STI CASE STUDIES

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ACHA Sexual Health Education and Clinical Care Coalition
ACHA FR 208 -- Objectives

- Describe the clinical presentation and management strategies for common STIs
- Discuss current controversies in STI testing and treatment
- Identify expected changes in the forthcoming 2010 CDC STD Treatment Guidelines

A presentation handout will be provided on the ACHA web site
Disclosures

- Craig Roberts is a speaker for Merck. No financial support was received for this program.
- Davis Smith has no disclosures to report
- Today’s presentation may include discussion of off-label use of medications.
- 2010 CDC STD Treatment Guidelines have not been published as of the date of this presentation. Inferences about what they will include are purely speculative on our part.
“please test me for everything”

- Katie, A 20 y.o. college student comes in for STI screening. She is taking a course in human sexuality and was prompted to seek testing. She recently had unprotected intercourse with a new partner. She has had two other lifetime partners. She is asymptomatic and asks to be “tested for everything.”

- What tests would you do? What not to do?
  - what else do you need to know first?
Since most screening is risk based, obtaining a sexual history from all patients is important.

- **Partners**: # in last 90 days & their gender
- **Practices**: sites of contact, injection drug use
- **Protection**: frequency of condom use
- **Past history**: previous STDs
- **Prevention** of pregnancy: contraception use

*The handout from last year’s presentation on this topic is available on the ACHA web site*
What is “screening”?

- Screening generally means initial identification of unrecognized disease or infection.
- In the context of this presentation, screening tests are those done to identify STIs in asymptomatic persons, as distinct from testing symptomatic persons to establish a diagnosis.
STI Screening Recommendations

sources

- **United States Preventive Services Task Force (USPSTF)**
  - issues recommendations based on careful review of the evidence/data, assessing the benefit (or harm) of each preventive service or screening test
  - each recommendation is graded for strength of evidence

- **Centers for Disease Control and Prevention**
  - issues guidelines based on expert opinion and evidence
  - usually agree with USPSTF

- **Professional organizations (ACS, ACOG, AAFP, etc)**
  - issues recommendations based on expert opinion and “best practice” for their field
  - may or may not be evidence-based
  - support accreditation standards (HEDIS, JCAHO)
  - ACHA guidelines in development
Routine STI Screening Summary:
Patient-based approach

- For most low risk, heterosexual students:
  - Chlamydia NAAT*, urine or swab
  - HIV, if not previously tested
  - Genital/pelvic exam optional

- Add these tests only if risk factors justify:
  - Gonorrhea, NAAT urine or swab
  - Syphilis serology
  - HSV serology
  - HBV, HCV serology

*nucleic acid amplification test
Gonorrhea Screening Guidelines

- Less evidence-based than chlamydia
- Patients at higher risk — screen for GC:
  - Men who have sex with men
  - ?African-American (20X increased incidence)?
  - STD history (esp chlamydia, syphilis, HIV, NGU, PID)
- Patients at uncertain risk — consider screening for GC:
  - Women under age 25 with multiple partners
  - High community prevalence (prevalence in patient’s sexual network probably more relevant)
  - Partner is nonlocal and/or nonstudent
- Patients at low risk — don’t screen for GC
  - Many college students are not in the above groups
Case Presentations

- These cases are designed to illustrate some typical and perhaps not-so-typical issues in the management of selected STIs
- We’ll also cover areas of uncertainty and controversy in testing or treating STIs
- These are actual cases representing real patients seen in college health centers. Names have been changed and other information may have been modified to protect confidentiality.
22 yo male, MSM, with 3 day history of acute dysuria and urethral discharge

Exam: purulent urethral discharge

Lab: Gram stain done in clinic shows full field PMNs, with Gram-negative intracellular diplococci

What’s the diagnosis?

Presumptive gonococcal urethritis
Management Questions

- Which other STI tests does he need?
- Does he need presumptive treatment pending urine GC/CT test results?
- Which drug(s)?

