New Developments in the Management of Sexually Transmitted Infections in Women

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Categories of STI Screening and Testing

• Routine screening
  – Population based risk factors
• Targeted screening
  – Personal behavioral risk factors
• Contact testing
  – Suspected or known exposure to a person w/ STI

Categories of STI Screening and Testing

• Co-infection testing
  – If one STI, greater risk of being co-infected
• Diagnostic testing
  – 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

• There are no relevant financial relationships with any commercial interests to disclose
Routine Screening: Cervical Chlamydia

• CDC (2010)
  – Annually in sexually active women < 25 years old
  – Older women with risk factors
  – If practice-site prevalence is ≥ 3% (CA STD Control Branch)

• USPSTF (2007)
  – All sexually active non-pregnant women < 24 [A]
  – Older women who are at increased risk [A]
  – Recommend against routinely screening women > 25, whether pregnant or not, if not at increased risk [C]

Why Routine Chlamydia Screening?

• Most prevalent in sexually active women < 26 years old
  – Larger ectropion → bigger target for Ct infection
  – More likely to have multiple sexual partners
  – Less likely to use barrier contraceptives

• Detection and treatment of asymptomatic Ct
  – Reduces PID rates by 56%
  – Reduces consequent infertility, chronic pelvic pain
  – Prevents horizontal transmission to sex partners

Are the Wrong Women Screened for Ct?

• 20-50% of women in target age range are not screened
  • Yet, in many systems, screening rates for women over age 25 are equal to women 25 and younger

So what??

• Ct rates in women over 25 are <1%; decline with age
  – Chlamydia infects the columnar epithelium of the cervical ectropion; recedes with aging
  – As prevalence decreases, positive predictive value declines
Strategies for Improving Ct Screening
Provider Level

- Screening procedures clear to all office staff
- Unlink Chlamydia screening from pelvic exam
  - With NAAT, vaginal or urine samples are preferred
- Practice “opportunistic prevention”
  - Screen at problem-oriented visits if necessary
- “Automate” office work flow
  - Kit on chart or exam room prep table in advance based on age or risk behaviors

Routine STI Screening: Gonorrhea

- CDC (2010)
  - Women under 25 years of age who are at increased risk for infection
  - Older women with risk factors
  - If PSP is > 1% (CA STD Control Branch)
- USPSTF (2005)
  - Screen all sexually active women, including pregnancy, if at increased risk for infection [B]
  - Do not screen men and women who are at low risk for infection [D recommendation]

USPSTF: Increased Risk for GC Infection

- Under 25 years of age
- New or multiple sex partners
- Previous GC or other STDs
- Inconsistent condom use
- Commercial sex work
- Drug use

Targeted Screening: Risk Factors

Ct screening in women > 26 years old, or
GC screening in women of any age, PSP <1%

- 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
  - Highly accurate: >98% sensitivity; >99% specificity
  - Men: first catch urine sample preferred
  - Women: vaginal swab preferred
    - Urine, cervical, LBC samples slightly less accurate
    - Sample endocervix only if speculum exam being done
- DNA probe test (Genprobe PACE-2) being phased out
- In *asymptomatic* heterosexuals who engage in oral or anal sex, CDC does *not* recommend pharyngeal or anal samples

**Is A Screening Pelvic Exam Necessary in Adolescents?**

In sexually active asymptomatic adolescents (<21 years of age), exam at STI and well women visits includes
- Blood pressure check, BMI, and PNP
  - PNP= Pee...not pelvic
- Pee: Chlamydia NAAT
- Pelvic exam: not until 21 years old
- Pap: not until 21 years old
- 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 2010: 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,
  - *Is cost* effective in high prevalence adult populations
    - IDU, MSM, sexual contacts of chronic carriers, persons from endemic countries
    - If screened, give 1st dose of vaccine at same time
**CDC 2010: 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
  - Ever been on long-term kidney dialysis
  - Evidence of liver disease (e.g., abnormal LFTs)

**Recommendations for Identification of Chronic Hep C Virus Infection, Persons Born 1945–1965**

MMWR 2012;61(RR04);1-18

- Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk, and
- All persons identified with HCV infection should receive a brief alcohol screening and intervention, followed by referral to appropriate care services for HCV infection

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

- 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 2010: Lower Genital Tract Chlamydia**

- **Preferred treatment**
  - Azithromycin 1 gm orally, directly observed
    - 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
- **NOTE:** Ciprofloxacin not effective!

