New Developments in the Management of Sexually Transmitted Infections

“A Rose By Any Other Name Is Still A Rose”

- Venereal Disease (VD)
- Sexually Transmitted Disease (STD)
- Sexually Transmitted Infection (STI)
- Reproductive Tract Infections (RTI)
- Sexually Transmitted Disorder (STD)

- Miller WC. Tell us what you think: Sexually transmitted disease, sexually transmitted infection, both, or neither. Sex Tm Dis 2015; 42: 170
CDC 2015: Top Updates

1) CT/ GC screening
2) CT/GC diagnostic tests
3) New-ish chlamydia treatment
4) Changes to GC recommended/alternative therapy
5) Partner management guidelines
6) HPV vaccine and Primary HPV screening
7) Trichomonas screening, diagnosis, and treatment

1) STD Screening for Women

- Sexually active adolescents & through age 24
  - Routine chlamydia and gonorrhea screening
  - Other STDs based on risk
- Women 25 years of age and over
  - STD screening and testing based on risk
- Pregnant women
  - Chlamydia
  - Gonorrhea (<25 years of age or risky behaviors)
  - HIV
  - Syphilis serology
  - Hepatitis BsAg
  - Hepatitis C (if high risk)

2) NAAT Vaginal Swab Is Preferred Specimen Source

- Sensitivity is equal or greater to cervical swabs or urine
- Self-collection option well accepted women of all ages
- Less specimen processing than with urine
- Check with your lab regarding specimen handling
- In asymptomatic heterosexuals who engage in oral or anal sex, sample single site most likely infected
- NAAT test (and CPT code) is the same, regardless of site

Routine Screening: Chlamydia and GC

- USPSTF (2014)
  - All sexually active non-pregnant women ≤ 24 [B]
  - Older women who are at increased risk [B]
  - Men: [ I ] No recommendation
- CA STD Control Branch
  - If practice-site prevalence (PSP) is...
    - Chlamydia ≥ 3%
    - Gonorrhea ≥ 1%
**Increased Risk for Ct/ GC**

- Previous or concurrent STI
- New or multiple sex partners
- A sex partner with concurrent partners
- A sex partner with an STI
- Inconsistent condom use among persons who are not in mutually monogamous relationships
- Exchanging sex for money or drugs

**Targeted Ct, GC Screening: Risk Factors**

Ct and GC screening in women 25 years and older, and PSP is low (Ct is <3% and GC is <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

**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

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**Chlamydia—Rates by Age and Sex, United States, 2010**

<table>
<thead>
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<th>Age</th>
<th>Rate (per 100,000 population)</th>
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<tr>
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<td>20–24</td>
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<td>25–29</td>
<td>590.0</td>
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<td>30–34</td>
<td>309.0</td>
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<tr>
<td>65+</td>
<td>2.8</td>
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<tr>
<td>Total</td>
<td>3,378.2</td>
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</table>

No senior epidemic!
**Strategies for Improving Ct Screening**

*Provider Level*

- Screening procedures clear to all office staff
- Unlink Chlamydia screening from pelvic exam
- 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

**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)
  - HBC, HBV (strategy for HBV is vaccination)

**CDC 2015: Screening for Hepatitis B**

- Have you previously been vaccinated for Hepatitis B?
  - Yes... no further evaluation
  - No... offer HBV vaccination if HB risk factors
  - Don’t know... check! If can’t find out, do serology
- 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 2015: Screening for Hepatitis C**

- Sexual transmission is very uncommon
- Candidates for targeted screening
  - Blood transfusion from a donor later positive for hep 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)
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

Treatment of GC + Chlamydia (Ct)

- Positive GC or Ct screening test
- Sexual partner with person with known GC or Ct
- Presumptive therapy of mucopurulent cervicitis or urethritis (treat both partners)
- Pelvic inflammatory disease (treat both partners)

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!