(btw, the patient reports a known allergy to cephalosporins)
Routine STI Screening for MSM

- GC and CT urine NAAT
- GC culture/NAAT from other exposed sites (pharynx and/or rectal)
- RPR or VDRL for syphilis
- HIV antibody
- HBsAg if not immunized prior to sexual debut
  - what about HBsAb if immunized?
Rectal and Pharyngeal Chlamydia and Gonorrhea

- CDC recommends NAATs for detection of rectal and pharyngeal infections

- Rectal and pharyngeal specimen types have not been cleared by the FDA for use with NAATs
  - Labs can offer if internally validated
  - Use culture if NAAT is not available

- Quest, LabCorp and other reference labs do offer NAAT testing for rectal and pharyngeal CT or GC
Gonorrhea Treatment

- **Gonorrhea treatment, 2010**
  - Third gen cephalosporins are the only real choice
    - Ceftriaxone 125/250mg IM – preferred
    - Cefixime 400mg PO – ok (but not for pharyngeal infection)
    - Cefpodoxime PO – avoid
  - Dual treatment with azithromycin 1g may enhance efficacy of cefixime
- Quinolones should **not be used** due to widespread resistance
- Routine use of azithromycin 2g PO discouraged
Gonorrhea Treatment

- GC treatment for cephalosporin-allergic patients is a challenge:
  - 😞 Quinolone - resistance is common, not recommended
  - 😞 Spectinomycin - not available in the U.S.
  - 😞 Azithromycin 2g PO – poorly tolerated, resistance concerns
    - But it’s the best choice for this patient!

- The patient took and tolerated his azithromycin; symptoms resolved
  - Other STI screening tests were negative
  - Partners lost to follow up

- Test-of-cure not usually recommended
  - But in this case it might be worth doing
Susan

- 25 yo grad student seen in primary care clinic with a 3 day history of urinary frequency, urgency, dysuria, nocturia, plus low back pain and nausea. No hematuria. She is afebrile and does not have any CVA tenderness. She took some cipro yesterday, left over from a prior UTI.
- Urine dipstick is negative
- Assessment: UTI, presumed pyelonephritis
- Plan: Urine culture, levofloxacin 500mg X 7 days, f/u visit next week.
Susan, visit 2, day 8

- On her return visit 5 days later she reports an itchy rash on her hands and a sensation of “electrical shocks” going down both legs. UTI symptoms are still present, dysuria is predominant. Also now notes some “crusty” vaginal discharge plus fever to 101.4 F.
- Exam: erythematous papular rash on hands. No genital lesions. Pharynx clear. Copious vaginal discharge, no odor. Cervix is friable, erythematous. Positive CMT, no adnexal tenderness
Cervical exam
Susan, visit 2, day 8

- **Assessment:**
  - “probable GC/CT/PID”
  - Possible levofloxacin allergy
  - Consider disseminated gonorrhea, tenosynovitis

- **Plan:**
  - Ceftriaxone 250mg IM plus 750mg IV
  - Doxycycline 100mg PO BID X 10 days
  - HIV, VDRL, GC, CT tests, plus CBC, chem panel
  - Return tomorrow for additional IV ceftriaxone
Symptoms slightly improved (rash, leg/foot pain, dysuria).

Repeated ceftriaxone 1g IV per plan

Urine culture from first visit: mixed flora x10^3

CT/GC from yesterday negative

Dermatology consult obtained, recommends biopsy

Assessment: “puzzling picture, w/ triad of urethritis, rash and anterior foot pain”

ECG, blood cultures, repeat UA, chem panel, cryoglobulins done today
Susan, visit 4, day 10

- Symptoms persist, pt frustrated
- Pelvic exam repeated, same findings
- Labs: GC/CT repeated, HSV PCR (urethral swab), HSV serology done
- Derm biopsy done; consider EM, vasculitis

So we still don’t have a definitive dx and have spent more than $1000 trying to figure it out. What’s going on?
Susan, resolution

- HSV PCR positive for HSV-2
- HSV serology also positive for HSV-2
- Derm biopsy result shows Gianotti-Crosti syndrome
- Pt was started on valacyclovir, symptoms resolved within one week
- Retrospective history: partner had a history of penile lesions one month earlier.
Gianotti-Crosti syndrome
(papular acrodermatitis)

