Value of STI Screening and Testing

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Hazards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detect infection</td>
<td>False positives</td>
</tr>
<tr>
<td>• Patient treatment</td>
<td>• Unnecessary W/Us</td>
</tr>
<tr>
<td>• Partner treatment</td>
<td>• Emotional impact</td>
</tr>
<tr>
<td>• Behavior change</td>
<td>Economic costs,</td>
</tr>
<tr>
<td>• PH Surveillance</td>
<td>esp if high NNT</td>
</tr>
<tr>
<td>Absence of infection</td>
<td></td>
</tr>
<tr>
<td>• Behavior change</td>
<td></td>
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<tr>
<td>• Reassurance</td>
<td></td>
</tr>
</tbody>
</table>

Goals of STI Testing
- Test the right patients
- For the right organisms
- With the right test
- Interpret result correctly

Case Study
- 27 year old woman requests STI screening
- In a monogamous relationship until 6 months ago
- 4 weeks ago, had unprotected sex with new partner
- Because she is concerned that she may have acquired an infection, wants to be screened “for everything”
Which STD screening test is considered to be unnecessary in this case?

1. Gonorrhea + chlamydia
2. Hepatitis B serology
3. Syphilis serology
4. HIV serology
5. All are considered to be necessary

Categories of STI Screening and Testing

- Routine screening
  - Population based risk factors
- Targeted screening
  - Personal behavioral risk factors
- Contact testing
  - Persons with suspected or known contact (exposure) to another person with a STI

- Co-infection testing
  - If diagnosed with one STI, there is an increased risk of being co-infected with another STI
- Diagnostic testing
  - Evaluation of a person with clinical symptoms or signs of a STI
- Test-of-cure
  - Testing after treatment to detect treatment failure
- Repeat screening
  - Screening after treatment to detect re-infection
“Routine” STI Screening

- Cervical Chlamydia (in women)
  - Annually in sexually active women thru 25 years old
- Cervical gonorrhea (in women)
  - Annually in sexually active women thru 25 years old
  - Only if practice-site prevalence is at least 1%
- HIV serology (CDC 2006); USPSTF (2007): [C] recommend
  - Screen once 13-64; repeat ≤ annually if “known risk”
  - Only if practice site prevalence is at least 0.1%
- Pregnant women
  - Syphilis, HIV, Chlamydia (under 26 years old)
  - Hepatitis B antigen (newborn treatment)

Are the Wrong Women Screened for Ct?

- Many women in the target age range (25 and younger) are not being screened
- Yet, in many systems, screening rates for women over age 25 are equal to women 25 and younger
  
  So what?
  
  - Rates of chlamydia in women over age 25 are <1%
  - As prevalence decreases, positive predictive value declines, making incorrect diagnoses more likely

Female Chlamydia Rates, 2004

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rates</td>
<td>3.9%</td>
<td>3.8%</td>
<td>3.7%</td>
<td>3.6%</td>
<td>3.5%</td>
<td>3.4%</td>
<td>3.3%</td>
<td>3.2%</td>
<td>3.1%</td>
<td>3.0%</td>
<td>2.9%</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

CDC, 2005
Targeted Screening: Risk Factors

GC + Ct screening
- History of GC, chlamydia, or PID in the past 2 years
- More than 1 sexual partner in the past year
- New sexual partner within 90 days
- Reason to believe that a sex partner has had other partners in the past year
- Syphilis, HIV screening
- Sexual history, partner behaviors, local prevalence

GC+Ct Screening Recommendations

- Nucleic acid amplification tests (NAAT) are preferred
  - Urine, vaginal swab, cervical, and LBC samples are highly accurate (>98% sensitivity; >99% specificity)
  - Sample endocervix only if speculum exam is being performed for another reason
- DNA probe tests are being phased out, since less sensitive (70%) and cervical or urethral samples required
- In asymptomatic heterosexual women and men who engage in oral or anal sex, CDC does not recommend pharyngeal or anal GC or Ct tests

Is A Screening Pelvic Exam Necessary in Adolescents?