3) New Chlamydia Treatment

Alternative Regimen: Non-pregnant
- Doxycycline (delayed release) 200 mg QD x 7 days
  - Equally efficacious to BID doxy, less GI side effects
  - More expensive

Moved to Alternative Regimen: Pregnant
- Amoxicillin 500 mg PO TID x 7 days
**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

- **Why dual therapy??**
  - Prevent (or delay) GC cephalosporin resistance
  - Co-treat “for chlamydia”, even if NAAT is negative
  - Preferably, simultaneously and direct observation

**4) Gonorrhea Dual Therapy**

**Uncomplicated Genital, Rectal, or Pharyngeal Infections**

- **Recommended regimens**
  - Ceftriaxone 250 mg IM in a single dose

- **Dual therapy**
  - Azithromycin 1 g orally (preferred) or
  - Doxycycline 100 mg BID x 7 days

- **Why dual therapy??**

  - Prevent (or delay) GC cephalosporin resistance
  - Co-treat “for chlamydia”, even if NAAT is negative
  - Preferably, simultaneously and direct observation

**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
  - Pharyngeal GC treated with an alternative regimen
  - Multi-day antibiotics with high failure rate
- Avoid non-culture tests within 3 weeks of treatment

**Gonorrhea Treatment Alternatives**

**Anogenital Infections**

**ALTERNATIVE cephalosporins**

- Cefixime 400 mg orally once
  - PLUS
- Dual treatment with azithromycin 1 g (preferred) or doxycycline 100 mg BID x 7 days, regardless of CT

**IN CASE OF SEvere ALLERGY:**

- Gentamicin 240 mg IM + azithromycin 2 g PO
- OR
- Gemifloxacin 320 mg orally + azithromycin 2 g PO
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 Post-Treatment

• Re-screening: women treated for chlamydia, GC or trichomonas should be re-screened in 3 months
  – Past infection is strong predictor of repeat infection
    • 20% will have a 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

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)
    • 2015 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 in the index patients’ name
  3. Write prescriptions in the partners’ names
  - Ideally with written instructions for the partner(s)

**Legal Status of Expedited Partner Therapy**

2016: www.cdc.gov/std/ept

**5) Partner Management**

- Clinical evaluation first-line option
- Concurrent patient-partner therapy (BYOP) may be effective for patients with one partner
- Offer PDPT routinely to heterosexual patients with CT/GC if partner cannot be promptly treated
  - Dual therapy (cefixime 400 mg + azithromycin 1 g) is crucial if PDPT is offered

**Routine STD Screening: HIV Serology**

- **CDC (2015), USPSTF (2012)**
  - Screen all individuals once between 13-64 years old
    - Only if practice-site prevalence (PSP) is at least 0.1%
  - Repeat annually or more often if “known risk”
  - Many labs switching to 4th generation HIV antigen/antibody test (e.g., Abbott “Architect” test), with “Multispot” confirmatory test
Routine STD Screening: Syphilis Serology

- **CDC (2015)**
  - All pregnant women; otherwise no recommendation
- **USPSTF (2004)…2016 update in progress**
  - Strongly recommends that clinicians screen persons at increased risk for syphilis infection [A]
  - MSM, and persons living with HIV highest risk
  - History of incarceration or commercial sex work, geography, race/ethnicity, male < 29 years old

6) HPV Vaccines

**Bivalent: GSK Cervarix**
- Types 16, 18
- Prevents cervical cancer
- FDA-approved for females 10-25
- 3-dose series; $365

**Quadrivalent: Merck Gardasil**
- Types 6, 11, 16, 18
- Prevents warts, cervical & anal cancer
- FDA-approved for females and males 9-26
- 3-dose series; $375

**Nonavalent: Merck Gardasil 9**
- Types 6, 11, 16, 18, 31, 33, 45, 52, 58
- FDA approved Dec 2013

### Summary of 9vHPV Vaccine

- Original HPV types (6,11,16,18)
  - Non-inferior anti-HPV responses vs 4vHPV vaccine
  - Similar protection against disease
- Additional HPV types (31, 33, 45, 52, 58)
  - 97% protection against disease due to these types
- Adverse effect profile similar to 4vHPV vaccine
- Well tolerated, highly immunogenic in prior HPVv recipients
- Can be co-administered with Menactra and Adacel

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**Relative Contribution of HPV Types in 9vHPV Vaccine to Cervical Cancers Worldwide**

Interchangeability of 9v and 4v HPV Vaccine

- If vaccination providers do not know or do not have available the HPV vaccine product previously administered, or are in settings transitioning to 9vHPV, any HPV vaccine product may be used to continue and complete the series for females.

