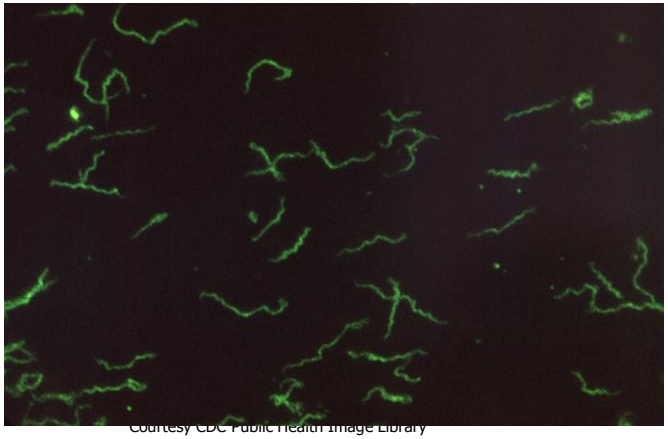
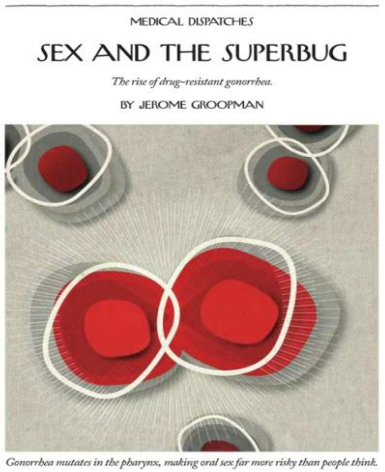


Courtesy CDC Public Health Image Library




# *STD Update for Primary Care Providers*

**Sharon Adler, MD, MPH**
California PTC
Assistant Clinical Professor, UCSF-FCM

National Network of STD HIV Prevention Training Centers

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# Disclosure Information

## *Sharon Adler, MD MPH*

☒ *I have no financial relationships to disclose*

☒ *I will discuss off label use of NAATs*

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# Presentation Overview

- CDC Surveillance Data for 2015
- STD Updates
  - ✓Screening Best Practices
  - ✓Diagnostics for GC/CT
  - ✓Gonorrhea treatment
  - ✓Antibiotic resistance: Gonorrhea
  - ✓Chlamydia treatment
  - ✓Urethritis: *Mycoplasma genitalium*
  - ✓Syphilis: Ocular Syphilis
  - ✓Vaginitis: Trichomoniasis

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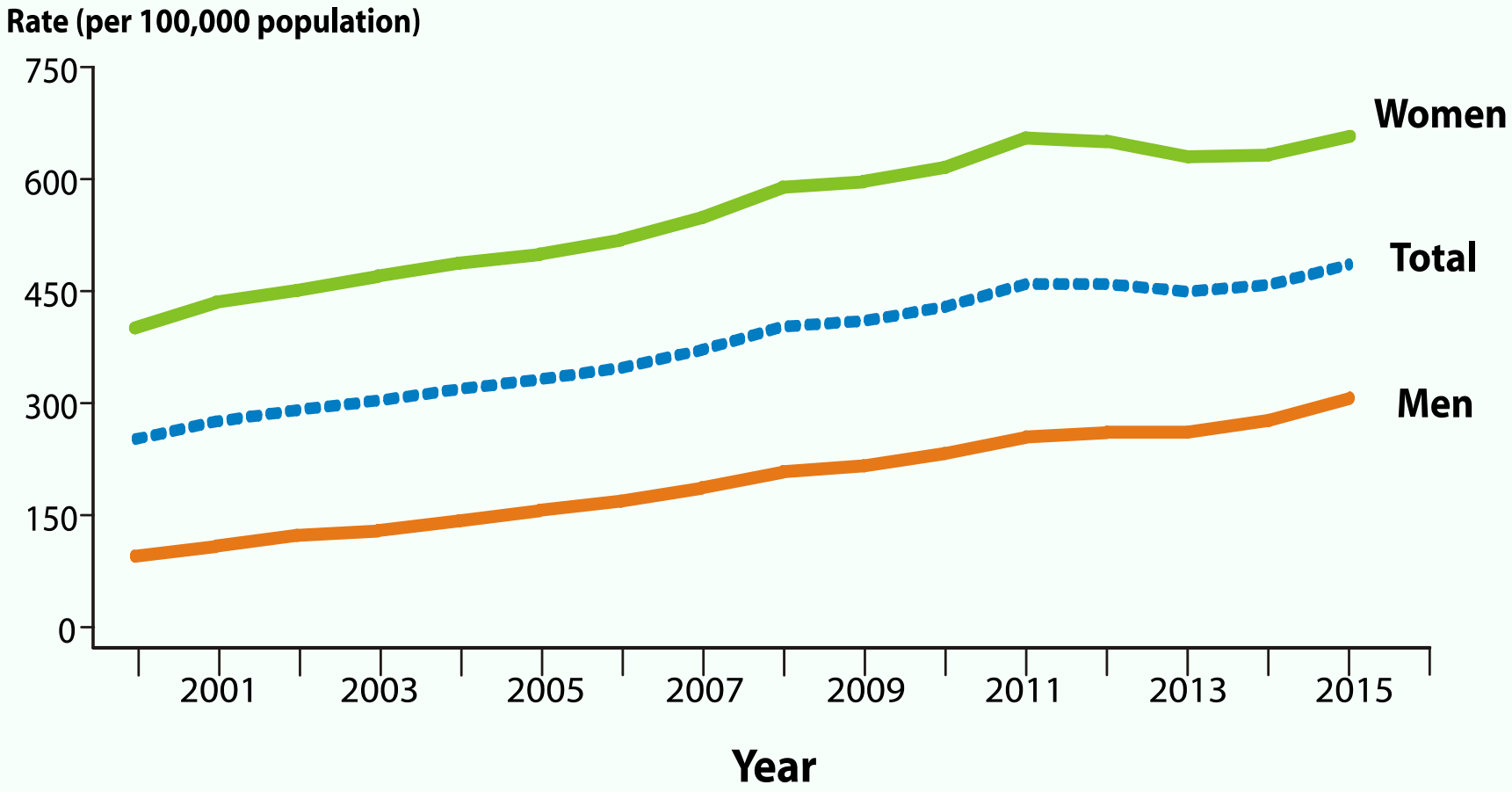
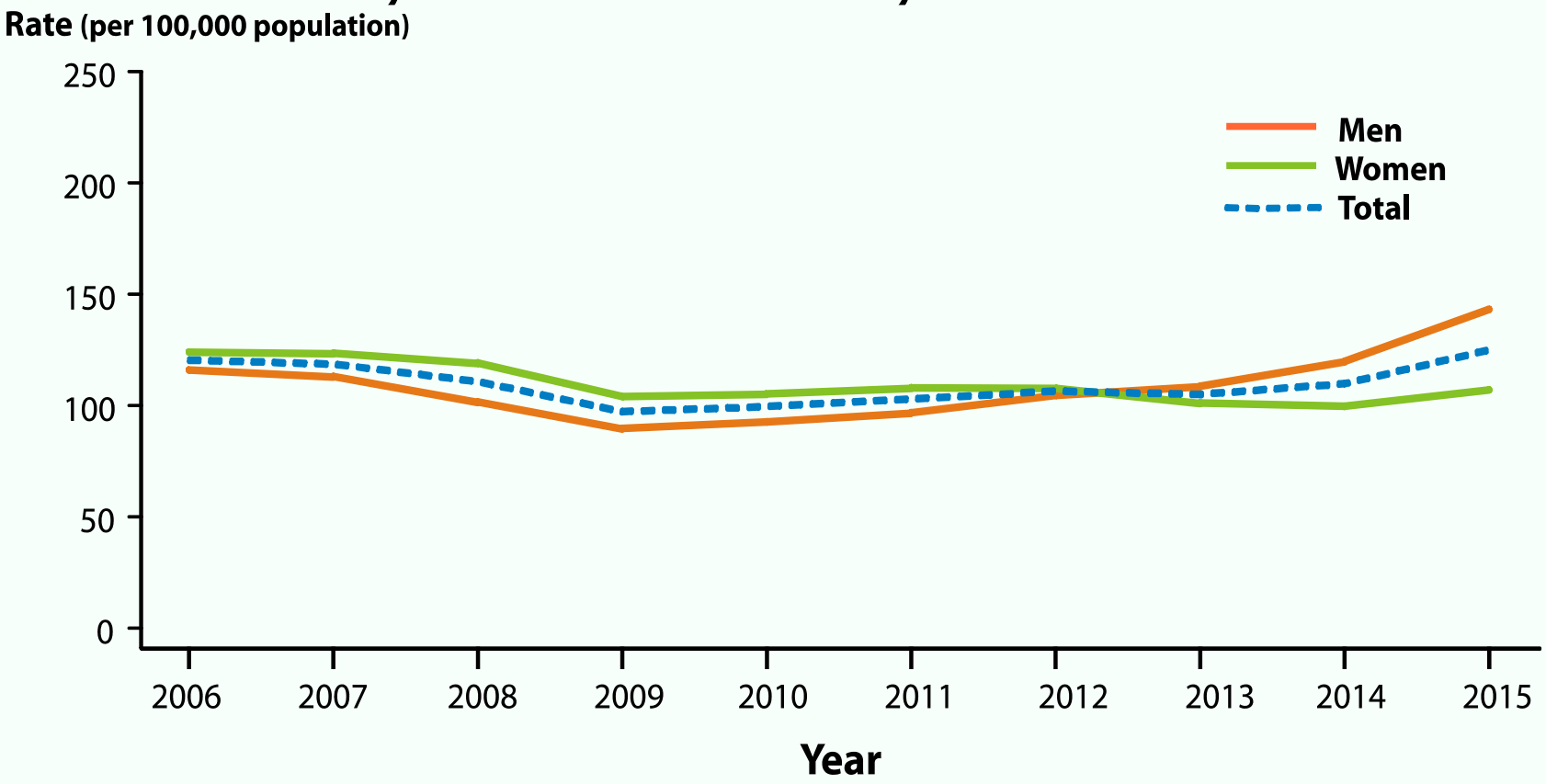
# Chlamydia — Rates of Reported Cases by Sex, United States, 2000–2015

