What’s New in Sexually Transmitted Infections?

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Objectives

- As a result of participating in this activity, participants will be better able to:
  - Implement current guidelines related to screening and treatment for sexually transmitted infections specific to the HIV-infected population.
  - Apply knowledge of current epidemiology of resistant gonorrhea to screening and management strategies in populations at high-risk.
Off-Label Disclosure

- This presentation will include discussion of the following non-FDA-approved or investigational uses of products/devices:
  - Oral and rectal testing for *N. gonorrhoeae* and *C. trachomatis* with:
    - Hologic Gen-Probe APTIMA Combo 2®
    - BDProbeTec™ ET
    - Roche COBAS® PCR
  - Testing for *T. vaginalis* utilizing:
    - Hologic Gen-Probe APTIMA Combo 2®
    - Roche COBAS® Amplicor PCR
Case

• 35yo black man with a 1 week history of yellow penile discharge and mild dysuria.

• 2 partners in the last 2 months – 1 female/1 male. Last contact 1 week PTA → unprotected receptive oral sex with a female commercial sex worker at a party while drinking and an HIV+ male partner 2 months ago (unprotected receptive and insertive rectal sex, active oral sex/fellatio). Never uses condoms with oral sex, uses them 100% of the time with insertive penile activities (vaginal/anal), and some of the time with receptive anal activities. No drugs or tobacco use. 2 glasses of wine a week. He is in graduate school.
Case continued...

PMH –

• HIV diagnosed Fall 2012
• Primary syphilis in 2010 and Fall 2012 (titer 1:128)
• HSV – 1 and HSV – 2 IGG positive
• Hepatitis A immune
• Hepatitis B naïve
What anatomical sites would you test for gonorrhea and chlamydia?

1. Urethra
2. Throat
3. Rectum
4. All sites for both pathogens
5. Urethra and rectum for both pathogens, throat for gonorrhea only
What anatomical sites would you test for gonorrhea and chlamydia?

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Case

- Treatment:
  - Ceftriaxone 250mg IM x 1
  - Azithromycin 1gm po x 1
Labs

- CD4 670 (29%); VL 2480
- UA – 1.033/mod LE/small bld/4-8 RBC/TNTC WBC; culture negative
- Urine CT positive
- Oral GC positive
- Rectal GC positive, CT negative
- RPR 1:32
Location of Participating Sentinel Sites and Regional Laboratories, Gonococcal Isolate Surveillance Project (GISP), United States, 2011

*NOTE: The Austin site is a regional laboratory only.
Percentage of *Neisseria gonorrhoeae* Isolates that are Ciprofloxacin-Resistant by Sex of Sex Partner, Gonococcal Isolate Surveillance Project (GISP), 1995–2011

*MSM*= men who have sex with men; *MSW*= men who have sex with women only.
Proportion of Isolates with MICs to Cefixime $\geq 0.25 \, \mu g/ml$

$n=52,785$

* $p_{trend} < 0.05$

Preliminary data

Gonococcal Isolate Surveillance Project (GISP)
Proportion of isolates with MICs to Cefixime ≥ 0.25 μg/ml by Region

n=52,785

3.3% (n=68)

* p_trend < 0.05

Preliminary data

Gonococcal Isolate Surveillance Project (GISP)
Proportion of Isolates with MICs to Cefixime \( \geq 0.25 \, \mu g/ml \) by Sex of Sex Partner

\( n=50,873 \)

\[ \frac{\text{Percentage of isolates}}{\text{Years}} \]

- **MSW**
- **MSM**

3.9% (n=64)

* \( p_{\text{trend}} < 0.05 \)

**Note:** MSM = Men who have sex with men; MSW = Men who exclusively have sex with women; Preliminary data.
Neisseria gonorrhoeae Treatment Failure and Susceptibility to Cefixime in Toronto, Canada

Cephalosporin-Resistant Gonorrhea in North America
Treatment failures of *N gonorrhoeae* infections due to strains with reduced susceptibility to cefixime were identified in the study clinic from May 1, 2010, to April 30, 2011.
Results

• **Treatment failures:**
  – 4 of 76 urethral (5.3%)
  – 2 of 7 pharyngeal (28.6%)
  – 3 of 39 rectal (7.7%)

• **Rx failure overall – 6.8% (95% CI – 3.1-12.5%)**
  – If cefixime MIC $\geq 0.12$ – 25%(95% CI 10.7-44.9%)
  – If cefixime MIC <0.12 – 1.9% (95% CI 0.23-6.7%)
  – RR 13.13 (95% CI 2.9-59.72)

