Sexually Transmitted Diseases (STDs)
2016 Update

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Disclosures

- I have no financial relationships to disclose.
- I will not discuss off-label use and/or investigational use in my presentation.
- Slides provided by various sources including AETC, CDC, DHHS, and Dr. Sharon Adler.

Arizona STDs

2014: 39,919 cases of STDs reported in Arizona:

- Maricopa (64.4%)
- Pima (16.8%)
- Pinal (4.1%)
- Yuma (2.6%)

  - 1.2% of investigated cases were co-infected with HIV
  - 22.8% of investigated cases were men who have sex with men (MSM)
  - 79.5% of all reported cases were young adults 15 – 29 years of age

Arizona STDs

- Pima County
  - 55 cases of syphilis in 2013
  - 142 cases of syphilis in 2014

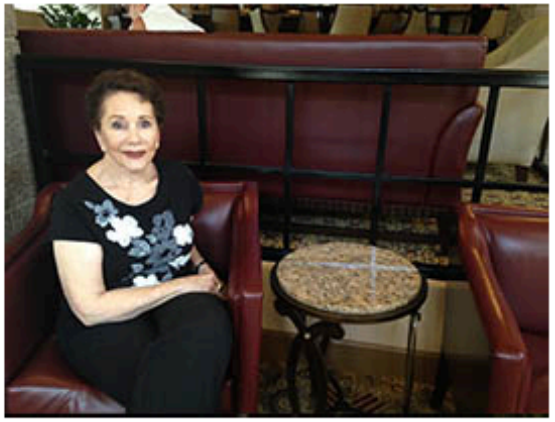
- As a result of the year to year increase, the syphilis rate in Pima County increased by 158% (14.2 cases per 100,000 population in 2014)

Cronkite News

Department of Health: STDs on the rise among Arizona senior citizens

Wednesday, April 29, 2015

By MACKENZIE CONCEPCION
Cronkite News



Lynn Brown Rosenberg, author of "My Sexual Awakening at 70," a book about her personal experience, said she urges fellow seniors to educate themselves about sex. State figures show a rise in

Figure CT 2: Comparison of 10 Year Reported Chlamydia Rates for Arizona and the United States, 2005-2014

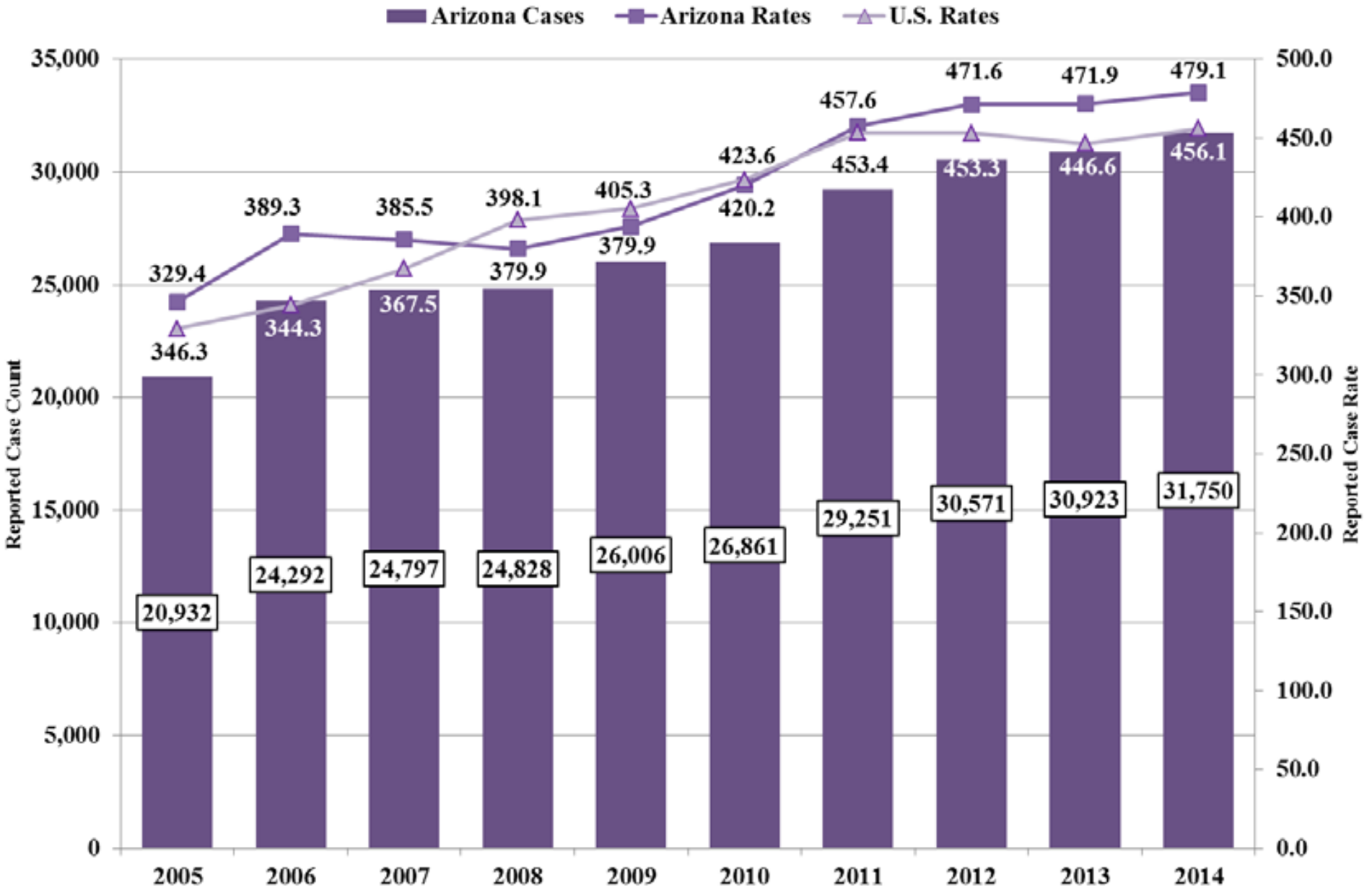


Figure CT 3: Chlamydia Rates by County, Arizona 2014

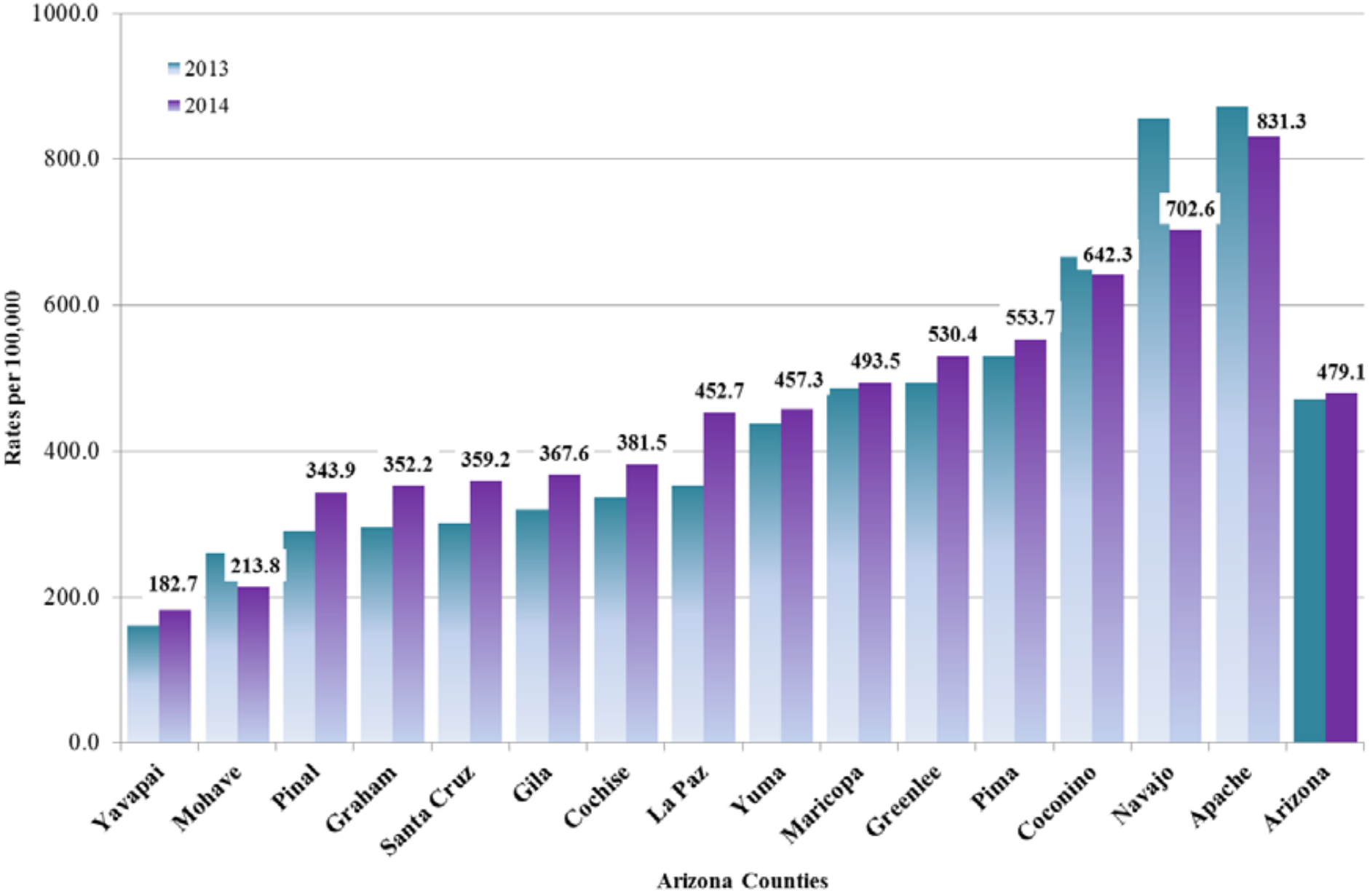


Figure GC 2: Comparison of 10 Year Reported Gonorrhea Rates for Arizona and the United States, 2005-2014