In sexually active asymptomatic adolescents (under 21 years of age), physical assessment at screening visits should consist of
- Blood pressure check, BMI, and PNP
- PNP= Pee, not Pap
- Pee: Chlamydia NAAT
- Pelvic exam: not until 21 years old
- Pap: not until 21 (or 3 years after sexual debut)
- With or without a contraceptive prescription

ACOG Comm on Gyn Practice, #431. OG 2009; 113:1190
Contact Testing for STI Exposure

- Test asymptomatic persons with high risk sexual exposure (new or multiple sexual partners) for:
  - Gonorrhea
  - Chlamydia
  - Syphilis
  - HIV
- Maybe: HSV-2 serology
- No contact testing for:
  - HSV (culture), HPV (DNA)
  - HBV, HBC (strategy for HBV is vaccination)

CDC 2006: Screening for Hepatitis B

- Have you previously been vaccinated for Hepatitis B?
  - Yes...no further evaluation
  - No...consider being vaccinated if HB risk factors
- If HB vaccine is offered, pre-vaccination HB serology
  - Is not cost effective in low prevalence groups, including adolescents
  - Is cost effective in high prevalence adult populations
    - IDU, MSM, sexual contacts of chronic carriers, persons from endemic countries
  - If screening is done, the first dose of vaccine should be given at the same time

CDC 2006: Screening for Hepatitis C

- Sexual transmission is very uncommon
- Candidates for targeted screening
  - Blood transfusion from a donor who later tested positive for hepatitis C
  - Injected illegal drugs, even if experimented a few times many years ago
  - Transfusion or organ transplant before 7/1992
  - Recipient of clotting factor(s) made before 1987
  - Ever been on long-term kidney dialysis
  - Evidence of liver disease (e.g., abnormal LFTs)
Testing for STI Co-Infection

<table>
<thead>
<tr>
<th>If positive for</th>
<th>Test for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia</td>
<td>GC, syphilis, HIV</td>
</tr>
<tr>
<td>GC</td>
<td>Chlamydia, syphilis, HIV</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Chlamydia, GC, HIV</td>
</tr>
<tr>
<td>Primary herpes</td>
<td>Chlamydia, GC, syphilis, HIV</td>
</tr>
<tr>
<td>Recurrent herpes</td>
<td>(?)… may be long standing</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>(?)…, may be long standing</td>
</tr>
<tr>
<td>Ext genital warts</td>
<td>(?)… may be long standing</td>
</tr>
<tr>
<td>BV, candida</td>
<td>Not STIs, therefore don’t screen</td>
</tr>
</tbody>
</table>

Diagnostic Testing for GC and Ct

- Women
  - Abnormal vaginal discharge
  - Abnormal vaginal bleeding
  - Dyspareunia, chronic pelvic pain, PID
  - Mucopurulent cervicitis
  - Cervical friability
  - Unexplained infertility

- Men
  - Dysuria
  - Urethral discharge
  - Testicular pain

Gonorrhea (GC) + Chlamydia (Ct) Indications for Treatment

- Positive GC or Ct screening test
- Sexual partner with known GC or Ct
- Presumptive therapy of mucopurulent cervicitis or urethritis (treat both)
- Pelvic inflammatory disease (treat both)
CDC 2006: LGT Chlamydia

- Preferred treatment
  - Azithromycin 1 gm orally
    » Dispensed as sachet (powder) or capsules
  - 2006: first line treatment in pregnancy
    » Doxycycline 100 mg PO BID for 7 days
      » Avoid prolonged sun exposure (photosensitivity)

- Alternative treatment
  - Ofloxacin 300 mg PO BID for 7 days
  - Levofloxacin 500 mg PO QD for 7 days
  - Erythromycin base or EES QID for 7 days

Update to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2006: Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections

- 2006 GISP findings of QRNG isolates (5% threshold)
  - Overall population: 13.3% (8.6% no CA, HI)
  - MSM: 38.3% (30.7% no CA, HI)
  - Heterosexual men: 6.7% (5.1% no CA, HI)
  - Philadelphia: 26.6%; Miami: 15.3%

