Laboratory Methods for Assessing Antimicrobial Resistance in Gonococcal Infections
CDC recently released updated gonorrhea treatment recommendations (available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm), which provide guidance on the use of tests for follow-up of patients treated for gonorrhea with oral antibiotics.

**Detecting Antibiotic Resistant Gonorrhea**

Assessing *N. gonorrhoeae* antibiotic susceptibility requires viable isolates from culture since accurate genetic markers of antibiotic resistance to front-line therapies remain to be documented. Agar plate dilution testing, which provides minimum inhibitory concentration (MIC) values of tested antibiotics, is the preferred method but may be too difficult to perform in laboratories with limited capacity and low testing volumes. Disk diffusion and Etest are the most practical methods for determining susceptibilities of gonococcal isolates, although cefixime Etest strips are not FDA cleared for use in the United States. Because there are no recommended interpretative criteria for *N. gonorrhoeae* resistance to cephalosporin antibiotics, it is recommended that isolates with MICs higher than the current Clinical Laboratory and Standards Institute interpretative criteria for susceptible organisms (http://www.cdc.gov/std/Gonorrhea/arg/criteria.htm) be submitted to CDC for reference testing using the agar plate dilution method. Procedures for agar dilution and disk diffusion can be found on the CDC website (http://www.cdc.gov/std/Gonorrhea/arg/lab.htm).

Clinicians who diagnose *N. gonorrhoeae* infection in a patient with suspected treatment failure should contact their local or state public health laboratory or local clinical laboratory for guidance on submitting specimens for culture and susceptibility testing. Local and state public health laboratory directors are encouraged to maintain capacity for culture and antimicrobial susceptibility testing for *N. gonorrhoeae* or if such testing has ceased, to identify public health or private laboratories in their area with such capacity.
Using Nucleic Acid Amplification Tests to Assess Patients with Possible Gonorrhea Treatment Failure

Following treatment for gonorrhea with an alternative treatment option (either dual therapy with cefixime or azithromycin monotherapy), CDC recommends use of culture 1 week after treatment to ensure the patient does not have persistent infection. If culture for *N. gonorrhoeae* is not readily available, then using a nucleic acid amplification test (NAAT) for gonorrhea is an option. Residual nucleic acid from bacteria rendered non-infective by antibiotics may still give positive NAAT results for a period of time after therapy. Studies have demonstrated differences in time periods during which residual nucleic acid from *Chlamydia trachomatis* and *N. gonorrhoeae* can be detected. NAATs may generate false-positive results from *C. trachomatis* residual nucleic acid for up to 3 weeks after treatment. In a study from the United States investigating the duration in which residual *N. gonorrhoeae* nucleic acid can be detected after treatment, over 90% of specimens were negative 5 days following treatment (95% of patients were treated with ofloxacin). The median time to a negative urine NAAT following treatment was 1 day for men and 2 days for women. This study used an older NAAT that is no longer marketed in the US. In a very small Norwegian study, researchers used an in-house *porA* pseudogene PCR (that is not FDA-approved) to follow patients after treatment with cefixime 400 mg. Among 19 patients tested within 4–7 days after treatment, 16 (90%) had negative follow-up tests. Of the 3 patients with positive follow-up NAATs, 2 were negative by day 11 and the third did not return until day 19 (at which time the test was negative). Available data suggest that most NAATs for *N. gonorrhoeae* will be negative within a week of treatment for gonorrhea. Additional data using specimens from the pharynx and rectum and using currently used NAATs may help to refine guidance. For patients with a positive NAAT on follow-up testing, every effort should be made to obtain a culture to confirm active infection. While awaiting culture results, these patients should be managed according to clinical history.
What kind of clinical specimens can be used for NAATs for gonorrhea?

The majority of commercial NAATs have been cleared by the Food and Drug Administration (FDA) to detect *N. gonorrhoeae* in endocervical swabs from women, urethral swabs from men, and urine from both men and women. NAATs have not been cleared by the FDA to detect *N. gonorrhoeae* in pharyngeal and rectal specimens. However, many laboratories have performed internal validation studies and now conduct NAATs to detect *N. gonorrhoeae* in extragenital specimens. The National Network of STD/HIV Prevention Training Centers maintains a list of laboratories providing this service (http://www.nnptc.org/PHLabs.html).

Can NAATs for gonorrhea be used for follow-up testing if the test is not FDA-approved for test-of-cure and the package insert states that the test cannot be used for test-of-cure?

Commercial NAATs are not FDA-approved for use as a test-of-cure following antibiotic therapy and cannot be marketed by manufacturers for this indication. Clinicians use their expertise and clinical judgment to tailor the best clinical management for their patients, and can determine whether follow-up tests are indicated for patients treated for gonorrhea. A positive post-treatment NAAT, if used after sufficient time to diminish the chance of detecting residual nucleic acid, may indicate failed therapy and require a culture follow-up.

References