What's New in the 2015 CDC STD Treatment Guidelines

Ina Park, MD, MS
California STD/HIV Prevention Training Center
UCSF Dept of Family and Community Medicine
STD Control Branch
California Department of Public Health

Outline

- Overview of CDC STD Treatment Guidelines Development Process
- Top 10 updates for primary care providers
  - 1) Screening recommendations for women
  - 2) Screening for men who have sex with men
  - 3) Recommendations for GC/CT diagnostic tests
  - 4) New-ish chlamydia treatment
  - 5) Changes to gonorrhea recommended/alternative therapy
  - 6) Partner management guidelines
  - 7) Rescreening and HIV testing after an STD
  - 8) HPV vaccine
  - 9) Primary HPV screening
  - 10) New STI: Mycoplasma genitalium and Bonus: ? Ebola?

Development of CDC STD Treatment Guidelines

- Enlistment of Subject Matter Experts
- Systematic Review of Evidence
- Background papers Tables of evidence
- Guidelines Meeting, April 2013
- Answer the "Key Questions"
- Rate the quality of the evidence
- Identify critical gaps in knowledge (research agenda)
- Write the Guidelines document

Online: www.cdc.gov/std/treatment

Disclosures

• None
1) STD Screening for Women

Sexually Active adolescents & up to age 25
- Routine **chlamydia** and **gonorrhea** screening
- Other STDs and HIV based on risk

Women over 25 years of age (non incarcerated)
- STD/HIV testing based on risk (new partner, multiple partners, partner w/ other partners, transactional sex, drug use)

Pregnant women
- Chlamydia
- Gonorrhea (<25 years of age or risk)
- HIV
- Syphilis serology
- HepBsAg
- Hep C (if high risk)

CDC 2014 STD Tx Guidelines-Draft at www.cdc.gov/std/treatment

2) STD Screening for MSM*

At LEAST annually:
- HIV
- Syphilis
- Urine GC and CT (NAAT)
- Rectal GC and CT (receptive anal)
- Pharyngeal GC (receptive oral)
- Hep C if IDU or other risk factor

Anal Cancer in HIV+ MSM: Annual digital rectal exam may be useful, some centers perform anal Pap and HRA

More frequent (3-6 months) if patient t or their sex partners have multiple partners, uses methamphetamine, or sexual performance enhancing drugs

CDC 2014 (draft recommendations)

3) Vaginal Swab is preferred specimen type for women

**Diagnostics for GC/CT**

**MMWR** Recommendations and Reports / Vol. 63 / No. 2
March 14, 2014

**Recommendations for the Laboratory-Based Detection of Chlamydia trachomatis and Neisseria gonorrhoeae — 2014**

NAATs recommended for detection of genital tract infections in men and women – with and without symptoms
- highly sensitive and specific compared to culture
- less dependent on specimen collection and handling

Optimal specimen types are:
- First catch urine for men, swabs for rectal/pharyngeal STDs in MSM
- Self collected vaginal swabs from women
Chlamydia

- Updated estimates: 2.8 million cases in US annually
- Hetero male screening: Still not routinely recommended, certain venues only (corrections, STD clinics, etc)
- Addition of a new (ish) treatment regimen

**Recommended treatment (non-pregnant):**
- Azithromycin 1 g orally in a single dose
- Doxycycline 100 mg orally twice daily for 7 days

**Recommended treatment (pregnant):**
- Azithromycin 1 g orally in a single dose
- Amoxicillin 500 mg po TID x 7 days

4) Chlamydia Treatment

**Proposed Changes**

**Additional Alternative Regimen (non-pregnant):**
- Doxycycline (delayed release) 200 mg QD x 7 d
  - Equally efficacious to BID doxy, less GI side effects
  - More $$$$

**Proposed Alternative Regimen (PREGNANCY):**
- Amoxicillin 500 mg po TID x 7 days
  - CT persistence documented in vitro after treatment prompted removal from recommended to alternate

Gonorrhea Treatment

**Pre-Antibiotics**
- 5 weeks of rest
- Avoid alcohol
- Avoid sex

**Urethral Dilation**
- 2 weeks of urethral irrigation

- Still recommended today
5) Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose PLUS*

Azithromycin 1 g orally (preferred) or Doxycycline 100 mg BID x 7 days

• Regardless of CT test result

Proposed: Move doxycycline from recommended to alternative for dual therapy

CDC 2010 STD Treatment Guidelines
www.cdc.gov/std/treatment

ARS audience poll:
A 25 year old MSW was treated presumptively for urethritis with azithromycin. His GC test result returns positive 4 days later, what do you do???

A. Do nothing, the azithromycin alone is good enough
B. Treat him with just ceftriaxone
C. Treat him with ceftriaxone and azithromycin

What does dual therapy mean?