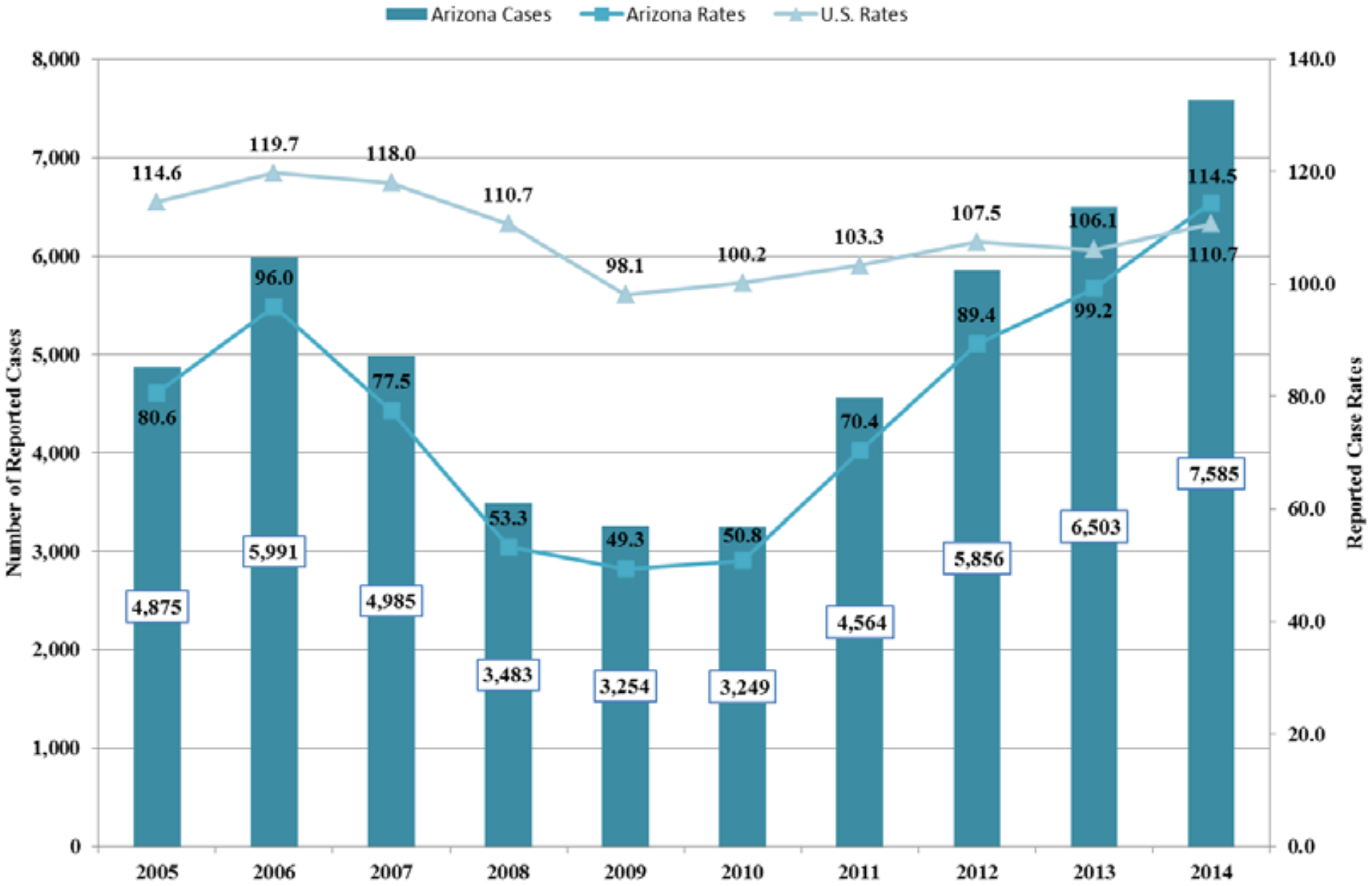


Figure GC 3: Gonorrhea Rates by County, Arizona 2014

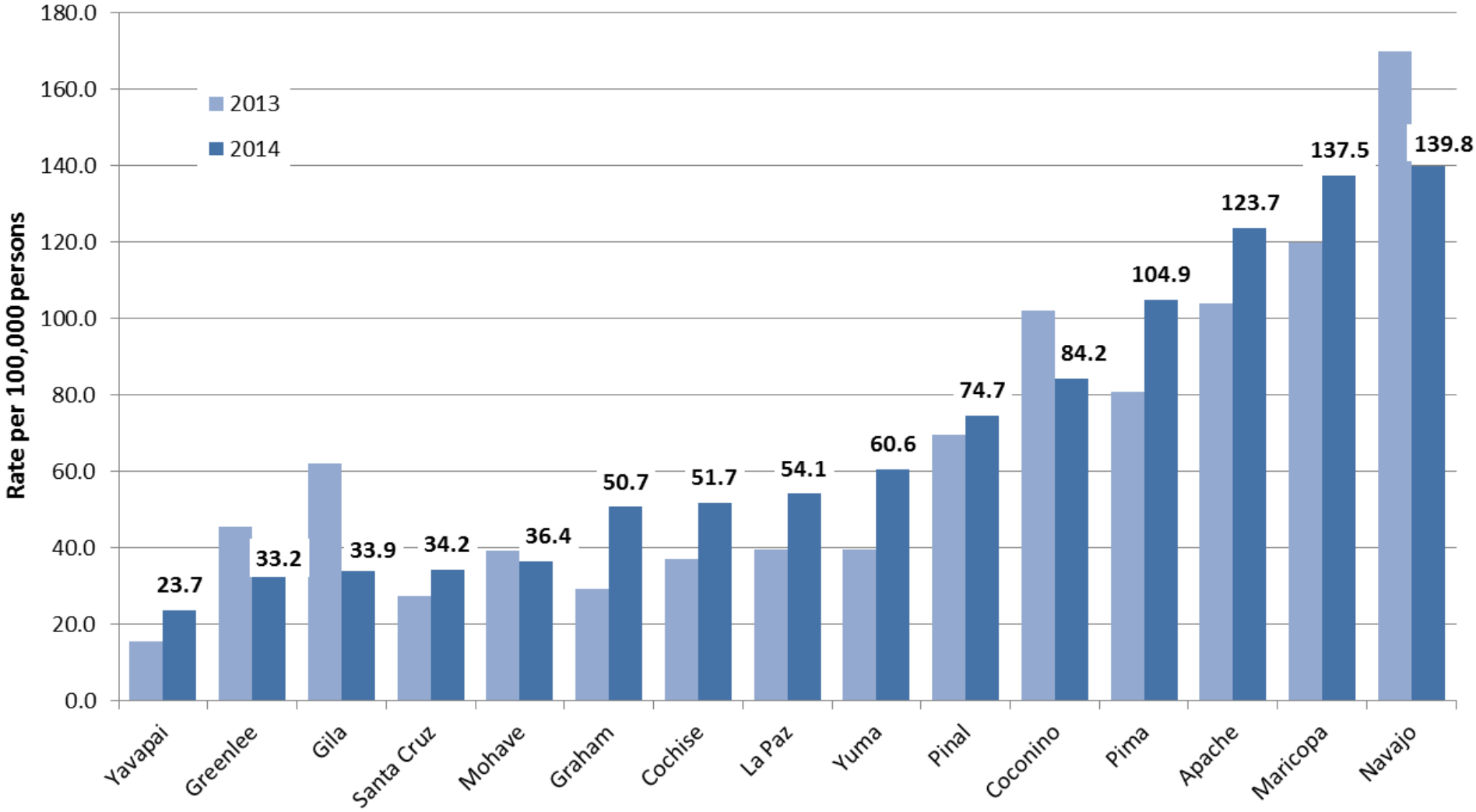


Figure S3: Reported Primary and Secondary Syphilis Case Rate
United States and Arizona 2005 - 2014