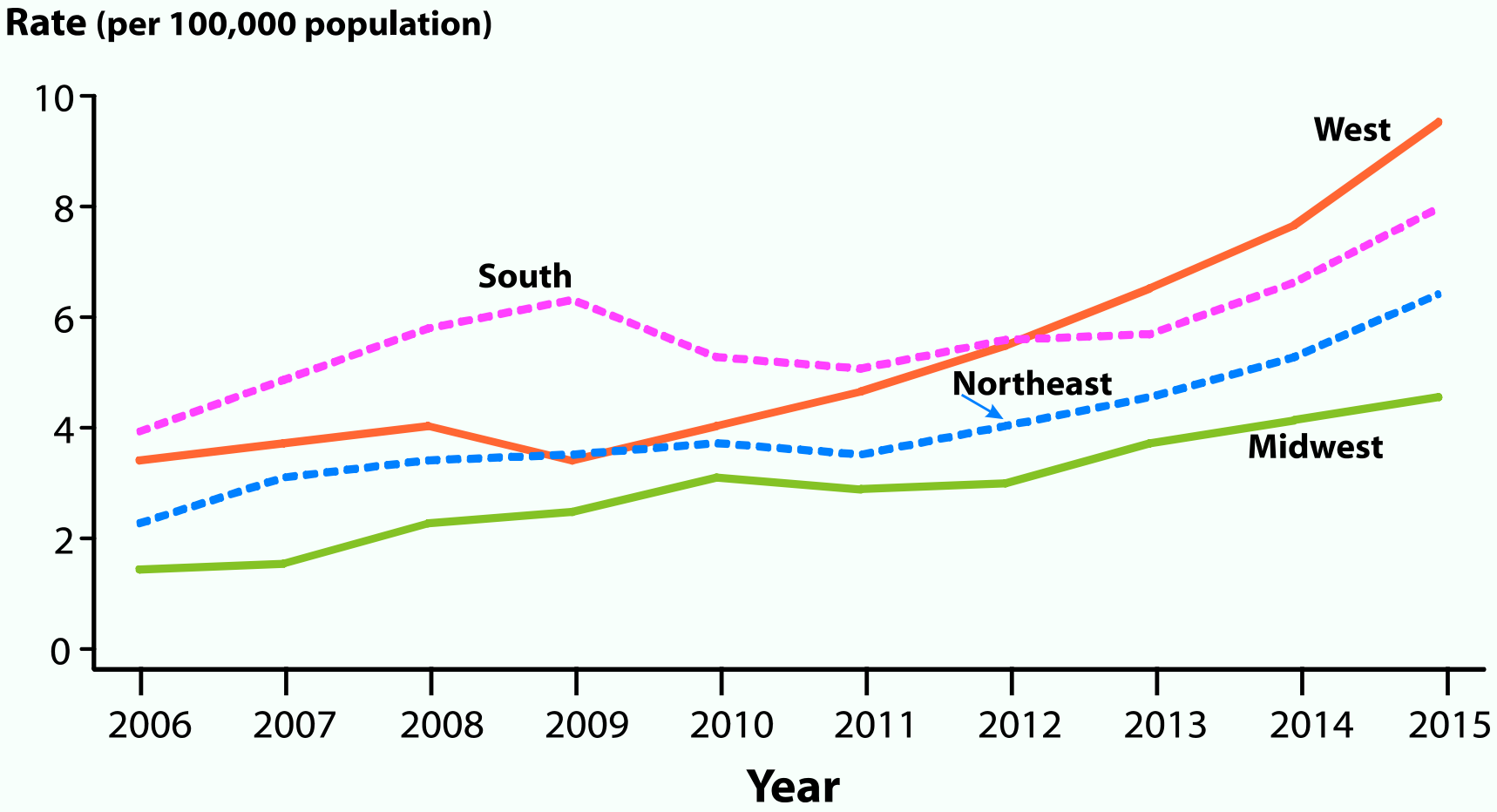



**NOTE:** Data collection for chlamydia began in 1984 and chlamydia was made nationally notifiable in 1995; however, chlamydia was not reportable in all 50 states and the District of Columbia until 2000. Refer to the National Notifiable Disease Surveillance System (NNDSS) website for more information: https://wwwn.cdc.gov/nndss/conditions/chlamydia-trachomatis-infection/.

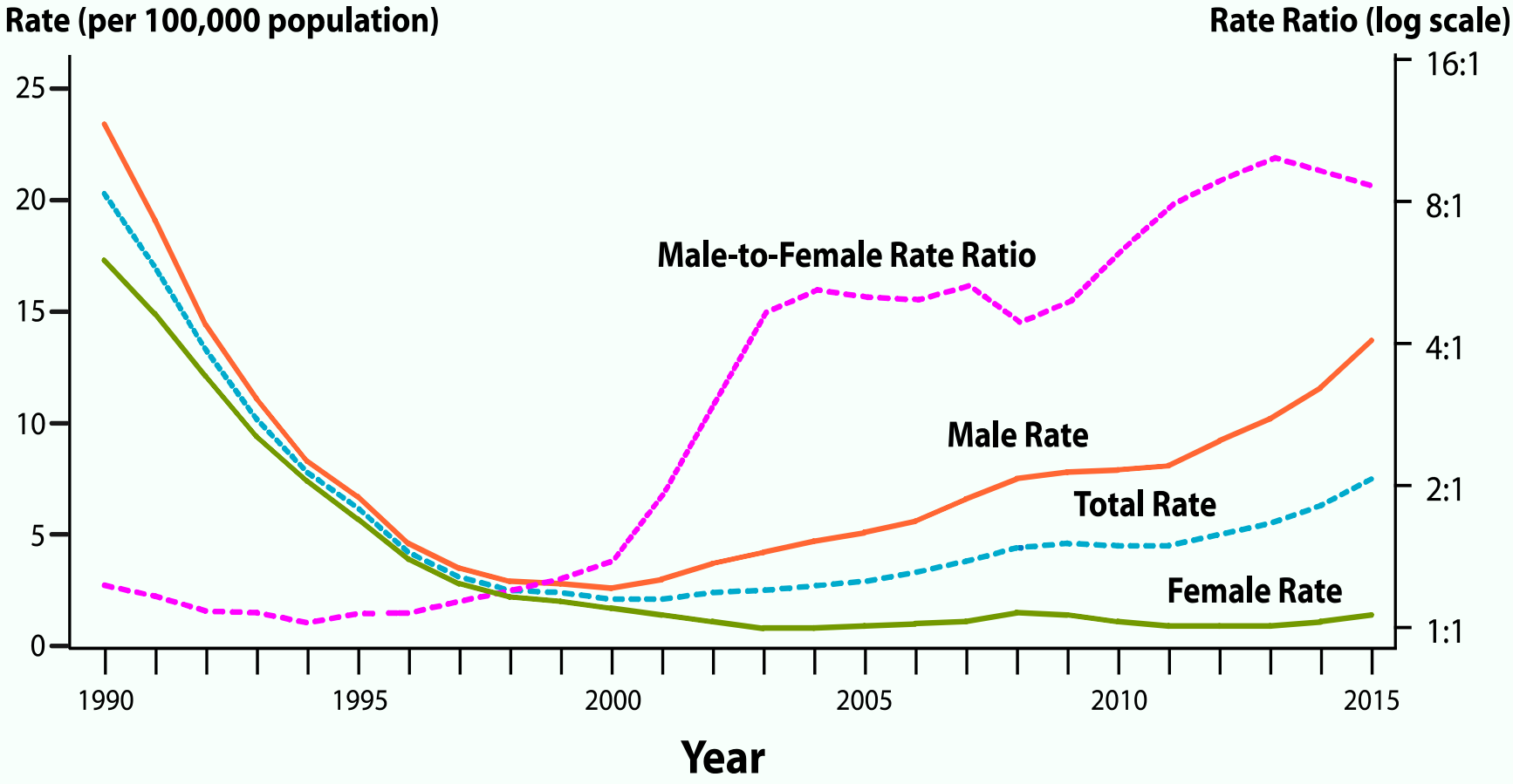
# Gonorrhea — Rates of Reported Cases by Sex, United States, 2006–2015



# Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2006–2015



# Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2015



# STDs in Indian Country

- AI/AN Chlamydia rate
  - 709.1 cases per 100,000 population (*stable* 2011-2015)
  - 3.8 times the rate among Whites
- AI/AN Gonorrhea rate
  - 192.8 cases per 100,000 population
  - 4.4 times the rate among Whites
  - **Increased 71.3% during 2011-2015**
- AI/AN P&S syphilis rate
  - 5.6 cases per 100,000 population
  - 1.4 times the rate among Whites
  - ***Increased* 90.3% during 2011-2015**

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http://www.cdc.gov/std/stats15/default.htm

# STD Screening for Women

Sexually Active adolescents & up to age 25

- Routine **chlamydia** and **gonorrhea** screening
- Other STDs based on risk

Women over 25 years of age

- STD testing based on risk

Pregnant women

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

*CDC 2015 STD Treatment Guidelines*

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# 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)
- Hepatitis C (HIV infected MSM, risk based)

Anal Cancer in HIV+ MSM: Data insufficient to recommend routine screening, some centers perform anal Pap and HRA

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

*CDC 2015 STD Treatment Guidelines*

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# STD Screening Recommendations: HIV-positive Men & Women

| STD | Testing site or test type |
|---|---|
| Chlamydia | Genital, rectal if exposed |
| Gonorrhea | Genital, rectal & oral if exposed |
| Syphilis | Serology |
| Trichomoniasis | Vaginal |
| Hep B – (HBsAg, HBsAb, HBcAb) | Serology |
| Hep C | Serology |
| HPV-related cancer | Cervical cytology for women<br>Anal cytology for MSM is controversial, digital anorectal exam may be useful for early detection |

*

* Screen at least annually; repeat screening every 3-6 months as indicated by risk.

