STD Update

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Women's Health Update CME 2015

• No conflicts of interest to disclose
• No FDA non-approved use of medications
• GC/CT NAATs are not FDA approved for use as test of cure

Objectives

• Upcoming changes to CDC STD Treatment Guidelines.. Due any day now...
  • Management of Transgender Populations
  • NAATs for Trichomonas
  • Alternative treatments for N.G.
  • Treatment options for genital warts
  • HPV counseling messages
  • Role of Mycoplasma genitalium in cervicitis

Transgender Care

• Transgenders are individuals whose gender identity differs from that which they were assigned at birth
  • Transgender Men (FTM): female sex at birth based on appearance of genitalia
  • Transgender Women (MTF): male sex at birth

• Transgenders are diverse
  • Sex with men, women, both
35 yo MTF patient accessing health care for the first time.

- What is the most important testing for her?
  - Pap smear
  - HIV test
  - Lipid panel
  - Mammogram

Transgender Women

- Highest HIV Prevalence in the US!
  - 27.7% for all
  - 56.3% for AA transgender women
- Majority have not had genital affirmation surgery so retain a functional penis
  - Insertive oral, vaginal or anal sex with men and women


24 year old FTM patient accessing care for the first time.

- What do you recommend?
  - Lipid panel
  - Pap smear
  - HPV vaccine
  - Mammogram
  - Chlamydia screening

Transgender Men

- Many still have vagina and cervix putting them at risk for bacterial STDs as well as cervical HPV and cancer.
- Some risky behavior but lower prevalence of HIV than transgender women.

Trichomonas: Who would you test?

- 30 year old presents with vaginal discharge and itching
- 45 year old for well woman exam; asymptomatic; recently incarcerated
- 26 year old whose boyfriend was recently treated for trichomonas
- 50 year old with trichomonads noted on liquid based pap

Risk Factors in Women

- Incarceration: 9.32% prevalence
- >40 years old: 11%
- Symptoms
  - 70-85% of infected persons are asymptomatic
- Recent sexual contact


Trichomonas: How would you test?

- Source?
- Wet Mount
- Pap smear
- Culture
- NAAT – Point of care; Lab based

Trichomonas-NAAT

<table>
<thead>
<tr>
<th>FDA + Test</th>
<th>Point of Care</th>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTIMA TV</td>
<td>No</td>
<td>RNA by transcription mediated amplification</td>
<td>95-100%</td>
<td>98-99%</td>
</tr>
<tr>
<td>OSOM Trich Rapid Test</td>
<td>Yes 10 min</td>
<td>Antigen detection</td>
<td>71-99%</td>
<td>99-100%</td>
</tr>
<tr>
<td>Affirm VP III</td>
<td>Yes 45 min</td>
<td>Nucleic acid probe hybridization</td>
<td>83-93%</td>
<td>99.9-100%</td>
</tr>
</tbody>
</table>

Trichomonas- Diagnosis

- Culture was gold standard
- Vaginal Secretions more sensitive than Urine
- Wet mount is most common
  - Sensitivity: 44-80%
  - Drops to 20% if delayed by 10 min
- Pap smear – not accurate


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Follow-Up Important

- Why? 17% rate of reinfection
- When? Re-test within 3 months
- Can re-test with NAAT as early as 2 weeks but why would you?

Williams JA et al. Time from treatment to negative PCR results for C. trachomatis, N. gonorrhoeae and T. vaginalis. National STD Prevention Conference; March 10-13, 2008; Chicago, IL.

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Trich Treatment

- Recommended Regimens
  - Metronidazole 2 g orally in a single dose
  - 84-98% cure rate
    OR
  - Tinidazole 2 g orally in a single dose
  - 92-100% cure rate
- Alternative Regimen
  - Metronidazole 500 mg orally twice a day for 7 days

- All sex partners should be treated at the same time to reduce reinfections. If needed, these regimens may be administered parenterally instead of orally. All persons with a known exposure to T. vaginalis infection should be treated routinely, with or without symptoms or a positive diagnostic test.

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Refractory Trich

- Consider re-infection
- Resistance
  - MTZ: 4-10%
  - Tinidazole: 1%
- Try MTZ or T 500mg po bid x 7d
- Try MTZ or T 2 gm x 7 d
- Get help: CDC 404-718-4141; www.cdc.gov/std
21 yo requests STD testing at the end of unrelated visit

- What are your options for GC/CT testing?
  - Skip it, she is likely low risk
  - Do a pelvic and collect endocervical swab for culture
  - Do a pelvic and collect vaginal swab for NAAT
  - Have her collect a vaginal swab for NAAT
  - Collect a first stream urine for NAAT

CT Rates in King County

* Create incidence rate with 95% confidence intervals.