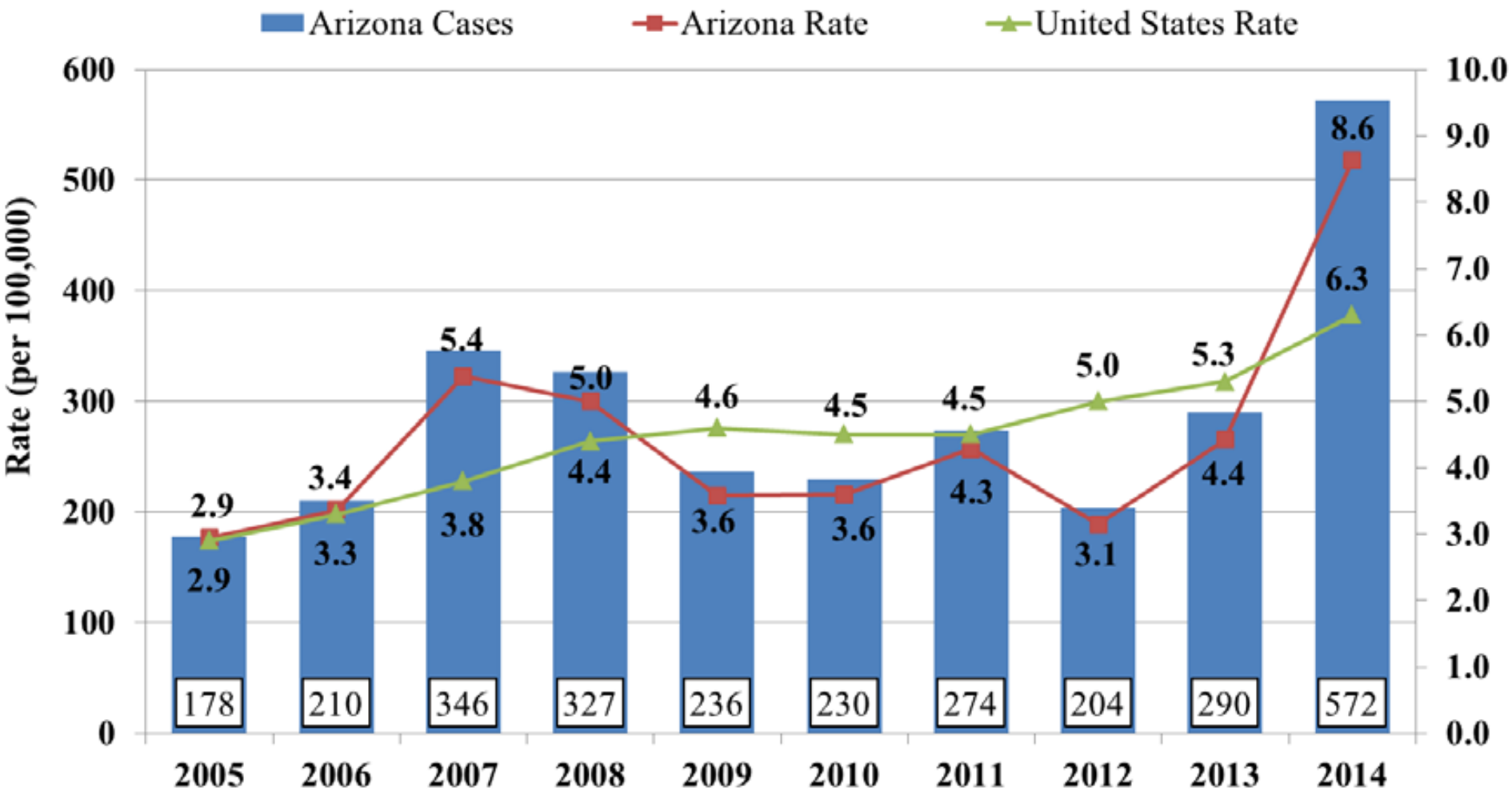
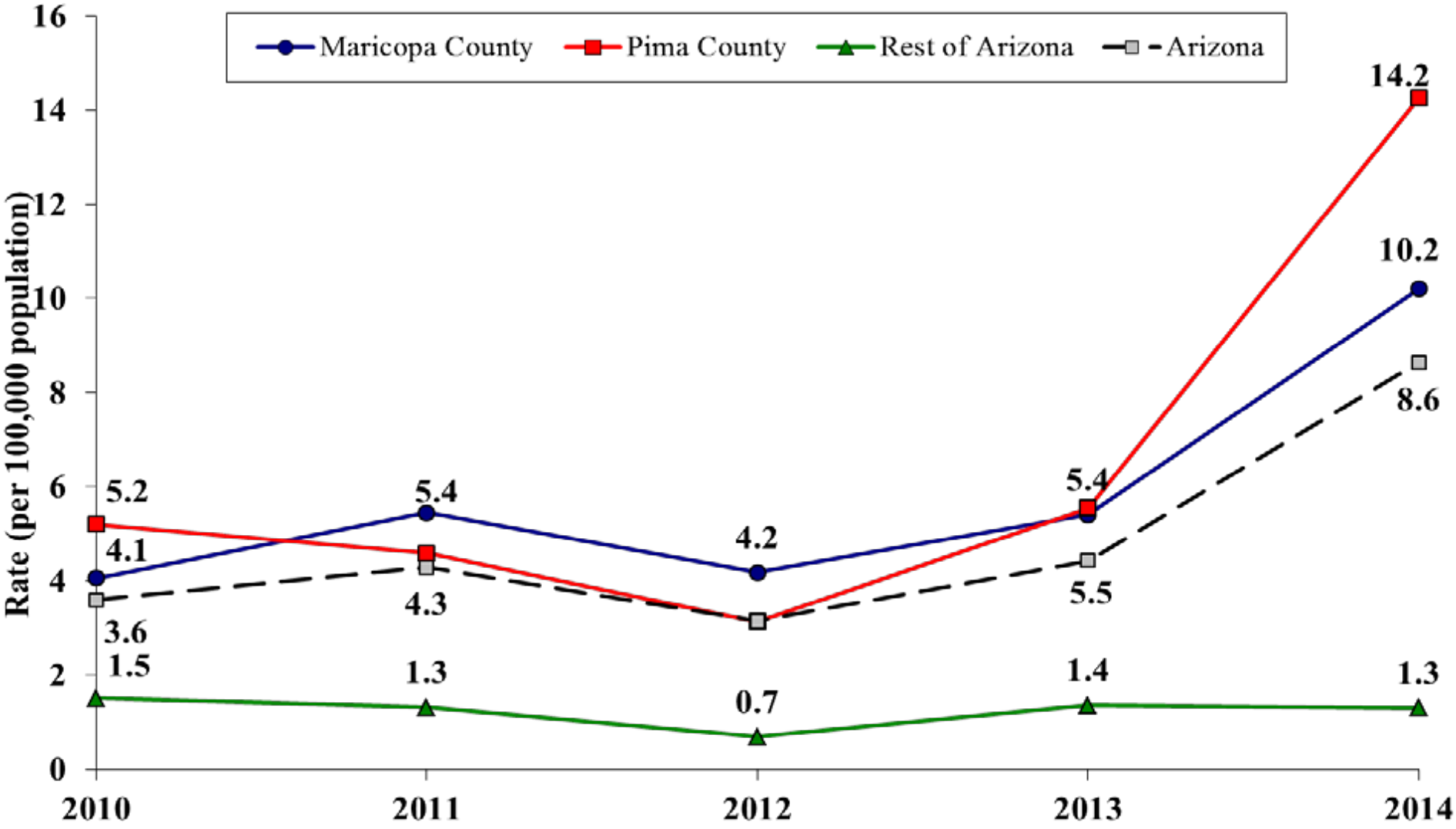


Figure S4: Reported Primary and Secondary Syphilis Case Rates by County of Residence, Arizona 2010 - 2014



Clinical Prevention Guidance

The prevention and control of STDs are based on the following 5 major strategies:

- Accurate risk assessment, education, and counseling on ways to avoid STDs through changes in sexual behaviors and use of recommended prevention services

- Pre-exposure vaccination of persons at risk for vaccine-preventable STDs (Human Papillomavirus and Hepatitis B Virus

- Identification of asymptomatically infected persons and persons with symptoms associated with STDs

Clinical Prevention Guidance

The prevention and control of STDs are based on the following 5 major strategies:

- Effective diagnosis, treatment, counseling, and follow up of infected persons

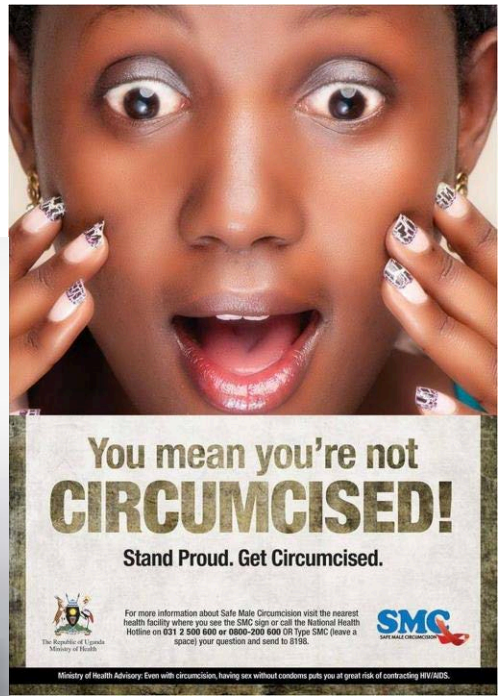
- Evaluation, treatment, and counseling of sex partners of persons who are infected with an STD

The Five P's approach to obtaining a sexual history

1. Partners
2. Practices
3. Prevention of Pregnancy
4. Protection
5. Past History

Prevention Methods

- Pre-exposure Vaccination
- Abstinence and Reduction of Partners
- Male Condoms
- Female Condoms
- Male Circumcision
- PEP and PrEP for HIV
- Expedited Partner Therapy



Case 1

- A 37 year old man presents with a lesion on his penis for 4 days and reports mainly discomfort surrounding the lesion
- He has been sexually active with 6 different partners during the last month (oral and anal receptive)
- He is HIV positive and is on antiretroviral therapy (ARV) with an undetectable viral load
- He reports no history of genital herpes

What is your differential diagnosis?

A. Herpes simplex virus (HSV)

A. *Haemophilus ducreyi* (Chancroid)

B. *Treponema pallidum* (Syphilis)

C. *Klebsiella granulomatis* (Granuloma inguinale)

D. Lymphogranuloma venereum (LGV)

Other Differential Diagnosis

- Behcet's syndrome
- Squamous cell carcinoma
- Reactive arthritis
- Contact Dermatitis
- Balanitis

Question 1

What tests would you order?

A. HSV PCR

B. HSV culture

A. RPR (rapid plasma reagin)

B. Culture for Chancroid

Case 1

- No previous history of syphilis and last RPR was negative during the last visit, 8 months ago
- Results: RPR non-reactive, HSV PCR negative
- Patient was notified and reported resolution of his lesion

Case 1

What is the most likely diagnosis?