Primary Care Guidelines for the Management of Persons Infected with HIV: 2013 Update by the HIVMA of the IDSA. Clin Infect Dis 2014;58(1):e1-e34. DHHS Guidelines for the prevention and treatment of OIs in HIV-infected adults and adolescents: recommendations from the CDC, NIH, HIVMA. Available at http://aidsinfo.nih.gov/contentfiles/adult_oi.pdf

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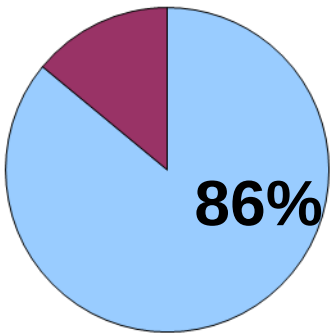
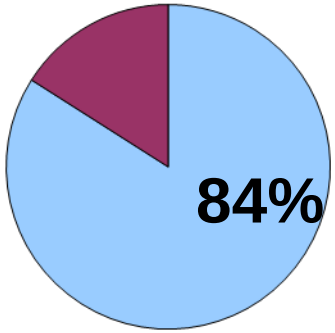
# Majority of Rectal Infections in MSM are Asymptomatic

Rectal Infections

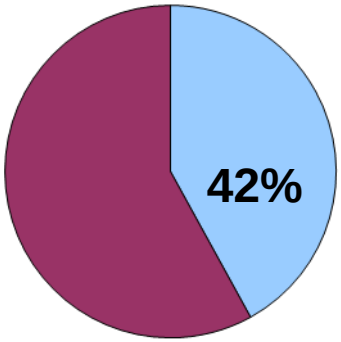



Chlamydia
n=316

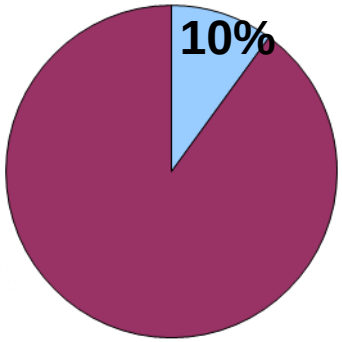



Gonorrhea
n=264

Urethral Infections




Chlamydia
n=315




Gonorrhea
n=364

Asymptomatic
Symptomatic

*Kent, CK et al, Clin Infect Dis July 2005*

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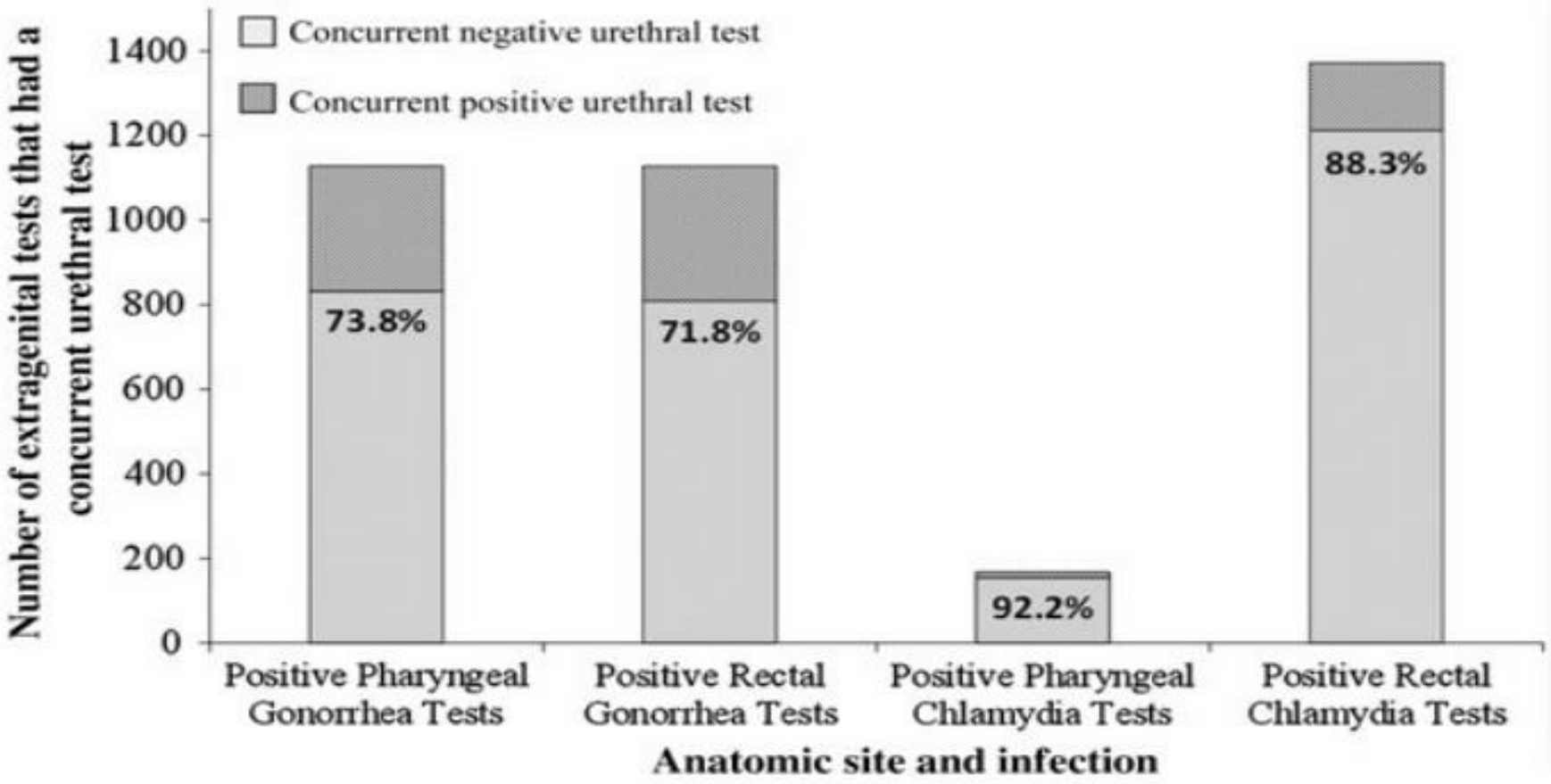
# High Proportion of Extragenital CT/GC Associated with Negative Urine Test, STD Surveillance Network (n=21994)

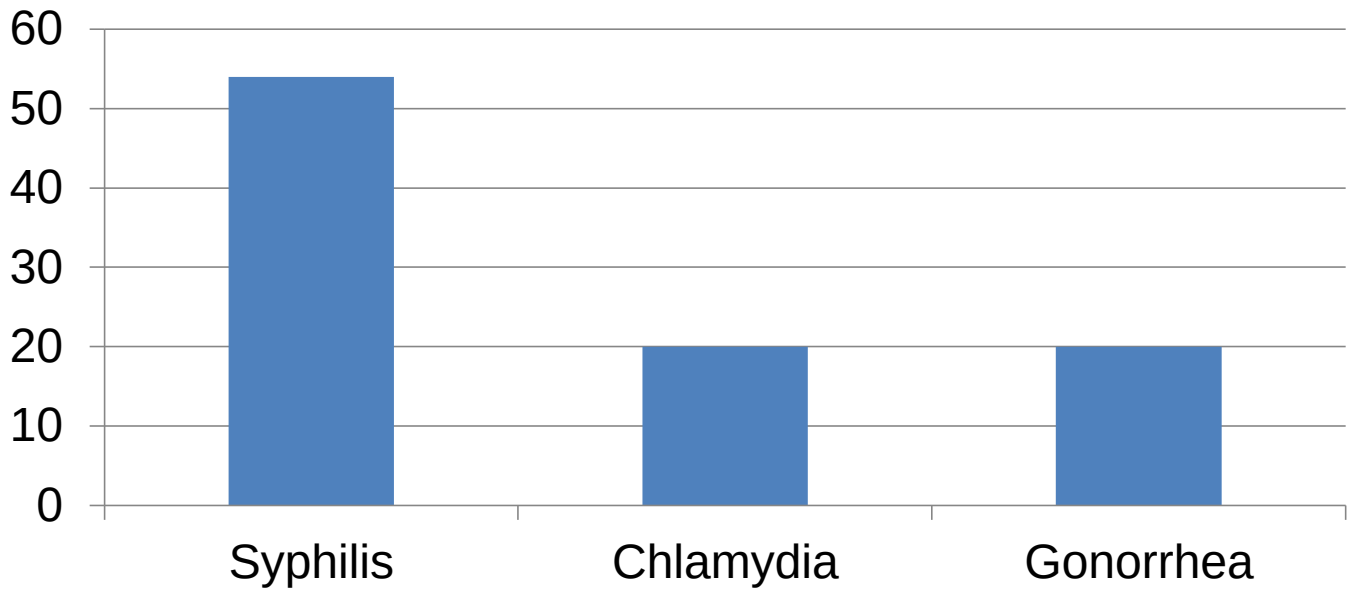



*Patton et al CID 2014*

# Suboptimal STD Screening among MSM in HIV Care

- N=4217 interviews and chart reviews from Medical Monitoring Project, nationally representative sample of adults in HIV care

