Centers for Disease Control and Prevention
Division of STD Prevention
Updated Gonorrhea Treatment Recommendations

Talking Points and Q&A for STD Prevention Partners

Overview

On December 17, 2020, CDC's Division of STD Prevention (DSTDP) released a special Morbidity and Mortality Weekly Report (*MMWR*) policy note, *2020 Update to CDC's Treatment for Gonococcal Infections*, to highlight key adjustments in gonorrhea treatment practices. DSTDP issued a Dear Colleague Letter that same day to outline the key changes and important implications for STD prevention.

Since 2015, dual therapy with ceftriaxone and azithromycin has been the only recommended regimen for uncomplicated gonorrhea. However, recent data from CDC's 2013-2019 Gonococcal Isolate Surveillance Project (GISP) showed growing azithromycin resistance and low prevalence of ceftriaxone resistance in gonorrhea in the U.S. CDC removed the medication azithromycin from its recommended treatment regimen for uncomplicated gonorrhea in adolescents and adults. Gonorrhea should now be treated with a single dose of ceftriaxone 500 mg administered intramuscularly to effectively eradicate gonorrhea infection.

The following talking points were developed to assist partners with communicating about CDC's updated gonorrhea treatment guidelines.

***Note**: This publication was not intended to address all clinical situations or all populations in which treating gonorrhea and other infections may be warranted. Providers should refer to the 2015 STD Treatment Guidelines for additional recommended treatment regimens.*

Four Key Messages about the Update

1. CDC updated its gonorrhea treatment recommendations to guard against additional resistance and ensure patients receive the most effective treatment, as effective treatment is the cornerstone of U.S. gonorrhea control efforts.
    - CDC has recommended a two-drug regimen of the injectable ceftriaxone and oral azithromycin uncomplicated gonorrhea since 2015; however, recent Gonococcal Isolate Surveillance Project (GISP) data and scientific literature suggests that gonorrhea is showing signs of resistance to azithromycin, making it less effective for gonorrhea and risking losing effectiveness for other infections (e.g. M. gen & shigella).
    - Changes to the gonorrhea treatment guidelines were prompted by three concerns:
        - Antimicrobial stewardship and the need to minimize antibiotic exposure unless the benefit clearly outweighs the risk, which is an increasingly important consideration for all infections, not just STIs.
        - Understanding the pharmacokinetics (how drugs move in the body) and pharmacodynamics (biochemical and physiologic effects of drugs) of ceftriaxone and identifying the optimal treatment dose.

        - Signs of azithromycin resistance is increasing.
    - While gonorrhea is still treatable in the U.S. (and we've not yet seen gonorrhea treatment failures), changes in treatment and continued monitoring are essential to preserve the last option for as long as possible.
2. Gonorrhea should be treated with just one, higher dosage injection of ceftriaxone – a two-drug approach is no longer recommended.
    - Although the treatment may change, our job does not: we must keep detecting, curing, and preventing this common infection, using the most effective treatment regimen currently available.
    - Our highest priority is to adjust treatment practices according to the latest science to ensure effective treatment and minimize the threat of drug resistance.
        - Treat gonorrhea with a single 500 mg injection of ceftriaxone. Gonorrhea should be treated along with chlamydia treatment (100 mg doxycycline orally twice a day for seven days), if chlamydia has not been ruled out.
        - A test-of-cure is not needed for people who receive a diagnosis of uncomplicated urogenital or rectal gonorrhea who are treated with any of the recommended or alternative regimens, unless symptoms persist.
        - A test-of-cure is recommended in people with pharyngeal gonorrhea by using either culture or NAAT 7-14 days after the initial treatment, regardless of the regimen.
        - Patients who have been treated for gonorrhea should be retested three months after treatment, to ensure reinfection hasn't occurred.
        - Providers also should facilitate partner treatment.
    - Our response can only succeed with immediate action from healthcare providers. They should continue to:
        - Follow CDC testing and treatment recommendations.
        - Identify a lab where they can send a gonorrhea culture test when their patient needs one, to avoid delays in susceptibility testing.
        - Monitor for and report suspected treatment failures to their health department STD program.
        - Retest patients who have been diagnosed and treated for gonorrhea three months after treatment.
        - Healthcare providers should continue to follow basic tenets of good STI prevention, including taking thorough sexual histories, ensuring partners are notified and treated, and considering early expedited partner therapy for those unable or unwilling to access care.
3. Drug-resistant gonorrhea remains an urgent public health threat, and we must continue monitoring and preparing for resistance.
    - Half of all gonorrhea infections are resistant to at least one antibiotic.[1]
        - There has been twice as many resistant infections since the first major CDC report on antibiotic-resistant threats in the U.S. was published in 2013.

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[1] Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019 [Internet]. Atlanta (GA): U.S. Department of Health and Human Services, CDC; 2019 [cited 2020]. 75-76 p. Available from: https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

        - Drug resistant gonorrhea costs $133 million in annual discounted lifetime medical costs.
    - Prevention and control efforts are critical in lessening the burden of gonorrhea.
    - Health departments and labs can help CDC keep a watchful eye on emerging drug resistance and enhance or re-build their ability to do culture testing, so that samples can be tested for treatment failures and resistance and reported to CDC when they occur.