A. Herpes simplex virus (HSV)

A. *Haemophilus ducreyi* (Chancroid)

B. *Treponema pallidum* (Syphilis)

C. *Klebsiella granulomatis* (Granuloma inguinale)

D. Lymphogranuloma venereum (LGV)

Case 1

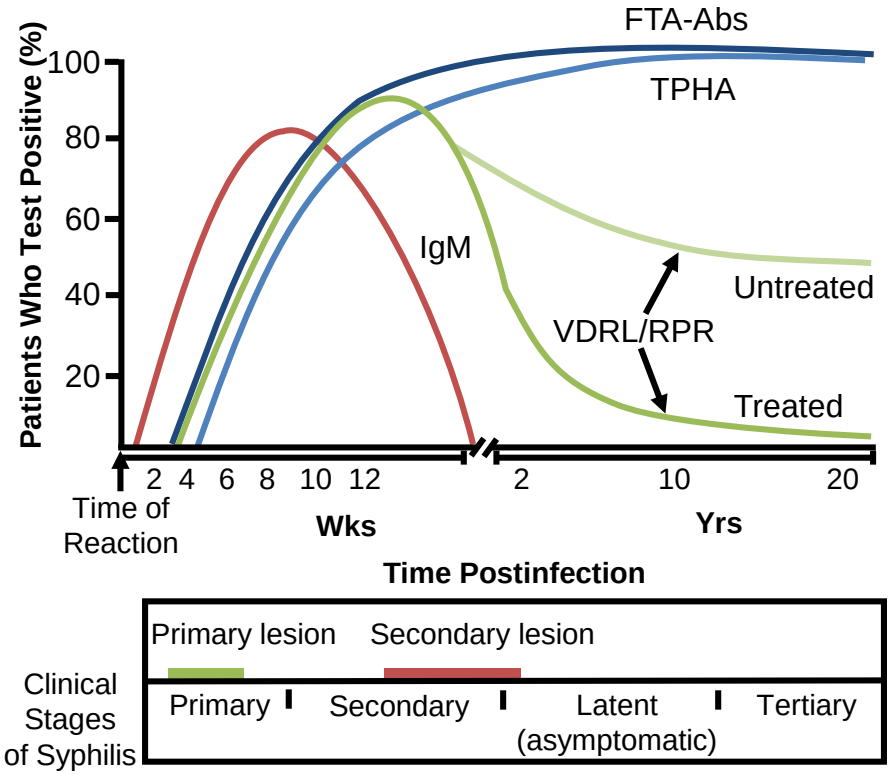
- Test Results:
  - RPR 1:256, *T. pallidum* passive particle agglutination assay (TP-PA) was Reactive
- Health Department notified
- Patient denied history of Penicillin allergy
  - Treated with one single dose of Benzathine penicillin G
- Scheduled for follow-up

Syphilis: Diagnosis

- A presumptive diagnosis of syphilis requires use of two tests:
  - A non-treponemal test
    - Venereal Disease Research Laboratory (VDRL)
    - Rapid Plasma Reagin (RPR)
  - A treponemal test
    - Fluorescent treponemal antibody absorbed test (FTA-ABS)
    - *T. pallidum* passive particle agglutination assay (TP-PA)
    - Enzyme immunoassays (EIAs)
    - Chemiluminescence immunoassays

Screening for Syphilis: Serological Tests

Common Patterns of Serological Reactivity in Syphilis Patients[1]



Serological Tests For Syphilis[1,2]

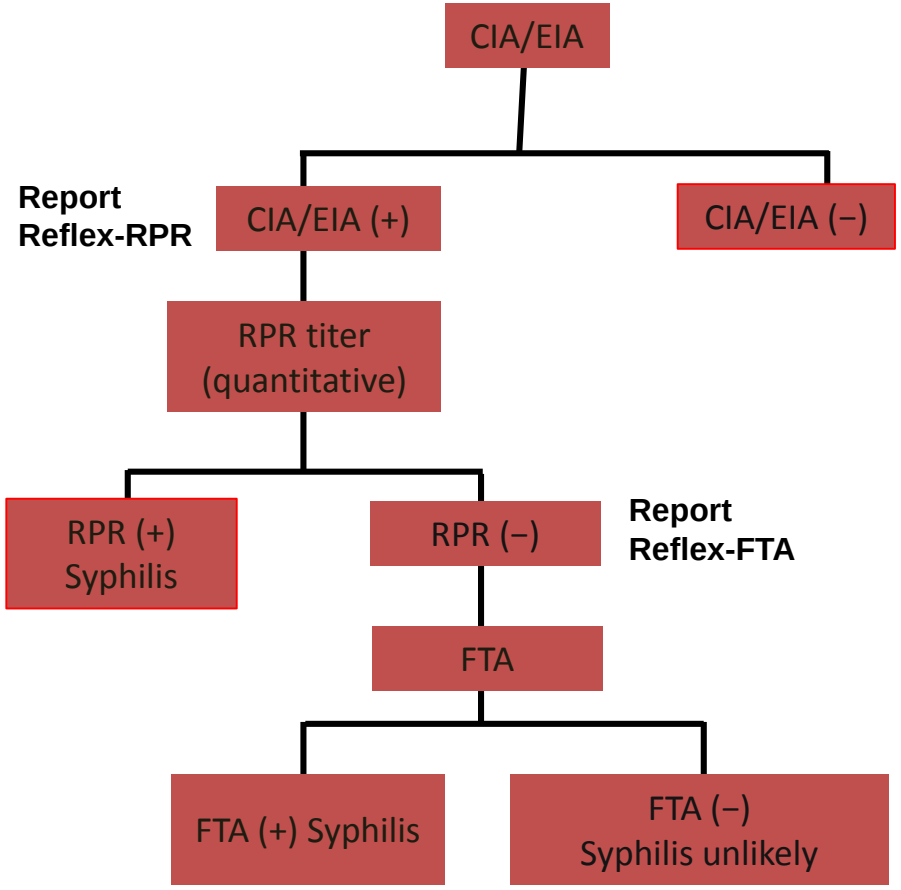
Nontreponemal Tests	Treponemal Tests
Complement fixation tests ▪ Wasserman reaction Flocculation tests ▪ RPR ▪ VDRL ▪ TRUST	▪ TPI ▪ FTA-Abs ▪ TPHA ▪ TPPA ▪ EIA ▪ WB and pseudoblots ▪ Automated chemi-luminescence platforms ▪ Chromatographic POC tests ▪ Microsphere Immunoassay

1. Peeling RW, et al Bull World Health Organ. 2004;82:439-446. 2. CDC. Reverse sequence syphilis screening.

Serologic Pitfalls in the Diagnosis of Syphilis

- Negative non-treponemal test may occur early in primary or late in tertiary syphilis
  - Check FTA-ABS or TP-PA
- Prozone Phenomenon: False negative due to lack of agglutination with elevated antibody titers
  - As the sample is diluted, agglutination occurs
- Serofast: Persistent, low level positive RPR titer after adequate treatment

Screening for Syphilis: Interpretation of Reverse Sequence Algorithm



Report
Reflex-RPR

Report
No serological evidence of infection with *Treponema pallidum*
Incubating or early primary syphilis cannot be excluded

Report
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

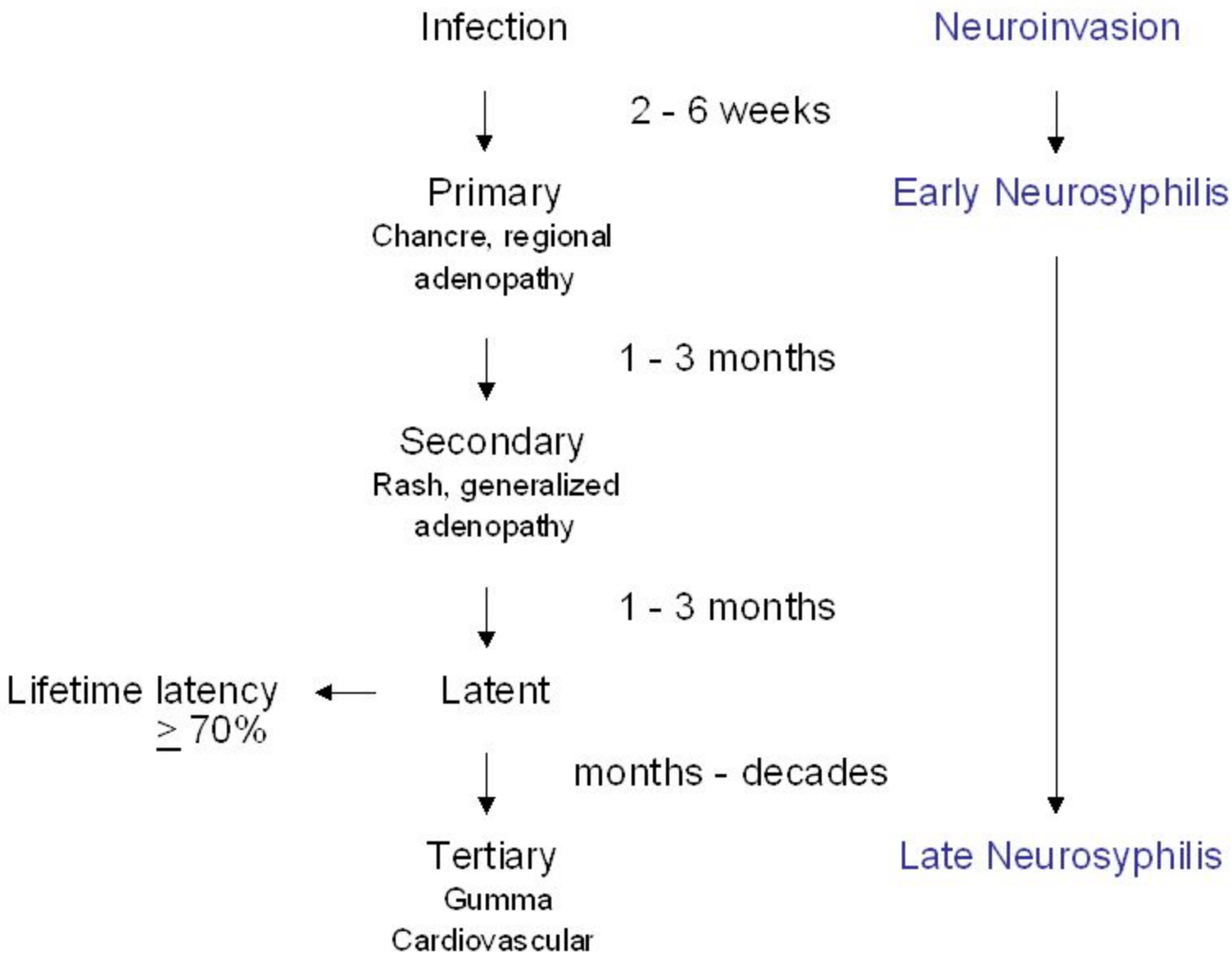
Report
Reflex-FTA

Report
Syphilis positive:
A. Early syphilis
B. Past treated syphilis
C. Past untreated syphilis

Report
Syphilis unlikely. Clinician may repeat testing in several wks if patient is at risk for syphilis

