STD Update for Clinicians

STD Top 10:
Highlights from the 2015 CDC
STD Treatment Guidelines

Alison O. Marshall, RN, MSN, FNP-C
Boston College Connell School of Nursing
Chestnut Hill, MA
Disclosures

• In the past 12 months, Ms. Marshall has **NOT** had significant financial interests or other relationships with manufacturer(s) of product(s) or provider(s) of service(s) that will be discussed in this presentation.

• This presentation will include discussion of pharmaceuticals or devices that have not been approved by the FDA.
  – “Off-label” use of extra-genital (rectal and pharyngeal) nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia
Goals

• Distinguish relevant updates to epidemiology, diagnosis, and treatment for bacterial, viral, and other STDs

• Highlight areas of 2015 CDC STD Treatment Guidelines that should be read carefully for detailed recommendations
CDC STD Treatment Guidelines Development

• Evidence-based on principal outcomes of STD therapy
  1. Microbiologic eradication
  2. Alleviation of signs & sx
  3. Prevention of sequelae
  4. Prevention of transmission
• Recommended regimens preferred over alternative regimens
• Alphabetized unless there is a priority of choice
• Reviewed April 2013; published 2015
• www.cdc.gov/std/treatment
  • Pocket guides, teaching slides, charts, app

Language in yellow highlighted boxes reflects changes between 2010 and 2015 guidelines
10. **Multi-Drug Resistant Gonorrhea**
CDC sets threat levels for drug-resistant 'superbugs'

By Miriam Falco, CNN
updated 5:48 PM EDT, Tue September 17, 2013

www.cdc.gov/drugresistance/threat-report-2013/

Microorganisms with the threat level of URGENT:

1. C. difficile
2. Carbapenem-resistant Enterobacteriaceae
3. Drug-resistant N. gonorrhoeae

Neisseria gonorrhoeae -- the drug-resistant form of this bacteria causes gonorrhea, the second most commonly reported infection in the United States. Gonorrhea can cause a variety of illnesses in men and women, including infertility. The CDC estimates there are 820,000 infections each year. In nearly a third of the cases, treatment of the sexually-transmitted disease, is hampered by growing antibiotic resistance.

Sexually-transmitted superbug could be major crisis

Frieden said if the current trends continue, "the medicine cabinet may be empty for patients who need them in the coming months and years."

To avoid what Frieden calls a "post-antibiotic" era, where none of the drugs available now would be able to stop the infections, he wants to see the US government and private industry push to develop new antibiotics to fight these superbugs.

Infections in the United States are managed by the Centers for Disease Control and Prevention. By empowering patients to take antibiotics only when necessary, they can help fight antibiotic-resistant infections.

Bacteria can become resistant to antibiotics by mutation. Infections in these resistant bacteria are difficult to treat because they can grow and multiply in the absence of antibiotics, and can make cells in the body more susceptible to infections.

Drug-resistant bacteria

Neisseria gonorrhoeae

HIDE CAPTION

STORY HIGHLIGHTS

• More than 2 million people get antibiotic-resistant infections

(CNN) -- Health officials have been warning us about antibiotic overuse and drug-resistant "superbugs" for a long time. But today the Centers for Disease Control and Prevention is announcing the

Patients should also only take antibiotics when they are really necessary. Changing the way antibiotics are used is perhaps "the single most important action needed to greatly slow the development and spread of antibiotic-resistant infections," Frieden said.

Patients need to demand fewer antibiotics and doctors have to resist patients requests for them when they know they won't work. Also, lowering the use of antibiotics in animals to only when it's
Historical Perspective, Gonococcal Antimicrobial Resistance in United States

(till the 1970s...)

