2010 STD Treatment Guidelines: Update for Primary Care Providers

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Overview
- CDC STD treatment guidelines process
- STD management highlights:
  - Clinical Prevention Guidance
  - Chlamydia and gonorrhea management issues
  - GC treatment options
  - New syphilis screening algorithm
  - HSV testing and treatment challenges
  - Syndromes Associated with STDs
    - PID, Cervicitis, NGU
    - Role of Mycoplasma genitalium
  - Vaginitis: Trich, BV
  - HPV

Prevention & Screening Issues
- STD screening in special populations:
  - Pregnant women: asymptomatic BV or trich screening or HSV-2 serologic screening still not recommended
  - Adolescents: Detailed screening rec for GC & CT
  - MSM: rectal and pharyngeal NAAT encouraged, HBsAg and HCV (for HIV+ MSM)
  - WSW: offer HPV vaccine and BV is common but screening not recommended
  - HIV+ women annual Trichomonas Screening
- STD screening in correctional facilities added

Key Questions
- Enlistment of Subject Matter Experts
- Systematic Review of Evidence
- Background papers
- Tables of evidence

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
**Chlamydia**

- **Diagnostic issues:**
  - Extra-genital NAAT testing
  - Self-collected vaginal swabs preferred specimen in females; urine preferred in males
  - Liquid cytology media OK for NAATs
- **Male screening:** venue-based (Corrections)
- **No change in treatment regimens**
- **Partner treatment:** EPT option, BYOP
- **Repeat testing 3 months after treatment:** all women and men infected with chlamydia or gonorrhea

**Chlamydia and gonorrhea NAA Testing**

...*not* FDA-cleared for rectal or pharyngeal specimens but now the preferred testing method over culture

**Nucleic Acid Amplification Tests**

- **Highest sensitivity for Chlamydia**
- **Able to detect 30-40% more infections**
- **Less dependent on specimen collection and handling**
  - Self-collected vaginal swabs
  - Urine

**But ...**

- **Validation procedures can be done by labs to allow use of a non-FDA-cleared test or application**
  - Test panel of known positive & negative samples against the cleared test technology to demonstrate good performance
- **Two commercial labs currently provide gc/chl NAAT for rectal/pharyngeal specimens**
  - Quest and LabCorp
**STD Screening for MSM**

- HIV
- Syphilis
- Urethral GC and CT
- Rectal GC and CT (if RAI)
- Pharyngeal GC (if oral sex)
- HSV-2 serology (consider)
- Hepatitis B (HBsAg)
- Anal Pap (consider for HIV+)

* At least annually, more frequent (3-6 months) if at high risk (multiple/anonymous partners, drug use, high risk partners)

**STD Screening for Women**

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

**Women over 25 years of age**
- STD/HIV testing based on risk

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

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**Case History**

- 20 year old male
- Presents with complaints of burning with urination and urethral discharge x 1 day
- 3 female sex partners during the past year—did not use condoms with these partners
- No known prior STDs

- Exam: yellow pus noted at urethral meatus, but no epididymitis, no inguinal adenopathy, and no systemic symptoms
ARS Question 1: How would you treat this patient?

1. Ceftriaxone 125 mg IM
2. Ceftriaxone 250 mg IM
3. Ceftriaxone 250 mg IM + azithromycin 1 g PO
4. Azithromycin 1 g PO

Gonorrhea

- **Treatment issues:**
  - Genital GC: increase ceftriaxone to 250 mg IM (efficacy = 99.2%, 95%CI = 98.8-100%)
  - Pharyngeal GC: increase ceftriaxone dose to 250 mg IM
  - Dual treatment for chlamydia regardless of test result
- **Partner treatment:** EPT option, BYOP
- **Repeat testing 3 months after treatment:** women and men infected with chlamydia or gonorrhea

