Update on Sexually Transmitted Infections

Michael S. Policar, MD, MPH
Professor Emeritus of Ob, Gyn, and Repro Sci
UCSF School of Medicine
michael.policar@ucsf.edu

I have no disclosures relevant to this talk

General Disclosures
• Bayer: litigation consultant
• Sebela Pharmaceuticals:
  – Investigator proctor in phase III trial of a copper IUD (VeraCept)
Routine Screening: Chlamydia and GC

- **USPSTF (2014)**
  - Annually for 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 $\geq 3\%$
    - Gonorrhea $\geq 1\%$
**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/drugs/safety/housing

**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
- Sex in conjunction with drug use
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
- Multi-site screening in MSM; no guidelines for females
  - Screen females based on sexual history…not routinely
  - NAAT test (and CPT code) same, regardless of site(s)

What About Rectal CT and GC in Women Seen in STD Clinics?

- Chandra et al, STI 2018
  - Rectal CT positivity overall: 6% (95% CI, 3.2-8.9%)
  - Rectal CT if reporting anal sex: 25.9% (95% CI 9-43)
  - Percentage of rectal infections that would be missed with only urogenital screening: 18-23%
  - Rectal GC: 1.9% ; pharyngeal GC: 2.1%
  - Rectal chlamydia: 8.7%; pharyngeal chlamydia: 1.7%
Let’s Talk About Technique

- Throat: Swab both tonsillar pillars (watch out for gagging)

- For rectal swab: Insert 3-4 cm and twirl the wrist 360°

GC/CT NAAT: Optimal Urine Specimen Collection

- 1st catch: don’t urinate an hour before providing specimen
  - If patient urinated < 1 hr before, ok to use specimen, but sensitivity may be reduced

- What if we only have a midstream urine?
  - 96/100 participants with first-void urine + for CT also had a positive midstream urine (CI 90-99%)
  - Ok to use specimen, but sensitivity slightly reduced

Mangin et al J Fam Pract 2012
Contact Testing for STI Exposure
aka: “Screen Me for Everything”

- 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)

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
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)

Lower Genital Tract Chlamydia

- **Preferred regimen**
  - 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 regimen**
  - 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!
Lower Genital Tract Chlamydia
added in 2015

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

Anogenital Gonorrhea

• Recommended regimens
  – Ceftriaxone 250 mg IM + dual therapy
• Dual therapy drugs
  – Preferred: azithromycin 1 gram PO
  – If azithromycin allergy, doxycycline 100 mg PO BID
• Why dual therapy??
  – Prevent (or delay) GC cephalosporin resistance
  – Co-treat “for chlamydia”, even if NAAT is negative
  – Preferably, simultaneously and direct observation
Anogenital Gonorrhea

**Alternative cephalosporins**

- Cefixime 400 mg orally once
  
  **PLUS**
  
  - Dual treatment with azithromycin 1 gm PO 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

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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
  - Pharyngeal GC treated with an alternative regimen
  - Multi-day antibiotics with high failure rate
- Avoid non-culture tests within 3 weeks of treatment
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
  - In young women, 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 #737, ObGyn, June 2018
**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)

**The Effectiveness of Expedited Partner Treatment (EPT) on Re-Infection Rates**

<table>
<thead>
<tr>
<th></th>
<th>GONORRHEA</th>
<th>CHLAMYDIA</th>
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</thead>
<tbody>
<tr>
<td>Usual Care</td>
<td>11%</td>
<td>13%</td>
</tr>
<tr>
<td>EPT</td>
<td>3%</td>
<td>11%</td>
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</table>

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
HIV Screening

- Screen all individuals once between 15-65 years old [A]
- Repeat annually or more often if “known risk”
  - Sex partner with HIV, injection drug use, commercial sex work, a new sex partner (since a prior HIV test) whose HIV status is unknown, care at STD or TB, correctional facility, or homeless shelter
- Use 4th gen HIV test; positive result 4 weeks earlier than 3rd
  - HIV-1, HIV-2 antibodies
  - HIV-1 p24 antigen

Primary and Secondary Syphilis:
Reported Cases, U.S., 1941–2017*

Primary and Secondary Syphilis Cases have increased 390% since 2001

CDC estimates more than 55,000 people are infected each year

Bolan, NRHC 2018
Congenital Syphilis (CS) Cases and Primary and Secondary (P&S) Syphilis Cases Among Females of Reproductive Age, U.S., 2007–2017*

In 2016, just seven states represented 70% of all congenital syphilis cases in the U.S.

