA, Klausner JD. Time to clearance of *Chlamydia trachomatis* ribosomal RNA in women treated for chlamydial infection. *Sex Health* 2011;8(1):69-73.
7. Dukers-Muijers NH, Morré SA, Speksnijder A, van der Sande MA, Hoebe CJ. *Chlamydia trachomatis* test-of-cure cannot be based on a single highly sensitive laboratory test taken at least 3 weeks after treatment. *PLoS One* 2012;7(3):e34108. Epub 2012 Mar 28.
8. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015;64(RR-03):1-137. Erratum in: *MMWR Recomm Rep* 2015;64(33):924.
9. Geisler WM. Diagnosis and management of uncomplicated *Chlamydia trachomatis* infections in adolescents and adults: summary of evidence reviewed for the 2015 Centers for Disease Control and Prevention Sexually Transmitted Diseases Treatment Guidelines. *Clin Infect Dis* 2015;61(Suppl 8):S774-84.



Clinical Inquiries are author-formulated questions that are answered with the best available current evidence, written by family medicine residency faculty and their residents through the **Family Physician Inquiries Network**. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (www.cebm.net). The Family Physicians Inquiries Network Clinical Inquiries series in *Canadian Family Physician* is coordinated by **Rick Guthmann, MD, MPH**, Editor-in-Chief for the series. If interested in submitting questions or writing answers for this series, go to www.fpin.org or e-mail ci@fpin.org. ©Family Physicians Inquiries Network. Used with permission.