Extragenital STI Testing

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Craig Roberts

Craig Roberts, PA-C, is an epidemiologist and physician assistant with more than 30 years of clinical and research experience in public health and infectious disease. He holds an appointment as an Emeritus Clinical Assistant Professor at the University of Wisconsin-Madison. He is a past chair of the Sexual Health Coalition of the American College Health Association, and served as the association’s liaison to the National Chlamydia Coalition. Mr. Roberts worked as a manager and clinician in the sexual health clinic at the University of Wisconsin-Madison University Health Services from 1984 to 2015. He also coordinated infectious disease surveillance, case investigation, and outbreak response at the student health service. An expert in sexually transmitted infections, he consults and lectures frequently on topics relating to college population health and infectious diseases of young adults.
Extragenital STI Testing

CLINICAL ESSENTIALS

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April 20, 2016

Topics covered in this webinar

- Overview of extragenital testing for gonorrhea and chlamydia
- Basics of NAAT tests and how they work
- Indications for screening: who gets tested and when
- Practical tips and how to test
- Clinical scenarios and common questions
- General Q&A

Definitions & Acronyms

GC: gonorrhea
CT: chlamydia
NAAT: nucleic acid amplification test
MSM: men who have sex with men
MSW: men who have sex with women
WSM: women who have sex with men
WSW: women who have sex with women
MTF: male-to-female (transgender woman, biologically male)
FTM: female-to-male (transgender man, biologically female)

What is “extragenital” testing?

- Testing for STIs at any body site other than genitourinary (urethral/urine/vaginal/cervix)
- Usually refers to rectal and pharyngeal sites
- Typically done only for gonorrhea and/or chlamydia
- Part of routine STI screening for men who have sex with men (MSM)

The burden of rectal & pharyngeal GC/CT

- Multiple reports demonstrate that both gonorrhea and chlamydia are common infections at rectal and pharyngeal sites in MSM
  - Pharyngeal GC positivity 3-9%
  - Pharyngeal CT positivity 1-2%
  - Rectal GC positivity 5-10%
  - Rectal CT positivity 5-11%
- You miss a lot of disease if you don’t screen MSM at all sites of exposure
  - SF clinic data: 53% of chlamydia and 64% of gonococcal infections in MSM were in non-urethral sites
- Rectal GC and CT infection is associated with risk of HIV acquisition
  - 8-fold increased risk with 2 prior rectal infections
    - Rectal GC or CT infection is a trigger indicator for initiating HIV PrEP


Proportion of CT and GC infections MISSED among 3398 asymptomatic MSM if screening only urine/urethral sites, San Francisco, 2006-2009

Chlamydia
Gonorrhea

Morse et al. STDs Oct 2011 38:492-4
UW-Madison screening data, cy2014

Pharyngeal gonorrhea: 5.0% positive, 32.8% of all GC cases
Rectal gonorrhea: 5.6% positive, 22.6% of all GC cases
Rectal chlamydia: 6.5% positive, 8.0% of all CT cases

Total extragenital cases identified: 51 positive tests, 18.6% of all CT/GC

In this population of college students, nearly 1 in 5 of all CT or GC infections were extragenital (oral and rectal combined).

Who to test: the sexual history

Identifying who should be tested at extragenital sites requires that a proper sexual history be obtained by the provider. At minimum this should include:

- Gender of recent sexual partners (“are your partners men, women or both?”)
- Then for MSM, ask this additional question: “have you had any receptive anal sex in the past 12 months?”
  - Note: not all MSM have anal sex. Some MSM have only receptive anal sex (“top”); Some MSM have only penetrative anal sex (“bottom”); Some MSM have both types of anal sex (“versatile”). Some MSM have only oral sex. You can’t assume any of this: you have to ask.
- And, “have you performed oral sex on your male partners” [i.e. receptive oral sex]
- Usually you should also ask about # of partners and frequency of condom use, but this does not affect which sites to test or what tests are ordered.

