Optimizing STD Prevention & Care in the U.S.
What’s Hot in the STD Treatment Guidelines

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## Disclosure

<table>
<thead>
<tr>
<th>Gail Bolan, M.D.</th>
<th>Commercial Interest</th>
<th>Role</th>
<th>Status</th>
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<tbody>
<tr>
<td>Nothing to disclose</td>
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Objectives

- Identify four areas of STD clinical uncertainty in the 2015 STD Treatment Guidelines
- List three STD treatment recommendation changes in the 2015 STD Treatment Guidelines
- Discuss two new STD diagnostic options in the 2015 STD Treatment Guidelines
Overview

- STD treatment guidelines history
- Changing landscape of STDs in the United States
- What’s hot in STD treatment and management
  - USPSTF chlamydia screening for young females
  - Treatment concerns for gonorrhea
  - Syphilis in pregnancy
  - Emerging Issues:
    - Genital Herpes
    - *Trichomonas vaginalis*
    - *Mycoplasma genitalium*
- Provision of quality STD clinical services
2015 STD TREATMENT GUIDELINES
Clinical Practice Guidelines We Can Trust

Robin Graham, Michelle Mancher, Dianne Miller Wolman, Sheldon Greenfield, and Earl Steinberg, Editors; Committee on Standards for Developing Trustworthy Clinical Practice Guidelines; Institute of Medicine
This PDF is available from the National Academies Press at:
http://www.nap.edu/catalog/13058/clinical-practice-guidelines-we-can-trust

- Be based on a systematic review of the existing evidence;
- Be developed by a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups;
- Consider important patient subgroups and patient preferences, as appropriate;
- Be based on an explicit and transparent process that minimizes distortions, biases, and conflicts of interest;
- Provide a clear explanation of the logical relationships between alternative care options and health outcomes, and provide ratings of both the quality of evidence and the strength of recommendations; and
- Be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations.
Want to know about 2015 STD Treatment Guidelines? There’s an app for that.

- CDC Treatment Guidelines App for Apple and Android
- Available now, FREE!
  - (accept no competitors)
STD Tx Guide Mobile app – New look

- Gonorrhea
- Bacterial Vaginosis
- Candidiasis - Vulvovaginal
- Cervicitis
- Chancroid
- Chlamydia
- Epididymitis
- Granuloma Inguinale
- Hepatitis

Recommended Regimen
- Ceftriaxone 250 mg IM in a single dose
- Azithromycin 1 g orally in a single dose

Alternative Regimen
- If ceftriaxone is not available
- Cefixime 400 mg orally in a single oral dose
- Azithromycin 1 g orally in a single dose
CHANGING LANDSCAPE OF STDs IN THE UNITED STATES
Main Messages:

1. CDC’s annual STD report finds that overall reported cases for chlamydia, gonorrhea and syphilis are increasing; some at an alarming rate

2. Young people are still at the highest risk of acquiring an STD and most vulnerable to their damaging effects

3. Greater awareness and action is needed at all levels to ensure good health for the nation’s youth and others disproportionately impacted by STDs
2014 Surveillance Report Overview

Case rate increases seen from 2013 - 2014:

- **Chlamydia**: 2.8% with 1,441,789 cases reported in 2014
  - Driven by a 6.8% increase among men
  - 1.3% increase among women
- **Gonorrhea**: 5% with 350,062 cases reported in 2014
  - Driven by a 10.5% increase among men
  - 0.4% decrease among women
- **P & S syphilis**: 15.1% with 19,999 cases reported in 2014
  - Increases seen in MSM, MSW, women
  - MSM accounted for 83% of P&S cases
- **Congenital syphilis**: total of 458 cases
  - Decreased from 2008-2012, increased slightly in 2013 and then rose by 27.5% in 2014
  - Increased in all regions with largest increases in the NE and West
WHAT’S HOT IN STD TREATMENT AND MANAGEMENT
STD Prevention – Key Principles

- Risk Assessment and counseling to reduce STD acquisition
- Screening of asymptomatic persons
- Diagnosis and treatment of symptoms
- Management of sex partners
- Vaccination
  - HPV
  - Hepatitis A & B
STD Prevention - The Clinicians’ Role