**Gonorrhea Treatment**

Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose  **PLUS**  Azithromycin 1 g orally

* Regardless of CT test result

Doxycycline demoted from recommended to alternative, because of tetracycline resistance in U.S. GISP isolates

CDC 2015 STD Treatment Guidelines

www.cdc.gov/std/treatment
Gonorrhea – Treatment Issues

• Dual therapy may hinder development of antimicrobial resistance

• Limited options in cephalosporin-allergic patients:
  – Spectinomycin is no longer manufactured
  – Consider azithromycin monotherapy, but
    • Requires 2 grams -- GI tolerance issues
    • Resistance likely increasing and treatment failures have been seen
Gonorrhea Treatment Alternatives
Just for Anogenital Infections

**IF CEFTRIAXONE UNAVAILABLE**

- Cefixime 400 mg orally once

**PLUS**

- Dual treatment with azithromycin 1 g

**IN CASE OF ALLERGY TO AZITHROMYCIN:**

- Cefixime 400 mg orally once

**PLUS**

- Dual treatment with doxycycline 100 mg BID x 7 days

**Azithromycin 2 g orally removed as an alternative regimen**

Prior TOC recommendation: Test of cure in 1 week for anyone treated w/ alternative regimens

**New TOC recommendations:** Limit TOC only to pharyngeal GC not treated with recommended regimen, perform TOC at 14 days with either NAAT* or culture

* Not FDA-approved for extragenital testing, but has been validated.
Back-Pocket GC Treatment Regimens: Alternatives for cephalosporin-allergic patients

- Trial conducted in Baltimore, Birmingham, Pittsburgh, San Francisco
- 401 men and women 15 - 60 yrs
- 202 received gent 240 mg IM + azithro 2 g PO: **100% effective**
- 199 received gemiflox 320 mg PO + azithro 2 g PO: **99.5% effective**

**Bottom line**
- Probably fine for urogenital gonorrhea, but trial not powered for extragenital gonorrhea (though it worked in the few cases enrolled)
- Efficacy limited by tolerance: 8% vomited in the gemiflox + azithro group and needed re-treatment with standard cftx + azithro

Kirkcaldy RD et al. *CID* 2014
9. RE-SCREENING FOR STIs IN THOSE PREVIOUSLY INFECTED, REACHES THOSE AT HIGHEST STI RISK
Repeat Testing after an STD infection

- Current CDC STD screening guidelines for GC and CT recommend screening persons at-risk, including those with a prior STD.
- Among sex workers with baseline GC, CT or trichomonas infection, the adjusted HR for any of these at follow up was 2.6 (95% CI 2.1-3.1) (Turner 2010).
- Project RESPECT in US STD clinic patients:
  - 25.8% of women had 1 or more new infections with CT, GC, or Trich at one year of follow up.
  - 14.7% of men had a new GC or CT infection.
  - Conclusion: patients with GC/CT or trich infections should return at 3 months because they are at high risk for new infections (Peterman 2006).
Sexually active female students 15-27 years old, enrolled in the British Prevention of Pelvic Infection (POPI) trial between 2004-06, who self-collected 2 vaginal swab specimens.

“One in four women with chlamydia infection at baseline retested positive, supporting recent recommendations to routinely retest chlamydia positives.”
Repeat Screening after an STD infection

- **Women with CT, GC or trich should be rescreened at 3 months after treatment.**
- **Men with CT or GC should be rescreened at 3 months after treatment.**
- **Patients diagnosed with syphilis should undergo follow up serologic serology per current recommendations.**
- **HIV testing should also be considered in all patients with a prior STD history**
8. TREATING SEX PARTNERS SIGHT UNSEEN (EPT) IS LEGAL (MOSTLY)
Legal Status of Expedited Partner Therapy (EPT)

The information presented here is not legal advice, nor is it a comprehensive analysis of all the legal provisions that could implicate the legality of EPT in a given jurisdiction.

To view information for each state, click on state in the map below. Summary Totals are here.

