SEXUALLY TRANSMITTED INFECTIONS AS THE GATEWAY TO HIV IN WOMEN

Arti Barnes MD MPH
Clinical Director, South Central AETC
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Disclosures

- None
Overview

- Epidemiology and economic impact of STDs in the US and Texas
- Factors affecting STD transmission
- 2015 CDC STD treatment guidelines - updates
The US problem

CDC’s estimates of sexually transmitted infections:

Annual new infections (Incidence)
- United States, 2008

20 million

Total infections (Prevalence)
- United States, 2008

110 million

Total medical costs
- United States (in 2010 dollars)

$16 billion

Estimated number of new sexually transmitted infections
- United States, 2008

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>Ages 15-24</th>
<th>Ages 25+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>19,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV*</td>
<td>41,400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>55,400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HSV-2</td>
<td>776,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>820,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>1,090,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia</td>
<td>2,860,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>14,100,000</td>
<td></td>
<td>49%</td>
</tr>
</tbody>
</table>

TOTAL: 19,738,800

*HIV incidence not calculated by age in this analysis

Bars are for illustration only; not to scale, due to wide range in numbers of infections
STIs place a significant economic strain on the U.S. healthcare system.

CDC conservatively estimates that the lifetime cost of treating eight of the most common STIs contracted is $15.6 billion.

However, the annual cost of curable STIs is $742 million.
**TABLE 1. Estimated lifetime cost per case, number of new cases among persons aged 15–24 and total direct medical costs of eight major STDs, United States, 2000**

<table>
<thead>
<tr>
<th>STD</th>
<th>Average lifetime cost per case* ($)</th>
<th>No. of new cases in 2000†</th>
<th>Total direct medical cost* ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>na</td>
<td>9.1 million</td>
<td>6.5 billion</td>
</tr>
<tr>
<td>HIV</td>
<td>199,800</td>
<td>15,000</td>
<td>3.0 billion</td>
</tr>
<tr>
<td>HPV</td>
<td>1,228 (women) 27 (men)</td>
<td>4.6 million</td>
<td>2.9 billion</td>
</tr>
<tr>
<td>Genital herpes</td>
<td>417 (women) 511 (men)</td>
<td>640,000</td>
<td>292.7 million</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>779</td>
<td>7,500</td>
<td>5.8 million</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>244 (women) 20 (men)</td>
<td>1.5 million</td>
<td>248.4 million</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>266 (women) 53 (men)</td>
<td>431,000</td>
<td>77.0 million</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>18</td>
<td>1.9 million</td>
<td>34.2 million</td>
</tr>
<tr>
<td>Syphilis</td>
<td>444</td>
<td>8,200</td>
<td>3.6 million</td>
</tr>
</tbody>
</table>

*In year 2000 dollars. †Excludes infections that were not sexually acquired. Notes: To calculate total costs, we assumed that men accounted for 50% of new HPV infections, 43% of new cases of genital herpes, 35% of new chlamydial infections and 41% of new cases of gonorrhea in this age-group (references 1, 2, 26 and 58). Totals may not match sum of individual items because of rounding. na = not applicable. Source: For incidence estimates, see reference 1.
Why do STDs matter?

- The STI and HIV epidemics are interdependent.
- Similar behaviors, such as frequent unprotected intercourse with different partners, place people at high risk of both infections.
- Individuals infected with STDs are two to five times more likely to get sexually acquired HIV infection.
Effect of Genital Tract Infections on Detectable HIV shedding in the Genital Tract (Johnson and Lewis 2008)

- Urethritis: OR 2.7
- Cervicitis: OR 2.5
- Genital Ulcer Disease: OR 2.2
- Cervical discharge: 1.9
- Gonorrhea/Chlamydia/Candidiasis: OR 1.8 for each condition
- HSV shedding: OR 1.5
- Bacterial vaginosis/trichomonas/syphilis: NS
STDs in Texas

- In 2014: 174,345 sexually transmitted disease (STD) cases, excluding HIV, were reported in Texas, an increase of 5.5% from 2013.

