Stemming the Tide of Rising STDs:
What a Clinician Needs to Know

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Disclosure

Gail Bolan, MD, has no relevant financial relationships with an entity producing, marketing, re-selling, or distributing health care goods or services consumed by, or used on patients.
Objectives

- Discuss the latest STD trends and epidemiology
- Describe the rising rate and challenges of congenital syphilis
- Review emerging treatment approaches for gonococcal infections in an era of increasing antimicrobial resistance
- Examine new approaches for the provision of quality STD clinical services
Outline

› Changing Landscape of STDs in the US
› Syphilis Strikes Back
› Enhanced Congenital Syphilis Response
› Underutilization of Effective STD Prevention Strategies: Screening and EPT
› Gonorrhea Treatment and Antibiotic Resistance
› Provision of STD Clinical Preventive Services Guidelines
STIs are on the Rise in the United States

1.69 million CASES OF CHLAMYDIA
5% increase since 2016

548,678 CASES OF GONORRHEA
17% increase since 2016

98,437 CASES OF SYPHILIS
12% increase since 2016

more than 900 Congenital Syphilis Cases in 2017

*Data are preliminary as of April 12, 2018; congenital syphilis data are preliminary as of July 10, 2018
Chlamydia — Rates of Reported Cases Among Women by Age Group, United States, 2008–2017*

*Data are preliminary, as of April 12, 2018
Gonorrhea — Rates of Reported Cases Among Women by Age Group, United States, 2008–2017*

15-19 yrs ↑ 13%
20-24 yrs ↑ 10%
25-29 yrs ↑ 17%
30+ yrs ↑ 24%

*Data are preliminary, as of April 12, 2018
Primary and Secondary Syphilis: Reported Cases, U.S., 1941–2017*

Primary and Secondary Syphilis Cases have increased 390% since 2001

CDC estimates more than 55,000 people are infected each year

*Data for 2017 are preliminary as of April 12, 2018
Congenital Syphilis (CS) Cases and Primary and Secondary (P&S) Syphilis Cases Among Females of Reproductive Age, U.S., 2007–2017*

*Data are preliminary, as of April 12, 2018.

*Data for 2017 are preliminary as of 06/08/2018.
In 2016, just seven states represented 70% of all congenital syphilis cases in the U.S.

<table>
<thead>
<tr>
<th>State</th>
<th>2012 Cases</th>
<th>2016 Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA</td>
<td>35</td>
<td>206</td>
</tr>
<tr>
<td>TX</td>
<td>78</td>
<td>71</td>
</tr>
<tr>
<td>FL</td>
<td>37</td>
<td>59</td>
</tr>
<tr>
<td>LA</td>
<td>33</td>
<td>48</td>
</tr>
<tr>
<td>GA</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td>MD</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>AZ</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>IL</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>OH</td>
<td>19</td>
<td>11</td>
</tr>
<tr>
<td><strong>U.S. Total</strong></td>
<td><strong>334</strong></td>
<td><strong>628</strong></td>
</tr>
</tbody>
</table>

201 of 3,141 counties (6%) reported at least 1 congenital syphilis case in 2016.
Syphilis Strikes Back
Overall Actions to Address Syphilis

Screening and Treatment

- Underutilization of frequent syphilis screening and timely, recommended treatment for MSM and pregnant females
- Penicillin shortages and stockpiling drugs
- USPSTF recommendations for more frequent screening in special populations could facilitate reimbursement
- PrEP visits may provide an opportunity for screening/Rx

Partnerships

- Partnering around prenatal care access, screening and unintended pregnancy prevention
- Working with DHAP and MSM providers and communities to sync HIV and syphilis messages
Stages of Untreated Syphilis

Neurologic complications can occur at any stage of syphilis. Syphilis can also be transmitted congenitally, most likely during early stages.

Early Syphilis
- Primary
  - ~ 3 weeks after infection

Secondary
- ~ 6 weeks after infection

Latent
- Early | Late
  - Weeks to years after infection

Tertiary
- Years to decades after infection
Syphilis Staging Flowchart

**SIGNs or SYMPTOMS**

- **YES**
  - Chancre/Lesions
  - Rash, Condyloma, etc.

