# FOLLOW-UP GUIDELINES FOR PATIENTS WITH SUSPECTED GONORRHEA TREATMENT FAILURE AND REDUCED SUSCEPTIBILITY TO SPECIFIC ANTIBIOTICS

California Department of Public Health
Division of Communicable Diseases Control
Sexually Transmitted Diseases Control Branch



## **Purpose**

Gonorrhea is the second most common sexually transmitted disease (STD) in California and is caused by *Neisseria gonorrhoeae*, a bacterium that has rapidly acquired resistance to each class of antibiotics used to treat it. The U.S. Centers for Disease Control and Prevention (CDC) has declared drug-resistant gonorrhea an urgent public health threat. Monotherapy with ceftriaxone is currently the only CDC recommended treatment regimen for gonorrhea. While alternative regimens exist for rectal and urogenital infections, no other antibiotic regimen reliably cures pharyngeal infections. Reported cases of cephalosporin resistance have occurred in Europe, Asia, Australia, and Canada, as has the first U.S. case of a *Neisseria gonorrhoeae* isolate harboring the mosaic *penA60* allele, which confers reduced susceptibility to cephalosporins and increases the risk of treatment failure. This guideline summarizes California Department of Public Health (CDPH) recommendations to enhance detection and management of suspected gonorrhea treatment failure cases.

## **Criteria for Suspected Gonorrhea Treatment Failure**

Clinicians should be alert for potential treatment failures. Consider the following 3 criteria:

- 1. Patients with persistent symptoms greater than three days despite appropriate treatment, and
  - o no sexual contact reported since treatment (reinfection unlikely), and
  - untreated infections (e.g., chlamydia, trichomoniasis, Mycoplasma genitalium) have been excluded. For those with pharyngeal symptoms, consider testing for common etiologies such as COVID-19 and Group A Streptococcus
- 2. Patients with a positive test-of-cure (TOC) who report no sexual contact since treatment.
  - A positive TOC is defined as the following:
    - A positive culture at least 72 hours after treatment, or
      - A positive nucleic acid amplification test (NAAT\*) obtained:
        - More than 7 days after treatment for anogenital gonorrhea
        - More than 14 days after treatment for pharyngeal gonorrhea
  - \*Note: BD Probetec\*\* NAAT testing may have false-positive results due to commensal *Neisseria* species in the oropharynx
- **3.** Patients with a positive TOC if there is evidence of decreased susceptibility to cephalosporins on antimicrobial susceptibility testing (AST)<sup>†</sup>, regardless of whether sexual contact is reported since treatment.

<sup>†</sup>Decreased susceptibility to cefixime = MIC ≥0.25 μg/mL Decreased susceptibility to ceftriaxone = MIC ≥0.125 μg/mL

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# **Reporting of Suspected Gonorrhea Treatment Failures**

If your local health department receives a notification of a patient suspected of having gonorrhea treatment failure (see 3 criteria above on page.1), the following steps should be taken to ensure adequate follow up:



Assess for reinfection and partner treatment:

- If reinfection likely
  - Retreat with standard regimen (refer to table below)
- If reinfection unlikely
  - Obtain specimens for culture AND NAAT\*
  - o Treat with:
    - 1. Ceftriaxone 1 g IM PLUS azithromycin 2 g orally **OR**
    - 2. Gentamicin<sup>‡</sup> 240 mg IM PLUS azithromycin 2 g orally (for cephalosporin allergy)

\*Note: BD Probetec\*\* NAAT testing may have false-positive results due to commensal *Neisseria* species in the oropharynx.

<sup>‡</sup>Gentamicin has poor efficacy for pharyngeal infection. For suspected pharyngeal treatment failure, ceftriaxone 1 g PLUS azithromycin 2 g should be used when possible



### Report to the STD Control Branch:

- Complete the Notification of Suspected Gonorrhea Treatment Failure Form and forward to <u>STDCB\_ARGC@cdph.ca.gov</u> via secure email within 24 hours and call within 1 business day regarding suspected treatment failure.
- Complete the Supplemental Information Form and forward it to <u>STDCB\_ARGC@cdph.ca.gov</u> via secure email within 5 business days.
- Consult STD Control Branch via email (contacts above) if any questions arise and if assistance with partner services is needed.



Ensure partner services investigation has been initiated. This involves:

- Interviewing the patient to understand sexual history and recent exposures. Recommending the patient refrain from sex until the patient has cleared the infection (as determined by TOC).
- Eliciting sex partners from the infectious period (starting 2 months before symptom onset or test date if asymptomatic) and ensuring they are tested at all sites of sexual exposure (pharyngeal, urogenital, rectal) with NAAT and culture (if available) and treated with the same regimen as patient (index case)
- Initiating partner services for any sexual partners who test positive for gonorrhea and ensure they get a TOC.

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Antimicrobial Susceptibility Testing Resources Available to CA Providers and Laboratories Contact <u>STDCB\_ARGC@cdph.ca.gov</u> if assistance is needed in obtaining antimicrobial resistance testing.

- → Maryland Public Health Laboratory (through CDC's ARLab Network) offers antimicrobial susceptibility testing for suspected gonorrhea treatment failures. Visit <u>submission guidelines</u> or contact <u>mdphl.arln@maryland.gov</u> for more information.
- → Quest Diagnostics\*\* offers gonorrhea culture with reflex to antimicrobial susceptibility testing (Test Code 38404; CPT Code 87081). If gonorrhea is isolated, antimicrobial susceptibility testing will be performed (CPT code(s): 87185, 87181(x4)). Contact Quest directly for more information on gonorrhea testing.
- → Washington DOH Lab offers antimicrobial susceptibility testing by gradient strip for suspected gonorrhea treatment failures. Visit their <u>lab test menu</u> or contact <u>ARLN@doh.wa.gov</u> for more information.

# Recommended Treatment for Uncomplicated Gonorrhea (Standard Regimen)

DISEASE	RECOMMENDED TREATMENT	ALTERNATIVE TREATMENT
Uncomplicated gonorrhea infections of the cervix, urethra, or rectum	For persons <150 kg (330 lb): Ceftriaxone 500 mg lM  For persons ≥150kg (330 lb): Ceftriaxone 1 g lM	Cefixime 800 mg orally, <b>OR</b> Gentamicin 240 mg IM <u>PLUS</u> Azithromycin 2 g orally
Uncomplicated pharyngeal gonorrhea <sup>††</sup>	For persons <150 kg (330 lb): Ceftriaxone 500 mg lM  For persons ≥150kg (330 lb): Ceftriaxone 1 g lM	No reliable alternative treatments are available. Conduct a thorough assessment of beta-lactam allergy. If history of anaphylactic or other severe reaction to ceftriaxone, consult an infectious disease specialist or STD Clinical Consultation Network (stdccn.org)

**Chlamydia:** If chlamydial infection has not been excluded, providers should treat for chlamydia with doxycycline 100 mg orally twice daily for seven days. If treating gonorrhea with azithromycin 2g as part of alternative therapy, the addition of doxycycline to treat chlamydia is not needed.

**Pregnancy:** During pregnancy, azithromycin 1g as a single dose is recommended to treat chlamydia.

<sup>††</sup>Pharyngeal gonorrhea: particularly when treated with an alternative regimen, a **TOC by culture** AND/<u>OR</u> NAAT is recommended. NAAT is more sensitive than culture, but to avoid false positive results (due to residual genetic material) we recommend TOC NAAT 14 days post-therapy.

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