

**FREQUENTLY ASKED CASE QUESTIONS:
UPDATE TO CDC'S TREATMENT GUIDELINES FOR GONOCOCCAL INFECTION, 2020**

[HTTPS://WWW.CDC.GOV/MMWR/VOLUMES/69/WR/MM6950A6.HTM](https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm)

(CDC SUMMARY BOX IS SHOWN AT END OF FAQ)

GONORRHEA (GC) TREATMENT GUIDELINES CHANGES

Q: GUIDELINES STATE THAT IF CO-EXISTING CHLAMYDIA (CT) "CANNOT BE EXCLUDED," ADD DOXYCYCLINE 100 MG X 7 DAYS TO CEFTRIAXONE. IF THROAT SWAB (+) FOR GONORRHEA (GC), SHOULD WE EMPIRICALLY TREAT WITH BOTH CEFTRIAXONE AND DOXYCYCLINE, SINCE OUR PHARYNGEAL NAAT TEST IS SPECIFIC ONLY FOR GONORRHEA AND DOES NOT TEST FOR CHLAMYDIA?

A. The guidelines say treat for CT if it cannot be excluded; therefore, if your test kit is specific to only GC, then you cannot exclude CT. However, if your test kit has both GC and CT in it, and the GC is positive and the CT is negative, you can simply treat for GC.

B. IF TREATING EMPIRICALLY FOR EXPOSURE TO EITHER GC OR CT BEFORE RESULTS COME BACK, DO YOU RECOMMEND USING DOXYCYCLINE OR AZITHROMYCIN?

B. Regarding the switch from Doxycycline to Azithromycin, this is obviously challenging to implement into practice. We recommend that if possible, please send throat swabs for both GC and CT as it's likely you are missing asymptomatic CT infections. However, if the throat swab is positive for GC and the NAAT does not test for both, we recommend a 7-day course of Doxycycline along with the Ceftriaxone.

The decision to move from Azithromycin to Doxycycline was made in consideration of both antimicrobial stewardship PK/PD properties. The guidelines imply that empiric treatment should be done with Doxycycline, and we use Doxycycline for empiric CT if rectal exposure is reported. For rectal CT, a recent RCT trial (presented at the 2016 CDC STD conference), was reportedly stopped early due to Azithromycin being inferior to Doxycycline for rectal CT.

CDC has emphasized the need for a shared decision-making approach with your patients. While Doxycycline is "recommended", Azithromycin remains an "alternative" regimen for CT. There may be instances when you and the patient decide that a single dose of Azithromycin is the right choice after considering cost/insurance issues, tolerability, and/or ability to go to the pharmacy to obtain the medication or compliance concerns.

Q: WITH THE NEW RECOMMENDATION FOR TEST OF CURE IN 7-14 DAYS S/P PHARYNGEAL GONORRHEA TREATMENT: WHAT ARE THE CHANCES THAT THE NAAT TEST MAY STILL BE POSITIVE FROM RESIDUAL NON-VIABLE ORGANISMS AFTER INITIAL TREATMENT, AND THUS BE A FALSE-POSITIVE RATHER THAN FAILED TREATMENT? HOW DO WE MANAGE THIS IF THE REPEAT TEST COMES BACK POSITIVE AGAIN?

A: With regard to repeat testing for pharyngeal treatment, we tend to err on the side of 2 weeks. While most patients will clear within one week, nearly all treated infections will test negative at the end of 2 weeks (PMID: [12354851](#)). In this study of specifically pharyngeal and rectal GC, DNA persisted in 8% of men 14 days after treatment however persistence was associated with elevated MICs to Ceftriaxone and Azithromycin (PMID: [25371490](#)). If the patient remains positive, consider whether reinfection or failure is more likely. If reinfection is more likely, the recommendation is to retreat with the initial regimen (Ceftriaxone 500mg x 1). If failure is suspected, we recommend trying to get culture/antimicrobial susceptibility testing while treating with the alternative regimen (Gentamicin 240mg IM x 1 and Azithromycin 2g PO x 1).

SUSPECTED GC TREATMENT FAILURE

Q. AN MSM PATIENT WHO IS ALLERGIC TO KEFLEX WAS TREATED FOR ORAL GC WITH GENTAMICIN AND AZITHROMYCIN 8/2020. HE TESTED NEGATIVE 10/2020 BUT POSITIVE AGAIN FOR PHARYNGEAL GC 1/2021. HE REPORTS HE HAS NOT HAD ORAL SEX SINCE 8/2020. WHAT TREATMENT/DOSE SHOULD THIS PATIENT BE GIVEN FOR POSITIVE ORAL GONORRHEA?