- It ranks 12th among states in chlamydia rates and gonorrhea rates, and 15th in syphilis rates in 2014

(CDC and 2014 Texas Health Report)
Understanding the STD Epidemic in Texas

- African Americans
  - 3.7 times higher rate of CT
  - 7 times higher rate of GC
  - 5 time higher rate of primary and secondary syphilis

- Hispanics
  - 2 times higher rate of CT
  - 1.5 times higher rate of GC
  - 1.5 times higher rate of Primary and secondary syphilis

(2013 Texas STD and HIV Epidemiological Profile)
STDs in Women in Texas

- The bulk of the epidemic is in 15-24 y/o

- Women account for
  - 75% of CT
  - 50% of GC
  - only 23% of syphilis

(2013 Texas STD and HIV Epidemiological Profile)
Percentage of Public Secondary Schools in which Specific HIV, STD, or Pregnancy Prevention Topics were Taught in a Required Course (CDC data)

<table>
<thead>
<tr>
<th>Grades 6, 7, or 8, 2010</th>
<th>TX %</th>
<th>US state %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required course covers how to prevent HIV, other STDs, and pregnancy</td>
<td>76.9%</td>
<td>77.3%</td>
</tr>
<tr>
<td>Required course covers how to access valid and reliable health information, products, and services related to HIV, other STDs, and pregnancy</td>
<td>65.4%</td>
<td>64.0%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grades 9, 10, 11, or 12, 2010</th>
<th>TX %</th>
<th>US %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required course covers how to prevent HIV, other STDs, and pregnancy</td>
<td>92.3%</td>
<td>94.2%</td>
</tr>
<tr>
<td>Condom use: Efficacy, Importance of consistent use and how to obtain them</td>
<td>34%</td>
<td>58.1%</td>
</tr>
</tbody>
</table>
Condom Use and Errors

- >99% effective when used correctly
- Late application among participants, with 17.0% to 51.1%
- Early removal at the participant level, with prevalence ranging from 13.6% to 44.7%
- Not inspecting the condom for damage was reported by 74.5% of men and 82.7% of women
- 3.2% of women and 4.7% of men used an oil-based lubricant

(Sanders 2012)
Adolescent Behavior

- Teenage females with a positive pregnancy attitude were significantly more likely to
  - Have public insurance (43% vs 20%)
  - Be poor (33% vs 10%),
  - Have reached menarche at an earlier age
  - Ever have HIV tested (35% vs 23%)
  - Be Hispanic (OR 3.1) or African American (OR 1.9)

(Lau 2014)
Women

- Young girls are more vulnerable to Chlamydia due to cervical ectopy
- ETOH (OR 6.13) and strict households (OR 1.49) were associated with higher PRESS scores (Smith 2014)
- AA adolescents whose boyfriend was their primary spending money source were 50% more likely never to use condoms (Rosenbaum 2012)
Gender differences in Transmission Risk

- **Chlamydia**: 25% per coital act
- **Gonorrhea**: Female to male: 20% per act
  - Male to female: 50% per act
- **Herpes**: Female to male: 1.5 per 10000 acts
  - Male to female: 8.9 per 10000 acts (Wald 2001)
- **Syphilis**: 60% per partner
- **Trichomonas**: >70% of male partners are infected (Hobbs 2006)
- **HPV**: 20% in a 6 month period (Burchell 2011)
Sexual Networks

- There is an association between social distance and geographic distance, in people at risk to acquire HIV (Rothenberg 2005)

- Concurrency: Reactive/transitional/compensatory and experimental
  - Experimental concurrency in women was associated with same sex behaviors and drug use
  - Reactive concurrency in women was associated with African-American race and having $>3$ lifetime partners (Hess 2012)
Understanding Risk Behavior in Sexual Orientation Groups

- Sexual debut occurred earlier among MSM than heterosexuals.
- New partnership during the previous year
  - MSM: 86% of 18- to 24 y/o and 72% of 35- to 39 y/o
  - MSW: 56% of 18-24 y/o and 21% of 35-39 y/o
  - WSM: 34% of 18-24 y/o and 10% 35-39 y/o.

(Glick 2012)
WSW

- WSW should not be presumed to be at low or no risk for STDs
  - Metronidazole-resistant trichomoniasis
  - Genotype-concordant HIV transmitted sexually between women
  - High prevalence of Bacterial Vaginosis
  - HPV
  - Syphilis through oral sex
Risk Based Testing?

- >10% of young adults with a laboratory-confirmed positive STD result reported abstaining from sexual intercourse in the 12 months before assessment and STD testing
  
  (DiClemente Pediatr 2011)

- 15.7% of AA adolescent females with an STI reported abstinence from vaginal sex during the reporting period of the past 6 months
  
  (Brown AIDS behavior 2012)
Chlamydia (CT) in Texas

- In 2014, TX ranked 12th among states in chlamydia rates

Figure 3. Chlamydia Diagnoses in Texas 1992-2013, Rates of Chlamydia diagnoses in Texas 2001-2013, and Rates of Reported Chlamydia Cases in the United States 2001-2013