Update to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2010: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infections
2010 STD Treatment Guidelines: Gonorrhea (amended)

- Recommended
  - Ceftriaxone 250 mg IM

  Plus (even if chlamydia test negative)

  - Azithromycin 1gm po x 1 or
  - Doxycycline 100mg po BID x 7d
**Alternative Regimens**

<table>
<thead>
<tr>
<th>Cefixime 400mg po x 1</th>
<th>If cephalosporin allergy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plus</td>
<td>Azithromycin 2gm po x 1</td>
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<tr>
<td>Azithromycin 1gm po x 1</td>
<td></td>
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<tr>
<td>Or</td>
<td></td>
</tr>
<tr>
<td>Doxycycline 100mg po BID x 7d</td>
<td></td>
</tr>
<tr>
<td>• TOC in 1 week</td>
<td>• TOC in 1 week</td>
</tr>
</tbody>
</table>

**Test of cure should be performed in 7 days!  MMWR August 10, 2012 / 61(31);590-594**
Resistant Gonorrhea

- If cephalosporin treatment failure
  - ID Consult
  - GC susceptibility testing
  - 250 mg IM Ceftriaxone + 2gm Azithro
    - If patient received alternative regimen initially
  - Ensure partner treatment
  - Report to state and CDC

Case

• 49 yo HIV+ male (CD4 410, HIV VL <48) presents for routine HIV f/u visit
• Reports 4 days of urethral burning.
• 3 male partners in previous 2 months.
  – HIV+ and HIV- partners; +100% disclosure
  – Receptive and insertive anal and oral sex
  – Receptive and insertive fisting
  – No condoms or gloves
NAATS for oral testing

• Oral GC testing:
  – Culture (se – 50%-65%; sp – 99.0 - 99.4%)
  – NAATS (se – 83.6-100%; sp -94.2-98.6%)
    • Gen-Probe APTIMA Combo 2®
    • BDProbeTec™ ET

• PCR not sufficiently specific for use at the oral site

NAATS - Detection of Rectal GC/CT

• GC
  – Culture se 66.7-71.9% and sp 99.7-100%
  – PCR se 91.4-95.8% and sp 96-98.5%
  – SDA se 97.1-100% and sp 96-98.8%
  – TMA se 100% and sp 95.5-98.3%

• CT
  – Culture se 36.1-45.7% and sp 99.4-99.7%
  – PCR se 80.1-95.5% and sp 91.8-98.5%
  – SDA se 92.2-100% and sp 89.6-96.4%
  – TMA se 100% and sp 88.8-95.6%

Case continued...

• Treatment:
  – Ceftriaxone 250mg IM x 1
  – Azithromycin 1gm po x 1

• RPR – nonreactive
• GC (pharynx) – positive
• GC (urine) – positive; CT (urine) – negative
• GC (rectum) – negative; CT (rectum) – positive
• Hepatitis C Ab+; HCV VL <20
STIs Detection Status Based on Urethral Testing Alone - Netherlands

- Detected: 14%
- Not Detected: 86%

Heiligenberg et al, Sexually Transmitted Diseases, Jan 2012
MEDICAL DISPATCHES

SEX AND THE SUPERBUG

The rise of drug-resistant gonorrhea.

BY JEROME GROOPMAN

Gonorrhea mutate in the pharynx, making oral sex far more risky than people think.
Highly active antiretroviral therapy does not completely suppress HIV in semen of sexually active HIV-infected MSM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adjusted OR (95% CI)</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>STI status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pt with STI</td>
<td>29.03 (2.60, 523.53)</td>
<td>0.003</td>
</tr>
<tr>
<td>- Pt without STI</td>
<td>1.0 (referent)</td>
<td></td>
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<tr>
<td>Unprotected IA sex with HIV+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Yes</td>
<td>7.34 (1.59, 47.73)</td>
<td>0.007</td>
</tr>
<tr>
<td>- No</td>
<td>1.0 (referent)</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Politch et al. AIDS 2012, 26:1535-1543
Hepatitis C Infection

1169* HIV+ men seen ≥2 times from 1/2008-6/2009

- 9 men excluded not MSM

1059 (91%) men ≥1 HCV Ab test

- 38 (4%) HCV Ab+ on 1st test at Fenway
- 26 (2%) known HCV Ab+ prior to first Fenway visit
- 995 (94%) HCV Ab negative on 1st test at Fenway

- 379 (38%) ≥1 additional HCV Ab test
- 616 (62%) no additional HCV Ab tests

- 23 (6%) incident HCV Ab positive
- 356 (94%) HCV Ab negative

Case

• KH is a 40+yo WM who presented to ED with fever and sore throat. Sore throat +/- odynophagia x 1 month

• ROS - +sores in mouth, +myalgias, +fever and chills, +cough due to throat irritation. Remainder negative.
More history...