**% of sexually active HIV+ MSM screened for STIs, N=1411**




*Flagg EW, 2015, STD*

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# Don’t forget the triple dip

Syphilis and HIV serology

Pharyngeal GC

Urine GC/CT

Rectal GC/CT

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Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 63 / No. 2
March 14, 2014

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

## Major conclusions

**NAATs recommended for detection of genital tract infections in men and women** – with and without symptoms

**Optimal specimen types are**:
First catch **urine** for men
Self collected **vaginal** swabs from women

**NAATs recommended for**: detection of **rectal** and **oropharyngeal** infections
- not FDA-approved for rectal or pharyngeal specimens but remain the preferred testing method over culture

# NAAT Laboratory Ordering and Billing Codes

| | Company-Specific Ordering Codes for Combined GC/CT Nucleic Acid Amplified Tests (NAATs) | | Company-Specific Ordering Codes for CT test only |
|---|---|---|---|
| | LabCorp* | Quest* | LabCorp |
| Rectal | 188672 | 16506 | 188706 |
| Pharyngeal | 188698 | 70051 | 188714 |
| NAATs are offered at (or from) any location in the country with these two codes. | | | |

For information on specimen collection and transportation, clinicians should contact the local reference laboratory representative.

| CPT Billing Codes | |
|---|---|
| CT detection by NAAT | 87491 |
| GC detection by NAAT | 87591 |

*CDC does not endorse these laboratories, however, they represent the largest laboratories nationally. There may be other private laboratories that have verified rectal and pharyngeal testing with NAATs. Many PHLs have also verified rectal and pharyngeal testing.

*Bolan, CDC webinar March 2011*

# Case Scenario

- 20 year old female
- Asymptomatic, no prior STDs
- STD Screening
  - NAAT testing for GC/CT

- What is optimal specimen to obtain NAAT GC/ CT

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Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 63 / No. 2
March 14, 2014

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

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**Optimal specimen types are**:
First catch **urine** for men
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**NAATs recommended for**: detection of **rectal** and **oropharyngeal** infections

- not FDA-approved for rectal or pharyngeal specimens but remain the preferred testing method over culture

# Self-collected Rectal/Pharyngeal STI Testing

- Highly acceptable, similar performance compared to clinician-collected specimens
- Self-collection can be performed at laboratory along with blood draw/urine collection or in the exam room before/after the provider visit
- May save patient an office visit
- May save the provider time

*Van der helm, 2009, STD; Sexton, 2013 J Fam Pract; Dodge, 2012 Sex Health Freeman 2011, STD; Alexander 2008, STI; Moncada 2009, STD*

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# Provider Barriers to Screening

- Discomfort with sexual history taking or genital examination
- Lack of knowledge about need for testing
- Patient reluctance
- Lack of time

*Barbee, 2015 STD*

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# Case Scenario

- 20 year old female
- Asymptomatic, no prior STDs
- STD Screening
  - NAAT testing for GC/CT

- GC positive
- CT negative

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# What is current recommended regimen to treat Gonorrhea?

1. Cefixime 400 mg PO + azithromycin 1 g PO
2. Azithromcyin 2 gm PO
3. Ceftriaxone 250 mg IM + azithromycin 1 g PO
4. Ceftriaxone 250 mg IM + doxycycline 100 BID x 7d

# Gonorrhea Dual Therapy

## Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose

**PLUS***

Azithromycin 1 g orally

* Regardless of CT test result

*CDC 2015 STD Treatment Guidelines*

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# What does dual therapy mean?

- Ceftriaxone and azithromycin administered on the same day
- Preferably simultaneously and under direct observation

*CDC 2015 STD Treatment Guidelines*

CALIFORNIA STD/HIV PREVENTION TRAINING CENTER

# What if she had a severe ceftriaxone allergy (anaphylaxis)?

1. Treat with Levofloxacin 500 mg for 7 days
2. Desensitize her so she can be treated with ceftriaxone
3. Azithromycin 2 gm PO — 2012 rec
4. Gemifloxacin 320 mg orally + azithro 2 gm PO — 2015 rec
5. Gentamicin 240 mg IM + azithro 2 gm PO

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# Gonorrhea Treatment Alternatives
## Anogenital Infections

***ALTERNATIVE CEPHALOSPORINS:***

- Cefixime 400 mg orally once

***PLUS***

- Azithromycin 1 g, regardless of CT co-infection

***IN CASE OF SEVERE ALLERGY:***

Gentamicin 240 mg IM + azithromycin 2 g PO
OR
Gemifloxacin 320 mg orally + azithromycin 2 g PO

CDC 2015 STD Treatment Guidelines www.cdc.gov/std/treatment

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# *Any downside to the new regimens?*

| | Gentamicin Regimen | Gemifloxacin Regimen |
|---|---|---|
| **Route** | IM (or IV) | Oral |
| **Nausea** | 27% | 37% |
| **Vomiting (<1 hour)** | 3% | 7% |
| **Availability** | OK | FDA reported shortage in May 2015 |
| **Other** | Need 6 cc (40mg/cc) | |

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# Pharyngeal gonorrhea <u>should not</u> be treated with oral cephalosporins

- Cefixime 400mg PO provides lower bactericidal levels compared to ceftriaxone 250mg IM
- Time above the MIC is not as prolonged
- Efficacy is reduced

- **Test of Cure ( TOC)** for patients with pharyngeal GC treated with an alternative regimen
  - 14 days after tx, culture or NAAT

*CDC 2015 STD Treatment Guidelines*

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THREAT LEVEL
**URGENT**

This bacteria is an immediate public health threat that requires urgent and aggressive action.

# DRUG-RESISTANT NEISSERIA GONORRHOEAE

**246,000** DRUG-RESISTANT GONORRHEA INFECTIONS

**188,600** RESISTANCE TO TETRACYCLINE

**11,480** REDUCED SUSCEPTIBILITY TO CEFIXIME

**3,280** REDUCED SUSCEPTIBILITY TO CEFTRIAXONE

**2,460** REDUCED SUSCEPTIBILITY TO AZITHROMYCIN

**820,000** GONOCOCCAL INFECTIONS PER YEAR

*Neisseria gonorrhoeae* causes gonorrhea, a sexually transmitted disease that can result in discharge and inflammation at the urethra, cervix, pharynx, or rectum.

## RESISTANCE OF CONCERN

*N. gonorrhoeae* is showing resistance to antibiotics usually used to treat it. These drugs include:

- cefixime (an oral cephalosporin)
- ceftriaxone (an injectable cephalosporin)
- azithromycin
- tetracycline

## PUBLIC HEALTH THREAT

Gonorrhea is the second most commonly reported notifiable infection in the United States and is easily transmitted. It causes severe reproductive complications and disproportionately affects sexual, racial, and ethnic minorities. Gonorrhea control relies on prompt identification and treatment of infected persons and their sex partners. Because some drugs are less effective in treating gonorrhea, CDC recently updated its treatment guidelines to slow the emergence of drug resistance. CDC now recommends only ceftriaxone plus either azithromycin or doxycycline as first-line treatment for gonorrhea. The emergence of cephalosporin resistance, especially ceftriaxone resistance, would greatly limit treatment options and could cripple gonorrhea control efforts.

In 2011, 321,849 cases of gonorrhea were reported to CDC, but CDC estimates that more than 800,000 cases occur annually in the United States.

| | Percentage | Estimated number of cases |
|---|---|---|
| Gonorrhea | | 820,000 |
| Resistance to any antibiotic | 30% | 246,000 |
| Reduced susceptibility to cefixime | <1% | 11,480 |
| Reduced susceptibility to ceftriaxone | <1% | 3,280 |
| Reduced susceptibility to azithromycin | <1% | 2,460 |
| Resistance to tetracycline | 23% | 188,600 |

Source: The Gonococcal Isolate Surveillance Project (GISP)–5,900 isolates tested for susceptibility in 2011.
For more information about data methods and references, please see technical appendix.

**U.S. Department of Health and Human Services**
Centers for Disease Control and Prevention

# 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


Unemo Eurosurveillance 2011 | Tapsall J Med Microbiol 2009 | Ohnishi EID 2011 | Allen JAMA 2012

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The NEW ENGLAND JOURNAL of MEDICINE

# Failure of Dual Antimicrobial Therapy in Treatment of Gonorrhea

TO THE EDITOR: Resistance to all antimicrobial agents has developed in some *Neisseria gonorrhoeae* strains. Dual antimicrobial therapy (ceftriaxone plus azithromycin) is a recommended first-line empirical treatment in many countries.[1-3] We describe treatment failure with dual therapy in a patient with gonorrhea.

In December 2014, a heterosexual man presented to a sexual health clinic in the United Kingdom with a 2-week history of urogenital symptoms (Table 1). Ten days previously, he had returned from Japan, where his Japanese female partner had been treated for gonorrhea. He reported having no other recent sexual partners.

*N. gonorrhoeae* was detected in a urine specimen and pharyngeal swab on nucleic acid amplification testing (Abbott RealTime CT/NG assay) and in a culture of a urethral specimen. All *N. gonorrhoeae*–positive specimens on nucleic

On day 98, *N. gonorrhoeae* was detected in a pharyngeal sample on the nucleic acid amplification test and culture. The patient received one dose of ceftriaxone at a dose of 1 g intramuscularly plus azithromycin at a dose of 2 g orally.[3] At the test of cure on day 112, the pharyngeal specimen was negative (according to the nucleic acid amplification test). Initial pretreatment specimens were unavailable for further analysis.