<table>
<thead>
<tr>
<th>State</th>
<th>2012 Cases</th>
<th>2016 Cases</th>
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<tbody>
<tr>
<td>CA</td>
<td>35</td>
<td>206</td>
</tr>
<tr>
<td>TX</td>
<td>78</td>
<td>71</td>
</tr>
<tr>
<td>FL</td>
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<td>IL</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>OH</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td>U.S. Total</td>
<td>334</td>
<td>628</td>
</tr>
</tbody>
</table>

201 of 3,141 counties (6%) reported at least 1 congenital syphilis case in 2016.
Syphilis Screening

June 2016

- **USPSTF**: Persons at increased risk for syphilis [A]
  - MSM (61% of syphilis diagnoses)
  - Men and women living with HIV
  - History of incarceration
  - History of commercial sex work
  - Certain racial/ethnic groups (AA > Hispanic > white)
  - Being a male younger than 29 years
  - Regional variations (hot spots)
What Can Women’s Health Providers Do?

- Check with your local or state health department to determine whether you are in a “hot spot” area
  - Ask your lab to supply a 2-year syphilis positivity rate
- In-service clinicians re: USPSTF syphilis screening guidelines
- Offer screening: intending pregnancy, infertility w/u, IUD or implant removal for pregnancy, preg test visit negative
- Offer treatment for confirmed syphilis cases, or have established referral pathway for treatment
- Collaborate with health department initiatives

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

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

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
ACIP: Routine HPV Immunization

Females: HPV Immunization with 9vHPV
Routine: 11- or 12-year-olds

Males: HPV Immunization with 9vHPV
Routine: 11- or 12-year-olds

MMWR Dec 16 2016/ 65(49);1405–1408

ACIP: Routine HPV Immunization

- The series can be given starting at age 9 years
- Catch-up immunization
  - Females 13-26 years old
  - Males 13-21 years old
- Males 22 - 26 years may be immunized

Special Populations:
HPV immunization is recommended thru age 26 for MSM and for immunocompromised persons (incl. HIV infection)

MMWR Dec 16 2016/ 65(49);1405–1408
ACIP: Routine HPV Immunization

- **2006**: administered in a 3-dose schedule
  - Each dose is 0.5 mL, administered IM
  - 2nd dose: 1-2 months
  - 3rd dose: 6 months
- **2016**: TWO dose schedule in 9 through 14 year olds
  - Zero and 6-12 months
- Can give with other vaccines (TDaP, TD, MCV4)
- Avoid if a hypersensitivity to yeast or any vaccine component

MMWR Dec 16 2016/ 65(49);1405–1408

10/5/18: FDA Approves Gardasil 9 to 27-45 Year Olds

- 9vHPV studied in 3,200 women 27-45 followed for 3.5 yrs
  - 88% decrease in persistent infection, genital warts, precancerous cervical, vaginal, vulvar lesions (covered types)
- In men 27-45 years, approval was based upon
  - Efficacy data in women for this age group
  - Earlier trials in boys and younger men
  - Immunogenicity data from 150 men in older age group

FDA Approval of Gardasil 9 for 27-45 Year Olds

- **Why does it work in older individuals?**
  - Even if previously exposed to a few types, can gain protection against HPV types not yet encountered
- **CDC ACIP has not modified their guidance yet**
  - Will it be recommended or permissive for 27-45 y.o.?
  - Impacts health insurance coverage and no cost-sharing feature of the ACA

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**The projected timeframe until cervical cancer elimination in Australia: a modelling study**

By Michaela T. Holl, Kate T. Simms, Jie-Bin Lew, Megan A. Smith, Julie M. Brotherton, Marion Saville, Ian H. Frazer, Karen Canfell

**Summary**

*Background* In 2007, Australia was one of the first countries to introduce a national human papillomavirus (HPV) vaccination programme, and it has since achieved high vaccination coverage across both sexes. In December 2017, if high-coverage vaccination and screening is maintained, and if an elimination threshold of four cases per 100,000 women is chosen, cervical cancer is on track to be eliminated as a public health problem in Australia within the next 20 years.