CDC EPT guidelines

“PDPT can prevent reinfection of index case and has been associated with a higher likelihood of partner notification...”

www.cdc.gov/STD/EPT
Infection During Follow-up Among Patients Completing The EPT Trial

- **Gonorrhea**: Standard care 10.6%, Expedited care 3.4%, P = .02
- **Chlamydia**: Standard care 13.2%, Expedited care 10.8%, P = .17
- **Gonorrhea or Chlamydia**: Standard care 13%, Expedited care 9.9%, P = .04

Golden MR, *NEJM 2005*
Chlamydia, Gonorrhea, and EPT

• EPT is supported by the CDC and permissible in at least 35 states

• Standard partner treatment for chlamydia infection is one oral dose of 1g of the antibiotic azithromycin

• Standard partner treatment for gonorrhea is one oral dose of 1g of the antibiotic azithromycin PLUS one oral dose of 400 mg of cefixime

• EPT has been shown to be safe and effective in the treatment of sex partners

• Most states with long-standing EPT programs also have had no reports of adverse events
A “partner pack” is a method of delivering medication for STDs to partners of diagnosed patients. David Ryder for The New York Times

Recently, while William, 21, was manning the chicken-wing fryer at a fast-food restaurant in suburban Seattle, he pulled aside his sort-of girlfriend, 18, a pizza deliverer there. He had bad news.

He had tested positive for gonorrhea and chlamydia. That meant she was very likely infected.

Loud, insult-fueled cross-accusations ensued. But the conversation did not disintegrate, as might otherwise be expected.
7. The epidemic of syphilis (& HIV co-infection) in MSM continues
HIV and Syphilis Diagnoses Have Increased in Young MSM

- Primary and secondary syphilis rates increased in 70% of areas
- Average increases in young black men
  - HIV: 68%
  - Syphilis: 203%

Torrone et al, JAIDS, 2011.
Syphilis/HIV Co-infection Common

Proportion of MSM Attending STD Clinics with Primary and Secondary Syphilis Co-infected with HIV, STD Surveillance Network (SSuN), 2013

CDC, Sexually Transmitted Diseases Surveillance, 2013
Can We Screen for Syphilis Control?

• Syphilis screening could lead to decreases in MSM population prevalence

\[ R_0 = T \cdot C \cdot D \]

• How do we scale up screening in MSM?

*Stay tuned ...*
Don’t forget the q3mth “triple dip” for at-risk MSM

- HIV/Syphilis/ HepC* Serologies
- Pharyngeal GC NAAT**
- Urinary GC/CT NAAT
- Rectal GC/CT NAAT**

*In HIV-coinfected individuals, screen Hep C at least annually

**Off-label use - not FDA-approved for testing at extragenital sites, but many reference labs have validated the assay for use
6. *Mycoplasma genitalium* has emerged
Mycoplasma genitalium: Epidemiology

• First identified in the early 1980’s
• Cause of male urethritis
  – 15-20% of non-gonococcal urethritis (NGU) cases
  – 20-25% of non-chlamydial NGU
  – 30% of persistent or recurrent urethritis
  – More common than *N. gonorrhoeae* but less common than *C. trachomatis*
  – Co-infection with *C. trachomatis* is not uncommon
• Unknown whether it can cause male infertility or other male anogenital tract disease syndromes
• Pathogenic role in women less clear
  – Found more commonly in those with cervicitis or PID than those without cervicitis or PID
Mycoplasma genitalium: Diagnostics

• Very slow-growing organism
  – Culture can take up to 6 months
  – Only a few laboratories in the world are able to recover clinical isolates

• Nucleic acid amplification testing (NAAT) is the preferred method to detect *M. genitalium*
  – Research settings
  – In-house PCR assays (?)
  – None commercially available (YET)
Mycoplasma genitalium: Treatment

• 7-day doxycycline regimen recommended for treatment of urethritis is largely ineffective against *M. genitalium* with a median cure rate of approximately 31%

• 1 gram single dose azithromycin significantly more effective against *M. genitalium* than doxycycline in two randomized trials
  – However, resistance to azithromycin appears to be rapidly emerging: median cure rate for both men and women is approximately 85%, but was only 40% in the most recent trial
  – Individuals with treatment failures after 1g azithromycin regimen frequently have macrolide resistant strains suggesting that single dose azithromycin therapy may select for resistance

• Moxifloxacin (400mg x 7, 10 or 14 days) successfully used to treat *M. genitalium* treatment failures in men and women, with cure rates of 100% in initial reports
  – However, moxifloxacin has been used in a relatively small number of cases and the drug has not been tested in clinical trials
5. *Trichomonas vaginalis* diagnostics have improved
Newer Testing Options for Trich

