STI Testing and Treatment-Influences on Mucosal Sampling

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STIs and BV

• Are prevalent, recurrent, persistent
• Many are asymptomatic even if untreated
• Major causes of inflammatory cytokine upregulation and immune cell recruitment
• BV may induce mixed cytokine profile
• Cause mucosal disruption (disruption of epithelial layers, tight junction integrity disruption…)
• Promote HIV replication (activating NF-kB)
Figure 1. Cervicovaginal (CVL) cytokine profiles of women who did not have a sexually transmitted infection (STI), compared with women who had asymptomatic or symptomatic infections. A, Cytokine concentrations were measured in CVL samples that were available for 227 of 242 participants in this study. Women who did not have an STI, bacterial vaginosis (BV), or vaginal discharge (blue dots or blocks), women who had an asymptomatic STI (yellow), and women who had a symptomatic STI (orange) were clustered according to their genital cytokine concentrations. Only the cytokines that differed significantly between these groups after adjustment for multiple comparisons were included in this analysis. Abbreviations: Max, maximum standardized cytokine concentration measured; Min, minimum standardized cytokine concentration. B, Principal component analysis was used to group either (1) all cytokines or (2) cytokines that differed significantly between the groups into single components and generate estimates representative of each component. P values were adjusted for multiple comparisons, using a false discovery rate step-down procedure in order to reduce false-positive results when multiple comparisons were made. Adjusted (adj.) P values <.05 were considered statistically significant.
Changes in cervical mucus over the menstrual cycle
Proliferative  Ovulatory  Secretory
Genital infections with *Chlamydia trachomatis* and *Neisseria gonorrhoeae*
Gonorrhea

• Incidence and prevalence of infection with *Neisseria gonorrhoeae* varies widely across communities
  – 2012: 334,826 cases reported

• Majority (50%) asymptomatic
Gonorrhea - Rates by State

Nationally: 107.5/100,000
Chlamydia

- Genital infection with *Chlamydia trachomatis* most frequently reported infectious disease in U.S.
  - 2012: 1.4 million cases reported
- 80-90% asymptomatic
- Plays a major role in development of PID
Chlamydia - Rates by State

Nationally: 456/100,000
Chlamydia - Rates by Sex

Rate (per 100,000 population)

Rate in women: 643/100,000

Year

1991 1993 1995 1997 1999 2001 2003 2005 2007 2009 2011

Women
Total
Men

NOTE: As of January 2000, all 50 states and the District of Columbia have regulations that require the reporting of chlamydia cases.

2011-Fig 1. SR
15-24 year olds disproportionately affected by GC and CT

Reported STDs in the United States
2012 National Data for Chlamydia, Gonorrhea, and Syphilis

Most Reported Chlamydia and Gonorrhea Infections Occur among 15-24-Year-Olds
How should we screen & test?
Laboratory testing

Recommendations for the Laboratory-Based Detection of Chlamydia trachomatis and Neisseria gonorrhoeae — 2014
Recommendations for GC and CT testing for women

- Nucleic acid amplification tests (NAATs) are the recommended test method.
- A self- or clinician-collected vaginal swab is the recommended sample type. Self-collected vaginal swab specimens are an option for screening women when a pelvic exam is not otherwise indicated.
- An endocervical swab is acceptable when a pelvic examination is indicated.
- A first catch urine specimen is acceptable but might detect up to 10% fewer infections when compared with vaginal and endocervical swab samples.
From cervix to salpinx...
Microbial Etiology

• Most common pathogens:
  – *N. gonorrhoeae*: recovered from cervix in 30%-80% of women with PID
  – *C. trachomatis*: recovered from cervix in 20%-40% of women with PID

• Most cases of PID are polymicrobial
  – Prevotella, Peptostreptococcus, Gardnerella, GBS, EColi, Mycoplasma, Ureaplasma
Normal fallopian tube  | Fallopian tube post chlamydia

*CDC Slide photo files.* Scanning electron microscopy photos (1200x) courtesy of D.L. Patton, University of Washington, Seattle, Washington.
Is *Neisseria gonorrhoeae* Initiating a Future Era of Untreatable Gonorrhea?: Detailed Characterization of the First Strain with High-Level Resistance to Ceftriaxone

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**TIME** Partners with ON

Scientists Discover Drug-Resistant Gonorrhea 'Superbug'  
By Laura Blue  
Monday, July 11, 2011

A new, untreatable strain of the sexually transmitted disease gonorrhea has been discovered in Japan, according to an international team of infectious disease experts. The strain, named H041, is resistant to all known forms of antibiotics.