MMWR, March 27, 2015; 64(11):300-304

7) Trichomonas

- Screening recommended for HIV+ women at least annually
- New recommendations
  - Consider screening women in corrections or STD clinics
  - Consider screening high risk-women (those with an STD or with new/multiple sex partners)
  - Use of NAATs and other highly sensitive/specific tests is recommended for detecting Trich (vaginal swabs or urine)
  - Retest women 3 months after treatment
    • NAAT can be done as soon as 2 weeks after treatment

Trichomoniasis Treatment

Recommended regimen
  • Metronidazole 2 g PO x 1 dose
  • Tinidazole 2 g PO x 1 dose
Women with HIV infection
  • Metronidazole 500 mg PO BID x 7 days
Alternative regimen
  • Metronidazole 500 mg PO BID x 7 days
Recommended regimen in pregnancy
  • Metronidazole 2 g PO x 1 dose (all trimesters)
  • Tinidazole is a Category C drug in pregnancy

Trichomoniasis: Treatment Failure

First treatment failure, re-treat with
  • Metronidazole 500 mg PO BID x 7 days
If repeat failure, treat with
  • Metronidazole 2 g PO x 5 days
  • Tinidazole 2 g PO x 5 days

Susceptibility testing: send isolate to CDC: 404-718-4141
“Never before in history has there been a situation where a bite from a mosquito can result in a devastating malformation”

- Dr. Thomas R. Frieden, CDC

ZIKV Effects In Pregnancy

- Initially thought that first trimester exposure was ‘danger zone’
  - (ie, time of neuro-development with microcephaly, intracranial calcifications)
- Now concern throughout pregnancy
  - Eye problems, neurological disorders
  - Premature birth
- Disruptive and destructive
  - Interferes with neural stem cells of brain tissue

What Is Microcephaly?

- Head smaller than expected
  - Abnormal brain development
- Seizures
- Developmental & Intellectual disability
- Problems with movement and balance
- Feeding problems
- Hearing loss
- Vision problems

Source: CDC, 2016

ZIKV: Implications for Women’s Health

- Primary prevention: prevent disease
  - Avoid ZIKV infection
- Secondary prevention: treat precursor to disease
  - Avoid maternal → fetal transmission
- Tertiary prevention: minimize damage from disease
  - Option of elective abortion
  - Monitor for fetal congenital anomalies
ZIKV: Implications for Women’s Health

• **Primary prevention**
  – Avoid mosquito-borne transmission
  – Avoid sexual horizontal transmission

• **Secondary prevention**
  – Avoid unintended pregnancy, esp in high risk situations...travel, partner travel, US endemic
  – Delay pregnancy after exposure or illness

• **Tertiary prevention**
  – Option of elective abortion if infected while pregnant
  – Monitoring for fetal congenital anomalies

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Sexual Transmission Recommendations

• Messages for men! (testes are a reservoir)

• Symptomatic illness
  – Women: wait 8 weeks after onset of symptoms
  – Men: wait 6 MONTHS before causing pregnancy

• Exposure and no symptoms
  – Women and men should both wait 8 weeks to conceive

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Providing Family Planning Care for Non-Pregnant Women and Men of Reproductive Age in the Context of Zika

www.hhs.gov/opa

• Zika Toolkit for Healthcare Providers
• Zika Toolkit Webinar for Healthcare Providers

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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)
• The free app is available for Apple devices (Apple Store)
• An Android app will be available this summer

Need Advice From An STD Expert? Contact Us!

STD Clinical Consultation Network
www.stdccn.org

In: CA, NV, AZ, HI, NM
1 (855) STD-AtoZ
1 (855) 783-2869

Reproductive Infectious Disease Resources

• Reproductive Infectious Disease Pager (24/7)
  – (415) 443-8726
• National Perinatal HIV Hotline (24/7)
  – (888) 448-8765
• Repro ID HIV listserv
  – Clinical cases, patient referrals, networking
  – Sponsored by UCSF National Clinicians’ Consultation Center, IDSOG, UCSF Fellowship in Repro Infectious Disease
  – Contact Shannon Weber at: sweber@nccc.ucsf.edu