CDC 2007: LGT Gonorrhea

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Adv Eff</th>
<th>AWP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone 125 mg IM</td>
<td>+ 2 (IM)</td>
<td>12.98</td>
</tr>
<tr>
<td>Cefixime 400 mg PO</td>
<td>+ 1</td>
<td>$6.76</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin 500 mg PO</td>
<td>+ 3</td>
<td>3.62</td>
</tr>
<tr>
<td>Ofloxacin 400 mg PO</td>
<td>+ 3</td>
<td>4.34</td>
</tr>
<tr>
<td>Levofloxacin 250 mg PO</td>
<td>+ 3</td>
<td>6.00</td>
</tr>
</tbody>
</table>

Co-treat Chlamydia, unless ruled out by NAAT

No longer recommended by CDC
CDC 2006: LGT Gonorrhea
Alternative Regimens

<table>
<thead>
<tr>
<th>Single oral dose</th>
<th>Dose</th>
<th>Adv Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Cefpodoxime</td>
<td>400 mg</td>
<td>+ 1</td>
</tr>
<tr>
<td>– Cefuroxime</td>
<td>1 gm</td>
<td>+ 1</td>
</tr>
<tr>
<td>– Azithromycin</td>
<td>2 gms</td>
<td>+ 2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Single IM dose</th>
<th>Dose</th>
<th>Adv Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Cefotaxime</td>
<td>500 mg</td>
<td>+ 2</td>
</tr>
<tr>
<td>– Cefoxitin</td>
<td>2 gm</td>
<td>+ 2</td>
</tr>
</tbody>
</table>

Screening and Testing Post-Treatment

- Test of Cure
  - Not after high efficacy, single dose treatment
  - Only after multi-day antibiotics with high failure rate
    » e.g., Erythromycin TID for 7 days
  - Still recommended after Chlamydia treatment in pregnant women
  - Avoid non-culture tests within 3 weeks of treatment, since dead organisms may be detected

Screening and Testing Post-Treatment

- Re-testing: women treated for chlamydia or GC should be re-tested in 3 months
  - Past Ct infection is strong predictor of subsequent infection
  - High likelihood of repeat infection by untreated partner or new partner
  - Short time to repeat positive test
Retesting for Ct and GC…
Improving Clinic Practice

- Initial patient counseling
  - Stress importance of retest
  - Make retest appointment at the time of treatment
- System to contact patient regarding retesting
  - Tickler system, with follow-up if no return visit
  - Reminders by mail (self-addressed letter or card)
  - Reminder phone calls, e-mails, or text messages
- Opportunistic testing
  - Flag chart
  - Test at any subsequent visit (3-12 months)

Partner Management Strategies

- Traditional approaches
  - Patient notification of partner
  - Provider notification of partner
  - Health department referral
Partner Management Strategies

- Expedited partner treatment (EPT)
  - Patient brings partner to provider site (“BYOP”)
- Patient-delivered partner therapy (PDPT)
  - Provide patient with drugs intended for partners
  - Write prescriptions in the partners’ names
  - Prescribe extra doses of medication in the index patients’ name

2006 CDC Criteria for Acute PID

- “Minimal criteria”
  - Lower abdominal pain AND
  - Cervical motion tenderness OR
  - Uterine tenderness OR
  - Bilateral adnexal tenderness
- If more severe clinical signs— at least 1 of

<table>
<thead>
<tr>
<th>Routine criteria</th>
<th>Elaborate criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature &gt;38.3°C</td>
<td>- Endometritis on EMB</td>
</tr>
<tr>
<td>Cervical mucopus</td>
<td>- TOA on sono, CT, MRI</td>
</tr>
<tr>
<td>▲WBC in vaginal fluid</td>
<td>- Laparoscopic confirmation</td>
</tr>
<tr>
<td>Elevated ESR (&gt;20 mm/hr)</td>
<td></td>
</tr>
<tr>
<td>Elevated C-reactive protein</td>
<td></td>
</tr>
<tr>
<td>Positive test for GC or Ct</td>
<td></td>
</tr>
</tbody>
</table>

Acute PID: Hospitalization

- Uncertain diagnosis; especially if appendicitis or ectopic pregnancy cannot be excluded
- Adnexal or pelvic mass consistent with pelvic abscess
- Pelvic infection in a pregnant woman
- HIV infection; other immunodeficiency state
- Severe nausea and vomiting or allergy that preclude oral therapy
- Failure to respond to treatment within 72 hours
- Hospitalization of adolescents based same criteria
**CDC 2006: PID Treatment Principles**