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The New Yorker, October 1, 2012, p.26
NOTE: Resistant isolates have ciprofloxacin minimum inhibitory concentrations (MICs) ≥1 µg/ml. Isolates with intermediate resistance have ciprofloxacin MICs of 0.125–0.5 µg/ml. Susceptibility to ciprofloxacin was first measured in GISP in 1990.
Gonorrhea treatment history

**Recommended regimens for urogenital infections:**

- Ceftriaxone 250mg IM x 1
- OR if ctx not available:
  - Cefixime 400mg po x 1
  - Other single dose injectible ceph
    - Ciprofloxacin 500mg po x 1
    - Ofloxacin 400mg po x 1
    - Levofloxacin 250mg po x 1

**Alternative regimens:**
- Cefpodoxime 400mg po x 1
- Cefuroxime 1g po x 1

**Recommended regimens for pharyngeal infections:**

- Ceftriaxone 250mg IM x 1

**Alternative regimens**
- None

Update to CDC's *Sexually Transmitted Diseases Treatment Guidelines, 2006*: Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections
Update to CDC’s *Sexually Transmitted Diseases Treatment Guidelines, 2010*: Oral Cephalosporins No Longer a Recommended Treatment for Gonococcal Infections

**FIGURE.** Percentage of urethral *Neisseria gonorrhoeae* isolates (n = 32,794) with elevated cefixime MICs (≥0.25 μg/mL) and ceftriaxone MICs (≥0.125 μg/mL) — Gonococcal Isolate Surveillance Project, United States, 2006–August 2011.
Gonorrhea Treatment
Uncomplicated Genital or Pharyngeal Infections

- Ceftriaxone 250 mg IM in a single dose
- Azithromycin 1 g orally (preferred)
orDoxycycline 100 mg BID x 7 days*

* Regardless of CT test result

Proposed: Doxycycline may be removed from recommended to alternative

CDC 2010 STD Treatment Guidelines
www.cdc.gov/std/treatment
Gonorrhea treatment & management issues

• Using two agents with different resistance mechanisms may delay emergence of resistance

• Treatment with non-recommended regimen requires test of cure in 1 week
  – Culture preferred, NAAT in 1-2 wks if no cx

• Suspected treatment failures should be cultured and reported to CDC if cephalosporin resistance
CT/GC Partner Treatment
Chlamydia Treatment
Adolescents and Adults

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

**Recommended regimens** (pregnant*):
- Azithromycin 1 g orally in a single dose

* Test of cure at 3-4 weeks only in pregnancy

Proposed: 1) May add Doryx (Delayed release doxycycline) 200 mg QD x 7 d an additional regimen
2) Amoxicillin as an alternative for pregnant women with CT
Retesting for Repeat Infection
Rapid Repeat Chlamydial Infection is Common in Women

Repeat Testing after an STD infection

- Current CDC STD screening guidelines: repeat testing for STIs ~3 mo after infection
- High risk of new infections
  - 25.8% of women had 1 or more new infections with CT, GC, or Trich at 1y f/u (Project RESPECT)
  - 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)
- Test of cure: only in pregnancy, for chlamydia

CDC 2010 STD Tx Guidelines, www.cdc.gov/std/treatment
Syphilis
Herpesvirus

• Genital Herpes (HSV 2)

Most common overall cause of genital ulceration in the world; prevalence in the U.S. is about 22%, 1 M new cases each year; most are asymptomatic

Sexual Transmission: 4x higher in women may be due to anatomic differences (greater mucosal area),

Clinical Manifestations:

First episode: fever, headache, malaise, myalgias (40% men vs 70% of women), peaks within first 3-4 days after onset of lesions, recede in subsequent 3-4 days
Genital Herpes