Taking an effective sexual history

- Interviewing and counseling skills characterized by respect, compassion, and a nonjudgmental attitude toward all patients are essential to obtaining a thorough sexual history and delivering effective prevention messages
- Use open-ended questions when you can
  - “What has your experience with using condoms been like?”
- But also use specific questions when needed
  - “Have you had sex with men, women, or both?”
- Use understandable, nonjudgmental language

Current CDC Recommendations for Exragenital Testing

- Test for rectal infection with N. gonorrhoeae and C. trachomatis in men who have had receptive anal intercourse during the preceding year [NAAT of a rectal swab is the preferred approach];
  and

- Test for pharyngeal infection with N. gonorrhoeae in men who have had receptive oral intercourse during the preceding year [NAAT is the preferred approach]
- Testing for C. trachomatis pharyngeal infection is not recommended

CDC 2015 STD Treatment Guidelines

Prevent STDs: Risk Assessment

- Behavioral risk assessment – take a sexual history
- Biological risk assessment – obtain appropriate laboratory tests

A comprehensive STD/HIV risk assessment should include STD screening, because STDs are biologic markers of risk, particularly for HIV acquisition and transmission.

CDC: “Persons seeking treatment or evaluation for a particular STD should be screened for HIV and other STDs as indicated by community prevalence and individual risk factors”

So why aren’t more MSM being tested?

The Provider Problem
- Poor sexual history skills, inexperience with rectal testing
  - Ignorance about STDs in general, and MSM sexual behaviors/risk in particular
  - Technically confusing (which swabs? which orders? which laboratory?)

The Laboratory Problem
- No FDA-cleared test commercially available
- Availability varies by lab, health system, region
- Lack of clear recommendations
- Site-specific collection requirements, assays, not always well communicated

Plus: resistance to change, and of course, cost

See excellent blog post by Bill Smith on this topic:
Standard STI screening for MSM

Routine:
- Urine NAAT for gonorrhea and chlamydia
- Pharyngeal NAAT for gonorrhea, if history of receptive oral sex
- Rectal NAAT for gonorrhea and chlamydia, if history of receptive anal intercourse
- HIV antigen/antibody combo test
- Syphilis serology

Supplemental:
- Hepatitis B serology, if not immunized prior to onset of sexual activity
- Hepatitis C serology, if HIV or history of IDU

Screen at least annually; more often as dictated by risk (e.g. multiple partners)

CDC 2015 STD Treatment Guidelines

What about testing non-MSM?

Pros:
- Anal sex among MSM/MSW is more common than you think
- Oral sex is a near universal behavior regardless of sexual orientation
- Potentially an important reservoir of disease in the population
- As many as 10-20% of CT infections in women may be extragenital

Cons:
- Incidence of rectal GC/CT is much lower than in MSM; is it high enough to justify screening?
- No direct link to reproductive health/fertility
- CDC insufficient data to support routine extragenital testing at this time

So: Test on a case-by-case basis when indicated by patient history or risk.

Insurance/payment coverage may not apply as it would for genital tests.

See article (Trebak) and editorial (Strobino) from STD 2015;42(5) for more on this topic

Situations where ExGen testing might be considered for non-MSM

- Post sexual assault, especially as part of a STI evaluation or for forensic testing, if relevant exposure occurred
- Women reporting receptive anal/oral sex with high risk male partners, including MSM partners
- There is a high prevalence of gonorrhea or chlamydia in the patient’s sexual network or local population, with anal/oral exposure
- Evaluation of rectal symptoms, as a diagnostic test (not screening)
- Exposure to a partner with known GC or CT infection where an extragenital contact is the only site of exposure

Clinical: rectal gonorrhea & chlamydia infections

- Gonorrhea infection is more common in some populations:
  - men who have sex with men (MSM)
  - urban, low income (esp. African American)
- Rectal GC and CT infections are common in MSM
- Usually asymptomatic, but can cause proctocolitis
  - rectal pain, discharge, bleeding
  - LGV-associated proctocolitis can be severe
- GC treatment: ceftriaxone 250mg IM plus azithromycin 1g PO
- CT treatment: azithromycin 1g PO or doxycycline 100mg BID X7 days
  - Some data suggests doxycycline is more effective for eradicating rectal infection; days X 3 weeks is recommended if LGV is suspected, or for azithromycin treatment failures
  - see CDC guidelines
- Conventional NAATs cannot identify LGV strains of chlamydia