- HIV dx 2004. Last CD4 1100 with VL <50 when last measured. Lost insurance and out of care since 2005
- RUE DVT
- Soc – lives with mom in W-S, no tobacco x 5yr (former 15pkyr), +”social” alcohol use (former heavy use assoc. with DUI 2000), +IV crystal meth (last 1 wk PTA)
Exam

- T-100.7, P – 80, R – 20, BP – 124/80, 100% sat on RA

- WNWD in NAD. OP- mild pharyngeal erythema, 0.5cm ulcer to left of uvula, shoddy submandibular LA. Skin – multiple tattoos.
What key part of the physical examination is missing?

1. Ear exam
2. Mental status exam
3. Genital/Rectal exam
4. Musculoskeletal exam
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Labs and such...

- CBC, hepatic and FBP nl
- Flu-
- UA -
- Blood cx x 4 –
- Throat cx – nl flora
- GC throat cx – neg
- HSV throat cx – neg
- HSV-1 Ab equivocal
- HSV-2 Ab+
- Hep A Ab-, HBsAb-, HbsAg-, HCV Ab-
- UDS - + amphetamines

- CXR – normal
- CT angio – No PTE. Prominent axillary, subpectoral and supraclavicular nodal tissue
- Echo – normal. No veg.
- Patient discharged...
RPR 1:256

3 weeks lapsed between discharge and presentation to clinic
Additional History

• Syphilis in 2004, treated in Atlanta with 2.4 million units of Bicillin. Stage total duration course. + Jarisch-Herxheimer rxn

• Former stripper, sex with men only, 10 partners/6mo, last contact 2 days ago, exposure at all orifices
Clinic Visit

• Throat pain and sores continue

• “Well yes, I do have places on my penis but I thought they were nothing....”

• “BTW...I have ringing in my ears and I don’t think I hear as well as I used to”
Secondary syphilis
Mucous patch of upper lip with typical adherent exudate.

Source: Sexually Transmitted Diseases, second edition
Wisdom & Hawkins
Secondary syphilis
Natal cleft.

Source: Sexually Transmitted Diseases, second edition
Wisdom & Hawkins
Secondary syphilis

Source: Sexually Transmitted Diseases, second edition
Wisdom & Hawkins
Additional work-up

- **LP**
  - WBC 55 (100% mono)
  - RBC 0
  - Protein 38 (15-45)
  - Glucose normal
  - VDRL 1:2

- **Now s/p 10d IV PCN G (in house)**

- **Repeat LP (9 mo)**
  - WBC 1
  - RBC 0
  - Protein and glucose nl
  - VDRL nonreactive
  - Serum RPR 1:8
Syphilis Treatment

- Drug of choice remains penicillin
- Alternatives: doxycycline, ceftriaxone- optimal dose not defined (1 gm IV/IM x 8-10 d for early disease)
- Azithromycin (2 gm)-emerging data on treatment failure, not recommended for tx or prophylaxis until further data available

CDC. MMWR 2010; 59 (RR-12)
Recommended Criteria for CSF Exam

- Neurologic or ophthalmic signs/sx regardless of stage
- Active tertiary syphilis
- Treatment failure
- Some experts advocate CSF exam for RPR $\geq 1:32$ or HIV+ CD4 $< 350$

CDC. MMWR 2010; 59 (RR-12)
TV Incidence and Prevalence

- Sexually transmitted parasite
- 248 million new cases world-wide in 2005 (WHO 2011)
- Estimated prevalence in US:
  - 3.1% in the general female population (2001-4)
    - Prevalence increases with age
    - Highest rates in AA (13.3%; 95%CI 10-17.7%)
    - Symptoms not predictive
  - 8.7% women from 21 states undergoing testing for GC/CT (N=7593)
  - 2.5-23.2% of adolescents
  - 8.6-38% of drug users

TV Prevalence rates for by age

![Bar chart showing prevalence rates by age group.](chart.png)
Trichomonas vaginalis and HIV

- Most common curable STD in HIV+ women
  - 6-44% prevalence
  - 18-36% repeat infection rate (8% in HIV-neg)
- Multiple studies support the epidemiological association between TV and HIV
- HIV-infected women with TV had higher prevalence of HIV RNA in vaginal secretions than those without TV and TV treatment reduced vaginal HIV shedding over a 1-3 month period