4. Protecting patients from gonorrhea has never been more important.
    - Gonorrhea is the second most commonly reported notifiable disease in the U.S..[2]
        - In 2018, 583,405 cases were reported – the most reported in more than 20 years.
        - Gonorrhea is vastly underreported because many infections are asymptomatic and go undetected - more than a million infections occur each year.
    - With treatment options dwindling, and the threat of untreated gonorrhea on the horizon, it's critical that patients take important steps to prevent infection. Encourage patients to:
        1. Use latex condoms the right way every time and limit their number of partners, if they are sexually active.
        2. Get screened: CDC recommends annual screening for sexually active females and pregnant people <25 for gonorrhea; annual screening for major STDs (including gonorrhea) for sexually active men who have sex with men (MSM).
            - If a patient is infected, they should get treated with a ceftriaxone injection right away to cure the infection and prevent transmission to others. It's also important that patients know the recommended treatment and ask for it.

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[2] Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2018 [Internet]. Atlanta (GA): U.S. Department of Health and Human Services, CDC; 2019. 11 p. Available from: https://www.cdc.gov/std/stats18/STDSurveillance2018-full-report.pdf

Key Questions & Answers about the Update

1. Why is CDC now recommending a single dose of ceftriaxone instead of dual therapy?

- CDC removed the medication azithromycin from its recommended treatment regimen for uncomplicated gonorrhea due to increasing concern for antimicrobial stewardship and the continued low incidence of ceftriaxone resistance in the United States.

- Antimicrobial stewardship (which aims to improve antibiotic prescribing and effectively treat infections, reduce unnecessary antibiotic use, and combat antibiotic resistance) has become a more prominent concern since the publication of the last guidelines.

- Additionally, there is more awareness of the effects of these treatments and the amount needed to treat infection at different locations in the body, which contributed to the need for an increased ceftriaxone dose.

- Finally, data from CDC's 2013-2019 Gonococcal Isolate Surveillance Project (GISP) showed growing azithromycin resistance in gonorrhea and continued low incidence of ceftriaxone resistance in the United States.

- Together, these factors tipped the scales in terms of the risk versus benefit of keeping dual therapy.

2. Why is CDC increasing the dosage of ceftriaxone?

- Several factors contributed to the need for an increased ceftriaxone dose:
  - A better understanding of the effects of these treatments and in the amount needed to treat infection at various locations in the body.
  - Globally, most reported treatment failures occur at the pharynx and this site may not be always tested. Infection in the pharynx requires higher doses of ceftriaxone to cure gonorrhea.
  - These factors contributed to the need for an increased dose of ceftriaxone.

- The most up-to-date research indicates a single dose of ceftriaxone 500 mg administered intramuscularly is the optimal dose to effectively clear gonorrhea infection.

3. How often will CDC need to update its gonorrhea treatment recommendations if we keep running out of effective drugs?

- CDC is working to preserve the effectiveness of the current gonorrhea treatment regimen for as long as possible, and there is continued need for U.S. surveillance to monitor for resistance patterns before clinical treatment failure occurs.

- Preserving effective gonorrhea treatment will require close monitoring of resistance to the drugs ceftriaxone, along with healthcare providers testing and reporting any treatment failures.

- We also need to continue ongoing gonorrhea prevention and control efforts and support the development of additional therapeutics to increase treatment options.

4. **How close are we to finding new treatment options for gonorrhea?**
    - We are down to our last highly effective antibiotic class to treat gonorrhea. Until new drugs are available, our best course of action is to prevent gonorrhea infection and to slow the emergence and spread of antibiotic-resistant gonorrhea through continued monitoring, adherence to CDC's treatment recommendation, and rapid detection and response to strains with decreased susceptibility.

    - There are several investigational agents currently being studied in clinical trials to determine their effectiveness against gonorrhea.

5. **Why are these recommendations coming out before the full STD treatment guidelines are updated?**
    - Antibiotic-resistant gonorrhea continues to be a threat in the U.S. and it is important that we provide the most current information on the optimal treatment regimen.

6. **Since CDC no longer recommends exclusively oral treatment for gonorrhea, how does CDC recommend EPT be practiced for gonorrhea?**

    - In cases where gonorrhea expedited partner therapy (EPT) is permissible by state law and the partner is unable or unlikely to seek timely treatment, the partner may be treated with a single 800 mg dose of cefixime, if a chlamydia infection in the patient has been excluded.

    - As has always been the case, medication or prescriptions provided as part of EPT should be accompanied by treatment instructions, appropriate warnings about taking medications (if the partner is pregnant or has an allergy to the medication), general gonorrhea health education and counseling, and a statement advising that partners seek personal medical evaluation, particularly women with symptoms of pelvic inflammatory disease (PID).