- Better to over-diagnose and treat, rather than to under-diagnose.
- Early, aggressive therapy helps to avoid hospitalization, infertility.
- Treatment must address:
  - *N. gonorrhoeae*
  - *Chlamydia trachomatis*
  - Anaerobic bacteria
  - (Concomitant) Bacterial vaginosis

**CDC 2006: Outpatient PID Treatment**

**Regimen A**
- Levofloxacin 500 mg QD for 14 days OR
- Ofloxacin 400 mg PO BID for 14 days

**Regimen B**
- Ceftriaxone 250 mg IM
  - then doxycycline 100 mg PO BID for 14 days OR
- Cefoxitin 2 grams IM plus probenecid 1 gram PO,
  - then doxycycline 100 mg PO BID for 14 days
  If BV is diagnosed or to improve anaerobe coverage
- Add: Metronidazole 500 mg BID for 14 days

**AWP Comment**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>AWP</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone IM + Doxycycline + MTZ</td>
<td>$31</td>
<td>Good for mild PID</td>
</tr>
<tr>
<td>Cefoxitin IM + Doxycycline + MTZ</td>
<td>$37</td>
<td>Cefoxitin usually not stocked in offices</td>
</tr>
<tr>
<td>Levofloxacin + MTZ</td>
<td>$164</td>
<td>Good for moderate PID</td>
</tr>
<tr>
<td>Ofloxacin + MTZ</td>
<td>$174</td>
<td>More daily doses; no advantage</td>
</tr>
</tbody>
</table>
QRNG and Treatment of PID

CDC, 2006

CA STD Treatment Guidelines, 2007

• Quinolones may be used for PID if the risk of GC is low, a NAAT test for GC is performed, and follow-up is likely
• If GC is documented, change to a medication regimen that does not include a quinolone or obtain a test of cure to ensure that the patient does not have a resistant GC infection

Genital Herpes

- HSV serotypes in genital infections
  - Majority of genital infections caused by HSV-2
  - 15-30% of genital infections caused by HSV-1
  - 30-40% new cases of genital HSV due to HSV-1
- Herpes seroprevalence
  - HSV-1 antibody: 60-95% (mean: 80%)
  - HSV-2 antibody: 20-25%
  - 90% of prior HSV infections unrecognized

Genital Herpes

- Recurrence risk after primary infection
  - HSV-2: 50%; HSV-1: 10%
- 95% of people with genital HSV-2 have intermittent subclinical shedding
  - Highest in 1st year after infection (25% of days), then declines; 4-6% of days for many years
  - Similar frequency in persons with and without recognized symptoms
  - Cause of most new cases of HSV-2 genital herpes
  - Uncommon in new cases of HSV-1 genital herpes
**Prevention of Genital Herpes**

- Partner HSV-2 serostatus; susceptible if negative
- Avoid intercourse/touch of lesions during outbreak
- Condoms will provide some degree of protection
- Patient treatment of during outbreak (or long term suppression) reduces shedding
- Daily prophylactic treatment reduces shedding
  - Incident HSV infection reduced by 1.7% over 1 year
    » 96.4% don’t seroconvert in absence of treatment
    » 1.9% seroconvert with treatment
- NNT: 59 people to prevent one case/ year

**HSV: Organism Tests**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensit</th>
<th>Specif</th>
<th>Cost</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR</td>
<td>+4</td>
<td>+4</td>
<td>$$$$</td>
<td>Not in most labs</td>
</tr>
<tr>
<td>HSV culture</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ELVIS rapid</td>
<td>+3</td>
<td>+4</td>
<td>$$$</td>
<td>1 day; no typing</td>
</tr>
<tr>
<td>ELVIS std</td>
<td>+3</td>
<td>+4</td>
<td>$$$</td>
<td>5 days; typing*</td>
</tr>
<tr>
<td>Cytopathic</td>
<td>+3</td>
<td>+3</td>
<td>$$</td>
<td>Phasing out</td>
</tr>
<tr>
<td>Herpes DFA</td>
<td>+2</td>
<td>+3</td>
<td>$$</td>
<td>Scrape; plate</td>
</tr>
<tr>
<td>Cytology</td>
<td>+1</td>
<td>+3</td>
<td>$$</td>
<td>Scrape; plate</td>
</tr>
</tbody>
</table>