• Microscopy is inferior to new options, including
  – Rapid antigen testing (OSOM)
  – Nucleic acid amplification testing
    • APTIMA TMA *Trichomonas vaginalis* assay
    • BD ProbeTec TV Qx Amplified DNA assay
    • May use same specimen types as used with gc/chl NAATs (i.e. vaginal swab, endocervical swab, urine)

<table>
<thead>
<tr>
<th>Test</th>
<th>Sens</th>
<th>Spec</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTIMA TMA</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>OSOM</td>
<td>90%</td>
<td>100%</td>
</tr>
<tr>
<td>Culture</td>
<td>83%</td>
<td>100%</td>
</tr>
<tr>
<td>Wet prep</td>
<td>56%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 3. Differences in test sensitivity stratified by the presence or absence of vaginal symptoms.

<table>
<thead>
<tr>
<th>Test method</th>
<th>Sensitivity, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (n = 330)</td>
</tr>
<tr>
<td>Wet mount</td>
<td>50.8 (37.7–63.9)</td>
</tr>
<tr>
<td>Culture</td>
<td>75.4 (62.7–85.5)</td>
</tr>
<tr>
<td>Rapid test</td>
<td>82.0 (70.0–90.6)</td>
</tr>
<tr>
<td>TMA</td>
<td>98.4 (91.2–99.9)</td>
</tr>
</tbody>
</table>

NOTE. The comparator was any test result positive for *Trichomonas vaginalis* infection. TMA, transcription-mediated amplification.
Trich Testing in Men

• No approved point of care tests
  – Wet prep not sensitive

• Culture available: urethral swab, semen or urine sediment
  – No conclusive studies on sensitivity/specificity

• Urine and urethral swab NAAT offered through certain labs using analyte-specific reagents (check before sending)

**MSM- *T. vaginalis* does not infect oral sites, and rectal prevalence is low. Do not test these sites.
4. GENITAL HSV EPIDEMIOLOGY IS CHANGING
NHANES HSV2 Seroprevalence

![Graph showing NHANES HSV2 Seroprevalence over different age groups and time periods.]

Johnson et al. *NEJM* 321:7-12, 321, 1989
Schillinger et al. *STD* 31:753-60, 2004
Xu et al. *JAMA* 296:964-73, 2006
Xu et al. *MMWR* 59:456-9, 2010
Bradley et al. *JID* 209:325-33, 2014
“Tip of the Iceberg”

9.2% Recognized infection

90.8% Unrecognized and asymptomatic infection

Iceberg represents persons with HSV-2 antibody

Almost 1 in 10 adolescents who 10 years ago already would have acquired HSV1 earlier in life now are vulnerable to getting a primary infection as they enter their sexually active years.

Kimberlin, JID 2013
What About Genital HSV-1?

• **HSV1 now causes MOST of first genital HSV episodes in young adults**
  – Among >3400 HSV double-seronegative women 18-30 yrs from control arm of herpes vaccine trial who acquired disease during a 20 month period:
    • 5.3% became infected
    • HSV1 2.3x *more common* than HSV2 infection
    • Genital HSV1 2.5x *more common* than oral HSV1
  – Increasing proportion of anogenital herpetic infections have been attributed to HSV-1 infection in women and MSM

• Primary genital HSV1 and HSV2 remain *indistinguishable* clinically, and are treated with the same antiviral regimens

• Genital HSV1 does not recur as often as genital HSV2

What are the implications for genital HSV vaccine development?