- A welcoming environment
- Routine sexual history and risk assessment
- Screen, appropriately
  - Appropriate anatomic sites with recommended tests
  - Alcohol, drug use, tobacco, depression, intimate partner violence
- Assure appropriate vaccination status (HPV, HBV/HAV)
- Prevention messages--condoms, HIV pre- and post-exposure prophylaxis (PrEP, PEP)
- Diagnosis and treatment
- Provide or refer partner services
- Report cases in accordance with state and local statutory requirements; keep reports confidential
Chlamydia—Rates of Reported Cases Among Women by Age Group, 2004–2015*

Average annual percent change during 2011–2015

Rate per 100,000

20–24: ↑0.7%

15–19: ↓3.7%

25–29: ↑4.9%

30+: ↑6.3%

*2015 data preliminary as of July 18, 2016
Possible explanations for declining rates of Chlamydia among females 15-19 yrs old

- Less clinical visits to screen because of:
  - Changes in Pap smear recommendations
  - Increase in LARC use
- Less access to free screening because of co-pays when females < 26 yrs are on parents health plans
- Less testing by providers b/c not considered a priority clinical prevention service
- Reduction in incidence of CT
Chlamydia — Screening Coverage Trends Among Sexually-Active Women,* by Age and Plan, HEDIS, 2001–2014

*Among women enrolled in commercial or Medicaid plans who had a visit where they were determined to be sexually active

Number of female family planning users aged 15–19 years tested for chlamydia and proportion tested, Title X Family Planning, 2005–2014

Average annual percent change during 2011–2014

- 10.6%

No change
STD Screening for Adolescent and Young Females

- **Sexually active adolescents & women < age 25**
  - ✔ Annual chlamydia and gonorrhea screening
  - ✔ HIV serology if no previous test and annual if risk
  - ✔ Syphilis serology if risk (high community prevalence)
  - ✔ Consider HSV type-specific serology if partner with genital herpes
  - ❖ No routine screening for trich, MG, BV, or HPV recommended

- **What about screening older women?**
  - ▪ If increased risk: New or multiple sex partners, partner with concurrent partners, or partner with an STI
  - ▪ If increased clinic or community prevalence

CDC 2015 STD Tx Guidelines and USPSTF 2014
What About Screening Heterosexual Men?

- **Screening men**
  - No documented substantial secondary prevention in women
  - Costly
  - Consider in certain venues with high prevalence: corrections, STD clinics, teen clinics

- **Highest risk: Partners of chlamydia-infected females**
  - Focus is on partner services
Evolving Landscape of EPT, 2006 – July 2016: Legal Status Summary

- EPT is Permissible
- EPT is Likely Prohibited
- EPT is Potentially Allowable
EPT Packs in WA State

Information provided with EPT

- Information about medications, allergies & STD
- Advice about complications and need for care (e.g. PID)
- Where to seek care
Or Send a Love Letter…

A past sexual partner may have exposed you to…

- Genital Warts
- Pubic Lice (Crabs)

Time of exposure reported as 1 week ago

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e-Card from a concerned friend re: your health - via inSPOT
getcheked@inspot.org

Sent: Thursday, February 26, 2015 2:18 PM
To: hliss@uw.edu

I got screwed while screwing, you might have too.

Get checked for Crabs and Scabies if you haven't recently. www.inspot.org

Sorry!

This is from a friend at inSPOT the [STD] Internet Notification Service for Partners Or Tricks.

www.inspot.org
www.dontspreadit.com
Chlamydia & Gonorrhea Diagnostic Tests

- Nucleic acid amplification tests (NAAT) recommended for men & women
- Optimal specimen: first-catch urine in men and vaginal swabs in women
- NAAT optimal for rectal and pharyngeal testing; not FDA approved but commercially available & validation protocols available for local labs
- Limitations: no antibiotic resistance testing with NAAT (need culture)

http://www.cdc.gov/mmwr 2014
Chlamydia Treatment

- Effectiveness of azithromycin may be less than doxycycline
  - Systematic review (Kong FY Clin Infect Dis 2015):
    - Possible small increased efficacy of up to 3% for doxy compared with azithro for treatment of urogenital chlamydia
    - 7% increased efficacy for doxycycline for treatment of symptomatic urethral infection in men
      - Double-blind, placebo-controlled trials needed