- **NO**
  - Latent
    - ANY IN PAST 1 YEAR?
      - Negative syphilis serology
      - Known contact to an early syphilis case
      - Good Hx of typical P&S signs/symptoms
      - 4-fold increase in titers

- **YES**
  - Early Latent (<1 year)

- **NO**
  - Unknown Duration or Late Latent
Screening Recommendations for Syphilis

Targeted screening recommendations

- MSM annually and every 3 months if high risk
  - Multiple anonymous partners, meth use
- Other at risk populations:
  - Corrections
  - STD clinics
  - Clients with other STDs
- Prenatal screening at first visit, third trimester, at delivery if high risk or high prevalence
  - Otherwise at first visit for all pregnant women
Evaluate clinically:
• Determine if treated for syphilis in the past
• Assess risk of infection
• Administer therapy according to CDC’s STD Treatment Guidelines if not previously treated

EIA/CIA-
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

EIA/CIA+

Quantitative RPR

RPR+
Syphilis (past or present)

RPR-

TP-PA

TP-PA+
Syphilis (past or present)

TP-PA-
Syphilis unlikely
If at risk for syphilis, consider treating vs repeat RPR in 2 to 4 weeks
Addressing the Benzathine Penicillin G Shortages and Pricing

- Pfizer is releasing requested allocations to wholesale distributors. Procaine penicillin G is NOT available.
- Work with your pharmacists to implement a usage strategy, if inventory is less than 2 months of product based on projected use:
  - Discourage the use of Bicillin L-A® for treatment of other infectious diseases where other antimicrobials can be used
  - Don’t over treat early syphilis
  - Contact your state STD program or CDC
- If product reaches a critical supply level (3 weeks or less) call the Pfizer Supply Continuity Team at 844.804.4677 for an emergency shipment. Also, alert your state STD program and CDC.
- Private sector pricing has increased recently and is of concern for those who do not have access to 340B pricing.
National Network of STD Clinical Prevention Training Centers (NNPTC)

Resources: National STD Curriculum

- Visit: www.std.uw.edu
- Seven Self-Study Modules
- Modular learning in any order with an individual progress tracker
- Free continuing education credits (CME and CNE)
Enhanced Congenital Syphilis Response

*Among states with at least 10 reported cases of syphilis among pregnant women.*

<table>
<thead>
<tr>
<th>State (number of reported syphilis cases among pregnant women)</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>State 1 (n=13)</td>
<td>92.3%</td>
</tr>
<tr>
<td>State 2 (n=50)</td>
<td>92.0%</td>
</tr>
<tr>
<td>State 3 (n=135)</td>
<td>90.4%</td>
</tr>
<tr>
<td>State 4 (n=26)</td>
<td>88.5%</td>
</tr>
<tr>
<td>State 5 (n=69)</td>
<td>88.4%</td>
</tr>
<tr>
<td>State 6 (n=32)</td>
<td>87.5%</td>
</tr>
<tr>
<td>State 7 (n=22)</td>
<td>86.4%</td>
</tr>
<tr>
<td>State 8 (n=35)</td>
<td>85.7%</td>
</tr>
<tr>
<td>State 9 (n=20)</td>
<td>85.0%</td>
</tr>
<tr>
<td>State 10 (n=12)</td>
<td>83.3%</td>
</tr>
<tr>
<td>State 11 (n=18)</td>
<td>83.3%</td>
</tr>
<tr>
<td>State 12 (n=105)</td>
<td>82.9%</td>
</tr>
<tr>
<td>State 13 (n=62)</td>
<td>82.3%</td>
</tr>
<tr>
<td>State 14 (n=383)</td>
<td>81.5%</td>
</tr>
<tr>
<td>State 15 (n=10)</td>
<td>80.0%</td>
</tr>
<tr>
<td>State 16 (n=28)</td>
<td>78.6%</td>
</tr>
<tr>
<td>State 17 (n=264)</td>
<td>77.7%</td>
</tr>
<tr>
<td>State 18 (n=31)</td>
<td>77.4%</td>
</tr>
<tr>
<td>State 19 (n=64)</td>
<td>76.6%</td>
</tr>
<tr>
<td>State 20 (n=68)</td>
<td>76.5%</td>
</tr>
<tr>
<td>US Total (n=2508)</td>
<td>75.0%</td>
</tr>
<tr>
<td>State 21 (n=189)</td>
<td>74.6%</td>
</tr>
<tr>
<td>State 22 (n=21)</td>
<td>71.4%</td>
</tr>
<tr>
<td>State 23 (n=28)</td>
<td>71.4%</td>
</tr>
<tr>
<td>State 24 (n=56)</td>
<td>71.4%</td>
</tr>
<tr>
<td>State 25 (n=13)</td>
<td>69.2%</td>
</tr>
<tr>
<td>State 26 (n=39)</td>
<td>69.2%</td>
</tr>
<tr>
<td>State 27 (n=37)</td>
<td>67.6%</td>
</tr>
<tr>
<td>State 28 (n=24)</td>
<td>66.7%</td>
</tr>
<tr>
<td>State 29 (n=37)</td>
<td>64.9%</td>
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<tr>
<td>State 30 (n=51)</td>
<td>58.8%</td>
</tr>
<tr>
<td>State 31 (n=492)</td>
<td>58.1%</td>
</tr>
<tr>
<td>State 32 (n=20)</td>
<td>55.0%</td>
</tr>
</tbody>
</table>