- A viral exanthem with characteristic symmetric eruption of multiple small papular or papulovesicular lesions, 1 to 10 mm in diameter; they may coalesce into plaques.
- The face, buttocks, extensor aspects of forearms and legs, and feet are predominantly affected.
- Originally associated with hepatitis B, now also with EBV, RSV, influenza, and many other viral and bacterial infections.
- Pathogenesis is unknown. One hypothesis suggests that GCS results from a delayed hypersensitivity reaction to viral illness.
papular acrodermatitis
Genital Herpes – teaching points

- Dysuria, with or without external genital lesions, is a common symptom in genital herpes.
- Herpes should be considered early in the differential of UTI symptoms that are atypical, recurrent or persistent.
- Herpes can also cause a florid cervicitis, as occurred in this patient.
- HSV PCR tests are highly sensitive and specific
  - Test of choice for lesion/symptom diagnosis
Mark

- CC: night sweats, body aches, blood in urine
- HPI: 21 y.o. male w/ night sweats X 1 week but no fever. Dysuria began 3 days ago with intense pain and some urgency. Now has urethral discharge X 1 day and bright red hematuria also noted yesterday. Reports 2 female sexual partners recently, including someone he “barely knows”, but used condoms 100% with these partners.
Mark, continued

- Additional history: was backpacking in Central America one month ago with friends. Developed profuse, watery, non-bloody diarrhea one week after returning. The diarrhea resolved shortly before the urinary symptoms started.
- Exam: temp 97.4F, VS normal, no abnormal findings except purulent urethral discharge.
- Assessment: urethritis, hematuria, night sweats
Mark, continued

- **Plan:**
  - Azithromycin 1g po single dose
  - Urine CT/GC
  - Urinalysis and urine culture
    - UA result: + LE, + Heme, + protein, WBC clumps, full field RBC, no bacteria
  - CBC and metabolic panel

Is this a straightforward case of urethritis? Why or why not?
Mark, continued

- Returns to clinic the next day reporting that his dysuria is worse and he has penile pain at rest.
- PE repeated, findings unchanged. Further history provides some additional details:
  - Last unprotected intercourse was 4 mo ago.
  - Diarrheal illness was followed by sweats/chills, arthralgias, fatigue, myalgias, then urinary sx.
- Due to concerns about possible prostatitis, he was started on a course of ciprofloxacin 500mg.
Mark, continued

Final lab results

- Chlamydia & gonorrhea: negative
- CBC/chem panel: normal
- Urine culture: positive isolate for Salmonella enterica javiana

Resolution

- Symptoms resolved quickly after starting cipro
- Dx: Salmonella Urethritis? Cystitis? Prostatitis?
Urethritis can have multiple etiologies
- Only 50% are chlamydia or gonorrhea
- Other causes include HSV, trich, adenovirus, mycoplasma
- Nearly always sexually acquired, in young men

...but probably not in this case

Salmonella as a cause of UTI is reported infrequently, usually with preceding gastroenteritis

Source could be hematogenous or direct spread secondary to diarrheal illness
Brittany

- Brittany is a 19 year old female who presented to the Women’s Health Clinic for “STI testing.”

- She was seen for an annual physical exam at her home clinic over the summer. At that time she tested positive on a cervical culture for *Ureaplasma urealyticum*. She was treated with a two week course of erythromycin and advised to undergo a test-of-cure in two months.
As testing for *U. urealyticum* is not performed at the SHS, and evidence does not support routine screening or treatment for this organism, we had little to offer this patient except reassurance.

The provider contacted the patient’s physician back home directly. That physician stated that the medico-legal environment and practice patterns in her area force practitioners to perform testing and treatment for *ureaplasma* despite the lack of data to suggest benefit.
What are Mycoplasmas?