Source: STD*MIS, 2013
Screening Trends

- Among sexually-active women aged 16-24 years, chlamydia screening increased
  - Commercial plans: from 23.1% in 2001 to 43.1% in 2010.
  - Medicaid: from 40.4% in 2001 to 57.5% in 2010
Oropharyngeal CT

- Clinical significance of oropharyngeal C. trachomatis infection is unclear
- Routine oropharyngeal screening for CT is NOT recommended
- Oropharyngeal C. trachomatis can be sexually transmitted to genital sites
- Detection of C. trachomatis from an oropharyngeal specimen should be treated with azithromycin or doxycycline
Uncomplicated Chlamydia

- **Follow up:** Repeat testing at 3 months or within 12 months of Rx.
- **Test of Cure:** 3-4 weeks after Rx-ONLY in Pregnant, suspected noncompliance, persistent infection
- **Partner Rx:** All partners within 60 days of symptoms or most recent
- **Pregnant:** Azithro 1g or Amoxicillin 500 mg TID X 7d
The Cost of Chlamydia (2000 rates)

- Costs per case
  - men - $20
  - Women $244

- In women: 82% of the estimated cost per case is attributable to sequelae

- In men: 78% of the estimated cost per case is attributable to acute infection

(Chesson 2004)
Gonorrhea in Texas

- Gonorrhea is the second most frequently reported STD in Texas.
- In 2013, 33,116 cases of gonorrhea were reported in TX.
Gonorrhea Management

- Uncomplicated Urethral/ cervical/ rectal
  - Ceftriaxone 250 mg in a single intramuscular dose
    PLUS
  - Azithromycin 1 g orally in a single dose
  OR
  - Doxycycline 100 mg orally twice a day for 7 days
- If no ceftriaxone then can use cefexime 400 mg instead but test of cure in 1 week
Gonorrhea

- Pharyngeal gonorrhea:
  - Ceftriaxone 250 mg in a single intramuscular dose + Azithromycin 1 g orally in a single dose (doxycycline 100 mg BID x 7 days)

- Gonococcal conjunctivitis
  - Ceftriaxone 1 g IM X once

- Disseminated gonococcal infection
  - Ceftriaxone 1 g q24 hr or cefotaxime 1 g q8h or ceftizoxime 1 g q 8h X 24-48 PO cefixime 400 mg BID X 1 week

- Gonococcal meningitis
  - Ceftriaxone 1-2 g q 12 h x 14 days
Gonorrhea Treatment

- Screening only for high risk women
- Diagnosis: Sensitivity of NAAT superior to culture
- Treatment: **Dual therapy!**
- Resistance: **Quinolones not recommended**
- New alternatives: Cefpodoxime, Cefuroxime for Urogenital- Rectal GC
In 2010, 89% of isolates with decreased susceptibility to cefixime were from MSM. 2/3 isolates in 2011 were from MSW.

Azithromycin resistance decreased from 0.5% in 2010 to 0.3% in 2011.

Quinolone resistant: 9.6% by 2009, and increased to 13.3% in 2011.

Percentage of *Neisseria gonorrhoeae* isolates that are Cirpofloxacin-Resistant by Sex of Sex Partner, Gonococcal Isolate Surveillance Project (GISP) 1995–2011
Figure 29. Primary Antimicrobial Drugs Used to Treat Gonorrhea Among Participants, Gonococcal Isolate Surveillance Project (GISP), 1988–2013

NOTE: For 2013, “Other” includes no therapy (0.9%), azithromycin 2g (1.7%), and other less frequently used drugs (<0.1%).

Figure 25. Neisseria gonorrhoeae — Percentage of Isolates with Elevated Ceftriaxone Minimum Inhibitory Concentrations (MICs) (>0.125 μg/ml), Gonococcal Isolate Surveillance Project (GISP), 2006–2013
The Cost of Gonorrhea

- Costs per case
  - men - $53
  - Women $266
- In women: 81% of the estimated cost per case is attributable to sequelae
- In men: 92% of the estimated cost per case is attributable to acute infection

(Chesson 2004)
Complications: Managing Pelvic Inflammatory Disease (PID)

• **Early follow up (within 72 hours)** must be arranged

• Hospitalization is required for patients who do not respond to treatment with oral therapy or who cannot take oral therapy owing to nausea and vomiting.

• Male partners of women with PID who have had sexual contact in the past **60 days** should be referred for evaluation and treatment.
The Cost of the Sequelae of Chlamydia and Gonorrhea

- Progression to PID in 20% in untreated cases and 4% in treated cases
  - Costs per case of PID, including acute PID, chronic pelvic pain, ectopic pregnancy and treated infertility, range from $1,060 to $3,626 in 2000$ (Chesson 2004)
Syphilis in Texas

- In 2012, Texas had the third highest rate of congenital syphilis in the nation with 79 cases (20.7 cases per 100,000 live births), which was nearly one fourth of the total number of cases in the U.S.