Clinical: pharyngeal gonorrhea

- Pharyngeal GC infection is important primarily because it represents a reservoir for anogenital disease occurring in partners
- Transmission dynamics, natural history not well studied. Probably transient.
- Usually no associated pathology, although there is a theoretical risk of invasive disease (disseminated GC), esp. in immunocompromised persons
- Almost always asymptomatic; pharyngitis is not typical
- Can be more difficult to eradicate; fewer drugs produce reliable cure
  - note: cefixime, an alternative regimen in prior guidelines for treatment of urogenital GC infection, is not effective for pharyngeal infection
- Use CDC recommended therapy: cefixime 250mg IM X azithromycin 1g PO
  - note: a test-of-cure at 14 days if any other regimen is used

Lymphogranuloma Venereum (LGV)

- Caused by a specific serovar (subtype) of chlamydia
- Associated with causing proctocolitis in MSM
  - more inflammatory than other serovars, often symptomatic
  - test for rectal chlamydia using NAAT
  - additional molecular testing for LGV can be done in specialized laboratories but is not generally available
- Treat presumptively with doxycycline X 21 days (100mg BID) if LGV is suspected based on clinical presentation (rectal pain + bleeding)
Clinical: pharyngeal chlamydia

- Very little data exists about prevalence, incidence, transmission, or natural history
- until NAATs, there was no easy or accurate way to test the pharynx for chlamydia
- no associated disease state or complication
- Pharyngeal CT infection is probably also a reservoir for anogenital disease
- At this point in time, no recommendation for routine screening/testing
- this may change in the future, as data accumulates with NAAT based testing
- Ideal treatment regimen uncertain; CDC recommends azithromycin 1g as for genital infection
- Genital chlamydia is a very common infection...
- and oral sex is a very common behavior...
- so a presumption of oral infection given exposure is reasonable

Nucleic Acid Amplification Tests (NAATs)

- NAAT is a generic term for a molecular-based test to detect organism DNA or RNA
- NAATs look for a specific sequence of nucleic acids representing a defined segment of the organism’s genome, and characteristic of a specific bacteria or virus
- These segments are usually conserved (common) across multiple subtypes/stains but are highly specific to the species
- Even tiny amounts of DNA/RNA in the sample get amplified so they can be easily detected, which makes the test very sensitive. A viable organism is not required.

NAATs: interpreting results

A positive test result means only that DNA/RNA was detected
- It does not mean that live and viable bacteria are present
- It does not always indicate the patient has a current infection

A positive test result can also result from:
- Non-viable bacteria transmitted by an infected partner (deposition)
- Residual bacterial nucleic acid persisting after a resolved infection. Allow a minimum of 4 weeks from the date treatment was initiated before any re-test. Six or eight weeks is better, 12 weeks is preferred (re-screen).
- Contamination from the external environment

Testing Methodology …in the old days

- Culture and isolation – grow the organism in a medium and then identify it. This has some major limitations:
- Requires that live and viable organisms be collected from the patient and then survive and grow in the laboratory
- For extragenital GC and chlamydia tests, the sensitivity of culture is <50%
- No longer recommended for routine GC/CT testing at any site
- But still important in determining patterns of GC resistance
- Increasingly difficult to find a lab that can perform GC culture if you need it though

Antigen Detection

- Older generation tests that detect antigens expressed by the organism
- Not recommended for GC/CT, as now eclipsed by NAAT
- Not FDA cleared for GC/CT tests from extragenital sites

Nucleic Acid Amplification Tests (NAATs)

- Multiple types of NAATs exist, each using a different methodology to detect DNA/RNA
- PCR (polymerase chain reaction) is one common method used for many infectious diseases
- Most commercial NAATs for STIs use other, proprietary methods (e.g. strand-displacement assay, transcription-mediated amplification, etc) that are different from PCR
- They are not all the same; performance characteristics vary from test to test and from lab to lab.