- Smallest known free-living life forms.
- Prokaryotes, but lack a cell wall.
- Cell membrane contains sterols.
- Extracellular parasites, attach to the surface of epithelial cells of the respiratory and genital tracts.
Genital Mycoplasmas

Several species of mycoplasma are known to colonize the genital tract:

- *Mycoplasma hominis*
- *Ureaplasma urealyticum*
- *Mycoplasma primatum*
- *Mycoplasma genitalium*
- *Mycoplasma spermatophilum*
- *Mycoplasma penetrans*

*M. hominis*, *M. genitalium* and *U. urealyticum* are potential urogenital pathogens, attributed to causing nongonococcal urethritis, cervicitis, and pelvic inflammatory disease.
Epidemiology

- *M. hominis* and *U. urealyticum* colonize the genital and urinary tracts of postpubertal females and males. As many as 40-80% of asymptomatic, sexually active patients are colonized by ureaplasma.

- Female colonization is maximal in the vagina and less in the endocervix, urethra, or endometrium.

- Male colonization occurs primarily in the urethra.

- Colonization rates are directly related to sexual activity and are highest among persons with multiple sexual partners.

- Research has not shown a definitive association between *M. hominis* or *U. urealyticum* and symptomatic infections in women; some have suggested a relationship with PID and/or infertility.
Management

- The relationship between *M. genitalium*, *U. urealyticum* and symptomatic infection in males is far more clear, and may account for as much as 30% of nongonococcal urethritis.

- Treat if symptomatic (NGU, cervicitis)

- Resistant to beta-lactams and to sulfonamides and trimethoprim.

- All are susceptible to tetracyclines, but usually treated with azithromycin 1g single dose.
Few definitive facts are known about genital mycoplasma infections. However, some evidence implicates these organisms as a cause of NGU, cervicitis, PID, possibly infertility, as well as pregnancy and neonatal complications.

*M. genitalium* may be a true pathogen rather than a commensal organism. Routine screening and treatment for *M. genitalium* may decrease rates of pelvic inflammatory disease and its sequelae.

- No commercial screening assay is yet available

Current data suggests that routine screening and treatment for *M. hominis* and *U. urealyticum* is not likely to benefit young healthy patients without symptoms.
Kendra

- Age 22, comes in for possible UTI symptoms
- Notes mild dysuria for 3 days. No urgency, frequency or hematuria. No fever or back pain.
  - What other history is important to obtain?
  - What lab tests should be ordered?
  - Would you treat empirically at this point?
- Has had 2 male partners in the last 3 months, unprotected. Both are asymptomatic.
- No prior STI or UTI history
Kendra

- Per clinic protocol, you collect a urine for both chlamydia and a UA
  - what is the indication for doing chlamydia?
  - should it be a first void, midstream or both?
    - Urine for chlamydia must be first-void, “dirty” catch
- UA shows moderate WBCs, no bacteria
- Treated empirically with TMP-SMZ X 3 days
- The next day, her chlamydia result is positive
  - What are the next steps to manage this infection?
  - What will you do about her partners?
Chlamydia Treatment
2006 CDC Treatment Guidelines

- Rx: Azithromycin 1 gm single dose
- OR
- Doxycycline 100 mg BID x 7 days
  - Contraindicated during pregnancy
- Effectiveness is equivalent
Provider’s Role to Prevent Reinfection

- Test for reinfection:
  - Rescreen **3-4 months** after treatment or whenever patient presents to clinic within next 12 months

- Partner notification
  - Provider referral (report to health dept)
  - Patient referral (refers partner to clinic)
  - Expedited partner therapy (Rx for partner)
Expedited Partner Therapy

aka Patient Delivered Partner Therapy

- Providers give the patient medication intended for the partner(s)
  
  OR

- Providers write the partner(s) a prescription for medication
Legal Status of EPT

Permissible in 24 states    Possible in 18 states    Prohibited in 8 states

Exception:
EPT is permissible in Baltimore, MD

http://www.cdc.gov/std/EPT/legal/default.htm
Providers should consider including EPT as part of their regular STI care

- EPT is “useful option” to further partner treatment
  - Especially for male partners of chlamydia- or gonorrhea-infected females
- CDC STD Treatment Guidelines recommend EPT as option for partner treatment among heterosexual persons with chlamydia or gonorrhea