* HSV typing is helpful for counseling regarding recurrence risk, but not for clinical management decisions

**HSV-2 Serology: Diagnostic Testing**

Used mainly to exclude genital herpes diagnosis
- History suggestive of HSV but no lesions to test, OR
- Culture negative recurrent lesion
  - Seronegative: not due to genital herpes
  - Seropositive: HSV lesion or prior infection
- Suspected 1st herpes more than 6 weeks ago with initial testing negative; serology repeated
  - Seronegative: not due to genital herpes
  - Seropositive: HSV infection confirmed
HSV-2 Serology: Screening

<table>
<thead>
<tr>
<th>Screening</th>
<th>Should be offered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen general population</td>
<td>Should not be offered</td>
</tr>
<tr>
<td>Universal screening in pregnancy</td>
<td>Should not be offered</td>
</tr>
<tr>
<td>Screening in HIV-positive patients</td>
<td>Should generally be offered</td>
</tr>
<tr>
<td>Screening in patients in partnerships with HSV-2 infected people</td>
<td>Should generally be offered</td>
</tr>
<tr>
<td>Screening in patients at risk for STD/HIV</td>
<td>Should be offered to select patients</td>
</tr>
</tbody>
</table>

Guidelines for the Use of HSV-2 Type-Specific Serologies, CA DHS 2003

CDC 2006: Treatment of Genital Herpes

<table>
<thead>
<tr>
<th></th>
<th>Acyclovir</th>
<th>Famiclovir</th>
<th>Valacyclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong>&lt;br&gt;(7-10 days)</td>
<td>400 mg TID&lt;br&gt;200 mg 5 times/d</td>
<td>250 mg TID</td>
<td>1 gm BID</td>
</tr>
<tr>
<td><strong>Recurrent</strong>&lt;br&gt;800 mg TID x2d&lt;br&gt;800 mg BID x5d&lt;br&gt;400 mg TID x5d</td>
<td>1 gm BID x1d&lt;br&gt;125mg BID x5d&lt;br&gt;1 gm BID x5d</td>
<td>500mg BID x3d&lt;br&gt;1 gm QD x5d</td>
<td></td>
</tr>
<tr>
<td><strong>Suppression</strong>&lt;br&gt;400 mg BID</td>
<td>250 mg BID</td>
<td>0.5-1.0 gm QD</td>
<td></td>
</tr>
<tr>
<td><strong>Prophylaxis</strong>&lt;br&gt;400 mg BID**</td>
<td>500 mg QD</td>
<td></td>
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</tr>
</tbody>
</table>

** Drug class extrapolation, based upon suppressive regimen

High Risk HPV DNA Testing

ASCCP Clinical Update 2009; aSCCP.org

Clinically useful for:
- Primary screening (HPV+Pap), age 30 and over
- Triage of ASC-US or AGC Paps (< 21 years old)
- Post-colposcopy and post-treatment follow-up, in lieu of Pap smears
- Triage of women who are HPV HR pos/Pap negative
  - HPV 16/18 genotyping must be used, if available
High Risk HPV DNA Testing
ASCCP Clinical Update 2009

HR HPV testing and genotyping not recommended
- Any application in women under 21 years old
- (Reflex) triage of ASC-H, LSIL, HSIL Paps
- Routine screening in women before 30 years old
- In women considering vaccination against HPV
- For routine STD screening
- Evaluation of patients with genital warts
- Evaluation of sex partners
- As part of a sexual assault evaluation

Take Home Messages
- Understand the 7 categories of STI screening and testing and stick with established indications
  - A sexual history is essential to determine whether targeted screening or contact testing is indicated
  - Screening without a clear indication may do more harm than good
- Single sample – multiple pathogen tests are preferred when testing all pathogens is intended
- Avoid multiple pathogen test panels which include pathogens that do not need to be “found”