Gonorrhea Treatment

**Uncomplicated Genital/Rectal Infections**

- Ceftriaxone 250 mg IM in a single dose
- Azithromycin 1 g orally or Doxycycline 100 mg BID x 7 days

* Regardless of CT test result

CDC 2010 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
  - CDC recommended desensitization but now states it is impractical
  - Consider azithromycin, but
    - Requires 2 grams -- GI tolerance issues
    - Resistance to azithro likely increasing and treatment failures have been seen
Gonorrhea Treatment Alternatives
Anogenital Infections

**ALTERNATIVE CEPHALOSPORINS:**
- Single dose IM cephalosporin regimens or
- Cefpodoxime 400 mg orally once or
- Cefuroxime axetil 1 g orally once

**PLUS**
- Dual treatment with azithromycin 1 g or doxycycline 100 mg BID x 7 days, regardless of CT test result

**IN CASE OF SEVERE ALLERGY:**
- Azithromycin 2 g orally once
  (Caution: GI intolerance, emerging resistance)

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Gonorrhea Treatment
Oropharyngeal Infections

**Ceftriaxone 250 mg**
IM in a single dose

**PLUS**
Azithromycin 1 g orally or
Doxycycline 100 mg BID x 7 days

**IN CASE OF ALLERGY:**
- Azithromycin 2 g orally once

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**Neisseria gonorrhoeae**
Isolates with Decreased Susceptibility or Resistance, CA GISP Data, 1987-2010

- **AZITHROMYCIN RESISTANT (>= 8.0)**
- **AZITHROMYCIN RESISTANT (>= 2.0)**
- **CEFPODOXIME RESISTANT (>= 1.0)**
- **CEFPODOXIME ALERT (>= .250)**
- **CEFIXIME ALERT (>= .250)**
- **CEFTRIAXONE ALERT (>= .125)**

* Cefixime was dropped from testing panel in 2007 and reinstated in 2009
** Cefpodoxime was added to testing panel in 2009

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**What should I do if I suspect a cephalosporin-related treatment failure?**

- Culture and susceptibility testing
- Rx ceftriaxone 250 mg IM, if oral regimen used
- Consult a specialist for treatment guidance
- Report case to CDC through state* and local HD
- Ensure partner evaluation and treatment
- See CDC or state health department websites for most current information

*In CA, call STD Control Branch at 510 620 3400 for consultation
CT/GC Partner Management Options

- Patient referral
  - Ask patient to notify partner and ensure treatment
  - Suggest patient bring partner to clinic for concurrent treatment (“BYOP”)
  - Internet-based anonymous notification
- Expedited partner treatment (EPT)
  - Patient-delivered partner treatment (PDPT)
  - Health department field-delivered treatment
  - Pharmacy-based
- Provider or clinic-based referral
- Health department referral

Retesting for Repeat CT/GC Infection

- Retest all women and men with CT or GC 3 months after treatment
- If client returns earlier than 3 months, consider retest
- If client does not return for retesting at 3 months, retest when possible
- Test of cure is not recommended, except in pregnancy

Despite treatment, our 20 yo male patient with urethritis...

- Returns 1 week later, and tells you although he initially felt a little better, the discharge never really went away
- The gc/chl NAAT you sent on his urine are negative
- Moreover, he swears he hasn’t had sex in the past week (REALLY)

ARS Question 2: What is causing his urethritis?

1. C. trachomatis (the test is falsely negative)
2. M. genitalium
3. E. coli
4. T. vaginalis
5. HSV type 2
Urethritis
Common Infectious Causes

- Bacterial STDs:
  - GC 5-20%
  - CT 15-40%
- Non-gonococcal urethritis (NGU)
  - *Mycoplasma genitalium* 5-25%
  - Ureaplasma 0-20%; data inconsistent
  - *Trichomonas vaginalis* 5-20%
  - HSV 15-30%
  - Adenovirus, enterics, Candida, anaerobes

ARS Question 3:
How would you treat now?