Clinical Manifestations of *T. vaginalis*

Abnormal genital discharge, dysuria, urinary frequency, itching, burning, dyspareunia, NGU in men

MOST TRICHOMEONAL INFECTIONS ARE ASYMPTOMATIC!!!
<table>
<thead>
<tr>
<th>Diagnostic test</th>
<th>Technique</th>
<th>Time to result</th>
<th>Specimen</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet Mount</td>
<td>Vag swab with saline microscopy</td>
<td>Minutes, in office</td>
<td>Vag swab</td>
<td>35-82%</td>
<td>99.6-100%</td>
</tr>
<tr>
<td>Culture</td>
<td>Media: Diamond’s, Trichosel, InPouch TV</td>
<td>24-120h; send out</td>
<td>Vag swab, urethral swab, urine, semen</td>
<td>F:75-87%</td>
<td>100%</td>
</tr>
<tr>
<td>APTIMA Trichomonas (GenProbe)</td>
<td>NAAT – TMA to detect species specific 16S rRNA</td>
<td>Hours; send out</td>
<td>Vag swab (F) Urine (F) ThinPrep (F) Urethral swab (M) Urine (M)</td>
<td>96.6-98.4%</td>
<td>98-100%</td>
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<td>87.5%</td>
<td>100%</td>
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<td>96-100%</td>
<td>98.8-99.9%</td>
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<td>95.2%</td>
<td>96.5%</td>
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<td></td>
<td>73.8%</td>
<td>98.4%</td>
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<tr>
<td>Affirm VPIII (BD Diagnostics)</td>
<td>Direct specimen nucleic acid probe assay</td>
<td>45 min; send out or equipped office</td>
<td>Vag swab</td>
<td>83-90.5%</td>
<td>99.8-100%</td>
</tr>
<tr>
<td>OSOM Trichomonas rapid test (Genzyme Diagnostics)</td>
<td>Immunochromatographic capillary flow assay with murine monoclonal antibody</td>
<td>10 min; in office</td>
<td>Vag swab</td>
<td>82-94.7%</td>
<td>98.8-100%</td>
</tr>
</tbody>
</table>

Adapted from Miller and Nyirjesy, Curr Infect Dis Rep 2011 13:595-603; Schwebke JCM Dec 2011; p4106-4111
2010 CDC STD Treatment Guidelines: Trichomoniasis

**New Episode**
- Tinidazole 2 g PO single dose OR
- Metronidazole 2 g PO single dose

-Metronidazole 500 mg po BID for 7 days (alternative)

**Treatment Failure of 2 g metronidazole single dose** *
- Metronidazole 500 mg BID x 7d

**Treatment Failure – Additional Options** *
- Tinidazole or Metronidazole 2 g PO daily x 5d

Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines, 2010. MMWR 2010;59(No. RR-12)
NGU

• 2.5-13% of NGU cases secondary to TV

• 2010 CDC STD Treatment guidelines recommend addition of TV-active agent for persistent/recurrent NGU

• The addition of tinidazole to initial NGU treatment regimen has not demonstrated higher clinical cure rates but does effectively eradicate TV

What about resistant *T. vaginalis*?

6 US Cities, STD Surveillance Network, 2009-2010

4.3% with low-level resistance (MIC 50-100ug/mL) to metronidazole; no mod-
high level resistance to metronidazole or tinidazole resistance!

Treatment Conundrums

5-nitroimidazole resistance

• New evidence that susceptibility testing leading to tailored treatment may have beneficial role for management of women with persistent TV*

5-nitroimidazole allergy

• Alternative regimens (poor efficacy)
• Desensitization

*Bosserman EA et al. Sex Trans Dis 2011; 38(10):983-987
Alternative Treatments

• Various regimens of high-dose 5-nitroimidazoles
  – Tinidazole 1g PO TID + 500mg PV TID x 14d
• Paromomycin (alone or with tinidazole→paromomycin 5% cream – 5g PV qd + Tinidazole 1g PO TID x 14d
• Clotrimazole
• Acetarsol Pessary
• Povidine-Iodine
• Nonoxynol-9
• Zinc-sulfate
• Furazolidone
• Trichofuran
• Other combinations (Tinidazole+Amp+Clotrimazole)
• Vaginal/bladder irrigation
• AVC Tablets (1.05g sulfanilamide, allantoin, aminacrine HCL)
Persistent TV?


• Is TV “undetectable” by culture for undefined period post-treatment?

• When is most appropriate time to retest for TV by culture post-rx?
Resources

www.stdptc.org

www.nnptc.org