Exgen NAATs: The challenge

- No commercial GC or CT NAAT has been cleared by the FDA for use in testing specimens collected from extragenital sites
- Using NAATs for extragenital tests is therefore technically “off label”
- in some cases this might mean insurance won’t cover it
- Each lab performing extragenital NAATs must complete an in-house validation of the test to ensure its performance is satisfactory
- Not all clinical laboratories that perform genital GC/CT tests are able or willing to do this, thus they are not capable of performing extragenital GC/CT tests
- Some clinics will find they need to split up specimens – genital specimens going to a local lab; extragenital specimens going to a regional or national lab, even though the test is essentially the same.
Specimen Types – Female Patients

<table>
<thead>
<tr>
<th>Specimen Types</th>
<th>Recommended for Screening Use?</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. trachomatis</td>
<td>Endocervical and vaginal swab</td>
<td>ARUP Laboratories</td>
</tr>
<tr>
<td>N. gonorrhoeae</td>
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</tr>
</tbody>
</table>

Source: ARUP Laboratories

Standard collection instructions

**ANAL/RECTAL SWABS**
- Use the lab-provided swab specimen collection kit.
- Insert the specimen collection swab approximately 3 to 5 cm into the anal canal.
- Rotate the swab for 5 to 10 seconds against the rectal wall (at least three times) to sample the mucosal surface.
- If the swab is grossly contaminated with feces, discard and repeat the collection.
- Withdraw the swab carefully, remove the cap from the swab specimen transport tube, and immediately place the specimen collection swab into the transport tube.
- Carefully break the swab shaft against the side of the tube at the scoreline and discard the top portion of the swab shaft; use care to avoid splashing of contents.
- Recap the swab specimen transport tube tightly.
- If needed prior to insertion, the swab can be moistened with water or saline solution.

Specimen Types – Male Patients

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- Carefully break the swab shaft against the side of the tube at the scoreline and discard the top portion of the swab shaft; use care to avoid splashing of contents.
- Recap the swab specimen transport tube tightly.

Specimen Collection: Anorectal

- Rectal Testing
  1. Use a swab from the manufacturer’s urogenital collection kit
  2. Insert the collection swab into the anal canal until just past the sphincter, ~3-5cm (1-2 inches)
  3. Leave it there for a few seconds, rotate
  4. Remove and place in transport media

Specimen Collection: Pharynx

- Pharyngeal Testing
  1. Use a swab from the manufacturer’s urogenital collection kit
  2. Swab the posterior pharynx and tonsils with the collection swab
  3. Place the swab in transport media
  4. Procedure is identical to collecting a swab for routine throat culture, strep screen, etc.
Always use the right swab and the right transport tube!

Or else:
“If the lab receives a swab specimen transport tube with no swab, two swabs, a cleaning swab, or a swab not supplied by Gen-Probe, the specimen must be rejected.”

- Hologic Gen-Probe Aptima Combo 2 package insert

You should also label the specimen with the collection site

What about anal Pap tests?

- No specific recommendation from CDC or USPSTF for or against
- There are currently insufficient data regarding the natural history of anal HPV infection, and the evolution of anal dysplasia, as well as data regarding the efficacy of anal Pap smears and subsequent interventions for the prevention of anal cancer
- Some experts perform anal Pap testing and high-resolution anoscopic (HRA) on their high risk (esp HIV+) patients as part of regular clinical care
- If an anal Pap program is embarked upon, it is important to set up a system of follow-up for abnormal anal Pap tests, as the frequency of abnormal Pap tests (particularly among HIV+ MSM) is high

Documentation & Coding

See http://www.ncsddc.org/basics-coding-third-party-billing

Standard ICD10 code for STI screening: Z11.3
- “encounter for screening for infections with a predominantly sexual mode of transmission”

CPT E/M code examples:
- 99385 Preventive visit new patient age 18-39
- 99402 Patient counseling 30 minutes

CPT code for GC NAAT (regardless of collection site): 87591
CPT code for CT NAAT (regardless of collection site): 87491

Develop a cheat sheet for providers to use

(examples)
Case Scenarios & FAQs

THINGS THAT AREN'T ALWAYS COVERED IN THE GUIDELINES...

My patient is transgender MTF. She reports having receptive oral sex with male partners. She does not have any penetrative insertive penile sex. What STIs should she be tested for?

A: Transgender patients should generally be screened based on their current anatomy and sexual behaviors. Risk of STIs varies and will depend on partner risk. If MSM partners, apply MSM screening protocols. Include rectal swabs for GC/CT, plus pharyngeal swab for GC if history of oral sex, plus HIV and syphilis serology. If this person has no sexual exposures involving her penis, urine testing could be deferred/optional.

See STD Treatment Guidelines for a brief discussion of the topic.

Can pharyngeal gonorrhea or chlamydia be acquired from or transmitted to a female oral sex partner via cunnilingus, and should I test for it if that is the exposure risk?