*includes laboratory, x-ray, and physical findings consistent with congenital syphilis infection

2012–2016 98% increase

2012–2016 150% increase
Factors Associated with Congenital Syphilis Cases: Mothers of Reported Congenital Syphilis Cases (n=628), US, 2016

<table>
<thead>
<tr>
<th>Missed Prevention Opportunities</th>
<th>% (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received no prenatal care</td>
<td>26% (166)</td>
</tr>
<tr>
<td>No screening ≥ 30 days prior to delivery</td>
<td>16% (100)</td>
</tr>
<tr>
<td>Screened, but acquired syphilis infection after negative test</td>
<td>16% (101)</td>
</tr>
<tr>
<td>Positive syphilis screening test, but inadequate treatment</td>
<td>14% (88)</td>
</tr>
</tbody>
</table>

*Data for reported congenital syphilis cases in the United States, 2016

Missing Data: unknown/inadequate prenatal care or unknown/inadequate treatment for **173 Cases**
**Prenatal Syphilis Screening Laws, 2016**

- **Required - Only First Visit**: Blue states
- **Required - Only First Visit and Third Trimester**: Orange states
- **Required – First Visit, Third Trimester, and Delivery**: Purple states
- **Not Required**: White states

*Includes state statutes and regulations effective as of 2016*
The Proportion of Female Syphilis Cases that Report Meth or Heroin Use, or Sex with a PWID, Has Tripled Since 2012
Actions to Address Congenital Syphilis

- Case review with infant morbidity review board model in selected states/counties to identify missed opportunities
- Developing a CS prevention cascade
- Developing tools to assess local context of CS cases and implement high impact interventions
- Working with federal agencies (MCH, OPA, OWH, Substance use) and partner organizations (ACOG, AAP, March of Dimes)
- Enhancing maternal and CS surveillance to capture stillbirths (DRH and BD-Zika collaborative), fetal syphilis, infant morbidity and CS cases averted
- Updating Guidelines for the Prevention and Control of CS
CS Supplement Recipients (n=9)

**Project Period:** October 1, 2017 – December 31, 2018

**Total Award Amount:** $4 million

**Goals:** 1) Sustainable improvements to CS-related activities; 2) Strengthen CS prevention through *prospective* and *retrospective* activities to identify opportunities for change and effective interventions.