• Ceftriaxone and azithromycin administered on the same day
• Preferrably simultaneously and under direct observation

Gonorrhea Treatment Alternatives
Anogenital Infections

ALTERNATIVE CEPHALOSPORINS:
• Cefixime 400 mg orally once
  PLUS
• Dual treatment with azithromycin 1 g (preferred) or doxycycline 100 mg BID x 7 days, regardless of CT

IN CASE OF SEVERE ALLERGY:
Gentamicin 240 mg IM or + azithromycin 2g PO
OR
Gemifloxacin 320 mg orally + azithromycin 2g PO
Alternative Urogenital GC Regimens

- Non-comparative randomized trial in adults with urethral or cervical gonorrhea
  1. Gentamicin 240 mg IM + azithromycin 2 g PO, or
  2. Gemifloxacin 320 mg PO + azithromycin 2 g PO
- Rationale for regimens
  ▪ Additive effect between gentamicin and azithromycin (in vitro)
  ▪ Gemifloxacin more active against GC with known ciprofloxacin resistance
  ▪ Drugs already available in U.S.
- Per-protocol efficacy:
  ▪ Gentamicin + AZ=100% (202/202)
  ▪ Gemifloxacin + AZ=99.5% (198/199)

Kirkcaldy, CID 2014

Any downside to the new regimens?

Nausea was common
  27% for gentamicin + AZ,
  37% for gemifloxacin + AZ

3% and 7% in each group vomited <1hr after administration

Kirkcaldy, CID 2014

Suspected GC Treatment Failure After Recommended Dual Therapy

What do I do?

CULTURE: if GC culture not available call your local health department STD controller

REPEAT TREATMENT: Gemifloxacin 320 mg + AZ 2g
OR gentamicin 240 mg IM + AZ 2g

REPORT: To your local health department STD program within 24 hours, or call CDC 404-639-8659 for advice

TREAT PARTNERS: Within 60 days with same regimen as patient receives

TEST OF CURE (TOC): Patient returns in 7-14 week for TOC culture and NAAT

* If reinfection suspected instead of treatment failure, OK to repeat treatment with CTX 250 + AZ 1g

Cephalosporin treatment failures

- Oral cephalosporin treatment failures reported worldwide
  - Japan, Hong Kong, England, Austria, Norway, France, South Africa, and Canada
- Ceftriaxone treatment failures in pharyngeal gonorrhea and a few isolates with high-level ceftriaxone resistance reported
ARS question

You diagnose a 22 yr old female with chlamydia and ask her to come in to be treated with azithromycin. She has 1 male partner, who is not currently your patient. What are the most effective ways to ensure he is treated?

A. Have her bring is him with her when she is treated.
B. Tell her to encourage her partner to see a provider
C. Give her medication or a prescription for her partner without evaluating her partner
D. More than one of the above

6) Partner Management Recs

- Clinical evaluation first-line option (but traditional referral has low rates of partner treatment)
- Concurrent patient-partner therapy may be effective for patients with one partner
- Offer Expedited Partner Therapy routinely to heterosexual pts with CT/GC if partner cannot be promptly treated (multiple RCTs showing efficacy)
  - Dual therapy (cefixime 400 mg + azithromycin 1 g) is crucial if this is offered
Legal Status of Expedited Partner Therapy, 9/2014

ARS question

Have you used expedited partner therapy?

A. YES
B. NO

Repeat Infections
Or the STD

Repeat Infection is Common and Dangerous

- 15% of women with CT are reinfected within 6 months
- Repeat CT infection leads to higher risk of complications: PID, ectopic pregnancy, infertility

7) Rescreen for STDs and HIV

Proposed: Women who test positive for CT/GC, or trichomonas should be rescreened three months following treatment.
Men who test positive for chlamydia or gonorrhea should be rescreened at three months after adequate therapy.

All patients with a bacterial STDs or trichomonas should be tested for HIV

8) HPV Vaccines

Bivalent: GSK Cervarix®
- Types 16, 18
- Prevents cervical cancer
- FDA-approved for females 10-25
- 3-dose series; $365

Quadrivalent: Merck Gardasil®
- Types 6, 11, 16, 18
- Prevents warts, cervical cancer, anal cancer
- FDA-approved for females and males 9-26
- 3-dose series; $375

Nonavalent: Merck Gardasil9®
- Types 6, 11, 16, 18, 31, 33, 45, 52, 58
- FDA approved on December 10, 2014

Reduction in pre-cancer endpoints
Nonavalent vs quadrivalent vaccine

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Nonavalent n=7099</th>
<th>Quadrivalent n=7105</th>
<th>% reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIN 2/3 or AIS, VIN2/3, ValN 2/3</td>
<td>1</td>
<td>30</td>
<td>96.7% (80.9-99.8)</td>
</tr>
</tbody>
</table>

Non-inferior immunogenicity for types 6/11/16/18

HPV 101
Over 170 types of HPV classified
Updated incidence/prevalence estimates (CDC):
- 14 million new infections per year
- 79 million people infected in the US

devilliers, P., Virology
Satterwhite, 2013, STD
Estimated HPV Vaccine Uptake*, Girls Ages 13-17

- 2007
- 2008
- 2009
- 2010
- 2011
- 2012
- 2013

![Bar chart showing HPV vaccine uptake by age and year](chart_image)

* ≥ 1 dose of HPV Vaccine

---

9) RIP to the PAP?