1. One week of doxycycline
2. One week of levofloxacin
3. One day of metronidazole
4. 10 days of valacyclovir
5. Nothing – wait for more test results to come back

Persistent NGU Treatment

**Recommended regimen:**
- Metronidazole 2 g orally in a single dose
  - OR
- Tinidazole 2 g orally in a single dose
- Azithromycin 1 g orally in a single dose
  (if not used for initial episode)

*Moxifloxacin 400 mg PO x 7d* effective for NGU treatment failures due to *M. genitalium*

Case History

A 28 y.o. woman who is 24 weeks pregnant

- Routine syphilis screening performed with EIA (Trep-Chek) is reactive
- No history of STD; 4 lifetime male partners, 1 prior partner had genital herpes, no known history of syphilis
- Exam is normal
ARS Question 4: What next???

1. Check serum RPR or VDRL
2. Treat for late latent syphilis
3. Treat for early latent syphilis
4. Check her partner’s serum EIA and treat her only if he’s reactive too
5. Ignore it—it’s probably a false +

Diagnosis of Syphilis

• Serology
  – Non-treponemal (non-specific, cardiolipin-based)
    • RPR or VDRL
  – Treponemal (specific to Treponema pallidum)
    • TP-PA, FTA-abs, EIA, CIA, MBIA

• Darkfield microscopy

Reverse Sequence Syphilis Screening

Treponemal tests (i.e., EIA, CIA)
  • SPECIFIC TO TP
  • QUALITATIVE
  • REACTIVITY PERSISTS OVER LIFETIME

Non-treponemal tests (i.e. RPR, VDRL)
  • NOT SPECIFIC TO TP
  • QUANTITATIVE
  • REACTIVITY DECLINES WITH TIME

CHALLENGES:
• Cannot distinguish between active/old disease (treated/untreated)
• Confusion re: management of patients with discrepant serology

Why switch to EIA/CIA for Screening?

• Automated
• Low cost in high volume settings
• Less lab occupational hazard (pipetting)
• More objective results
• No false negatives due to prozone reaction

180 tests per hour, no manual pipetting
Reverse Sequence Syphilis Testing Algorithm - Draft

Treponemal Test (EIA/CIA)

Quantitative Non-trep Test (RPR, VDRL)

2nd Trep Test (TP-PA)

No infection, Early infection or False Negative

Probable false positive EIA If high risk: repeat trep EIA (and RPR if EIA still+)

INFECTION: old vs. new

INFECTION: old vs. late/early untreated Assess for hx of treated syphilis, sx/signs If treated, no further action If untreated, stage and rx If low risk, consider repeat trep EIA in 1 month (and RPR if EIA still +)

Syphilis Treatment

Primary, Secondary & Early Latent:
- Benzathine penicillin G 2.4 million units IM in a single dose
- Late Latent and Unknown Duration:
  - Benzathine Penicillin G 7.2 million units total, given as 3 doses of 2.4 million units each at 1 week intervals
Neurosyphilis:
- Aqueous Crystalline Penicillin G 18-24 million units IV daily administered as 3-4 million IV q 4 hr for 10 -14 d

*** No enhanced efficacy of additional doses of BPG, amoxicillin or other antibiotics even if HIV infected

Syphilis Resistant to Azithromycin!

Alternatives (non-pregnant penicillin-allergic adults):
- Doxycycline 100 mg po bid x 2 weeks
- Tetracycline 500 mg po qid x 2 weeks
- Ceftriaxone 1 g IV or IM qd x 10-14 d
- Azithromycin 2 g po in a single dose

* Should be used with caution and not in MSM or pregnant women

CDC 2010 STD Treatment Guidelines www.cdc.gov/std/treatment
When is an LP indicated?