A: While we know that most treatment failures are due to reinfection, there are higher rates of failure for pharyngeal GC than other sites. Your case is particularly unusual because the patient had a negative test of cure in October but was positive again in January without having had oral sex. It would be helpful to know which assay was used as some assays can cross react with other Neisseria species, causing a false positive result (PMID: [21813721](#)).

In this case, if you suspect treatment failure, we would recommend obtaining a culture with antimicrobial susceptibility now and consider re-treating with Gentamicin 240mg IM and Azithromycin 2g PO. Please consider a test of cure 14 days after treatment with both a NAAT and another culture and sensitivity that could direct to alternative regimens if needed.

Q: A PATIENT WAS TREATED FOR GONORRHEA OF THE PHARYNX ON 12/31/20 WITH CEFTRIAXONE 250MG IM AND AZITHROMYCIN 1G PO. THE PATIENT WAS RETESTED ON 1/14/21 AND STILL POSITIVE FOR GONORRHEA OF PHARYNX. PATIENT DENIES POSSIBLE REINFECTION AS THEY HAVE NOT BEEN SEXUALLY ACTIVE SINCE BEING TREATED. I AM CONCERNED WITH TREATMENT FAILURE. HOW SHOULD THE PATIENT BE TREATED NEXT?

A: The CDC updated their treatment guidelines for GC infection on 12/18/20. These [updated guidelines](#) recommend that if treating only GC the recommended treatment is now Ceftriaxone 500mg IM x 1 without concomitant of Azithromycin.

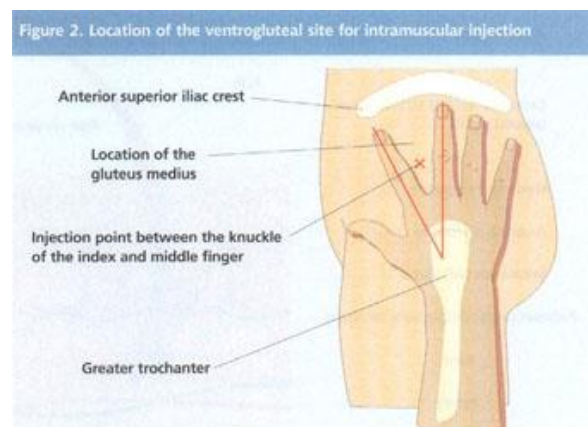
One of the many reasons for this change is that: “most reported Ceftriaxone-based regimen treatment failures have involved treatment of pharyngeal gonorrhea.” Ceftriaxone concentrations are more variable in the pharynx, and the higher likelihood of treatment failures in the pharynx was one of the major reasons for the recommendation to increase the Ceftriaxone dosage to 500 mg.

Therefore, we would treat the patient with Ceftriaxone 500mg IM x1 with plans for a test of cure 10-14 days after treatment. We would also consider getting a culture and antimicrobial susceptibility in addition to NAAT testing at the time of test of cure so that we have additional information on susceptibility patterns for your population which might impact antibiotic management.

ADMINISTERING MEDICATIONS

Q: OUR WAREHOUSE AND SITES HAVE 250 MG VIALS OF ROCEPHIN (CEFTRIAZONE) THAT ARE DILUTED WITH SALINE OR LIDOCAINE. WHAT IS THE RECOMMENDED PROCESS TO DILUTING THE CURRENT TREATMENT DOSE? WHAT LENGTH NEEDLE DO YOU USE?

A: It is the same dilution (e.g. dilute the 250mg/mL vial as you normally do. Give either two 1-mL injections or one 2 mL injection of the solution). Immunizations and medication doses between 1-2 mL should be administered in the deltoid muscle. Medication doses between 2-3 milliliters should be administered in the ventrogluteal muscle. You can dilute each vial as you normally do and then pull up the full dose in a separate syringe to combine the 2 vial doses together. For the patient's benefit, we generally recommend a single 2mL deep intra-gluteal injection to minimize the number of injections they have to receive (see image below). Either a 22 to 23 gauge needle (1 to 1.5 inches) will work, depending on the patient's size.