**Eligibility:** Reported 14 or more CS cases to CDC in 2015
Supplement Activities

1. Improve data collection of maternal, fetal and infant epidemiologic and clinical risk factors
2. Improve ascertainment of pregnancy status among female syphilis cases
3. Strengthen CS Morbidity and Mortality Case Review Boards
4. Match syphilis surveillance data with vital statistics data
5. Strengthen partnerships with MCH & healthcare providers
6. Work with one or two local counties
7. Participate in CDC-led Special Interest Groups (SIGs)
Health Impact Pyramid

- Counseling and Education
- Clinical Interventions
- Long-Lasting Protective Interventions
- Changing the Context to Make Individuals’ Default Decisions Healthy
- Socioeconomic Factors
Underutilization of Effective STD Prevention Strategies: Screening and EPT
STI Screening for Women

- Sexually Active adolescents & adults <25 years old
  - Routine annual chlamydia and gonorrhea screening (vaginal/cervical swab)
  - Others STIs and HIV based on risk

- Women 25 years of age and older
  - STI/HIV testing based on risk

- Pregnant women
  - Chlamydia and Gonorrhea (<25 years old or at risk)
  - Syphilis serology
  - HIV
  - Hep B sAg
  - Hepatitis C (If high risk)

CDC 2015 STD Tx Guidelines and USPSTF Guidelines 2017
Number of Female Family Planning Users aged 15–19 years tested for chlamydia and proportion tested, Title X Family Planning, 2007–2016

# tested ↓36.7% during 2007-2016

% tested ↑20.2% during 2007-2016

What About Rectal CT/GC Screening for Women?

- Of 5499 women w/rectal CT/GC tests (AND other sites tested) rectal positivity was 10.8%
- Almost ½ of women with CT/GC had a rectal infection only

*Women with rectal CT/GC rectum were more likely to have genital or pharyngeal CT/GCT*
What About CT/GC Screening for 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 men: Partners of chlamydia-infected females**
  - Focus is on partner services
    - BYOP- bring in your partner
    - EPT- expedited partner therapy
Expedited Partner Therapy (EPT)

“the practice of treating the sex partners of persons with sexually transmitted diseases without an intervening medical evaluation”

Core Elements

- Harm reduction strategy
- Treatable with oral medication
- Patient is willing to deliver medication to partners
- Written health education materials must accompany medication
  - Information about medications, allergies & STDs
  - Advice about complications and need for care (e.g. PID)
  - Where to seek care for a complete STD evaluation

* CDC. Expedited partner therapy in the control of sexually transmitted diseases. 2006
Evolving Landscape of EPT: Legal Status Summary

2006
- EPT is Permissible
- EPT is Likely
- Prohibited
- Potentially Allowable

2018
- EPT is Permissible
- EPT is Likely
- Prohibited
- Potentially Allowable
Gonorrhea Treatment and Antibiotic Resistance
2015 Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal 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 2015 STD Treatment Guidelines
www.cdc.gov/std/treatment
2015 Gonorrhea Treatment Alternatives
Anogenital Infections

Alternative Cephalosporins:

- Cefixime 400 mg orally once
- Azithromycin 1 g (preferred)

In Case Of Severe Allergy:

- Gentamicin 240 mg IM + azithromycin 2 g PO
- OR
- Gemifloxacin 320 mg orally + azithromycin 2 g PO
Prevalence of Penicillin, Tetracycline, and Fluoroquinolone Resistance and Cefixime, Ceftriaxone, and Azithromycin Elevated Minimum Inhibitory Concentrations (MICs) among *N. gonorrhoeae* isolates, United States, 2000-2016

Fluoroquinolone-R: ≥1.0 μg/ml  
Tetracycline-R:       ≥2.0 μg/ml  
Penicillin-R:            ≥2.0 μg/ml/  
Ceftriaxone-Elevated MIC:    ≥0.125 μg/ml  
Cefixime*-Elevated MICs:       ≥0.25 μg/ml  
Azithromycin-Elevated MIC: ≥1.0 μg/ml (2000-2005) ≥2.0 μg/ml (2006-2016)

*Cefixime not tested in 2007 & 2008
Percentage of Isolates with Elevated Azithromycin MICs and Elevated Ceftriaxone MICs with Other Resistance Phenotypes, 2016

Azithromycin-RS† (n=190)
- Tetracycline-R
- Penicillin-R
- Ciprofloxacin-R
- Ceftriaxone-RS