**CDC 2010: Anogenital Gonorrhea**

- **Recommended regimens**
  - Preferred: ceftriaxone 250 mg IM + dual therapy
  - If IM not an option: cefixime 400 mg PO + dual tx
- **Dual therapy drugs...either**
  - Azithromycin 1 gram PO, or
  - Doxycycline 100 mg BID for 7 days
- **Purpose of dual therapy**
  - Prevent (or delay) GC cephalosporin resistance
  - Co-treat “for chlamydia”, even if NAAT is negative

**CDC 2010: Anogenital Gonorrhea**

- **Alternative oral cephalosporins**
  - Cefpodoxime 400 mg PO, or
  - Cefuroxime axetil 1 gram PO
- **Alternative single IM dose**
  - Ceftizoxime 500 mg
  - Cefotaxime 500 mg
  - Cefoxitin 2 gm
- **Alternative regimen if cephalosporin allergic**
  - Azithromycin 2 grams PO x single dose
  - **Perform test of cure**
**CDC 2014: Anogenital Gonorrhea**

- **Recommended regimen**
  - Ceftriaxone 250 mg IM x1 dose

**plus Dual therapy**
- Azithromycin 1 gram PO
- **Doxycycline 100 mg BID for 7 days**

- **Alternative therapy**
  - If IM ceftriaxone not an option or EPT:
    - Cefixime 400 mg PO + azithromycin 1 gram PO

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**CDC 2010: Oropharyngeal Gonorrhea**

- **Recommended regimen**
  - Ceftriaxone 250 mg IM + dual therapy
  - All other cephalosporins have lower cure rates

- **Dual therapy drugs...either**
  - Azithromycin 1 gram PO, or
  - Doxycycline 100 mg BID for 7 days

- **Alternative regimen** if cephalosporin allergic
  - Azithromycin 2 grams PO x single dose
  - **Perform test of cure**

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**Test of Cure After Ct or GC Treatment**

- *Not after high efficacy, single dose treatment*
- Exceptions...perform test of cure
  - Pregnancy
  - Noncompliant with therapy
  - Persistent symptoms despite therapy
  - Suspect early reinfection after adequate therapy
  - Multi-day antibiotics with high failure rate
    - e.g., Erythromycin TID for 7 days
  - Avoid non-culture tests within 3 weeks of treatment, since dead organisms may be detected

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**Check List: Management of Ct and GC**

- **Ensure timely and appropriate treatment**
  - Within 14 days of specimen collection
- **Test for other STDs**
  - GC, syphilis, HIV
- **Patient education and counseling**
- **Report case to the local health department**
- **Schedule follow-up test in 3 months**
- **Ensure that sex partners are treated**
  - All partners in the past 2 months
Ct & GC Screening and Testing
Post-Treatment

- **Re-testing:** women treated for chlamydia or GC should be re-tested in **3 months**
  - In young women, past infection is strong predictor of repeat infection
    - 20% (14-26%) rate of new infection(s) by an untreated partner or new partner within 12 months
  - Short time to repeat positive test
  - 4x risk of PID, 2x risk of ectopic pregnancy

Retesting for Ct & GC...Improving Clinic Practice

- **Initial patient counseling**
  - 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 re-testing**
  - Flag chart to ensure retesting opportunity not missed
  - Test at any subsequent visit (3-12 months), but not earlier than 4 weeks from treatment

Partner Management: WHO?

- Treat ALL sexual partners within 2 months of positive gonorrhea or chlamydia test
  - Ask how many people she has had sex with during the previous 2 months
  - Ask regardless of marital/relationship status
  - If last sexual contact was longer than 2 months ago, treat most recent partner

Partner Management: HOW?