Slide courtesy of Barbara Detrick, JHH

Natural History of Syphilis



Primary Syphilis

- Serologic tests are negative in 25% of primary cases
- Non-treponemal tests may have slightly lower sensitivity than treponemal test in early primary syphilis
  - If serology negative and suspicion is low, schedule follow-up and repeat 2-4 weeks later
  - If serology is negative and suspicion is high, empirically treat and repeat serology 1 week after treatment

Primary Syphilis – Penile Chancre

Primary Syphilis
Multiple Vulvar Chancres

Mosby *STD Atlas, 1997*

SFCC

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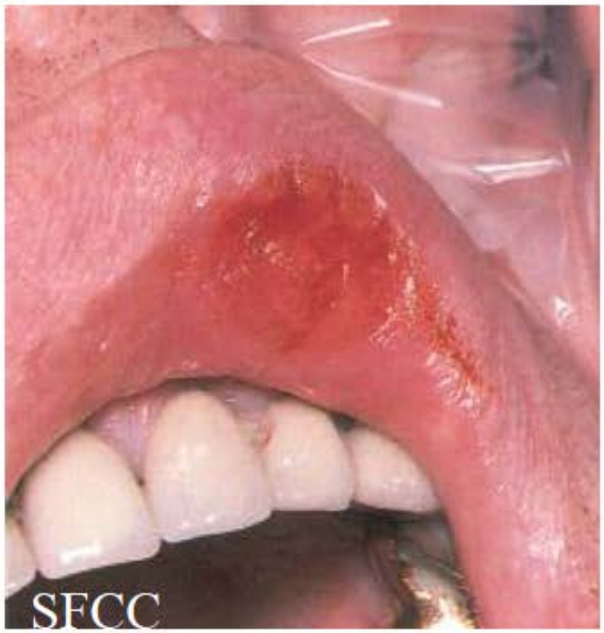
Primary Syphilis

Less Common Locations



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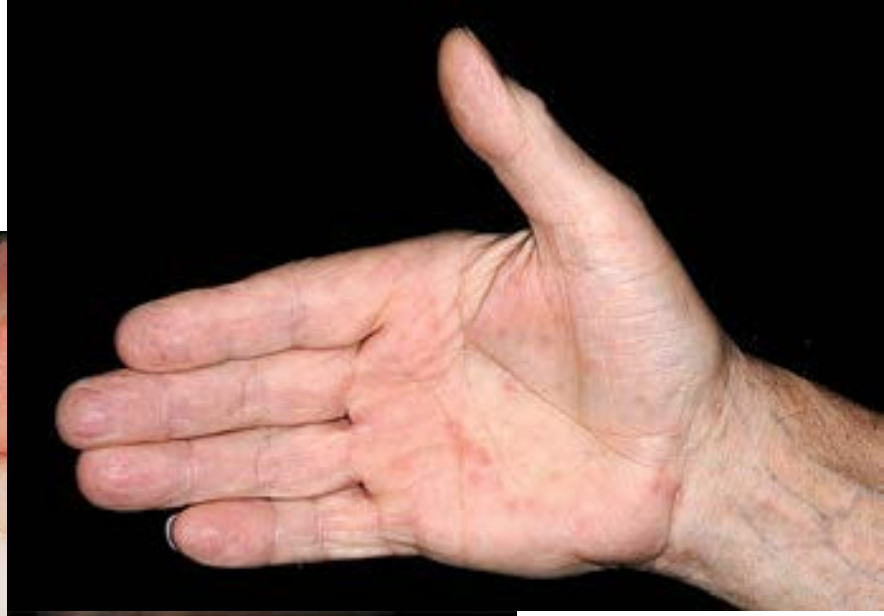
Primary and Secondary Syphilis



Secondary Syphilis
Condyloma Lata

Courtesy: Gregory Melcher, UC Davis
Susan Philip, SF DPH & UCSF

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Rash of Secondary Syphilis

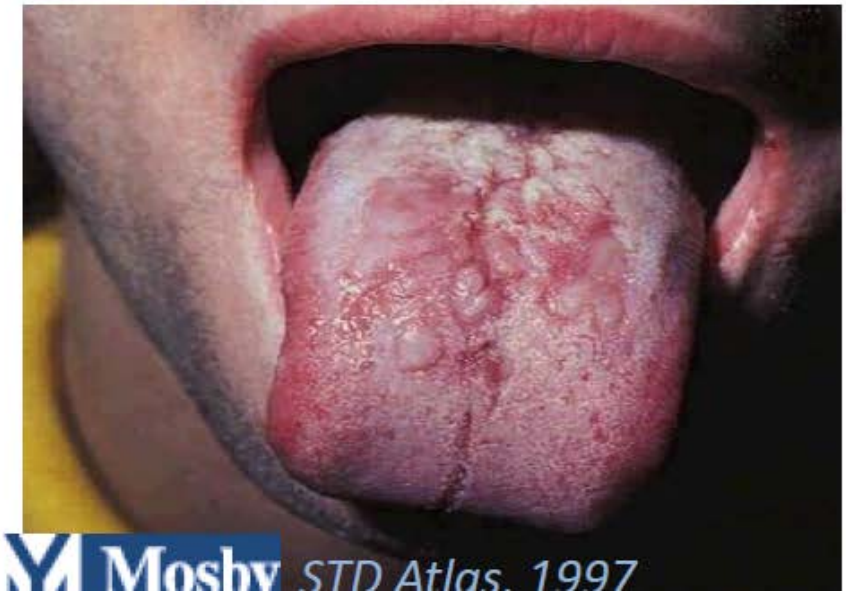
The NEW ENGLAND JOURNAL of MEDICINE

IMAGES IN CLINICAL MEDICINE

Papulonodular Syphilis

Annular Secondary Syphilis

Secondary Syphilis: Mucous Patches



Courtesy: Gregory Melcher, UC Davis
Susan Philip, SF DPH & UCSF

Mosby *STD Atlas, 1997*

Tertiary Syphils

Alopecia

Moth-Eaten

Diffuse

Mosby *STD Atlas, 1997*

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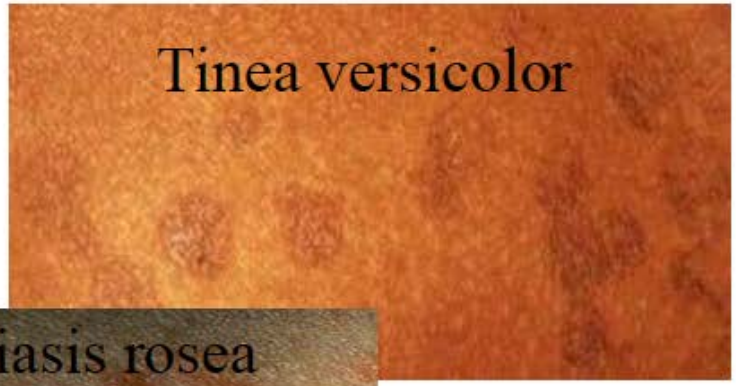
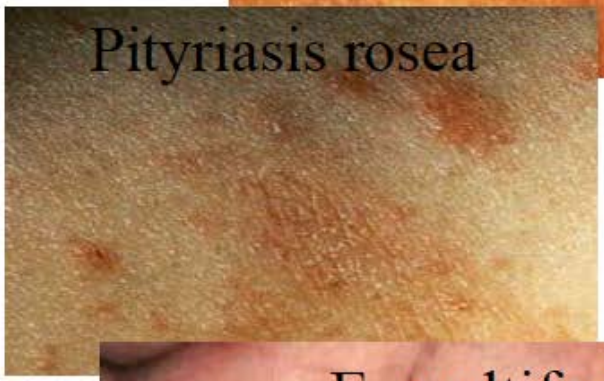
Differential Diagnosis of Secondary Syphilis Rash

- Tinea versicolor
- Pityriasis rosea
- Drug reaction
- Erythema multiforme
- Guttate psoriasis
- Scabies
- Viral Exanthem





December 2014 - March 2015: 12 cases of ocular syphilis were reported from San Francisco and Seattle