Greenway K. (2004). Using the ventrogluteal site for intramuscular injection. *Nursing standard* (Royal College of Nursing (Great Britain) : 1987), 18(25), 39–42. [https://doi-org.ezproxy.cul.columbia.edu/10.7748/ns2004.03](https://doi.org.ezproxy.cul.columbia.edu/10.7748/ns2004.03)

Original source: Zelman S (1961) Notes on the techniques of intramuscular injection. *The American Journal of Medical Science*. 241, 5, 47-58.

Q: IS IT APPROPRIATE TO MIX THE 500MG CEFTRIAZONE WITH 1.8 ML XYLOCAINE 1%? WE HAVE ALWAYS MIXED THE 250 MG CEFTRIAZONE WITH .9 ML 1%, SO I "ASSUME" THIS WOULD BE THE CASE. I WOULD LIKE TO ADD A CITATION TO OUR POLICY FOR THIS, SO ANY GUIDANCE IS APPRECIATED.

A: The 500mg Ceftriaxone vials recommend that they be diluted with 1 mL of 1% Lidocaine or saline. In our clinic we generally mix them with just 1 mL (listed on the vial) and have not had an issue with the solution dissolving. [FDA Ceftriaxone package insert for injectable - https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/50585s057,50624s027lbl.pdf]

Q: HOW ARE OTHER CLINICS ADMINISTERING THE ALTERNATIVE TREATMENT OF GC WITH 240 MG GENTAMICIN? THE MOST CONCENTRATED VERSION WE CAN GET FROM THE PHARMACY IS 80MG/2ML. THAT IS A LARGE INJECTION OF 6 ML TO GIVE THE TOTAL 240 MG GENTAMICIN. IS IT TYPICALLY GIVEN 3 ML PER GLUTE?

A: Yes, we recognize that this is a large injection however we have the same issue with 80mg/2mL vials. We generally end up doing two 3mL injections which patients have been able to tolerate.

CHLAMYDIA TREATMENT

Q: ARE THE NEW CDC RECOMMENDATIONS TO TREAT CHLAMYDIA INFECTION WITH ONLY DOXYCYCLINE, AND NO LONGER TO USE SINGLE DOSE AZITHROMYCIN WITH DOCUMENTED INFECTION WITH THIS ORGANISM?

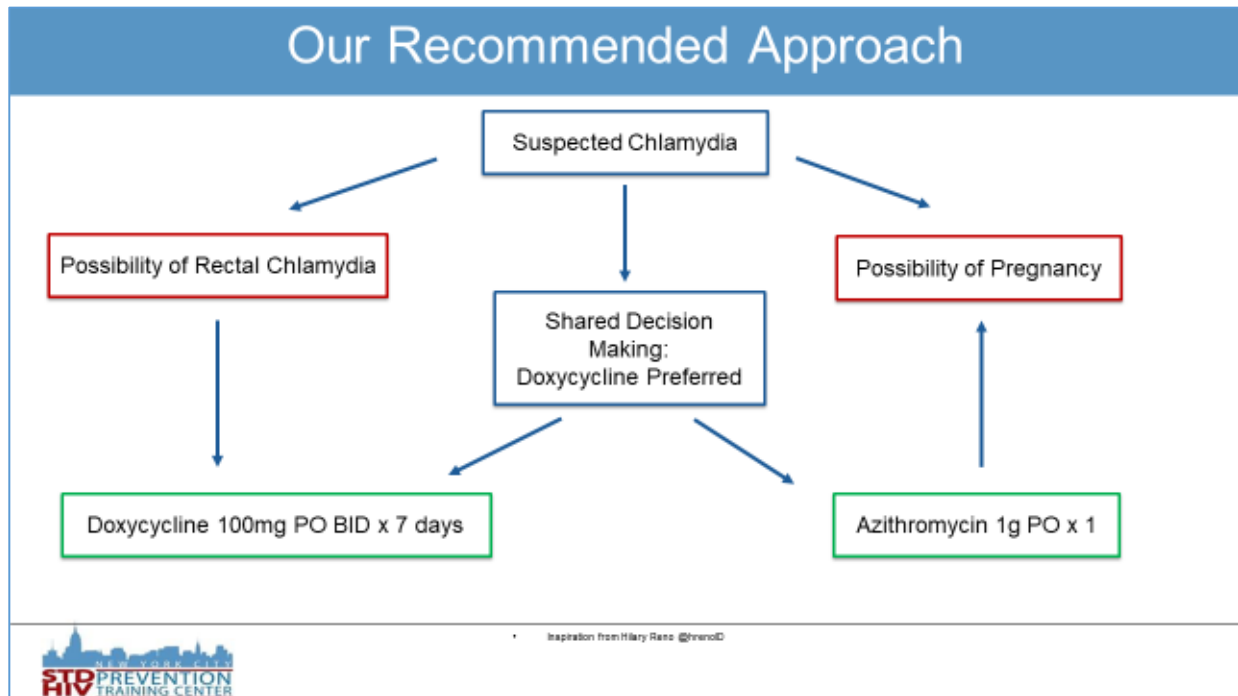
A: The CDC has currently only updated the GC guidelines; formal recommendations for CT will be included in the 2021 guideline update. In general, the CDC recommendations are to take a shared decision-making approach to this discussion with doxycycline as the preferred agent and azithromycin as an alternative. Some things to consider are 1) pregnancy 2) patient issues acquiring the medications 3) patient issues taking medications for multiple days and 4) GI intolerance with doxycycline or medications in general.