- Neurologic, ocular, auditory symptoms/signs
  - Cranial nerve dysfunction, meningitis, stroke, altered mental status, loss of vibration sense, iritis, uveitis
- Evidence of tertiary disease
  - aortitis, gumma
- Serologic treatment failure

In HIV infection, unless neurologic symptoms, there is no evidence that CSF exam is associated with improved outcomes

ARS Question 5: For which patient(s) is HSV-2 serology testing recommended?

1. 20-year-old male college student starting a new relationship
2. Female recently diagnosed with genital warts
3. Client with undiagnosed recurrent genital symptoms
4. Prenatal patient with history of chlamydia
5. All of the above
6. None of the above

Genital Herpes – Testing Issues

- Diagnostics
  - Virologic tests (culture or PCR) should be available
  - IgM serologic testing not useful
- Type-specific HSV-2 serology tests may be useful:
  - Recurrent/atypical symptoms with negative culture
  - Clinical diagnosis without lab confirmation
  - Patients with a partner with genital HSV
- Some experts recommend serology tests:
  - Patients who request testing or “comprehensive STD evaluation”
  - Patients with multiple partners, HIV-infected, MSM at high HIV risk
- Universal screening NOT recommended

Genital Herpes Treatment Issues

- All patients with initial genital HSV should receive treatment
- Episodic therapy for recurrent HSV:
  - Added Famciclovir 500 mg PO x 1, then 250mg BID for 2 days
  - Famciclovir is less effective for suppressive therapy than valacyclovir
- Suppressive HSV therapy does not reduce the risk of HIV in HSV-2 infected individuals
- Antiviral therapy recommended late in pregnancy in women with symptomatic HSV to reduce C-sections
**Mycoplasma genitalium**

- Sexually transmitted pathogen
- Associated with acute and persistent NGU in men, endometritis in women
- Diagnostic test in development
- Azithro superior to doxy for *M. genitalium* urethritis: 82% vs 39%
- Moxifloxacin effective for persistent NGU caused by *M. genitalium*

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**Cervicitis – Diagnostic Issues**

- Diagnostic criteria:
  - Endocervical mucopus OR cervical friability
- Vaginal wet mount with >10 WBCs associated with CT and GC infection
- Quantification of WBCs on gram stain of cervical exudate generally not useful
- Evaluate for PID, BV and trichomonas; consider HSV
- Test for GC and CT

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**Cervicitis – Treatment**

**Treat for chlamydia:**
- Age 25 or younger
- STD risk: new/multiple partners, partner with other partners, unprotected sex
- Follow-up unlikely

**Treat for gonorrhea:**
- High prevalence (>5%)

**Treat BV if present**

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**Pelvic Inflammatory Disease**

- Some association with *M. genitalium*
- No change in criteria for diagnosis or hospitalization
- Fluoroquinolone Resistant GC/ FQs not recommended
  - If parenteral treatment not feasible and GC prevalence and individual risk low, FQs may be considered
- Limited data: Ceftriaxone 250 mg IM + azithro 1g PO q wk x 2
- When to use metronidazole:
  - Oral regimens only
  - Assess for BV and if present, use metronidazole
  - If no wet mount available, use metronidazole
PID: Oral Treatment Regimens

Oral regimens:

- Ceftriaxone 250 mg IM (or other parenteral 3rd generation cephalosporin) x 1 or
- Cefoxitin 2 g IM with probenecid 1 g orally once
- Doxycycline 100 mg orally twice daily for 14 days
- Metronidazole 500 mg orally twice daily for 14 days

*Assess for BV and if present, use metronidazole. Also, if no wet mount available, use metronidazole

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

Trichomoniasis

- Increased HIV risk
- Diagnostic testing:
  - Aptima TV analyte-specific reagents
  - Urine NAAT preferred diagnostic in men
  - POC tests (Aptima VP III, OSOM Trichomonas Rapid Test)
  - Trich on Pap may need confirmation, liquid cytology more sensitive