- Doxycycline delayed release 200 mg tablets

- Amoxicillin moved to alternative regimen in pregnancy
  - In vitro studies: Penicillin induces persistent viable noninfectious chlamydia that can revert to a replicative form
  - Early amoxicillin studies in pregnancy had major limitations
  - RCT by Kacmar et al showed higher test of cure using azithromycin vs. amoxicillin (95% vs. 80%)
TREATMENT CONCERNS FOR GONORRHEA
Antibiotic Resistance Threats in the U.S., 2013

Seven Threat Assessment Criteria:
- Clinical impact
- Economic impact
- Incidence
- 10-year projection of incidence
- Transmissibility
- Availability of effective antibiotics
- Barriers to prevention

Three Urgent Threats:
- *Clostridium difficile*
- *Carbapenem-resistant Enterobacteriaceae*
- Drug-resistant *Neisseria gonorrhoeae*
Percentage of *Neisseria gonorrhoeae* isolates with reduced cefixime susceptibility†

Gonococcal Isolate Surveillance Project (GISP), 2006–2015*

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>2006</td>
<td>0.05</td>
</tr>
<tr>
<td>2007/2008</td>
<td>1.0</td>
</tr>
<tr>
<td>2009</td>
<td>1.5</td>
</tr>
<tr>
<td>2010</td>
<td>2.0</td>
</tr>
<tr>
<td>2011</td>
<td>2.0</td>
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<tr>
<td>2012</td>
<td>1.5</td>
</tr>
<tr>
<td>2013</td>
<td>0.5</td>
</tr>
<tr>
<td>2014</td>
<td>1.0</td>
</tr>
<tr>
<td>2015*</td>
<td>0.5</td>
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†Minimum inhibitory concentration (MICs) ≥0.25 µg/ml
*2015 data are preliminary as of March 7, 2016
†† Cefixime susceptibility not tested in 2007 and 2008

Revised Tx Recommendations
12/2010
Increased Ceftriaxone to 250 mg from 125 mg

Revised Tx Recommendations
8/2012
Dual therapy for GC
Proportion of Gonorrhea-Infected Patients treated with a CDC-Recommended Antibiotic Regimen for Gonorrhea

Data Source:
- SSuN
- AAPPS

*Based on 6 months of data
2015 CDC Treatment Recommendations for Gonococcal Infections

- Ceftriaxone 250 mg IM x 1
  PLUS
- Azithromycin 1 g po x 1

Alternatives
If ceftriaxone not available or for EPT:
- Cefixime PLUS azithromycin 1 g
If cephalosporin allergy:
- Gentamicin (240mg IM or 5 mg/kg IM) /azithro 2 g PO
  or
- Gemifloxacin 320 mg PO /azithro 2 g PO

TOC if alternative regimen used for pharyngeal GC at ~14 days
If treatment failure, perform culture, AST and retreat
SYPHILIS IN PREGNANCY
Congenital Syphilis (CS) Rate and Rate of Primary and Secondary (P&S) Syphilis Among Females, United States, 2008–2015*

*2015 data are preliminary as of July 18, 2016
### Characteristics of Mothers Who Gave Birth to Infants with Congenital Syphilis, United States, 2014

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number (N=458)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not receive prenatal care</td>
<td>100</td>
<td>21.8%</td>
</tr>
<tr>
<td>Received prenatal care (N=314, 68.6%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>135</td>
<td>29.5%</td>
</tr>
<tr>
<td>Treated &lt;30 days prior to delivery</td>
<td>78</td>
<td>17.0%</td>
</tr>
<tr>
<td>Non-penicillin therapy</td>
<td>3</td>
<td>0.7%</td>
</tr>
<tr>
<td>Inadequate regimen for stage</td>
<td>13</td>
<td>2.8%</td>
</tr>
<tr>
<td>Adequate treatment</td>
<td>43</td>
<td>9.4%</td>
</tr>
<tr>
<td>Unknown treatment status</td>
<td>42</td>
<td>9.2%</td>
</tr>
<tr>
<td>Unknown prenatal care status</td>
<td>44</td>
<td>9.6%</td>
</tr>
</tbody>
</table>
## Characteristics of Mothers Who Gave Birth to Infants with Congenital Syphilis and Did Not Receive Treatment, United States, 2014