Policy makers should remove systemic barriers to EPT

Chlamydia Diagnosis:
Nucleic Acid Amplification Test (NAAT)

- Amplifies specific nucleic acid sequences (ie, DNA)
- Does not require viable organisms
- Highly sensitive and specific, >99% in most settings
- Can test endocervical, urethral, urine, or vaginal* specimens
  - self-collected vaginal swabs are recommended
  - first void urine in women is also acceptable
- Can detect GC and CT in single specimen

*note: only Aptima and BD ProbeTec QX are FDA cleared for vaginal specimens
Ralph

- 23 y.o. undergrad student presents with dysuria for 1 week. No discharge. Also complains of left index finger pain and swelling for several days.
- Reports same female partner for past 7 months. Always uses condoms. No prior STIs diagnosed.
- Patient has a history of orolabial herpes
Exam:
- Left inguinal adenopathy to 1cm, slightly tender. Penis with erythema at meatus. No discharge.
- Erythema from tip of finger to DIP joint. There is swelling as well as a collection of fluid at the medial nailfold. Mild pressure yields clear fluid. No regional adenopathy.

UA: no WBCs, no RBCs, no bacteria
Ralph, continued

- Urine CT NAAT
- Urine culture
- Are there other lab tests that should be done?
- Would you treat empirically?
  - Azithromycin or doxycycline
Ralph, continued

- Chlamydia test and urine culture were negative
- Symptoms resolved without treatment
- Left index finger HSV culture positive, type 1
  - positive culture result supports the clinical impression that his finger lesion is a herpetic whitlow
  - He presumably innoculated himself by touching an oral or genital lesion
  - But wasn’t he immune from prior oral infection?
Dysuria, with or without external genital lesions, is a common symptom in genital herpes

- His dysuria may have been due to herpetic urethritis
  - Would need urethral swab PCR to confirm (pt declined)
  - Whether he acquired this by receiving oral sex from his girlfriend or by auto-inoculation via his finger is unclear

Herpes should be considered early in the differential of UTI symptoms that are atypical, recurrent or persistent.

HSV-1 is a common cause of genital herpes

- account for ~50% of GH cases in ACHA STI survey
- Most patients presenting with symptomatic genital HSV-1 have a new primary infection
Herpes: Who Should I Test?  
What Test Should Be Used?

**Use culture/PCR when patient ....**
- Presents with an open lesion (diagnosis)

**Use type-specific serology to.....**
- Confirm an uncertain clinical diagnosis
- Diagnose patients with atypical or unrecognized infection
- Manage partners of persons with genital herpes
- ? screen patients at increased risk?

What about routine screening?

CDC. *MMWR* 2006;54(RR-11):16-17.
Serologic screening for HSV

- Routine screening of adolescents & adults is not recommended (USPSTF, CDC)
- Screening of persons at increased risk of infection may make sense
  - prevalence increases with age (and sexual experience)
  - MSM, HIV+, contact to partner with HSV all have high rates
- Arguments pro and con:
  - Prevalent STD with known complications & risks
  - Low PPV (<50%) in adolescents and young adults
  - Confirming results is complex and expensive

## Prevalence of HSV-2 Infection

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>14-19</td>
<td>1.6%</td>
</tr>
<tr>
<td>20-29</td>
<td>10.6%</td>
</tr>
<tr>
<td>30-39</td>
<td>22.1%</td>
</tr>
<tr>
<td>40-49</td>
<td>26.3%</td>
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<tr>
<td>overall</td>
<td>17.2%</td>
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Xu et al JAMA 2006;296(8):966

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<th># Lifetime Partners</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>1</td>
<td>3.8%</td>
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<tr>
<td>2-4</td>
<td>13.3%</td>
</tr>
<tr>
<td>5-9</td>
<td>20.8%</td>
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### Adolescent Females, 14-19

1.9%

Forhan et al Pediatrics 2009;124(6):1507

### College Students, Maryland

3.6% (mean age 24.5)