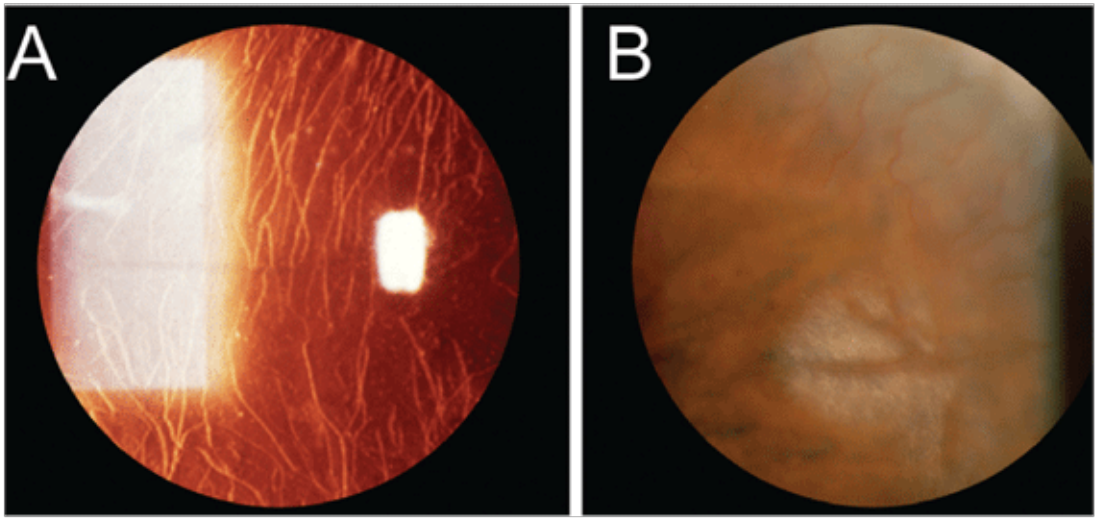
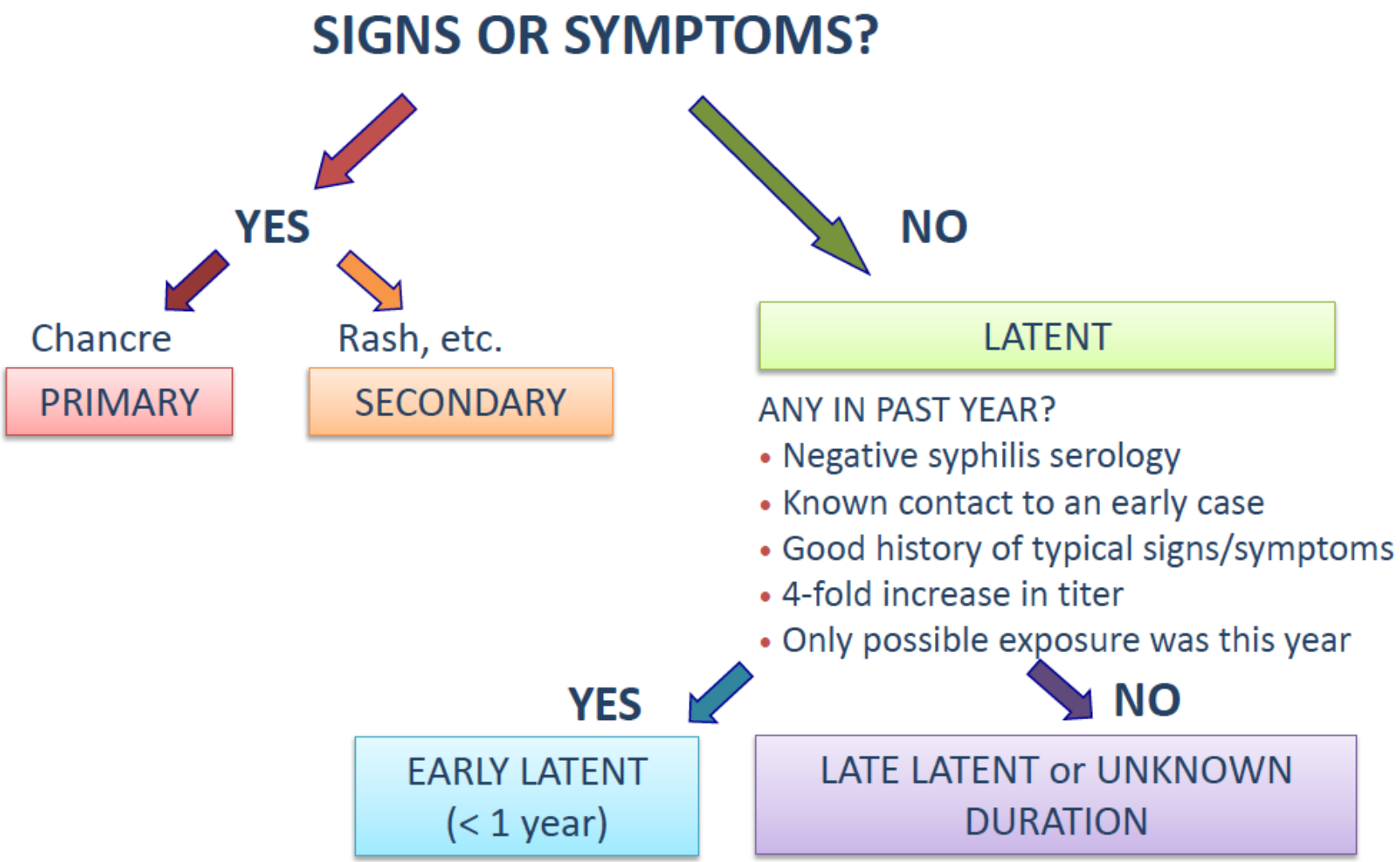


Figure 1. Syphilitic interstitial keratitis showing: A) inactive deep stromal vessels in retroillumination; and B) active deep stromal vessels with perivascular leukocytic cuffing in direct illumination.

Ocular Syphilis

- Neurosyphilis can occur during any stage of syphilis including primary and secondary syphilis
- Ocular syphilis, a manifestation of neurosyphilis, can involve almost any eye structure, but posterior uveitis and panuveitis are the most common
- Additional manifestations: anterior uveitis, optic neuropathy, retinal vasculitis and interstitial keratitis
- Treatment is same as neurosyphilis

Syphilis Staging Flowchart



Treatment

Primary Syphilis

Recommended Regimen for Adults*
Benzathine penicillin G 2.4 million units IM in a single dose

* Recommendations for treating syphilis in persons with HIV infection and pregnant women are discussed elsewhere in this report (see Syphilis among Persons with HIV infection and Syphilis during Pregnancy).

Early and Late Latent Syphilis

Recommended Regimens for Adults*
Early Latent Syphilis **Benzathine penicillin G** 2.4 million units IM in a single dose
Late Latent Syphilis or Latent Syphilis of Unknown Duration **Benzathine penicillin G** 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

* Recommendations for treating syphilis in persons with HIV infection and pregnant women are discussed elsewhere in this report (see Syphilis in Persons with HIV infection and Syphilis during Pregnancy).

Syphilis Follow-up

- All persons who have syphilis should be tested for HIV infection
- Quantitative non-treponemal serologic tests should be repeated at 6, 12, and 24 months (3, 6, 9, 12, and 24 months for HIV)
- A CSF examination should be performed if:
  - A sustained fourfold increase or greater in titer is observed
  - An initially high titer (≥1:32) fails to decline at least fourfold within 12–24 months of therapy
  - Signs or symptoms attributable to syphilis develop

Tertiary and Neurosyphilis Treatment

Recommended Regimen

Tertiary Syphilis with Normal CSF Examination
Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals

Recommended Regimen

Neurosyphilis and Ocular Syphilis
Aqueous crystalline penicillin G 18–24 million units per day, administered as 3–4 million units IV every 4 hours or continuous infusion, for 10–14 days

Alternative Regimen

Procaine penicillin G 2.4 million units IM once daily
PLUS
Probenecid 500 mg orally four times a day, both for 10–14 days

Neurosyphilis Follow-up

- If CSF pleocytosis was present initially, a CSF examination should be repeated every 6 months until the cell count is normal

- Follow-up CSF examinations also can be used to evaluate changes in the CSF-VDRL or CSF protein after therapy

- If the cell count has not decreased after 6 months, or if the CSF cell count or protein is not normal after 2 years, retreatment should be considered

Genital Herpes Simplex Infections

- Both HSV-1 and HSV-2 can cause genital herpes
- Most recurrent cases are caused by HSV-2 (approximately 50 million persons in the US)
- Acquisition of genital HSV-1 is increasing, and genital HSV-1 can be asymptomatic

Genital Herpes Simplex Infections

- Recurrences and subclinical shedding are more frequent for genital HSV-2 infection than for genital HSV-1 infection

- Prognosis and the type of counseling needed depend on the type of genital herpes (HSV-1 or HSV-2) causing the infection

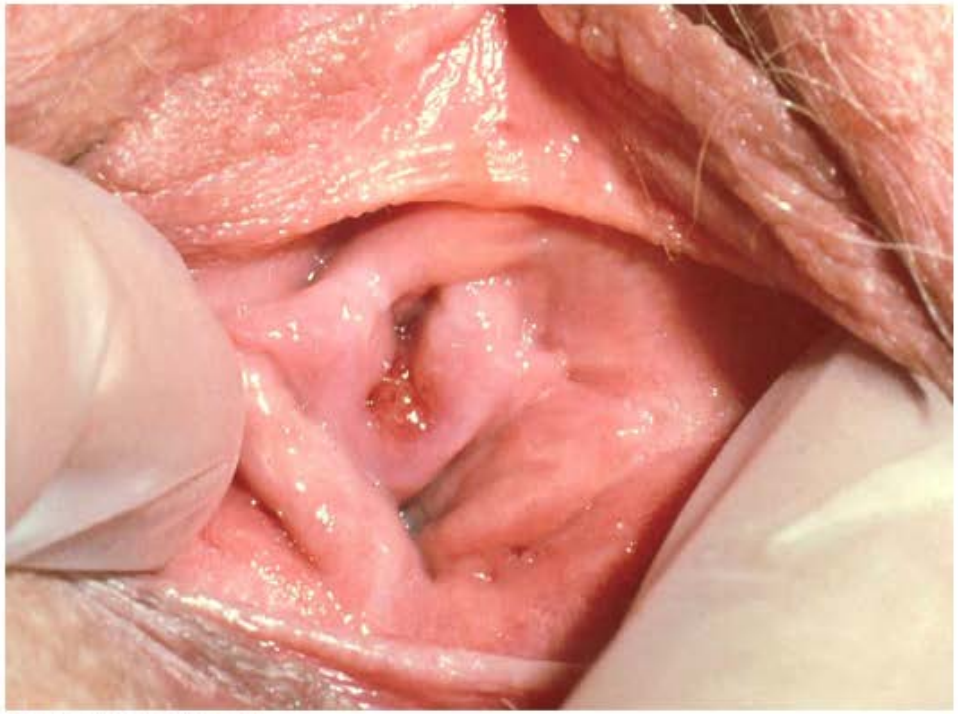
- The clinical diagnosis of genital herpes should be confirmed by type-specific laboratory testing







Atypical Herpes Lesions in Women



Courtesy: SF City Clinic

Atypical Herpes Lesions in Men

Courtesy: SF City Clinic

Virologic Tests

- Cell culture and PCR are the preferred HSV tests
- The sensitivity of culture is low (lower with healing lesions)
- Nucleic acid amplification methods, including PCR for HSV DNA, are more sensitive and are increasingly available
- Cytologic detection of cellular changes is an insensitive for diagnosing genital lesions (i.e., Tzanck preparation) and should not be relied on

Type-Specific Serologic Tests

- Because nearly all HSV-2 infections are sexually acquired, the presence of type-specific HSV-2 antibody implies anogenital infection

- The sensitivities of these glycoprotein G type-specific tests for the detection of HSV-2 antibody vary from 80%–98%

- False-negative results might be more frequent at early stages of infection

Type-Specific gG-Based HSV Serology:

	Sensitivity	Specificity
HerpeSelect-2™ ELISA (Focus)	96-100	97-100
HerpeSelect™ Immunoblot (Focus)	97-100	98
HerpeSelect Express (Focus)	86-100	97-100
Biokit™HSV-2 (biokitUSA)	93-100	94-97
Cobas®-HSV-2 (Roche)	93	98
Captia Select-HSV-2 (Trinity)	90-92	91-99

- Cost varies; $20-$140
- Western blot assay, considered gold standard, available through University of Washington

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Utility of Serologic Tests

- Recurrent genital or atypical symptoms with negative HSV PCR or culture
- Clinical diagnosis without laboratory confirmation
- A patient whose partner has genital herpes
- Testing should be considered for persons presenting for an STD evaluation, HIV infection, and MSM
- Screening for HSV-1 and HSV-2 in the general population is not indicated

Treatment

- All patients with first episodes of genital herpes should receive antiviral therapy

Suppressive Therapy for Recurrent Genital Herpes

- Suppressive therapy reduces the frequency of genital herpes recurrences by 70%–80% in patients who have frequent recurrences

- Treatment decreases the rate of HSV-2 transmission in discordant couples

Recommended Regimens
Acyclovir 400 mg orally twice a day OR **Valacyclovir** 500 mg orally once a day* OR **Valacyclovir** 1 g orally once a day OR **Famiciclovir** 250 mg orally twice a day

* Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).