Age Specific CT Rates in King County


GC Rates King County

* Create incidence rate with 95% confidence intervals.

**Age Specific GC Rates**

![Graph showing age-specific gonorrhea incidence rates by gender, King County, 2012](http://www.doh.wa.gov/Portals/1/Documents/Pubs/347-634-KingProfile12.pdf, accessed 3/15/2014)

*Age-specific gonorrhea incidence rate with 95% confidence intervals.*

**GC & CT Testing**

- Nucleic acid amplification tests (NAATs) are the recommended test method.
- A self- or clinician-collected vaginal swab is the recommended sample type.
  - Self-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated.
  - An endocervical swab is acceptable when a pelvic examination is indicated.
  - A first catch urine specimen is acceptable but might detect up to 10% fewer infections when compared with vaginal and endocervical swab samples.
  - An endocervical swab specimen for *N. gonorrhoeae* culture should be obtained and evaluated for antibiotic susceptibility in patients that have received CDC-recommended antimicrobial regimen as treatment, and subsequently had a positive *N. gonorrhoeae* test result (positive NAAT ≥ 7 days after treatment), and did not engage in sexual activity after treatment.

**CT Treatment**

**Recommended Regimens**

- Azithromycin 1g orally in a single dose OR
- Doxycycline 100 mg orally twice a day for 7 days

**Alternative Regimens**

- Erythromycin base 500 mg orally four times a day for 7 days OR
- Erythromycin ethylsuccinate 800 mg orally four times a day for 7 days OR
- Levofloxacin 500 mg orally once daily for 7 days OR
- Ofloxacin 300 mg orally twice a day for 7 days

**GC – Dual Therapy**

**Recommended Regimen**

- Ceftriaxone 250 mg in a single intramuscular dose (99.2%, 98.9% Pharynx) PLUS
- Azithromycin 1g orally in a single dose

*If ceftriaxone is not available:*

- Cefixime 400 mg in a single oral dose PLUS
- Azithromycin 1g orally in a single dose*

*If azithromycin is not available or if the patient is allergic to azithromycin, doxycycline 100 mg by mouth twice daily may be substituted for azithromycin as the second antimicrobial.*
Why **Dual** Therapy?

- Prevention of antibiotic resistance
- In 2007, emergence of fluoroquinolone-resistant *N. gonorrhoeae* in the US prompted CDC to no longer recommend fluoroquinolones for treatment of gonorrhea, leaving cephalosporins as the only remaining class of antimicrobials recommended for treatment of gonorrhea
- Cephalosporin resistance emerging in Asia and Europe; cefixime failures


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**Suspected Cephalosporin Failure**

- Perform culture and susceptibility testing
- Consult a specialist for guidance in clinical management, and
- Report the case to CDC through state and local public health authorities.

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**27 yo Noted Bumps on her Perineum**

What is most likely diagnosis?
- Normal Variant
- Skin Tag
- Genital Warts
- Genital Herpes

Do you need to biopsy?

What are the treatment options?
- Do nothing
- Cryotherapy
- Surgical excision
- Imiquimod 3.75% qhs

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**HPV 6, 11**

- Dome-shaped warts
- Flat or slightly raised warts
- No warts, but HPV stays in the skin and virus can still be passed on

Genital wart appearance
Treatment Options

- **Podofilox 0.5% solution or gel**
  - BID x 3 d; may repeat q 4 d x 4
  - Wart area <10cm²; no more than 0.5mL/d
- **Imiquimod 3.75% or 5% cream**
  - 3.75% q hs x up to 16 wks
  - 5% q hs three times/wk
- **Sinecatechins 15% ointment**
  - Tid up to 16 wks


HPV Counseling

- Very common – almost all sexually active people get it and partners share it.
- Usually body’s natural defenses fight HPV before it can cause health problems.
- HPV warts do not cause cancer
- No way to test partner
- Condom use can decrease but not eliminate transmission risk
- Warts may regress on their own. Treatment is for symptoms. Treatment does not prevent transmission.