<table>
<thead>
<tr>
<th>Mothers with prenatal care but no treatment</th>
<th>Number (N=135)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never tested during pregnancy</td>
<td>21</td>
<td>15.6%</td>
</tr>
<tr>
<td>1st test negative, later test positive</td>
<td>52</td>
<td>38.5%</td>
</tr>
<tr>
<td>Positive test, but not treated</td>
<td>62</td>
<td>45.9%</td>
</tr>
</tbody>
</table>
Algorithm for reverse sequence syphilis screening

If incubating or primary syphilis is suspected, treat with benzathine penicillin G 2.4 million units IM x 1 and/or repeat in 1-2 weeks

Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to CDC’s STD Treatment Guidelines if not previously treated

If at risk for syphilis, repeat RPR in 2 to 4 weeks
Syphilis Treatment
Primary, Secondary, Early Latent

- Penicillin treatment of choice +/- HIV
  - Benz PCN 2.4 mu IM x 1
- Penicillin is the only recommended treatment in pregnancy
- PCN alternatives in non-pregnant patients
  - Doxycycline, ceftriaxone
  - Azithromycin 2 gm (A2058G mutation/tx failure)
    - MSM>MSW
    - Do not use azithromycin in MSM or pregnancy
- PCN shortages
EMERGING ISSUES:
GENITAL HERPES
TRICHIOMONAS VAGINALIS
MYCOPLASMA GENITALIUM
Genital Herpes

- Increasing proportion of anogenital infections HSV-1 (young females, MSM)
- IgM testing not useful
- Type specific serologic tests
  - HerpeSelect HSV-2 ELISA may be false + at low index values (1.2-3.5) - confirmed with Biokit or WB
  - HerpeSelect HSV-1 ELISA insensitive for HSV-1 (80%)
- No change in recommended therapy
  - Famiclovir is out of alphabetical
Genital Herpes

- Increasing proportion of anogenital infections are HSV-1
  - Young females and MSM
- Type specific PCR is the preferred GUD diagnostic test
- IgM testing not useful
- Type specific serologic tests indicated for:
  - Recurrent or atypical genital symptoms with negative HSV PCR
  - Clinical diagnosis of genital herpes without lab confirmation
  - Partner with genital herpes
  - HerpeSelect HSV-2 ELISA may be false + at low index values (1.2-3.5)- confirm with Biokit or Western Blot
  - HerpeSelect HSV-1 ELISA insensitive for HSV-1 (80%)
- No change in recommended therapy
  - Famiclovir is out of alphabetical
**Trichomonas vaginalis**

- Test in women with vaginal discharge
- Consider screening in high prevalence settings
  - STD clinics, corrections
  - No data if screening/treatment reduces adverse health events or reduces community burden of infection
- Retesting 3 months after treatment
- Treatment: Metronidazole or Tinidazole 2 gm
- Management of persistent infection
  - Up to 17% at 3 months
  - Reinfection from untreated partner is common
  - Infection with MTZ-resistant strain: ~4-10%
    - Tinidazole-resistant ~1%
    - No clear relationship to clinical treatment failure
  - Susceptibility testing if resistance suspected (404-718-4141)
“New” Testing Options for Trich

- **Rapid antigen test (Genzyme)**
  - Significantly better than wet mount
  - Results in 10 minutes

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>OSOM</td>
<td>83.3%</td>
<td>98.8%</td>
</tr>
<tr>
<td>Wet prep</td>
<td>71.4%</td>
<td>100%</td>
</tr>
</tbody>
</table>

- **Nucleic Acid Amplification Test* (Gen-Probe)**
  - May use same specimen type as used with CT/GC NAAT for females
  - Not FDA cleared for use in men

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>95.2%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Vaginal/cervical swab</td>
<td>100%</td>
<td>99.0% to 99.6%</td>
</tr>
</tbody>
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- Consider a molecular test-resolved algorithm (negative wet prep followed by NAAT)