The *N. gonorrhoeae* species was verified with the use of the Phadebact Monoclonal GC Test and matrix-assisted laser desorption ionization–time of flight mass spectrometry. Antimicrobial susceptibility testing with the use of Etest showed that the strain was resistant to ceftriaxone, azithromycin, cefixime, cefotaxime, penicillin, tetracycline, and ciprofloxacin, but it was susceptible to spectinomycin. Whole-genome sequencing of one isolate with the use of

Fifer et al. NEJM 2016;374:2504-6.

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# Azithromycin Treatment Failure in California

NOTE

## Failure of Azithromycin 2.0 g in the Treatment of Gonococcal Urethritis Caused by High-Level Resistance in California

*Severin O. Gose, DrPH,* Olusegun O. Soge, PhD,† James L. Beebe, PhD,‡ Duylinh Nguyen, MPH,* Juliet E. Stoltey, MD, MPH,§ and Heidi M. Bauer, MD, MPH§*

**Abstract:** We report a treatment failure to azithromycin 2.0 g caused by a urethral *Neisseria gonorrhoeae* isolate with high-level azithromycin resistance in California. This report describes the epidemiological case investigation and phenotypic and genetic characterization of the treatment failure isolate.

index patient was treated with ceftriaxone 250 mg IM, which he tolerated well with no allergic reaction. On day 14, the index patient reported improvement in his symptoms.

The isolate's presumptive identification was confirmed by the San Francisco Department of Public Health Laboratory based on NAAT (Aptima Combo 2; Hologic Inc, Bedford, MA) and a species-specific biochemical test (API NH; BioMérieux

*Gose et al. STD 2015;42:279-80.*

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# New Warning Signs:
## Gonorrhea Treatment May be Losing Effectiveness

- 7 Gonorrhea isolates from Hawaii GISP with very high azithromcyin MIC
- 5 of the isolates also had alert-value Ceftriaxone MIC
- First time highly resistant GC found in the U S
- All of the patients responded to RX
- New oral agent performed well in one RCT: ETX0914

www.cdc.gov/nchhstp/newsroom/2016/2016-std-prevention-conference-press-release.html

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# Suspected GC Treatment Failure

## TEST WITH CULTURE AND NAAT:

- If GC culture not available, call your local health department

## REPEAT TREATMENT:

- Gemifloxacin 320 mg + AZ 2g OR Gentamicin 240 mg IM + AZ 2g
- If reinfection suspected, repeat treatment with CTX 250 + AZ 1g

## REPORT:

- To your local health department within 24 hours

## TEST AND TREAT PARTNERS:

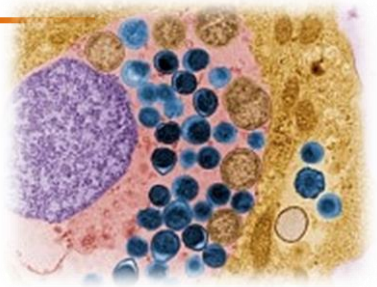
- Treat all partners in last 60 days with same regimen

## TEST OF CURE (TOC):

- TOC 7-14 days with culture (preferred) and NAAT

# 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

***Doxycycline delayed-release 200 mg tablet QD x 7 d added as alternative regimen -- same efficacy, better GI tolerance, more $$$***

**Recommended regimens** (pregnant*):

- Azithromycin 1 g orally in a single dose
- ~~Amoxicillin 500 mg orally TID x 7 days~~

***Amoxicillin 500 TID moved to alternative for pregnant women because CT persistence documented in vitro after treatment***

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

CDC 2015 STD Treatment Guidelines www.cdc.gov/std/treatment

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# Azithromycin versus Doxycycline for Treatment of Urogenital Chlamydia

- RCT comparing azithromycin with doxycycline
- DOT adolescents in youth correctional facilities
- Primary end point was treatment failure at 28 days after treatment
  - Treatment failure determined on basis of NAAT, sexual history, and genotyping of CT strains
- Efficacy for Urogenital CT:
  - Azithromycin 97% effective
  - Doxycycline 100% effective

*Geisler et al. NEJM 2015;373:2512-21.*

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# *Is azithro adequate treatment for rectal chlamydia infection?*

| Population | Treatment | Repeat positive |
|---|---|---|
| MSM in Australia (N=85) | Azithro 1 g | 13% |
| MSM in Seattle (N=407) | Azithro 1 g | 22% |
| (N=95) | Doxy 100 BID x 7 | 8% |

*Based on retrospective uncontrolled observational clinical data: Dummond, Int J STD AIDS 2011; 22:478 and Khosropour, STD 2014; 41:79*

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# Testing after an STD Infection

- **CT Test of Cure**
  - Only for Pregnant women 3 weeks after treatment
- **GC Test of Cure**
  - Patients with pharyngeal GC treated with an alternative RX. TOC 14 days after treatment ( culture or NAAT)
  - Suspected treatment failure

- Women treated for CT/GC, **or Trichomonas**
  - Retest 3 months following after treatment

- Men treated for CT/ GC
  - Retest 3 months after treatment

Retesting target is 3 months; retest opportunistically when patient returns 1-12 months

*CDC 2015 STD Treatment Guidelines* www.cdc.gov/std/treatment

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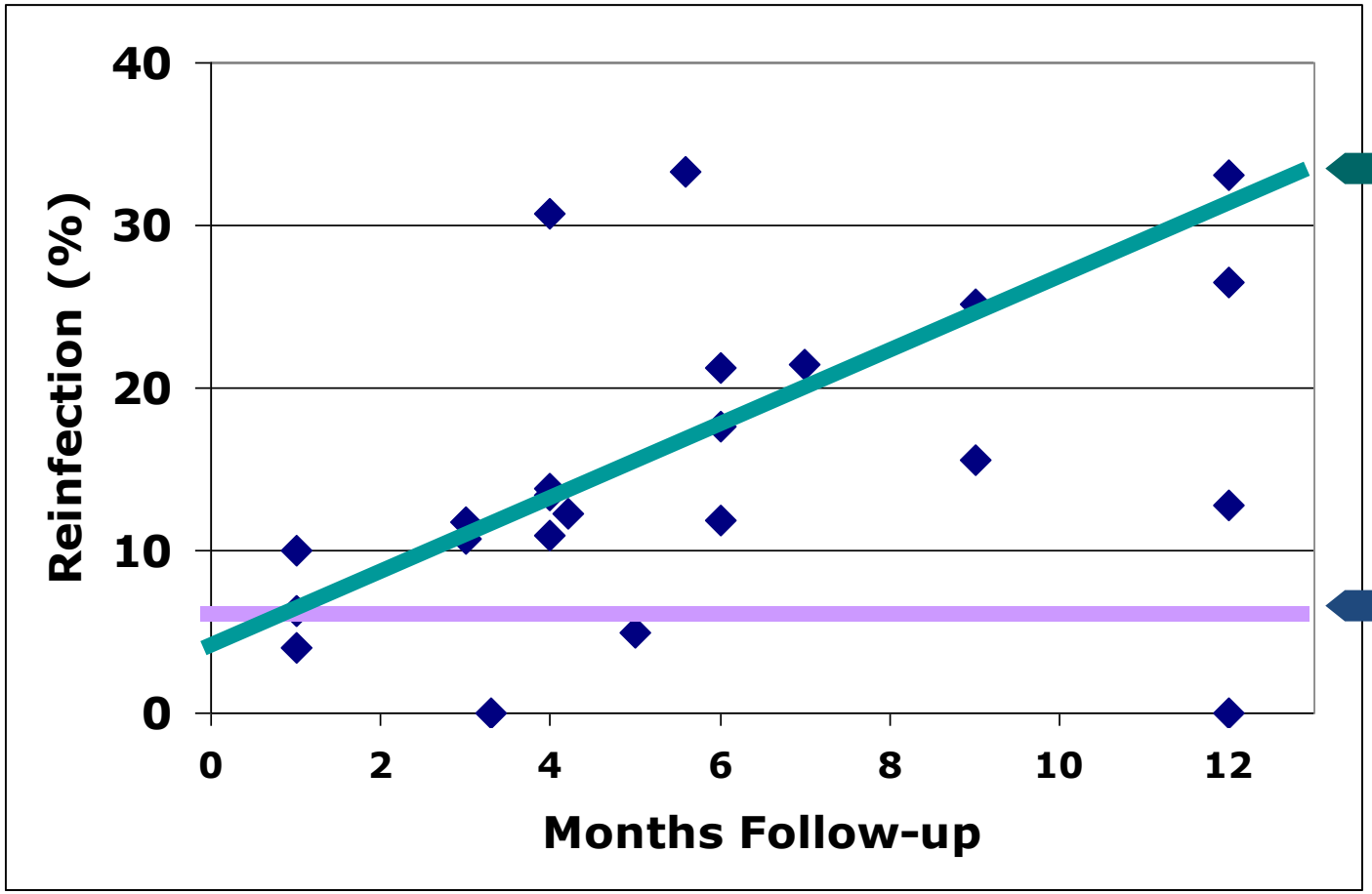
# Repeat Chlamydial Infection is Common among Females




*Hosenfeld C, et al. Sex Transm Dis. 2009 Aug;36(8):478-89*

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# *How soon can I retest for CT/GC?*

- Need to wait at least **3 weeks** for CT to clear for NAAT testing
- GC clearance is generally thought to be 1 week, but possibly up to 2 weeks for pharyngeal infection
- Limited evidence for timing of GC test of cure using modern NAAT (Wind et al. CID 2016)
    - Anogenital GC Median time to clearance **2 days**
    - Range 1-7 days for RNA-based NAAT
    - Range 1-15 days for DNA-based NAAT

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*CDC 2015 STD Tx Guidelines, [www.cdc.gov/std/treatment](www.cdc.gov/std/treatment)*

# Nathan

## Persistent Urethral Discharge

Seattle PTC

- 20 Year old Male complaint of persistent dysuria & urethral discharge.
  - Seen 1 week ago and treated for urethritis (Ceftriaxone 250 IM plus Azithromycin 1 gm PO)
  - States the discharge never really went away. No sexual exposures in past week ( h/o female partners)
  - GC/CT NAAT both negative from prior visit
- Urethral discharge confirmed on exam today

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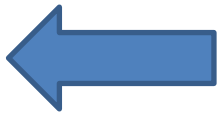
# How would you treat his persistent urethritis?