Pain, itching, dysuria, vaginal/urethral discharge, tender inguinal adenopathy
pustular or ulcerative lesions on external genitalia most frequent presenting sign
Viral shedding: with systemic symptoms, vesicles, pustules, wet ulcer, about 12 days
70-90% of women will have HSV cervicitis

**Recurrent Genital Herpes:**

localized to the genital area, pain, itching, ranges from 6-12 days; prodromal symptoms like mild tingling, shooting pains to the buttocks or legs or hips, lesions usually confined to one side
If untreated, duration of viral shedding is 4 days; 90% may develop recurrence
Genital Herpes

**Diagnosis:**
Clinical signs and symptoms
Cell culture, PCR, for HSV DNA

**Therapy:**
- **First episode** (oral therapy)
  - Acyclovir 400mg TID for 7-10 days or 200mg 5x a day for 7-10 days
  - Famciclovir 250mg TID for 7-10 days
  - Valacyclovir 1g BID for 7-10 days
Genital Herpes

**Treatment:**

**Recurrence:**
Acyclovir 400mg TID for 5 days, 200mg 5x a day for 5 days, 800mg BID for 5 days
Famciclovir 125mg BID for 5 days
Valacyclovir 500mg BID for 5 days

**Suppressive Therapy:**
Acyclovir 400mg BID
Famciclovir 250mg BID a day
Valacyclovir 500mg once a day, 1g once a day
Human Papillomavirus

At least 40 of the over 100 different HPV types primarily infect the genital tract

**Incidence and Prevalence:** >6M infected annually; estimated 20 million (15%) have HPV; over half in 15-25 years old

**Condyloma acuminata:** 6,11, 42-44, 54 (1.4 M)

Noncondylomatous lesions and/or CIN: 6,11, 16,18,30,31,33,34,35,39,40,42,43,51,52,55,56,57-59,61,62,64,67-70

**Carcinoma:** 16,18,31,33,35,39,45,51,52,54,56,66,68

More common, more persistent in HIV-infected women

May be detectable only transiently
HPV

- 14,000 cases of invasive cervical cancer (US) and estimated 5,000 women will die
- Worldwide: estimated 450,000 cervical CA and 200,000 deaths
- Virtually all cervical CA are related to HPV
- 70% caused by HPV 16 or 18
- 80-90% of anal cancers are caused by HPV 16 or 18 (4,000 people annually with 620 deaths)
Bacterial vaginosis

**Diagnosis:** Gram stain, Amsel’s criteria

**Treatment:**
- Metronidazole 500mg orally BID for 7 days
- Clindamycin cream 2% 5g intravaginally at bedtime for 7 days
- Metronidazole gel 0.75%, 5g intravaginally twice a day for 5 days

**Alternatives:** Tinidazole 2 gm for 3 days
- Clindamycin 300mg orally BID for 7 days

No routine treatment of sex partners

Studies ongoing on the need to treat asymptomatic BV
Trichomoniasis

Caused by a protozoan, diffuse malodorous, yellow-green discharge with vulvar irritation, can cause premature rupture of membranes in pregnancy leading to preterm delivery, PID

Diagnosis:
Wet mount, culture, InPouch, OSOM NAAT

Treatment:
Metronidazole 2g orally single dose or 500mg BID for 7 days
Tinidazole 2 gm orally single dose
Need to treat sexual partner
Vulvovaginal Candidiasis

Caused by Candida albicans or occasionally by other Candida sp., Torulopsis sp., or other yeasts. 75% of women will have at least one episode of VVC and 40-45% will have 2 or more episodes. 5% will have recurrent VVC.

Pruritus, vaginal discharge, vaginal soreness, vulvar burning, dyspareunia, external dysuria

Diagnosis:
Wet Mount, Gram stain, culture

Treatment:
Topical azole drugs
Nystatin
Fluconazole 150mg tablet, single dose
HIV Genital Aphthous Ulcer
STIs and BV

• Need to screen for STIs (asymptomatic)
• Most protocols rescreen in 45 days
• Change in quality of secretions affect sampling methods/composition of sample
• Friable tissues, ulcers, bleeding
• Endocervical cytobrush?
• Limited sampling: biopsy?
• Patient discomfort
• Treatment: effect on genital environment