*Schwebke, J Clin Micro 2011*
Trichomonas and HIV

- TV increases genital shedding of HIV
  - Increased risk of preterm birth, PID, vertical HIV transmission
  - Treatment of TV decreases HIV genital shedding
- Routine screening of HIV infected women
  - At entry to care
  - Annually if sexually active
  - At first prenatal visit if pregnant
  - Rescreen 3 months after therapy
- Treatment issues
  - Single dose MTZ 2 g PO not as effective as 500 mg PO BID x 7 days
  - Preferred regimen is 7 day course
Role of *Mycoplasma genitalium*

- Good evidence for role in urethritis (20%)
- May play role in cervicitis, PID, infertility, preterm delivery
- No commercially-available test for *M. genitalium* (in house NAATs)

Treatment implications

- Azithromycin is better than doxycycline because of resistance to doxycycline but new concerns of emerging resistance to Az
- Conflicting data on single dose vs extended dosing
- Moxifloxacin 400 mg po for 7-14 days has been studied as an alternative (cure rates 85-100%)
Guidelines for the Provision of Quality STD Clinical Services
History of STD Clinical Practice Guidelines

- 1991 STD Clinical Practices Guidelines
- 2005 Program Operation Guidelines: Medical and Laboratory Services
- Focus was on STD clinics and programs
Levels of STD Clinical Care Definitions

- **Basic STD Care:** Delivery of basic recommended STD clinical preventive services:
  - RA, screening and treatment of those with asymptomatic infection
  - Basic partner services (BYOP, EPT) and counseling, as needed
  - Treatment of patients with non-complex symptomatic infection

- **Specialized STD Care:** Delivery of more confidential, comprehensive and complex STD clinical services - including basic care plus:
  - On-site stat diagnosis (e.g. Gram stain, RPR)
  - Advanced diagnostics (e.g. gonorrhea culture, extra genital GC/CT NAATS)
  - On-site injectable antibiotics to treat syphilis and gonorrhea
  - Offers same day service for those likely to be infected (those with symptoms suggestive of an acute STD and those who report a partner with an acute STD)
  - Offers culturally expert care to those at highest risk of STD (youth and LGBT)
  - Ensures protection of confidentiality
More to Come... Stay Tuned!

- **HIV Pre-exposure Prophylaxis (PrEP)**
  - Ipergay study showed promise with peri-coital dosing
  - Long acting depo formulations
  - Vaginal microbicides & vaginal rings

- **GC**
  - Molecular tests with resistance markers

- **Syphilis**
  - Rapid testing

- **HPV testing instead of Pap?**
- **Extra-genital screening in women?**
- **Rectal Chlamydia resistance to Azithromycin?**
- **HSV and CT vaccines?**
- **Living STD Treatment Guidelines document?**
Know your STD Clinical PTC

STD Clinical Prevention Training Centers

- University of Washington PTC
- Denver PTC
- St. Louis PTC
- Ratelle PTC
- New York City PTC
- PTC at Johns Hopkins
- California PTC
- AL/NC PTC
STD Clinical Consultation Network (STDCCN)

- Provides STD clinical consultation services within 1-3 business days, depending on urgency, to healthcare providers nationally
- Your consultation request is linked to your regional PTC’s expert faculty
- Just a click away! www.STDCCCN.org
Take-Home Messages

- Screen, appropriately!
- Rescreen for chlamydial and gonococcal infections 3 months after treatment
- Be aware of antibiotic-resistant GC
- Syphilis: it’s not going away and know about the EIA syphilis test

Sexual health
- Vaccinate for HPV (but continue Pap test screening) and HBV
- Prevention messages including condoms
- PrEP
Save the Date!

2016 STD Prevention Conference

Atlanta, GA
September 20-23, 2016
www.cdc.gov/stdconference/

A collaborative conference between
- Centers for Disease Control & Prevention
- American Sexually Transmitted Diseases Association
- National Coalition of STD Directors
- American Sexual Health Association
- Pan American Health Organization
- Public Health Agency of Canada
Thank you!
gyb2@cdc.gov

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.