Implementation Questions for DSTDP-funded partners

1. **When should our STD program implement these gonorrhea treatment changes?**
   - The gonorrhea (GC) treatment guidelines published in the December 18, 2020 MMWR are currently in effect, and you should start the process for implementing these changes when feasible.
   - The new treatment recommendations reflect a change in practice for healthcare providers and STD programs. It is expected that there will be a transition period where these recommendations are disseminated and adopted.
   - **It is important to remember that treatment failures have not been reported using the old regimen.** If it takes some time to implement the new guidelines, you will still be effectively treating patients with the old regimen during these next few months of transition.

2. **At what point will we consider the previously recommended gonorrhea treatment regimen to be an "inadequate treatment"? Do we need to encourage patients to go back to their provider for additional ceftriaxone treatment or will there be a grace period?**
   - **Patients do not need to return to the clinic for additional treatment if they received the 2015 recommended regimen for GC**. While you should implement the new GC treatment guidelines with all due speed, it is important to know that there have not been treatment failures using the old regimen. Even if you take some time to implement the new guidelines, you'll still be effectively treating patients during this transition period over the next few months.

3. **When will the full set of STI Treatment Recommendations be published?**
   - The estimated timeline is early 2021, but there is no set date yet.

4. **Can we wait for the new full set of STI treatment guidelines to be published before we implement changes for GC treatment?**
   - At a minimum, we recommend that you begin promoting changes to the recommended GC treatment regimen. If you are inclined to delay provider outreach until you can promote the full suite of STI treatment guidelines updates, you can still take action now by updating internal documents, revising report forms, developing dissemination strategies, preparing health alerts, etc.
   - Because there is not a clear date for the release of the 2021 STI Treatment Guidelines, please let your STD PCHD Project Officer know if you are waiting for the complete 2021 STI treatment guidelines to be published before implementing the updated GC treatment.

5. **Do you have any guidance on how we should implement changes for GC treatment?**
   - **Promote Changes Internally:** Consider holding meetings with data entry, surveillance, and/or disease investigation staff who work with gonorrhea morbidity to review these changes. Ask front-line staff how this will impact their day-to-day processes, and help answer any questions they might have. Establish a process for staff to elevate additional questions or concerns that might come up as these changes roll out.

- **Promote Changes to Partners:** Consider drafting a Health Alert, or disseminating the [Dear Colleague Letter] to relevant provider networks. We recognize that provider attention may be limited due to the impact of COVID-19, and the best strategy will depend on your local context. If your program has limited bandwidth, focus your first efforts on local health department clinics, those most closely affiliated with you, and those that diagnose the most gonorrhea.

- **Update Treatment Reporting & Documentation**: Review your paper and/or electronic provider report forms and initiate the process for updating treatment information fields to match the new guidance. You also should assess your surveillance/case management system for any changes and update treatment documentation data fields and edit checks, as needed. Depending on how your system is set up, you may want to hold off on implementing changes until the full set of STI Treatment Recommendations is released, so you can implement any other changes at the same time. If updates are substantial, consider how deployment of those changes fits in with other priorities, and set yourself a clear timeline.

- **Review & Update Resource Documents:** Review your STD program's web page to see if any content or links need to be updated. Consider updates that may need to be made to internal job aids, or patient and provider education materials. If you have expedited partner therapy (EPT) Recommendations, review and update those guidelines to reflect recommended treatment.

- **Review Analysis & Reporting Processes:** If you have any auto-generated reports, review the underlying code and flag areas that need to be revised/updated to reflect the new recommendations. Consider whether you need to build any new reports to establish baseline measures of provider change by particular priority categories.

- **Update Medication Management & Inventory:** If your program directly orders STD medications, or facilitates medication ordering through partner organizations, review your current inventory and adjust ordering practices to reflect the new dosage recommendations. If you have a stockpile of the previous recommended treatment, you should continue using that until it is exhausted, and plan to adjust ordering and treatment practices moving forward.

6. Should we update our Year 3 STD PCHD work plans to reflect changes in GC treatment?

- Yes. Consider where you should adjust your objectives for sub-strategies 2A, 2B, and/or 11A in your Year 3 work plan. The focus in Year 3 (2021) should be on establishing processes for assessing treatment adherence and establishing new baselines. You may want to focus on process/milestone objectives, including promotional activities, making necessary system changes, and producing baseline analyses. We encourage you to include these changes in your response to the Year 3 Technical Review (responses due by February 1, 2021).

7. How will the GC treatment change impact STD PCHD Performance Measures?

- We expect to measure 2020 based on the guidelines current during that period, so the Performance Measures submitted this year (based on 2020 data) will not change. We have not yet developed the approach for 2021 measures, but the Evaluation Team will update STD PCHD recipients on those changes once they are finalized.

8. How does this change impact enhanced GC surveillance activities required in STD PCHD?

- If you have unique data collection forms for enhanced GC surveillance, you may want to review and update those to reflect recommended treatment options. The aim of enhanced GC sampling is to do follow up on a systematic random sample of cases, so the changes to GC treatment guidelines should not impact those processes. If you are conducting enhanced sampling in 2020, you may want to consider a focused analysis of treatment information from those provider/patient interviews as a method of assessing adoption of the new recommendations.