Q: WE DO GRAM STAINS AS WELL AS NAAT TESTING. IN CASES WHERE WE CAN IDENTIFY GC, BUT NOT CT, DO YOU RECOMMEND TREATING FOR CT AT THAT TIME OR WAIT FOR CONCLUSIVE TESTING? IN PREVIOUS GUIDELINES, THE ALTERNATIVE TREATMENT FOR PREGNANT WOMEN WHO HAD GC INCLUDED 2 GM OF AZITHROMYCIN. IS THIS STILL A RECOGNIZED TREATMENT?

A: Regarding use of gram stain and diagnosis of GC, this is very good for men with GC but not useful for women. The current guidelines say to treat for GC alone if CT has been excluded, which is not possible in women. In addition, although gram stain indicates that GC is present, it cannot exclude CT (co-infection occurs in about 30% of cases) and therefore, you should treat for both GC and CT in both men and women when you are treating empirically for symptomatic persons. Treatment is 500mg IM of Ceftriaxone (unless person is >150kg- then use 1 gram of

Ceftriaxone) and Doxycycline 100mg BID for 7 days. If adherence is an issue, you can use a shared decision-making model and give Azithromycin instead of the Doxycycline.

Previous versions of the guidelines indicated that pregnant women should be treated with Ceftriaxone and Azithromycin 1 gram which is the same in the current guideline update (Ceftriaxone 500mg IM and Azithromycin 1 gm single dose). We have moved away from 2 grams of Azithromycin as there is an increasing rate of resistance to Azithromycin when treating GC in many populations but most prevalent among MSM. If there is a Ceftriaxone allergy, then you can use Gentamicin 240 mg IM and Azithromycin 2 grams to treat GC and CT in pregnant women.



SUMMARY OF CDC GONORRHEA TREATMENT GUIDELINES 2020

BOX. CDC recommended regimens for uncomplicated gonococcal infections, 2020

Regimen for uncomplicated gonococcal infections of the cervix, urethra, or rectum:

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb).

- For persons weighing ≥ 150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

Alternative regimens for uncomplicated gonococcal infections of the cervix, urethra, or rectum if ceftriaxone is not available:

Gentamicin 240 mg IM as a single dose plus azithromycin 2 g orally as a single dose OR

Cefixime 800 mg orally as a single dose. If treating with cefixime, and chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.

Recommended regimen for uncomplicated gonococcal infections of the pharynx:

Ceftriaxone 500 mg IM as a single dose for persons weighing <150 kg (300 lb).

- For persons weighing ≥ 150 kg (300 lb), 1 g of IM ceftriaxone should be administered.
- If chlamydia coinfection is identified when pharyngeal gonorrhea testing is performed, providers should treat for chlamydia with doxycycline 100 mg orally twice a day for 7 days. During pregnancy, azithromycin 1 g as a single dose is recommended to treat chlamydia.
- No reliable alternative treatments are available for pharyngeal gonorrhea. For persons with a history of a beta-lactam allergy, a thorough assessment of the reaction is recommended.*
- For persons with an anaphylactic or other severe reaction (e.g., Stevens Johnson syndrome) to ceftriaxone, consult an infectious disease specialist for an alternative treatment recommendation.

Abbreviation: IM = intramuscular.

Source: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6950a6.htm>