4 isolates from Hawaii
CRO MIC = 0.125
AZI MIC = 16

Azithromycin-RS† (n=14)
- Tetracycline-R
- Penicillin-R
- Ciprofloxacin-R
- Ceftriaxone-RS

0.08% of all GISP isolates

† Azithromycin-RS=reduced azithromycin susceptibility (MIC ≥2 µg/ml); ceftriaxone-RS=reduced ceftriaxone susceptibility (MIC ≥0.125 µg/ml)
2016 data are preliminary ; NOTE: Resistance categories are not mutually exclusive
Suspected GC Treatment Failure

TEST WITH CULTURE AND NAAT:
- If GC culture **not** available, call your local health department

REPEAT TREATMENT:
- If reinfection suspected, repeat treatment with CTX 250 + AZ 1g

REPORT:
- To your local health department within 24 hours

TEST AND TREAT PARTNERS:
- Treat all partners in last 60 days with same regimen

TEST OF CURE (TOC):
- TOC 7-14 days with culture (preferred) and NAAT
Provision of STD Clinical Preventive Services Guidelines
Levels of Care: Basic & Specialized

Basic STD Care

- Recommended risk assessment
- Screening and treatment of those identified with asymptomatic infection
- Diagnosis and treatment of patients with common symptomatic infection

Specialized STD Care

- Comprehensive, confidential STD clinical services
  - Basic STD Care
  - Same day diagnostic and treatment services
Quality STD Clinical Services

- Sexual History and Physical Examination
- Prevention
- Partner Services
- Screening
- Evaluation of STD-related Conditions
- Laboratory Tests
- Treatments
**Partner Services**

### Basic and Specialized STD Care

- The following partner services *should be* available as a basic and specialized STD service:
  - Guidance regarding notification and care of sex partners
  - Expedited partner therapy (where legal)

### Specialized STD Care

- The following partner services *should be* available as a specialized STD service:
  - Interactive counseling for partner notification
  - Health Department Disease Intervention Specialist partner elicitation and follow-up
Screening

Basic and Specialized STD Care

- Screening and assessment for the following **should be** available:
  - Gonorrhea
  - Chlamydia
  - Syphilis
  - Hepatitis B
  - Hepatitis C
  - HIV
  - Cervical cancer

Specialized STD Care

- Screening and assessment for the following **should be** available:
  - *Trichomoniasis*

- Screening and assessment for the following **could be** available:
  - *Anal cancer*
Laboratory Tests – Clinical Laboratory

Basic and Specialized STD Care

- The following tests *should be* available through a clinical laboratory:
  - Urogenital NAAT for gonorrhea and chlamydia
  - Extragenital (pharynx, rectum) NAAT for gonorrhea and chlamydia
  - Quantitative non-treponemal serologic test for syphilis
  - Treponemal serologic test for syphilis
  - HSV viral culture or PCR
  - HSV type specific serology
  - 4th generation antigen/antibody HIV test
  - Oncogenic HPV NAATs with Pap smear
  - nPEP and PrEP
  - Serologic tests for hepatitis A, B, C
  - Test for pregnancy

Specialized STD Care

- The following tests *should be* available:
  - Gonorrhea culture
  - Gonorrhea antimicrobial susceptibility testing
  - NAAT for trichomonas
STD Resources

CDC: cdc.gov/std/default.htm

STD Treatment Guidelines: www.cdc.gov/std/tg2015/default.htm

NNPTCs: www.nnptc.org www.STDCCN.org

National Coalition for Sexual Health: www.ncshguide.org/providers www.ncshguide.org
National Network of STD Clinical Prevention Training Centers (NNPTC)

Resource: www.nnptc.org | www.STDCCCN.org

University of California, San Francisco

University of Washington

Denver Public Health

Washington University in St. Louis

Johns Hopkins University

Massachusetts Department of Public Health

University of Alabama at Birmingham

Columbia University

Offering STD treatment resources
2018 STD PREVENTION CONFERENCE

“Intersecting Epidemics, Integrated Solutions”

https://www.cdc.gov/stdconference/default.htm

WASHINGTON, DC      AUGUST 27-30, 2018      OMNI SHOREHAM HOTEL