Episodic Therapy for Recurrent Genital Herpes

Recommended Regimens
Acyclovir 400 mg orally three times a day for 5 days
OR
Acyclovir 800 mg orally twice a day for 5 days
OR
Acyclovir 800 mg orally three times a day for 2 days
OR
Valacyclovir 500 mg orally twice a day for 3 days
OR
Valacyclovir 1 g orally once a day for 5 days
OR
Famciclovir 125 mg orally twice daily for 5 days
OR
Famciclovir 1 gram orally twice daily for 1 day
OR
Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days

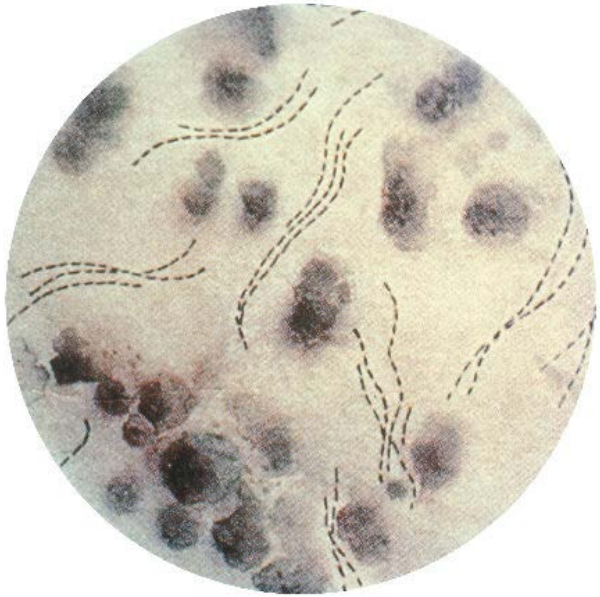
- Effective episodic treatment of recurrent herpes requires initiation of therapy within 1 day of lesion onset or during the prodrome that precedes some outbreaks

The combination of a painful genital ulcer and tender suppurative inguinal adenopathy suggests the diagnosis of?

- A. HSV-2
- B. LGV
- C. Chancroid
- D. Syphilis

Chancroid

- The prevalence of *H. ducreyi* (chancroid) has declined in the United States
- Like genital herpes and syphilis, chancroid is a risk factor in the transmission and acquisition of HIV infection
- A definitive diagnosis of chancroid requires the identification of *H. ducreyi* on special culture media that is not widely available
- The combination of a painful genital ulcer and tender suppurative inguinal adenopathy suggests the diagnosis of chancroid



Chancroid

- A probable diagnosis can be made if all of the following criteria are met:
  - The patient has one or more painful genital ulcers
  - The patient has no evidence of *T. pallidum*
  - The clinical presentation, appearance of genital ulcers and, if present, regional lymphadenopathy are typical for chancroid
  - A test for HSV performed on the ulcer exudate is negative

Chancroid

Recommended Regimens

Azithromycin 1 g orally in a single dose

OR

Ceftriaxone 250 mg intramuscularly (IM) in a single dose

OR

Ciprofloxacin* 500 mg orally twice a day for 3 days*

OR

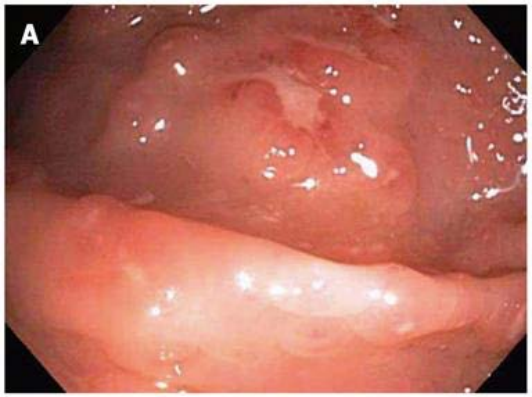
Erythromycin base 500 mg orally three times a day for 7 days

* Ciprofloxacin is contraindicated for pregnant and lactating women.

- If treatment is successful, ulcers usually improve symptomatically within 3 days and objectively within 7 days after therapy

Lymphogranuloma Venereum (LGV)

- LGV is a sexually transmitted infection caused by serovars L1, L2, and L3 of *C. trachomatis*
- LGV commonly presents in its classic or bubonic form as a chronic, systemic illness with a genital lesion, and prominent regional lymphadenopathy
- LGV can also cause a severe systemic proctitis and proctocolitis that occurs primarily in MSM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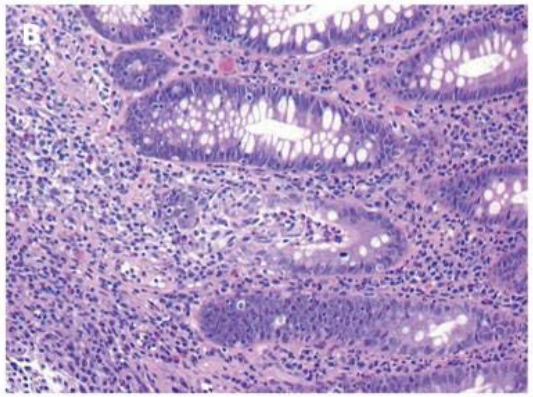
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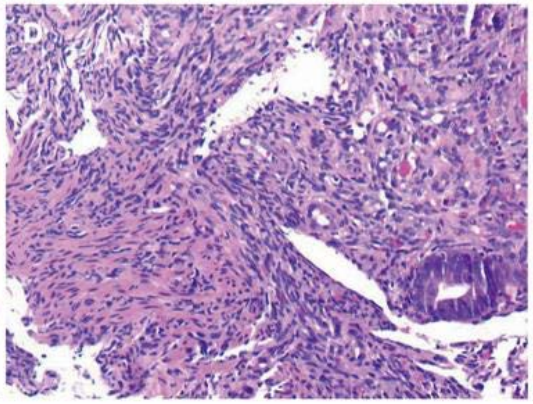
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Lymphogranuloma Venereum (LGV)

There are three distinct stages in classic LGV

1. The first stage is formation of a primary lesion, usually on the genital mucosa

2. The secondary stage is marked by systemic manifestations, including fever, headache, and myalgias followed by the rupture of the fluctuant inflammatory mass (bubo)

3. If untreated, some patients progress to a chronic tertiary stage of the infection (elephantiasis)

Lymphogranuloma Venereum (LGV)

- The disease can extend into the colon, and a granulomatous inflammatory process is present in the bowel wall, with both non-caseating granulomas and crypt abscesses

- Patients with LGV proctitis have mucopurulent anal discharge, as well as rectal pain, ulceration, and bleeding


I Got This Burning Sensation When I Pee Doc., Do You Think It's Serious?

Urethritis

Common Infectious Causes

- Bacterial STDs:
  - GC ~20%
  - CT 15-40%
- Non-gonococcal urethritis (NGU)
  - *Mycoplasma genitalium* 15-25%
  - Ureaplasma <15%?; data inconsistent
  - *Trichomonas vaginalis* ~5-15%
  - HSV 2-3%(in absence of skin lesions)
  - Adenovirus, enterics, Candida, anaerobes

Sexually Transmitted Diseases, 4th Edition, Holmes et al

Chlamydial Infections

- Chlamydia is the most frequently reported infectious disease in the US, and prevalence is highest in persons aged 24 and less

- Asymptomatic infection is common among both men and women but can be complicated by PID, ectopic pregnancy, and infertility

- Annual screening of all sexually active women aged <25 years and frequent testing of high risk men is recommended

Chlamydial Infections

Chlamydia and gonorrhea NAA Testing

- …*not* FDA-cleared for rectal or pharyngeal specimens but now the preferred testing method over culture
- Validation procedures can be done by labs to allow use of a non-FDA-cleared test or application
- Two commercial labs (Quest & LabCorp) currently provide GC/CT NAAT for rectal/pharyngeal specimens

	QUEST DIAGNOSTICS TEST CODES	LabCorp Test Codes
Pharyngeal	70051X	188698
Rectal	16506X	188672
Urine / Urethral	11363X	183194

CLIA Verified Labs for non-genital CT and GC NAATs list on NNPTC website (www.stdhivpreventiontraining.org) under Training Resources/Clinical Practice References.