1. Ceftriaxone 250 mg plus azithromycin 1gm orally
2. Doxycycline 100 mg orally BID for 7 days
3. Metronidazole 2 gm orally
4. Moxifloxacin 400 mg orally QD for 7 days plus metronidazole 2 gm orally once



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# Urethritis
## Common Infectious Causes


- Bacterial STDs:
  - GC 5-20%
  - CT 15-40%
  - ***Mycoplasma genitalium* 15-25%**
- Other etiologies:
  - *Trichomonas vaginalis* 5-20% (regional differences)
  - HSV
  - Ureaplasma 0-20%; data inconsistent
  - Adenovirus, enterics, Candida, anaerobes

Sexually Transmitted Diseases, 4th Edition, Holmes et al

*CDC 2015 STD Treatment Guidelines*

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# Appropriate Management of Persistent Urethritis

- Document urethritis
- Rule out noncompliance
- Rule out untreated partner/re-infection
- Consider *M. genitalium- particularly if initially treated with doxycycline*
- Consider *T. vaginalis** in MSW
  - trichomonas culture
  - NAAT (*If lab does CLIA validation, ASR - analyte-specific reagents can be used with urine or urethral swabs from men).

* MSM – low probability of *T. Vaginalis*

# *Emerging Issues:*
## *Mycoplasma genitalium*

- Sexually transmitted pathogen
  - Urethritis: studies support association
    - Etiology ~15-25% acute urethritis
      ~ 30% persistent urethritis
  - Cervicitis and PID (data suggestive)
- Azithromycin superior to doxycycline for *M. genitalium* urethritis
  - 82% vs 39% ( older studies)
  - *(*AZ efficacy may be declining for M.genitalium)*
- Moxifloxacin effective for *M.genitalium*
- ***No FDA-approved diagnostic test***

**Manhart et al, CID 2013*

# Persistent NGU Treatment

**If azithromycin NOT given for 1st episode:**

- **Azithromycin 1 g orally in a single dose**

**PLUS**

- **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**

**Urology referral if symptoms persist**

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# Brian

## MSM with Rash and Blurry Vision

-31 y/o MSM, methamphetamine use

-Symmetric macular rash on trunk and palms

-1 month of blurry vision

-Feels generally unwell

-No meds, allergies or travel



*Photos: Engelman, SFCC*

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# Diagnostic Work-up

- Ophthalmologist diagnosis: Retinitis
- Rapid HIV positive (CD4 50, VL 75,000)
- Normal CBC, electrolytes
- Neg PPD
- Neg RPR



*Photos: Engelman, SFCC*

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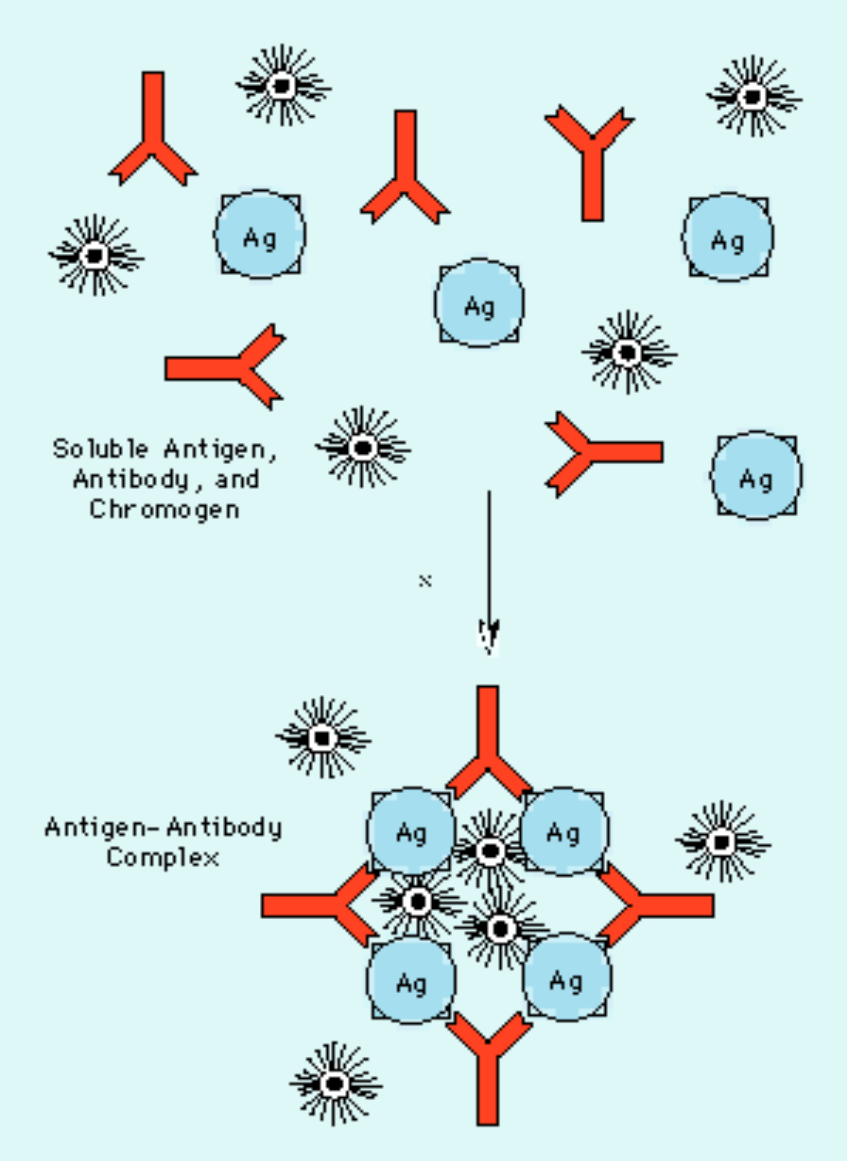
# What might explain this patient's rash and ocular manifestations??

1. Acute HIV rash with CMV retinitis
2. Prozone phenomenon & ocular syphilis
3. Rash & retinitis have separate etiologies
4. None of the above

# Prozone Phenomenon

- False Negative RPR
  - High Ab titers prevent antibody/antigen lattice formation
- Rare
  - Occurs ~0.3-2% (early syphilis/ secondary)
  - May be more common in HIV+ and neurosyphilis




*Jurado RL et al. Arch Intern Med 1993, **153:**2496–2498.*
*Geisler MG. South Med Jour 2004, **97**: 327-328.*
*Liu LL et al. Clin Infect Dis 2014, 59:384-9.*

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# Diagnosis: Secondary Syphilis w/ocular involvement + Prozone

- Repeat RPR 1:1024
- Patient initial RPR was
  False Negative
- Retinitis is manifestation of
  Ocular Syphilis



*Photos: Engelman, SFCC*

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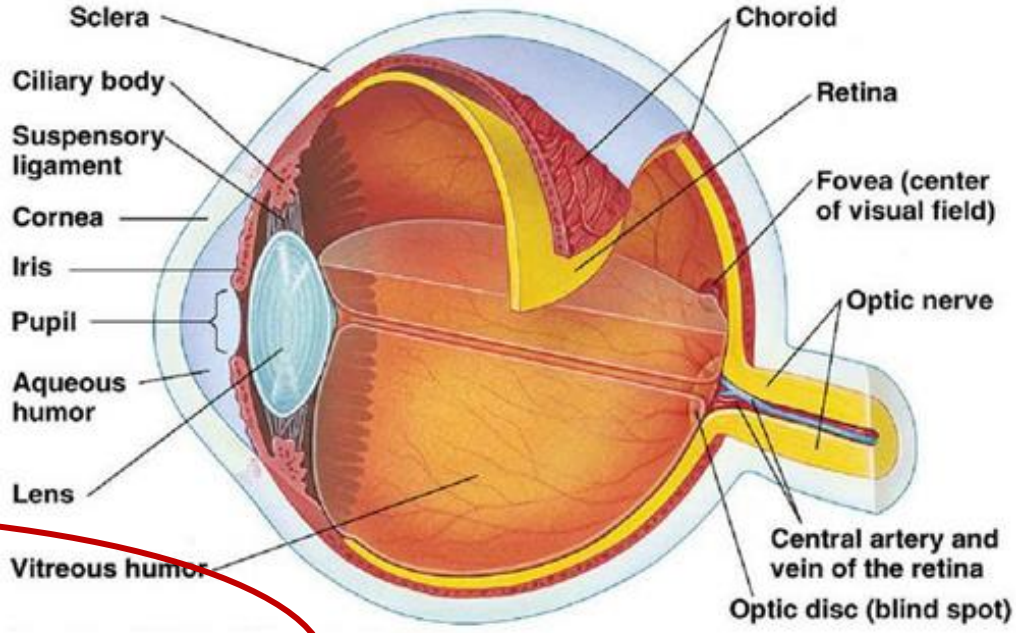
# Ocular Syphilis

Manifestations:
- Conjunctivitis, scleritis, and episcleritis
- **Uveitis**: anterior and/or posterior
- Elevated intraocular pressure
- **Chorioretinitis**, retinitis
- Vasculitis

Symptoms:
- Redness
- Eye pain
- Floaters
- Flashing lights
- Visual acuity loss
- Blindness

Diagnosis:
- Ophthalmologic exam
- Serologies: RPR, VDRL, treponemal tests
- Lumbar puncture




*Slide courtesy of Sarah Lewis, MD*

Wender, JD et al. How to Recognize Ocular Syphilis. Review of Ophthalmology. 2008.

