

Literature Review

National STD Curriculum Podcast

# Treatment Options for Trichomoniasis

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Season 2, Episode 7

This episode focuses on some of the literature supporting seven days of metronidazole treatment for *Trichomonas* infection recommended in the CDC 2021 STI Treatment Guidelines.

Topics:

- STI
- Trichomonas
- T. vaginalis
- Trich
- STD
- Trichomoniasis

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[Disclosures](#)

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### [00.00] Introduction

Hello everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STD [sexually transmitted disease] literature review for health care professionals who are interested in remaining up-to-date on the diagnosis, management, and prevention of STDs.

## [00.20] Background

Kissinger P, Mena L, Levison J, et al. A randomized treatment trial: Single versus 7-day dose of metronidazole for the treatment of *Trichomonas vaginalis* among HIV-infected women. J Acquir Immune Defic Syndr. 2010 Dec 15;55(5):565-71. [[PubMed Abstract](#)]

We're going to focus this episode on *Trichomonas vaginalis*. It's a parasite that is one of the most common STIs [sexually transmitted infections] worldwide, and it can lead to serious reproductive morbidity and poor birth outcomes. The CDC 2021 STI Treatment Guidelines now recommend a multidose metronidazole regimen for the treatment of *Trichomonas* as first-line therapy. The previous guidelines in 2015, they recommended a single 2-gram dose of metronidazole for first-line treatment among women without HIV, but for women with HIV, a multidose regimen was recommended. And this recommendation for women with HIV was based on data from a randomized treatment trial that was published in 2010 by Dr. Kissinger and colleagues, which showed that the 7-day metronidazole dose was more effective than a single dose but in this particular population. So let's review some of the literature supporting the multidose metronidazole treatment for *Trichomonas* in the 2021 STI Treatment Guidelines and look at one newer option to treat *Trichomonas*, which is called secnidazole

## [01.24] Paper #1

Kissinger P, Muzny CA, Mena LA, et al. A randomized trial of metronidazole in a single 2 g dose versus 500 mg twice daily for 7 days for the treatment of trichomoniasis in women. Lancet Infect Dis. 2018 Nov;18(11):1251-1259. [[PubMed Abstract](#)]

This first article for review was published in *Lancet Infectious Diseases* by Dr. Kissinger and colleagues in November of 2018. It was titled "A randomized trial of metronidazole in a single 2-g dose versus 500 mg twice daily for 7 days for the treatment of trichomoniasis in women."

1. This was a randomized, open-label trial of 623 women without HIV and not pregnant to evaluate the effectiveness of a single dose of metronidazole versus a multidose 7-day regimen for the treatment of trichomoniasis. It included women seen in STD clinics in Birmingham, Alabama; Jackson, Mississippi; and New Orleans, Louisiana.
2. In these areas, there were legal or institutional restrictions, so none of the clinics routinely provided expedited partner treatment, but some partners were given expedited partner treatment at the medical provider's discretion.
3. They used an open-label design to simulate real-world conditions and accommodate for the potential lack of adherence and sexual reexposure difference among women who received treatment over multiple days. And a test-of-cure was done at four weeks after completion of treatment by nucleic acid amplification test as well as culture. And 87% of individuals returned for the follow-up visit. There was a self-reported adherence in both arms that was greater than 95%. So patients were taking their medications.
4. The authors found that 11% of participants in the 7-day dose arm were *Trichomonas vaginalis* positive by nucleic acid amplification test or culture at the test-of-cure visit compared to 19% in the single-dose arm and that had a relative risk of 0.55.
5. The authors did not find any difference in sexual exposure to either baseline or new partners.

So, overall in this study, a 7-day regimen of metronidazole treatment resulted in 45% fewer treatment failures than participants receiving a single high dose of metronidazole at 2 grams for *Trichomonas vaginalis* infection. So I can see why the guidelines were updated to recommend a 7-day treatment for *Trichomonas* infection in women, both with and without HIV. We just have enough data to show that treatment effectiveness is better with the multiday regimen.

### [03.33] Paper #2

Gatski M, Martin DH, Levison J, et al. The influence of bacterial vaginosis on the response to *Trichomonas vaginalis* treatment among HIV-infected women. *Sex Transm Infect.* 2011 Apr;87(3):205-8. [[PubMed Abstract](#)]

Muzny CA, Mena LA, Lillis RA, Schmidt N, Martin DH, Kissinger P. A Comparison of single-dose versus multidose metronidazole by select clinical factors for the treatment of *Trichomonas vaginalis* in women. *Sex Transm Dis.* 2022 Mar 1;49(3):231-236. [[PubMed Abstract](#)]

Now, there was some evidence from the randomized treatment trial that was published in 2010 that among women with HIV and *Trichomonas* infection, a diagnosis of bacterial vaginosis may alter treatment efficacy. A secondary analysis of the original data was published by Dr. Gatski and colleagues in 2011, and they suggested a superiority of the 7-day treatment regimen, especially among those participants who also had concurrent bacterial vaginosis. And it was possibly due to altered vaginal flora interfering with a single-dose treatment. So an article published in *Sexually Transmitted Diseases* in March of 2022 by Dr. Muzny and colleagues evaluated if select clinical factors influenced the effect of multidose treatment in women without HIV. The manuscript is titled “A comparison of single-dose versus multidose metronidazole by select clinical factors for treatment of *Trichomonas vaginalis* in women.”