A: Probably not. This is mostly data-free zone, but transmission is unlikely to occur in this circumstance. The risk is similar to mouth-to-mouth kissing contact, which is negligible. The risk of infection from saliva or vaginal fluid contact alone is remote.

Transmission of pharyngeal GC/CT infection in most circumstances requires direct penile pharynx contact (fellatio).

But exceptions can occur.

Carlos

22 y.o. gay male, asymptomatic. Reports his partner was just diagnosed with urethral gonorrhea.

What do you test him for? What anatomic sites get tested?

A: Sexual history is important here. What type of sexual contact did he have with this partner?

- receptive oral sex (fellatio): throat swab for gonorrhea
- receptive anal sex: rectal swab for both gonorrhea and chlamydia
- screen for other STIs (urine GC and CT, HIV and syphilis serology)
- condom use does not influence testing decisions

and of course, treat him empirically.

I sent a throat swab for gonorrhea to our lab, but they tested it positive. How do I manage this?

A: Many labs won’t run gonorrhea tests separately from chlamydia. They probably don’t have good data about the specificity of pharyngeal chlamydia tests, but positive results should be assumed to be correct. Treat as for genital chlamydia (azithromycin or doxycycline) and also treat recent sexual partners exposed to this person’s throat (eg persons they performed fellatio on).

This should also be reported to local public health as you would for genital infection.

I’m seeing a male college student who is taking a Women’s Studies course. The professor advised the class that everyone should get tested for STIs each year. His only sexual experience is performing oral sex on female partners, twice. He has never had any type of penetrative intercourse. Should he get a throat culture? Other tests?

A: Not really. He is not at risk for anything you should test him for.

Technically, CDC guidelines state that all adults should be screened for HIV regardless of sexual history, so that could be done. But it is a teachable moment. Encourage him to return for future testing when he has intercourse. Discuss the risk of genital herpes transmission from mouth to genitals, and if he has a history of cold sores this is important.
My patient is an adolescent female coming in for an annual visit. She has had oral sex (fellatio) with multiple male partners but denies ever having vaginal or anal intercourse. She is asymptomatic. Should I do a throat culture?

A: Per CDC guidelines, routine screening for pharyngeal infection is not indicated in this patient. If you, the patient, or the parent, is particularly concerned about risk for GC or CT, then you could do it anyway. This is a very common sexual history for adolescents. And presents another teachable moment, etc.

A male patient saw recently had a positive rectal chlamydia test and was treated with azithromycin. He returned three weeks later to get retested and the test is still positive. How should this be managed?

A: This could happen for several reasons: reinfection from an untreated partner, or a false positive chlamydia NAAT test, or azithromycin treatment failure

I would re-treat the patient with a 7-day course of doxycycline and then wait at least 6-8 weeks before testing again (ideally 12 weeks). Ensure all partners get treated.

NAATs are very sensitive and can detect residual DNA for several weeks after successful treatment. Rescreening is recommended at 2-3 months and not sooner, in part to prevent a false positive result. Test of cure tests are generally not recommended.

Attempting to test for chlamydia treatment failure or document “resistance” in this circumstance is not practical...

References & Further Reading


Benzon et al. Rectal gonorrhea and chlamydia re-infections is associated with increased risk of HIV seroconversion. J Acquir Immune Defic Syndr 2011;56(4)

Barlow et al. Effect of nucleic acid amplification testing on detection of extragenital gonorrhea and chlamydial infections in men who have sex with men sexually transmitted disease clinic patients. Sex Transm Dis 2014;41(1)

Marcus et al. Infections missed by oropharyngeal screening for chlamydia or gonorrhea detection among men who have sex with men. Sex Transm Dis 2011;38(4)

Trepakh et al. Nonsusceptible gonorrhea and Chlamydia trachomatis among women reporting extragenital exposures. Sex Transm Dis 2015;42(2)

Drummond K. Do women need screening for extragenital gonococcal and chlamydial infections? Sex Transm Dis 2013;40(2)


General Q&A

Thanks for your attention!

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Upcoming Events

Wisconsin State Lab of Hygiene Update
May 12th, 12-1pm

STD Summit
November 16th
Rothschild, WI

Please complete the sign-in and evaluation forms:
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Scan and email to:
jdecker@hcet.org