- March 2014: Roche HPV testing with 16/18 genotyping recommended 13-0 by FDA advisory panel
- Would replace Pap starting at 25 years of age
  - Larger FDA body agreed with advisory panel
  - Professional societies (ASCCP, ACS, etc) decide whether to recommend it in national guidelines

---

10) New bugs: Man with a “Drip”

- A 23 yo male presents for evaluation of a urethral discharge without dysuria
- He has been seen in STD clinic 15 times between 5/22/12 and 9/2/14
  - Sometimes visible discharge on exam, sometimes not
  - On 9 occasions a urethral Gram stain performed
    - 5 times <5PMN/hpf
    - 4 times >5PMN/hpf
- GC documented 5/23/13, otherwise, tested for GC and CT at each of the 15 visits and always negative
- Most recently treated with 1gm Azithromycin orally once; partner received treatment; GC and CT neg
Today he presents with thick, white discharge...now what?

Source: Diepgen TL, Yihune G et al. Dermatology Online Atlas

ARS question:
What is your next step?
A. Give up
B. Give him longer course of azithromycin
C. Get a urine culture
D. Try a different antibiotic
E. Get a consult from ID
F. More than 1 of the above

10) New Section: Mycoplasma genitalium

M. genitalium
More common than you think

Young adults 18-24 yrs1,2
STD Clinic/ED Attendees3-9

<table>
<thead>
<tr>
<th></th>
<th>MG</th>
<th>CT</th>
<th>GC</th>
<th>TV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seattle</td>
<td>13.4%</td>
<td>7.9%</td>
<td>12.1%</td>
<td>19.2%</td>
</tr>
<tr>
<td>New Orleans</td>
<td>15.2%</td>
<td>9.0%</td>
<td>22.4%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Cincinnati</td>
<td>19.2%</td>
<td>12.1%</td>
<td>15.2%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Baltimore</td>
<td>22.4%</td>
<td>19.2%</td>
<td>15.2%</td>
<td>19.2%</td>
</tr>
<tr>
<td>Durham</td>
<td>19.2%</td>
<td>19.2%</td>
<td>15.2%</td>
<td>19.2%</td>
</tr>
</tbody>
</table>

1 Miller 2004; 2 Manhart 2007
3 Totten 2001; 4 Mena 2002; 5 Manhart 2003; 6 Huppert 2003
7 Gaydos 2009a & 2009b; 8 Mobley 2012
L. Manhart, with permission
M. genitalium & Reproductive Tract Disease

- Definitely associated with NGU in men
- Study of association with:
  - Cervicitis
  - PID
  - Infertility
  - Preterm delivery
- Summary OR = ~2.0 for all conditions
  - Statistically significant for all but infertility

Detecting MG infections?

No FDA-approved diagnostic test

- Hologic Gen-Probe TMA assay
  - Research use only
- Commercial Laboratories & PCR tests
  - Limited test-performance information

MG cure rates with doxycycline and azithromycin

Randomized Trials

Doxycycline (100mg bid x 7d) vs. Azithromycin (1g)

CONCLUSION: AZM (1g) is superior to DOX (100mg bid x 7d). However, efficacy of AZM is not consistently high and may be declining

MG Treatment

Moxifloxacin 400mg po x 7-14d

- Highly effective for treatment failures
  - 100% cure rates in most places
- Public health 340b pricing available
  - Usual price for 7 day course ~ $100+
  - Negotiated price to $1.21/pill
- Caveat: Moxifloxacin treatment failures emerging (Japan, Seattle, Australia)
Persistent NGU Treatment (proposed)

If azithromycin NOT given for 1st episode:
- Azithromycin 1 g orally in a single dose
- Metronidazole 2 g orally in a single dose OR
- Tinidazole 2 g orally in a single dose

If azithromycin given for 1st episode:
- Moxifloxacin 400 mg orally qd x 7d
  PLUS
- Metronidazole 2 g orally in a single dose OR
- Tinidazole 2 g orally in a single dose

Epilogue

- Patient takes moxifloxacin 400 mg po x 7 days.
- Symptoms finally resolve.

- Take home point: Think about *M. genitalium* in cases of cervicitis and urethritis treatment failure.

Bonus: Is Ebola an STI?

Ebola updates

- Story leads: ‘An Indian man who survived Ebola was quarantined when his blood tested negative but his semen tested positive.’
Ebola updates

- Ebola has been detected in blood, and many body fluids:
  - Saliva
  - Mucus
  - Vomit
  - Feces
  - Sweat
  - Tears
  - Breast milk
  - Urine
  - Semen

Ebola updates

- After a negative blood test for Ebola, semen can test positive for up to 3 months.
- The testes are considered immunologically ‘privileged’ sites; easier for virus to hide from immune system
- Theoretically Ebola could be transmitted via semen, but there have not been any documented transmissions via this route

Ebola updates

- CDC advises men who have recovered from Ebola to abstain from sex (including oral sex) for three months.
- If abstinence is not possible, condoms should be used.

Want to know more about STDs? There’s an app for that.

CDC Treatment Guidelines App for Apple and Android
Available now, FREE!
(Search “STD TX” on app store)
Download the app now…

Any burning questions?

Thank you!!

Contact information
ina.park@cdph.ca.gov