1. This was a secondary analysis of the randomized, controlled trial of a single-dose versus multidose metronidazole treatment for trichomoniasis we just spoke about that was published by Dr. Kissinger and colleagues in 2018.
2. All the women enrolled had a confirmed diagnosis of trichomoniasis at the study entry. And the investigators looked at whether the participants had a prior history of *Trichomonas vaginalis*, genital symptoms at baseline, or a concurrent diagnosis of bacterial vaginosis—and that was in addition to the new *Trichomonas* infection at baseline—to determine if multiday or single-dose treatment recommendations could be targeted for specific populations.
3. The authors found that on multivariate analysis, only a prior history of *Trichomonas* infection and single-dose metronidazole treatment was associated with a test-of-cure result that was positive for *Trichomonas vaginalis*.
4. The unadjusted analysis found a trend of women with *Trichomonas vaginalis* randomized to a single dose of metronidazole having a greater odds of being repeat test positive at test-of-cure than women randomized to the multidose regimen if they had baseline genital symptoms, but this finding was not significant in multivariable analysis.
5. There was no significant difference in the odds of being repeat positive at test-of-cure for *Trichomonas vaginalis* among women with a baseline diagnosis of bacterial vaginosis or a baseline diagnosis of gonorrhea compared with those without these infections.

So, this study reinforces the multidose treatment regimen for trichomoniasis, especially in women with a history of this previous infection, although I must note this was a self-reported history. While the mechanism for this was not studied, the authors note possible reasons might be related to the organism being relatively resistant to metronidazole or possibly non-vaginal reservoirs of infection that require longer dosing for effective treatment. I think further studies are just needed in this area.

### [06.26] Paper #3

Muzny CA, Schwebke JR, Nyirjesy P, et al. Efficacy and safety of single oral dosing of secnidazole for trichomoniasis in women: Results of a phase 3, randomized, double-blind, placebo-controlled, delayed-treatment study. *Clin Infect Dis.* 2021 Sep 15;73(6):e1282-e1289. [[PubMed Abstract](#)]

The question remains, what other treatments are available for *Trichomonas* infection? The last article to review was also published by Dr. Muzny and colleagues in *Clinical Infectious Diseases* in September of 2021. It is titled “Efficacy and safety of single oral dosing of secnidazole for trichomoniasis in women: Results of a phase 3, randomized, double-blind, placebo-controlled, delayed-treatment study.”

1. So first, a little bit of a brief background on secnidazole. It’s a potent 5-nitroimidazole antimicrobial agent with a longer half-life than metronidazole or tinidazole. It was approved by the FDA for bacterial vaginosis in women in 2017, and in 2021 it was approved to treat *Trichomonas* infection.
2. This study evaluated 131 women with trichomoniasis, confirmed by a positive *Trichomonas vaginalis* culture, that were enrolled in ten sites in the United States. The women were randomized to receive oral secnidazole 2 grams as a single dose or placebo for the treatment of their infection.
3. A test-of-cure was done by culture 6-12 days after treatment. At the test-of-cure visit, participants were given the opposite treatment and then followed for resolution of infection.
4. Now, overall, secnidazole was generally well tolerated.
5. And the authors found that the cure rates were significantly higher in the secnidazole group at 92% compared to the placebo group at 1.5%. Cure rates were 100% in women with HIV—and that was four out of four patients—and 95% in women with concomitant bacterial vaginosis.

The results of this study support secnidazole as a treatment of trichomoniasis. Given the long half-life of about 17 hours, this might be a good single-dose option, especially if patients might not be able to adhere to the multidose metronidazole treatment regimen. I wonder if we’ll be seeing more information on secnidazole for the treatment of *Trichomonas* infection in the future, particularly a treatment study comparing secnidazole to metronidazole.

#### **[08.29] Summary**

To conclude, I’d like to summarize some key points from this session:

1. A 7-day regimen of metronidazole treatment was more effective at treating *Trichomonas* infection in women than a single high dose of metronidazole.
2. A baseline diagnosis of bacterial vaginosis does not seem to influence the superiority of a 7-day metronidazole treatment regimen.
3. Women with a self-reported prior history of *Trichomonas* infection were more likely to fail with a single-dose metronidazole treatment.
4. A single dose of secnidazole was found to treat *Trichomonas* in women with high cure rates compared to placebo.

#### **[09.06] Credits**

This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by the Centers for Disease Control and Prevention.

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