Myoplasma genitalium

- Smallest free living bacteria
- Genome only 521 genes
- Second complete bacterial sequence ever sequenced
- First isolated in 1980 from 2/13 men with NGU
- Difficult to culture
- Fastidious with slow growth (>50 days)

Does MG cause Cervicitis and PID?

- Cervicitis – 17 studies (5 new)
  - 9 (53%) significant assoc.
  - 5 (29%) elevated OR, but NS
  - 3 (18%) no association
  - OR range 1.2 – 5.7
  - Suggests an association

- Endometritis/PID – 14 studies (7 new)
  - 3 sero-studies – conflicting
  - 10 PCR-based studies
  - 6 (40%) significant assoc.
  - 3 (21%) elevated OR but NS
  - OR range 2.1 – 6.3
  - Suggests a causal association

What Diagnostic Tests are Available for MG?

- No commercially available diagnostic tests currently approved in US
- Some large medical centers have in-house PCR assays available to general patients, but this is rare.
- In-house PCR assays used in research settings, but not generally available to patients not participating in research studies.
- APTIMA RUO TMA assay often used in research studies, but results cannot be used for treatment decisions. Not currently pursuing FDA approval.
- At least 2 multiplex MG assays are commercially available in Europe
  - Bio-Rad (C/L/CT/MG)
  - Sacace Biotechnologies, CTMG (U M. hominis) for Sacace.
- Cepheid may develop MG test for Genetarget platform, but not on current agenda.
- APT may be pursuing FDA approval

What is the Efficacy of Moxifloxacin (400mg x 7d) against MG?

<table>
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<th>Syndrome</th>
<th>Moxifloxacin dose</th>
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<tr>
<td>Jernberg 2006</td>
<td>PID</td>
<td>400mg x 14 days</td>
<td>93% (100%)</td>
</tr>
<tr>
<td>Bradshaw 2006</td>
<td>STD sx, or partner sx or NS&gt; + or CT+</td>
<td>400mg x 7 days</td>
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CONCLUSION: Moxifloxacin appears to be superior to other treatments for MG, but the drug has not been tested in clinical trials, and resistance may be emerging.

Does MG cause Female Infertility, Adverse Birth Outcomes?

- Infertility – 6 studies (2 new)
  - All but one with elevated ORs (range 2.5 – 6.3)
  - 2 strongest studies show significant association
  - Suggests an association

- Preterm birth – 7 studies (1 new)
  - Adverse birth outcomes rare in studies (4/7)
  - Limited evidence conflicting
  - Insufficient evidence

- Ectopic Pregnancy
  - Single study – no assoc.
  - Insufficient evidence

What is the Efficacy of Azithromycin (AZM1g x 7d) against MG?

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CONCLUSION: Azithromycin appears to be effective against MG, with a 99% cure rate for 7 days of treatment.
Should the recommended therapies for MPC, and/or PID be altered?

**MPC**
- Existing evidence does not support a recommendation to alter the currently recommended therapies for cervicitis.
- MG should be considered in cases of persistent cervicitis and treatment with moxifloxacin 400mg po qd x 7 days should be considered.

**PID**
- Current PID treatment regimens are not effective against MG.
- Given the relatively low prevalence of MG in women with PID, the existing evidence does not support a recommendation to change the current therapies for PID in the absence of diagnostic testing for MG.
- However, clinicians should consider MG in cases that fail to respond to MG within 2-3 days and treat with moxifloxacin 400mg/day x 14 days.
- Where MG testing is available, clinicians should test women diagnosed with PID for MG, and when MG is detected moxifloxacin 400mg/day x 14 days should be prescribed.

**Summary**
- Transgender care: anatomy & history; HIV
- Trich: Vaginal swab NAAT
- CT/GC: Vaginal swab NAAT; Dual therapy for GC
- Genital Warts: Imiquimod 3.75% qhs; HPV counseling
- Emerging pathogens: *M. Genitalium*

**Resources**
- HMC STD Clinic
- HMC Virology Research Clinic – HSV
- CDC website
- [http://www.cdc.gov/mobile/mobileapp.html](http://www.cdc.gov/mobile/mobileapp.html)
- [http://www.doh.wa.gov/YouandYourFamily/illnessandDisease/sexuallytransmitteddisease/expeditedpartnerstherapy.aspx](http://www.doh.wa.gov/YouandYourFamily/illnessandDisease/sexuallytransmitteddisease/expeditedpartnerstherapy.aspx)
- cgardef@uw.edu with questions