# Ocular Syphilis Management

- Patients with suspected ocular syphilis should receive a lumbar puncture and be treated for neurosyphilis
  - Note: a negative LP does not rule out ocular syphilis
  - Treatment for ocular syphilis is IV PCN (neurosyphilis regimen) *even if the CSF lab tests are negative*

- **HIV test** if not already known to be HIV-infected
- **Report** cases of ocular syphilis to the local health department within 1 business day.

*CDC 2015 STD Treatment Guidelines*

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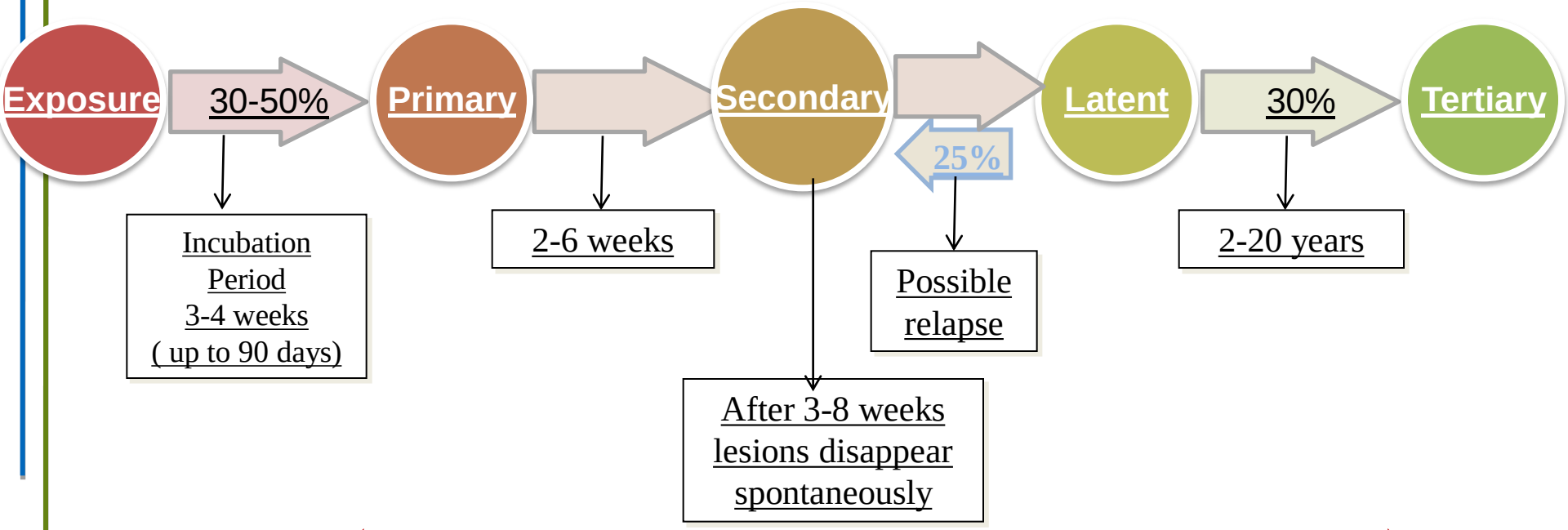
Photo Courtesy: Dr. Kees Rietmeijer, STD Control , Denver PHD

# Syphilis Natural History




**Ocular or Neurosyphilis can occur at any stage**

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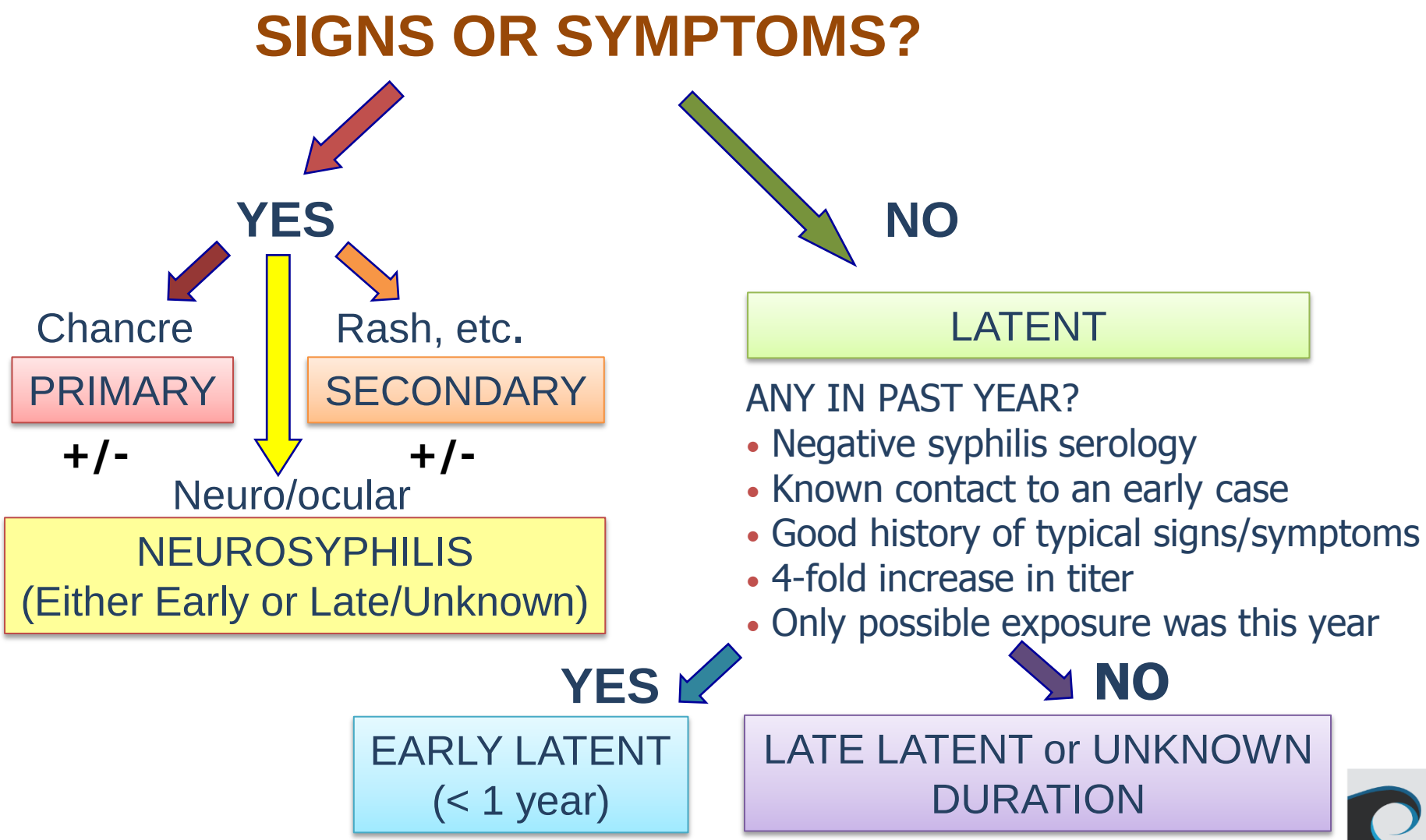
# Syphilis Staging Flowchart

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# Syphilis Staging → Treatment

NEUROSYPHILIS (Either Early or Late/Unknown)

**Aqueous Crystalline Penicillin G** 18-24 million units IV daily administered as 3-4 million IV q 4 hr for 10 -14 d

** BIC IM may be added for late/unk duration to achieve 3-week course*

PRIMARY

SECONDARY

EARLY LATENT (< 1 year)

**Benzathine penicillin G** 2.4 million units IM in a single dose

** Only one dose of BIC is recommended for early syphilis in HIV-infected persons, extra doses not needed*

LATE LATENT or UNKNOWN DURATION

**Benzathine Penicillin G** 7.2 million units total, given as 3 doses of 2.4 million units each at 1-week intervals

** Max interval = 14 days; 7 days if pregnant*

*Always order an RPR on the day of treatment!