Bernstein DI et al., *CID* 2013
Whitley RJ, *CID* 2013
Ryder N et al., *STI* 2009
Roberts CM et al., *STD* 2003
They are in the majority, not the minority ...
3. HPV9 VACCINE ROLL-OUT THIS YEAR
www.cdc.gov/vaccines/acip/
2. HIV PREVENTION INCLUDES PrEP FOR THOSE AT HIGHEST RISK FOR ACQUISITION
MSM in SF City Clinic
Diagnosed with Rectal Chlamydia or Gonorrhea 2003-05

HIV Seroconversion by Number of Prior Rectal Infections

<table>
<thead>
<tr>
<th>Rectal Chl or GC</th>
<th>Annual HIV Incidence</th>
<th>Adjusted HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>2.25%</td>
<td>--</td>
</tr>
<tr>
<td>2 or more episodes</td>
<td>15.00%</td>
<td>8.81</td>
</tr>
</tbody>
</table>

Bernstein et al. JAIDS, 2010
MSM in SF City Clinic
Diagnosed with Rectal Chlamydia or Gonorrhea 2003-05

HIV Seroconversion by Number of Prior Rectal Infections

<table>
<thead>
<tr>
<th>Rectal Chl or GC</th>
<th>Annual HIV Incidence</th>
<th>Adjusted HR</th>
<th>Still HIV Uninfected</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>2.25%</td>
<td>--</td>
<td>97.75%</td>
</tr>
<tr>
<td>2 or more episodes</td>
<td>15.00%</td>
<td>8.81</td>
<td>85.00%</td>
</tr>
</tbody>
</table>

Bernstein et al. JAIDS, 2010
HIV Treatment as Prevention

Antiretroviral treatment should be offered to all HIV-infected persons not only to provide benefit to individual health but also to reduce transmission to sex partners.

HIV pre-exposure prophylaxis should be available to HIV-negative men and women who are sexually active or injecting illicit drugs who are at substantial risk of HIV infection. All clients requesting PrEP should be counseled that high levels of adherence are needed for the best efficacy.


http://www.cdc.gov/hiv/prevention/research/prep/
Prescribing PrEP: CDC Guidance for MSM, Heterosexual Couples, IVDUs

<table>
<thead>
<tr>
<th>Component</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk assessment</td>
<td>PrEP indicated for those at high HIV risk</td>
</tr>
<tr>
<td>Eligibility</td>
<td>HIV negative, adequate renal function</td>
</tr>
<tr>
<td>Dosing</td>
<td>1 tenofovir/emtricitabine tablet, once daily</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Testing for HIV every 3 mos&lt;br&gt;Counseling on risk reduction and testing creatinine at 3 mos and then annually&lt;br&gt;Testing for STIs every 6 mos, even if asymptomatic</td>
</tr>
<tr>
<td>Discontinuation</td>
<td>PrEP not meant for lifelong administration but rather for periods of highest risk</td>
</tr>
</tbody>
</table>
2. HIV prevention includes PrEP for those at highest risk for acquisition
3. HPV9 vaccine roll-out this year
4. Genital HSV epidemiology is changing
5. *Trichomonas vaginalis* diagnostics have improved
6. *Mycoplasma genitalium* has emerged
7. The epidemic of syphilis (& HIV co-infection) in MSM continues
8. Treating sex partners sight unseen (EPT) is legal (mostly)
9. Re-screening for STIs in those previously infected, reaches those at highest STI risk
10. The specter of MDR GC

Drum roll please ...
1. CDC STD TREATMENT GUIDELINES
Sexually Transmitted Diseases Treatment Guidelines, 2015

Misnomer!
- Prevention
- Screening
- Counseling
- Management

AND
- Treatment Guidelines

- Harmony with USPSTF screening guidelines on gonorrhea/chlamydia in adolescents
- New hepatitis C screening recommendations for HIV+ MSM
- New information on clinical management of transgender men and women
Want to know more about STDs?

*There’s an app for that.*

CDC STD Treatment Guidelines App for Apple and Android

Available now, **FREE!** (accept no competitors)

Search “STD Treatment” in App store
NEW!!!!
- Provides STD clinical consultation services within 1-5 business days, depending on urgency, to healthcare providers nationally
- Your consultation request is linked to your regional PTC’s STD faculty
- Just a click away!
- www.STDCCN.org
References

- CDC. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2010;59(No. RR-12).
- CDC. Sexually transmitted diseases treatment guidelines. MMWR Recomm Rep 2015;61(Supp 8).
References con’t


References con’t