Chlamydia Treatment

Recommended Regimens

- **Azithromycin** 1 g orally in a single dose
- **Doxycycline** 100 mg orally twice a day for 7 days

Alternative Regimens

- **Erythromycin** base 500 mg orally four times a day for 7 days
- **Levofloxacin** 500 mg orally once daily for 7 days

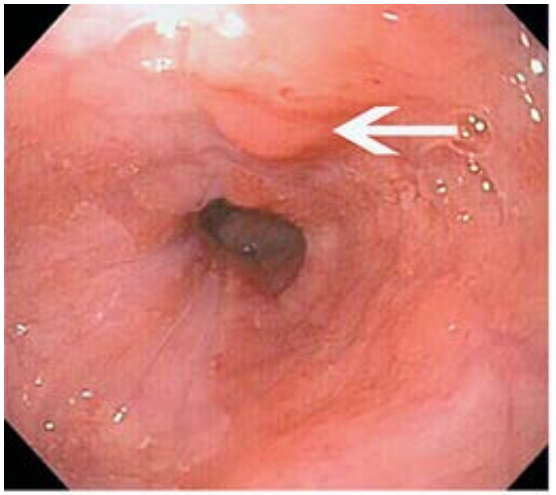
- **Ofloxacin** 300 mg orally twice a day for 7 days

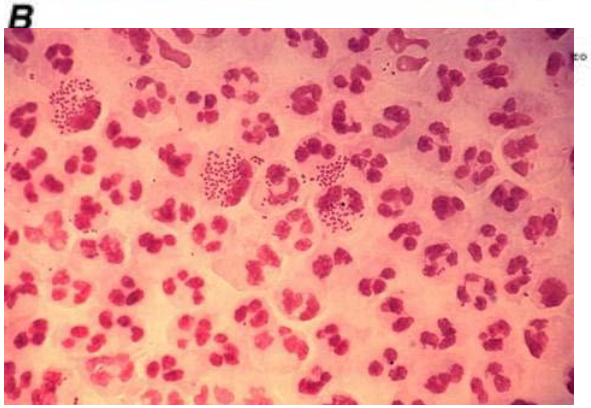
Chlamydia Follow-up

- Test-of-cure to detect therapeutic failure (i.e., repeat testing 3-4 weeks after completing therapy) is not advised except in pregnancy

- Men and women who have been treated for chlamydia should be retested approximately 3 months after treatment

Gonococcal Infections





Gonococcal Infections

- In the US, an estimated 820,000 new *N. gonorrhoeae* infections occur each year
- Gonorrhea is the second most commonly reported communicable disease
- Annual screening for *N. gonorrhoeae* infection is recommended for all sexually active women aged <25 years and for older women at increased risk for infection
- Subgroups of MSM are at high risk for gonorrhea and should be screened at sites of exposure

Gonococcal Infection: Diagnosis

- Specific microbiologic diagnosis of infection with *N. gonorrhoeae* should be performed in all persons at risk
- Culture and NAAT are available for the detection of genitourinary infection with *N. gonorrhoeae*
- Culture is available for detection of rectal, oropharyngeal, and conjunctival gonococcal infection
- NAAT is not FDA-cleared for use with these specimens

Antimicrobial-Resistant *N. gonorrhoeae*

- In 2007, emergence of fluoroquinolone-resistant *N. gonorrhoeae* in the US prompted CDC to cease recommending fluoroquinolones for treatment of gonorrhea

- CDC's 2010 STD treatment guidelines recommended dual therapy

- Treatment failures with cefixime or other oral cephalosporins have been reported in Asia, Europe, S. Africa, and Canada

Updated CDC GC Treatment Recommendations

- First line:
  - Ceftriaxone 250 mg IM x 1 + Azithromycin 1 g PO x 1
  - Use dual therapy even if *C. trachomatis* is ruled out
- Alternate (if Ceftriaxone is not available)
  - Cefixime 400 mg PO x 1 + azithromycin 1 g PO x 1

- Azithromycin allergy: doxycycline (100 mg twice a day for 7 days) can be used as an alternative second antimicrobial when used in combination with ceftriaxone or cefixime

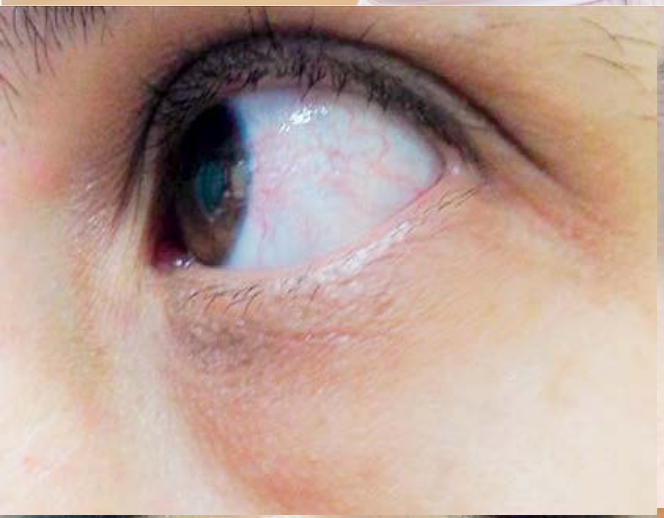
CDC. Morb Mortal Wkly Rep. 2012;61:590-594.

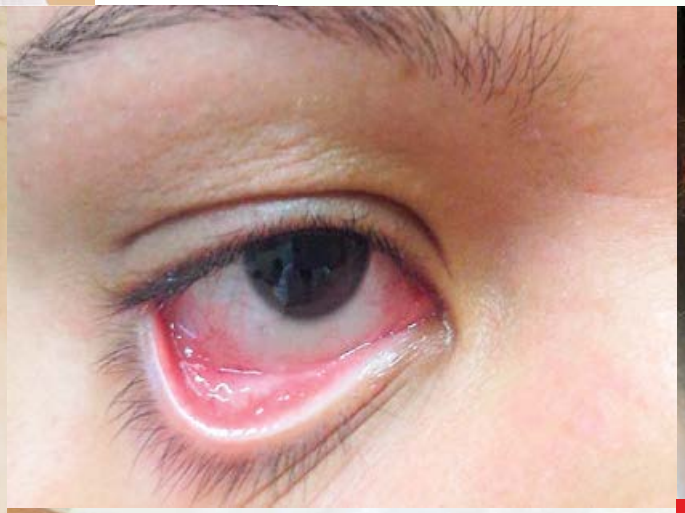
Other Antimicrobial Options

- Recent randomized trial of:
  - Intramuscular gentamicin 240 mg + oral azithromycin (2 g)
    - 100% effectiveness
  - Oral gemifloxacin (320 mg) + oral azithromycin (2 g)
    - 99.5% effectiveness
- Many trial participants reported adverse effects from the drugs, mostly gastrointestinal issues

Kirkcaldy RD. Sex Transm Infect. 2013;89:A14-A15.

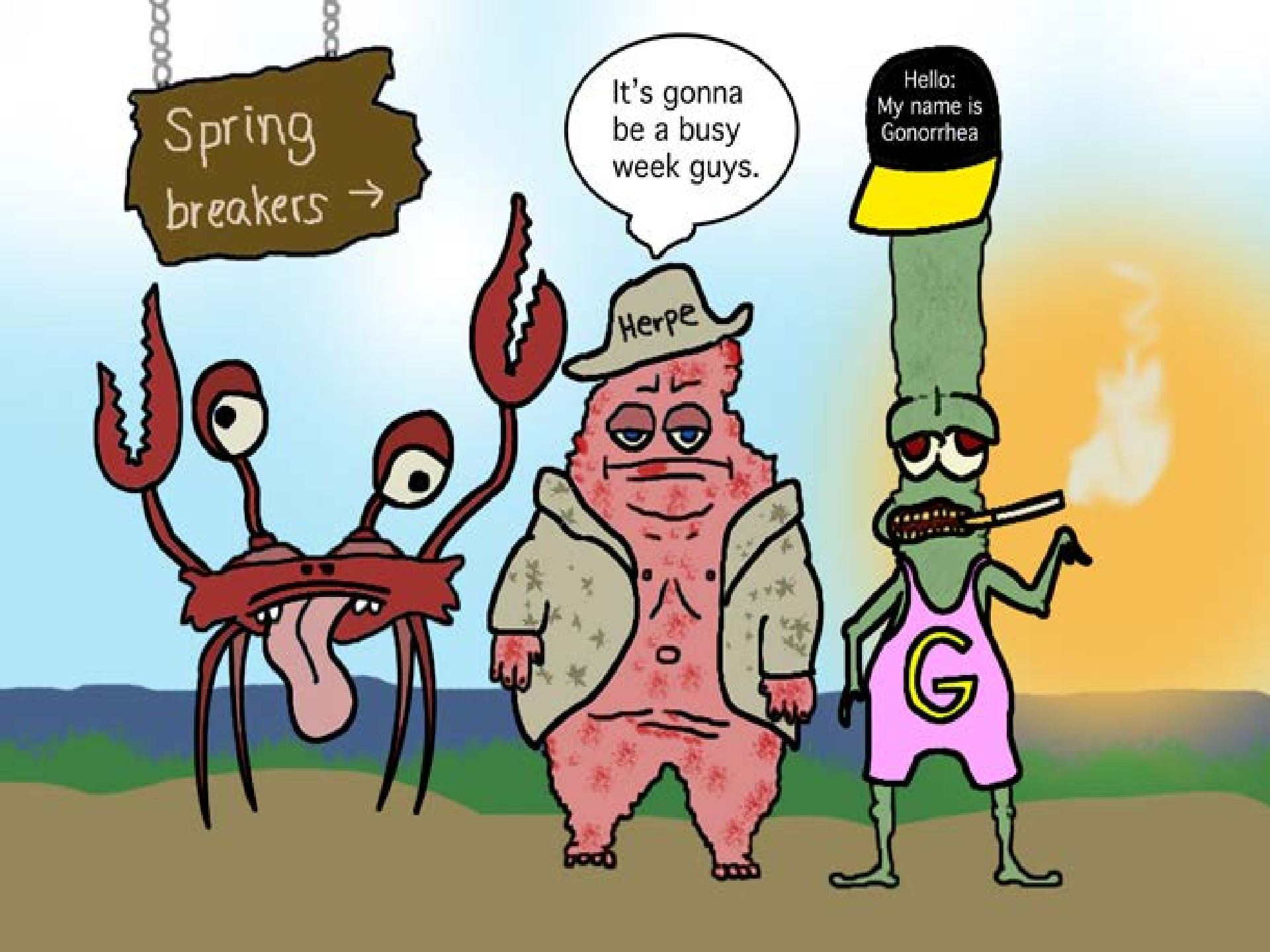
ZIKA & PREGNANCY





Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 64 / No. 3
June 5, 2015

Sexually Transmitted Diseases Treatment Guidelines, 2015


Spring breakers →
It's gonna be a busy week guys.
Herpe
Hello: My name is Gonorrhea
G