- Antimicrobial resistance significant (5-10%)
- Treat all recent sex partners; consider EPT

Trichomoniasis Testing and Screening Recommendations

- Test women with vaginal discharge
- Screening recommended for HIV+ women
- Consider screening in those at high risk for infection:
  - new or multiple partners
  - history of STDs
  - exchange sex for payment
  - use injection drugs
- Consider retest in 3 months

Trichomoniasis Treatment

Recommended regimen:

- Metronidazole 2 g PO x 1
- Tinidazole 2 g po x 1

Consider treating HIV-infected women:

- Metronidazole 500 mg PO BID x 7d

Alternative regimen:

- Metronidazole 500 mg PO BID x 7d

Recommended regimen in pregnancy:

- Metronidazole 2 g PO x 1

Note: Vaginal therapy is ineffective
Tinidazole is a Category C drug in pregnancy

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

First treatment failure, re-treat with:
- Metronidazole 500 mg PO BID x 7 days

If repeat failure, treat with:
- Metronidazole 2 g PO x 5 days
- Tinidazole 2 g PO x 5 days

Susceptibility testing: send isolate to CDC
Consultation is available from CDC: 404-718-4141

Bacterial Vaginosis

- Insufficient evidence to support screening high risk pregnant women; against screening in low risk (USPSTF)
- Pre-procedural screening/treatment not recommended
- Some rapid tests have acceptable Sen/Spec
  - Affirm VP III, Pip Activity Test Card & OSOM BV
- Prevention: use condoms, avoid douching

Susceptibility testing: send isolate to CDC
Consultation is available from CDC: 404-718-4141

BV Treatment

Recommended regimens:
- Metronidazole 500 mg PO BID x 7 d
- Metronidazole gel 0.75% 5 g per vagina QD/BID x 5 d
- Clindamycin cream 2% 5 g per vagina QHS x 7 d

Alternative regimens:
- Tinidazole 2 g PO QD x 2 days
- Tinidazole 1 g PO QD x 5 days
- Clindamycin 300 mg PO BID x 7 d
- Clindamycin ovelles 100 mg per vagina QHS x 3 d

Recurrences:
- Metronidazole gel 2x weekly x 4-6 weeks
- Oral nitroimidazole followed by intravaginal boric acid and suppressive metronidazole gel

HPV, Warts, & Cervical Cancer Prevention

- New treatment for genital warts: 15% sinecatechins (Veregen)
- More detailed information on:
  - HPV vaccine
  - HPV-associated cancers
  - Screening guidelines
  - HPV test indications
  - ASCCP management guidelines
  - Counseling messages

Susceptibility testing: send isolate to CDC
Consultation is available from CDC: 404-718-4141

CDC 2010 STD Treatment Guidelines
www.cdc.gov/std/treatment
**Who should get the HPV vaccine?**

- Routine vaccination with either HPV vaccine for prevention of cervical cancers and precancers:
  - Females ages 11-12 years (as young as age 9 years)
  - Females 13-26 years if not previously vaccinated
- Vaccination with the quadrivalent HPV vaccine
  - For added prevention of genital warts in females
  - May be given to males 9-26 to prevention genital warts

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**Take-Home Messages**

- CT/GC: dual treatment for GC; retest for CT/GC 3 months after treatment
- Trichomoniasis: better diagnostic tests; consider screening
- Genital herpes: serology screening, suppressive therapy regimens
- Syphilis: reverse sequence syphilis screening
- HPV: Vaccine
- Sexual health: promote prevention, routine screening

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**Online STD Resources**

- CDC Treatment Guidelines
  - [www.cdc.gov/std/treatment](http://www.cdc.gov/std/treatment)
- California STD/HIV Prevention Training Center
  - [www.stdhivtraining.org](http://www.stdhivtraining.org)
- California Department of Public Health STD Control Branch
  - [www.std.ca.gov](http://www.std.ca.gov)

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**THANK YOU!**