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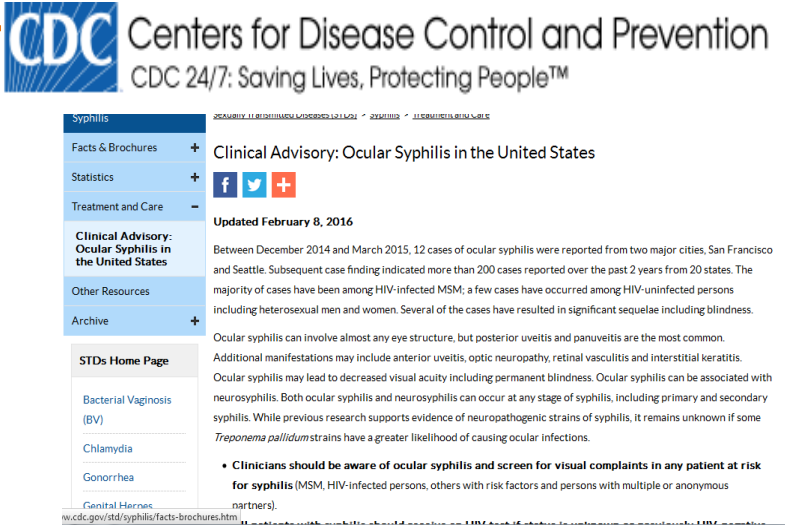
# Ocular Syphilis: CDC Clinical Advisory




200 Cases ocular syphilis in past 2 years from 20 states

- **Majority HIV-infected MSM**
  Few HIV-uninfected heterosexual men and women
- **Significant sequelae including blindness**

- Numerous ophthalmologic manifestations including:
  - **Posterior uveitis, panuveitis,** anterior uveitis, retintitis, optic neuropathy,interstitial keratitis, retinal vasculitis

•Prior research has documented neuropathogenic strains
  – ?unknown if oculo-tropic strain role in these cases

http://www.cdc.gov/std/syphilis/clinicaladvisoryos2015.htm

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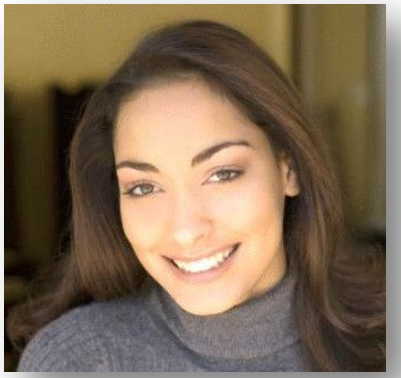
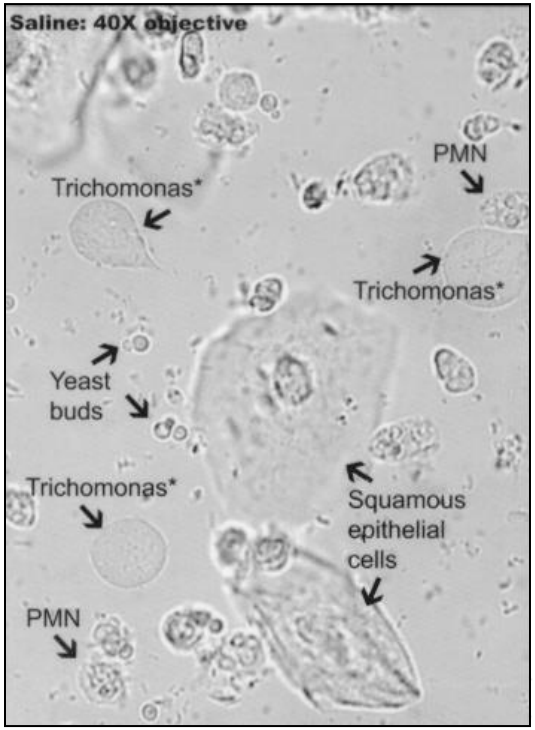
# Nadine

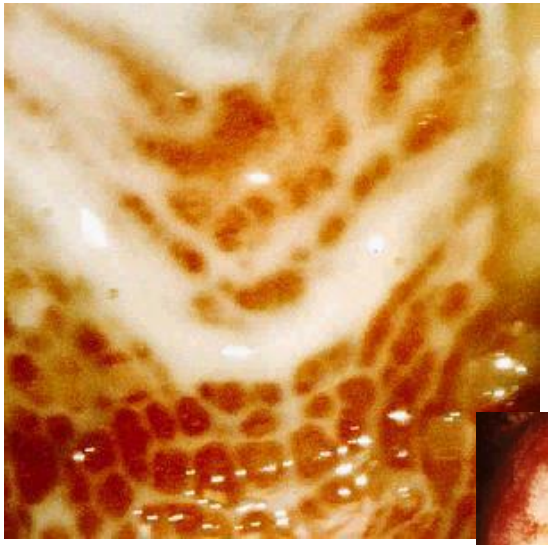


**A 26 y.o. HIV+ woman presents with c/o vaginal discharge.**

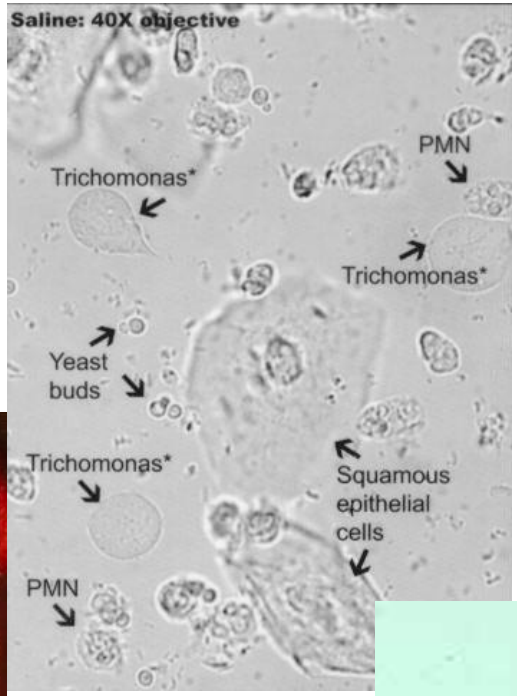
- Motile trichomoniasis seen on wet mount
- What is appropriate treatment?



# Trich: Exam and Lab Findings



Mosby
STD Atlas, 1997




Seattle STD/HIV PTC

CDC

Sensitivity of wet mount for trich: 60-70%

# Trichomoniasis Treatment

Recommended regimen:

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

Women with HIV infection:

- 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 (at all stages)

Note:

Vaginal therapy is ineffective

Tinidazole is a Category C drug in pregnancy

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# Trichomonas ( TV)

- **Prevalence estimates ~3.7 million**
- Most common curable STD in HIV+ women
  - 6-44% prevalence
  - 18-36% repeat infection rate (8% in HIV-neg)
- HIV+ women with TV higher prevalence of HIV RNA in vaginal secretions
  - TV treatment decreases vaginal HIV load/shedding

**Screening for TV in HIV+ women recommended**

**Retesting** recommended within 3 months after treatment for all women

- (insufficient data to recommend for men)

# Newer Trichomonas Diagnostics

| Test | Sensitivity | Specificity | |
|---|---|---|---|
| OSOM | 82-95% | 99-100% | 10 min POC, CLIA waived |
| Affirm VPIII | 83-90% | ~ 100% | 45 min POC |
| Hologic APTIMA BD Probe Tec Q$^{x}$ (NAAT) | 95.3-100% | 95.2-100% | **FDA approved ( women)*** |

FDA approved for vaginal specimen



*If lab does CLIA validation, ASR ( analyte-specific reagents) can be used with urine or urethral swabs from men.

Miller and Nyirjesy, Curr Infect Dis Rep 2011 13:595-603;
Schwebke JCM Dec 2011; p4106-4111

# Trichomoniasis Recurrence/ Resistance

- Cure rate over 90%
- Assess drug adherence, re-exposure
- Low-level metro resistance 4%–10%
  - High-level resistance rare
- Most respond to tinidazole or higher doses of metronidazole

# Single dose vs multi-dose Metronidazole: Trich Recurrence

- Meta-Analysis of 6 studies
- Pooled analysis showed higher treatment failure for single dose vs multi-dose
  - 1.87 Risk Ratio (95% CI 1.23-2.82, p<0.01)
- Study suggests that all women would benefit from multi-dose regimen for Trich (similar to what is recommended for HIV+ women)
  - RCT underway to assess further

*Kissinger et al. Single Dose Compared to Multi-Dose Metronidazole For the Treatment of Trichomoniasis in Women: A Meta-Analysis . Oral Session 4A4. 2016 National STD Prevention Conference. Atlanta GA Sept 2016*

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# 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*

CDC Consult & *T. vaginalis* susceptibility (404-718-4141)

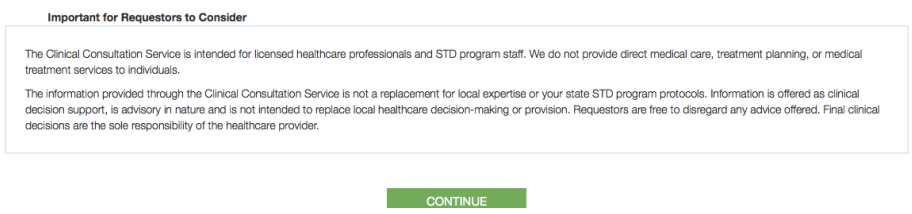
Alternative regimens not systemically studied: Anectodal reports of success with intravaginal paromocyin & high dose tinidazole

# STD Clinical Consultation Network (STDCCN)

- Provides STD clinical consultation services within 1-3 business days, depending on urgency, to healthcare providers nationally
- Your consultation request is linked to your regional PTC's expert faculty
- We are just a click away!
- www.STDCCN.org

National Network of STD Clinical Prevention Training Centers

STD Clinical Consultation Network



# Additional Resources for Clinicians

- CDC 2015 STD Treatment Guidelines
  - http://www.cdc.gov/std/tg2015/
  - CDC STD Treatment Guidelines free App

- National Network of STD/HIV Prevention Training Centers
  - http://nnptc.org/
- California Prevention Training Center
  - http://californiaptc.com/

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Questions?

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# What about HIV-infected women?

- Baseline Pap: Screen within 1 year of onset of sexual activity, no later than age 21
- 2nd Pap: 6-12 months after baseline
- 3rd Pap: 12 months after 2nd Pap
- If all 3 are normal, **Pap every 3 years**

HIV-infected women over 30

- HPV-Pap co-testing can be performed
- If negative co-test, **repeat co-test in 3 years**

CDC-IDSA-HIVMA-NIH Opportunistic Infections Guidelines (9/25/2015)
https://aidsinfo.nih.gov/contentfiles/lvguidelines/Adult_OI.pdf

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