Haley D et al. Sex Trans Dis 2007;34:681
**HSV Serology**

- Use a type-specific, gG-based ELISA test
- 4-6 weeks to develop antibody typical
- No role for IgM testing
- Confirm low values (<3.0) with another test or WB
  - WB is not commercially available but can be sent to Univ. of Washington ($250)
- A positive result for HSV-2 antibody means:
  - the patient is **infected** with genital herpes (rarely oral)
  - the patient is **infectious** with genital herpes
  - management is the **same** as for lesion-based diagnosis
Ryan

- Ryan is a 19 y.o. sophomore. He recently started having sex with men and comes to the clinic for routine STI screening. He is concerned about a bump near his anus and wonders if it is a hemorrhoid. He has had receptive anal intercourse only a few times, most recently about 1 month ago. No other symptoms or concerns.
Ryan

- Exam: 1 cm fissure noted near the anus, not tender, firm edges
- Lab: HSV PCR swab of lesion, plus routine STI screening (GC, CT, VDRL, HIV)
- Plan: Reassurance and self-care recommended.
Ryan

- HSV PCR was negative

- VDRL was reactive at 1:64, with positive TP-PA confirmatory test

- Diagnosis: primary syphilis

- Treatment: Benzathine penicillin G 2.4 million units IM
  - If PCN allergy then doxycycline X 2 weeks

- Plan follow up VDRL at 3, 6, 12 months
- Infrequent in college students, usually are MSM
- U.S. incidence near 50-year low, but recent increases among MSM

Syphilis Incidence Rates by Risk Group, 2007

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>Cases/100K Population</th>
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<tbody>
<tr>
<td>MSM</td>
<td>121</td>
</tr>
<tr>
<td>MSW</td>
<td>2 61X</td>
</tr>
<tr>
<td>WSM</td>
<td>1.3 95X</td>
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CDC, 2010 STD Conference LB2
Syphilis Pearls

- Routine screening for syphilis is indicated mostly for MSM, IDU, and pregnant women
  - Strong association with HIV infection (50% HIV+)
- The incidence in other countries may be different
- Diagnostic testing is important in the workup of unusual rashes or suspicious lesions (regardless of risk factors)
- Primary syphilis lesions (chancres) are often subtle, usually painless, and sometimes internal (vaginal, rectal, pharynx). Syphilis more typically presents as a secondary rash or is found on routine screening.
Is this a yeast infection?

- A 24 y.o. female college student presents with a complaint of vulvar itching for 3 days. She has had similar symptoms twice in the last year.

- ROS: Acne, being treated with doxycycline 100 mg daily. She is also on oral contraceptives, has had the same boyfriend for 15 months, and does not use condoms.
Exam: Minimal vulvar erythema, with a small superficial fissure noted in a labial fold. Vaginal wet prep reveals moderate WBCs and a few yeast are present.

How would you manage this patient?
- Treat for yeast?
- Test for STIs?

- A viral culture from this lesion was positive for HSV-2
Diagnostic Tests for Herpes

Visual exam alone
- Poor to fair, even with experienced clinician

Viral culture
- Good to very good, especially with first episode disease.

Nucleic acid amplification (PCR)
- Highly sensitive and specific, best test where available

Antigen tests, Tzanck smear
- Poor sensitivity and specificity, not recommended

Serology (gG based)
- Good to excellent, depending on the timing
Genital Herpes -- Discussion

- Herpes is often subtle and goes unrecognized
- Have a high index of suspicion for herpes and test open genital lesions
  - PCR is the test of choice for lesion diagnosis
  - HSV-2 increases the acquisition risk of HIV 2-5X
  - Serology can be useful for evaluation of atypical or recurrent symptoms
- Offer treatment with antivirals to all positive pts
What have we learned?

- Dysuria doesn’t always mean cystitis. It’s also a common symptom of herpes and chlamydia, in both men and women.
- Gonorrhea continues to develop resistance to most drugs we use and there are few options for tx.
- It’s important to routinely screen for syphilis in MSM, but probably nobody else.
- Ureaplasma is something best left untested for.
- Use nucleic acid tests (for HSV, CT, GC) when available, rather than older technologies.
Questions?

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