- The overall rate of congenital syphilis in Texas fell to 18.3 cases per 100,000 live births in 2013.
Syphilis Management

- **Primary, Early latent and Secondary**
  - 2.4 MU PCN IM X 1
  - Doxy 100 mg BID X 14 d
  - Azithromycin 2 g X 1
  - Check RPR at 6M, 1 yr

- **Late latent, unknown duration, tertiary (non neurosyphilis)**
  - 2.4 MU PCN IM weekly X 3 weeks
  - Check RPR 6, 12, 24 M

- **Neurosyphilis**
  - PCN G IV 18-24 units over 24 hours X 10-14 d
  - Procaine PCN G 2.4 MU IM + Probenicid 500 mg QID daily X 10-14 d
  - Check CSF pleocytosis titres q6M till they normalize
  - Checking VDRL titres less useful
The Cost of Syphilis (2000$)

- Cost per case was $444
- Neurosyphilis: $56,806 - $166,374
  - Assumptions based on end stage neurosyphilis especially dementia similar to 10 year costs for Alzheimer’s patient
- Primary/secondary and early latent: $53

(Chesson 2004)
Trichomonas

- Yellow-green vaginal discharge. No oral and low rectal prevalence
- Diagnosis: Wet prep 60-70% sensitive
  - NAAT based tests/rapid tests >83% sensitive
- Treatment: Metronidazole 2g X 1 or 500 mg BID X 7d OR Tinidazole 2 g X 1
- HIV: Metronidazole 500 mg BID X 7d
- Rescreen at 3 months
Expedited Partner Treatment (EPT)

- In 2006 CDC recommended expedited partner treatment
  - CT in Women: No difference
  - GC and CT in men and women: EPT was more effective in preventing GC (OR 0.32) than CT (OR 0.82) on F/U
  - Urethritis in men: Decreased persistent or recurrent infection (OR 0.38)
  - Trichomonas in Women: No difference
- EPT resulted in same or increased partner treatment and better behavioral outcomes
EPT for GC- CDC recommendations

“Under these new guidelines every effort should be made to ensure that a patient’s sex partners from the past 60 days are evaluated and treated with a recommended regimen.

However, because that is not always possible, providers can still consider EPT with cefixime or azithromycin for **heterosexual** partners of patients diagnosed with gonorrhea who are unlikely to access timely evaluation and treatment.”
EPT for GC- CDC recommendations

- Not treating partners is significantly more harmful than is practicing EPT for gonorrhea.
- EPT should be accompanied by
  - Treatment instructions
  - Appropriate warnings about taking medications (if the partner is pregnant or has an allergy to the medication)
  - STD health education and counseling
  - Statement advising that partners seek personal medical evaluation, particularly women with symptoms of PID.

- The partner should receive a test-of-cure approximately one week after finishing their medication
  - information on where they can receive a test-of-cure should be provided.
EPT Challenges

- Undiagnosed STDs in partners
- PID in women - should include education on warning signs
- EPT is not routinely recommended for MSM because of a high risk for coexisting infections, especially undiagnosed HIV infection, in their partners.
- No data on Syphilis
EPT in the US
Who Diagnoses STDs?

Figure 21. Gonorrhea — Percentage of Reported Cases by Sex and Reporting Source, United States, 2013
Sexual Assault Prophylaxis

- **Diagnostics:**
  - NAATs for C. trachomatis and N. gonorrhoeae.
  - Wet mount and culture or point-of-care testing of a vaginal-swab specimen for T. vaginalis.
  - A serum sample for immediate evaluation for HIV infection, hepatitis B, and syphilis.

- **Postexposure hepatitis B vaccination,** without HBIG and HIV regimen within 72 hrs of assault.

- **Empiric antimicrobial regimen for CT/GC/Trich.
- **Emergency contraception if warranted.**
Summary

- Dual therapy for GC decreases resistance rates
- Retesting at 3 months for GC, CT, Trich
- Close follow up needed for syphilis post Rx
- Screen routinely not just based on risk
- Screen for all, not just one STD at a time
- Partner management is CRITICAL - consider expedited partner therapy
Lastly...

- Know your affected communities
- Improve access and quality of STD services
- Understand the changing epidemiology of STDs
- Implement guideline based management of STDs
Links

- CDC pocket guide

- Texas DHHS
  - https://www.dshs.state.tx.us/hivstd/
References


References

- CDC Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea (November 19, 2012)
References

Thank you!