- **Traditional approaches**
  - Patient notification of partner
  - Provider notification of partner
  - Health department referral
- **Preferred approach**
  - Expedited Partner Therapy (EPT)
    - 2010 CDC STD Treatment Guidelines
    - ACOG Committee Opinion #506, ObGyn, Sept 2011
Expedited Partner Treatment (EPT)

- Bring Your Own Partner (“BYOP”)
  - Bring her partner(s) at the time of her treatment
- Patient-delivered partner therapy (“PDPT”)
  1. Provide patient with drugs intended for partners
  2. Prescribe extra doses of medication in the index patients’ name
  3. Write prescriptions in the partners’ names
    - Ideally with written instructions for the partner(s)
  - Other states: www.cdc.gov/std/ept for US map

Chlamydia and Gonorrhea Clinical Management in a Nutshell

“Screen, Treat, Treat, Screen”

- Screen all appropriate patients for Ct and GC;
- Treat all infected patients promptly;
- Treat all of their recent partners; and
- Screen all treated patients again three months after treatment (retest)

Routine STI Screening: HIV Serology

- CDC (2010), USPSTF (2012)
  - Screen all individuals once between 15-64 years old
    • Only if practice-site prevalence (PSP) is at least 0.1%
  - Repeat annually or more often if “known risk”
- Many labs have switched to Updated HIV Testing Algorithm
  - CDC: Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations (6/27/14)

2014 CDC HIV Testing Algorithm

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>3rd or 4th generation HIV serology</td>
<td>Multi Spot</td>
</tr>
<tr>
<td>Positive HIV-1, 2 or both</td>
<td></td>
</tr>
<tr>
<td>HIV-1 NAT Qualitative</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Negative (false pos screen)</td>
<td></td>
</tr>
<tr>
<td>Positive (false neg DA)</td>
<td></td>
</tr>
</tbody>
</table>

Note: Western Blot no longer used
Routine STI Screening: Syphilis Serology

- CDC (2010)
  - All pregnant women; otherwise no recommendation
- USPSTF (2004)
  - Recommends against routine screening of asymptomatic persons who are not at increased risk for syphilis infection [D recommendation]
  - Strongly recommends that clinicians screen persons at increased risk for syphilis infection [A]

Syphilis Screening

- Traditional protocol
  - Quantitative, non-treponemal assay (RPR, VDRL) → Confirmatory qualitative treponemal test (TPPA)
- New protocol
  - New treponemal tests EIA/CLIA → Non-treponemal test (RPR, VDRL)
  - If discordant EIA+/RPR negative → 2nd treponemal test (TPPA)

HSV-2 Serology: Screening

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Recommendation</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 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 DHCS

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
- Treatment of during outbreak 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
**CDC 2010: Treatment of Genital Herpes**

<table>
<thead>
<tr>
<th></th>
<th>Acyclovir</th>
<th>Famciclovir</th>
<th>Valacyclovir</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong> (7-10 days)</td>
<td>400 mg TID</td>
<td>250 mg TID</td>
<td>1 gram BID</td>
</tr>
<tr>
<td><strong>Recurrent</strong></td>
<td>800 mg TID x2d</td>
<td>1 gm BID x1d</td>
<td>500 mg BID x3d</td>
</tr>
<tr>
<td></td>
<td>800 mg BID x5d</td>
<td>125mg BID x5d</td>
<td>1 gm QD x5d</td>
</tr>
<tr>
<td></td>
<td>400 mg TID x5d</td>
<td>500 mg once, then 250 BID x2d</td>
<td></td>
</tr>
<tr>
<td><strong>Suppression</strong></td>
<td>400 mg TID</td>
<td>250 mg BID</td>
<td>0.5-1 gm QD</td>
</tr>
<tr>
<td><strong>Prophylaxis</strong></td>
<td>400 mg BID**</td>
<td>250 mg BID</td>
<td>500 mg QD</td>
</tr>
</tbody>
</table>

**Take It To Your Practice**

- Use the 7 categories of STI screening and testing
  - Automate office to support routine Ct screening
  - Sexual history is essential for targeted screening
  - Screening _without_ indication = more harm than good
- Pelvic exam is unnecessary for GC and Ct screening
- Treat partners (know your state law)
- Optimize office procedures to support
  - Rescreening of patients treated within 3-12 months
  - Expedited partner therapy (BYOP, PDPT)

**Reproductive Infectious Disease Pager (24/7)**
- (415) 443-8726

**National Perinatal HIV Hotline (24/7)**
- (888) 448-8765

**ReproIDHIV listserv**
- Clinical cases, patient referrals, sharing protocols/upcoming events, networking
- Sponsored by UCSF National Clinicians’ Consultation Center, Infectious Disease Society of Obstetricians and Gynecologists (IDSOG), UCSF Fellowship in Reproductive Infectious Disease
- Contact Shannon Weber at: sweber@nccc.ucsf.edu