



Sexually Transmitted Diseases (STDs): Presentation, Diagnosis, & Management

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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

Centers for Disease Control and Prevention

MMWR

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Sexually Transmitted Diseases Treatment Guidelines, 2015

Arizona STDs

In 2013, 37,924 cases of STDs were reported in Arizona: Maricopa (63.9%), Pima (16.2%), Pinal (4.0%) and Yuma (2.5%)

- 1.2% of investigated cases were co-infected with HIV
- 3.96% 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
- 13 congenital syphilis cases were reported



Public Health Alert

Syphilis is on the rise in Pima County

Syphilis is a sexually transmitted infection. It is easy to become infected and it is easy to cure with testing and treatment.

In 2012 there were 31. As of July 2014, the number of cases has reached 77. Most (72%) cases occurred in men less than 40 years of age who report sex with other men. In this population 1 of 3 report being infected with HIV.

Symptoms may include

- A painless sore that appears inside or near the mouth, genital or anus
- A rash that appears on the palm of hands, bottom of feet, or on the body between the armpits and upper thighs

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**That rash might be
SYPHILIS**



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

 Recommend { 14  Tweet { 10  G+1 { 0  

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, 2003-2012

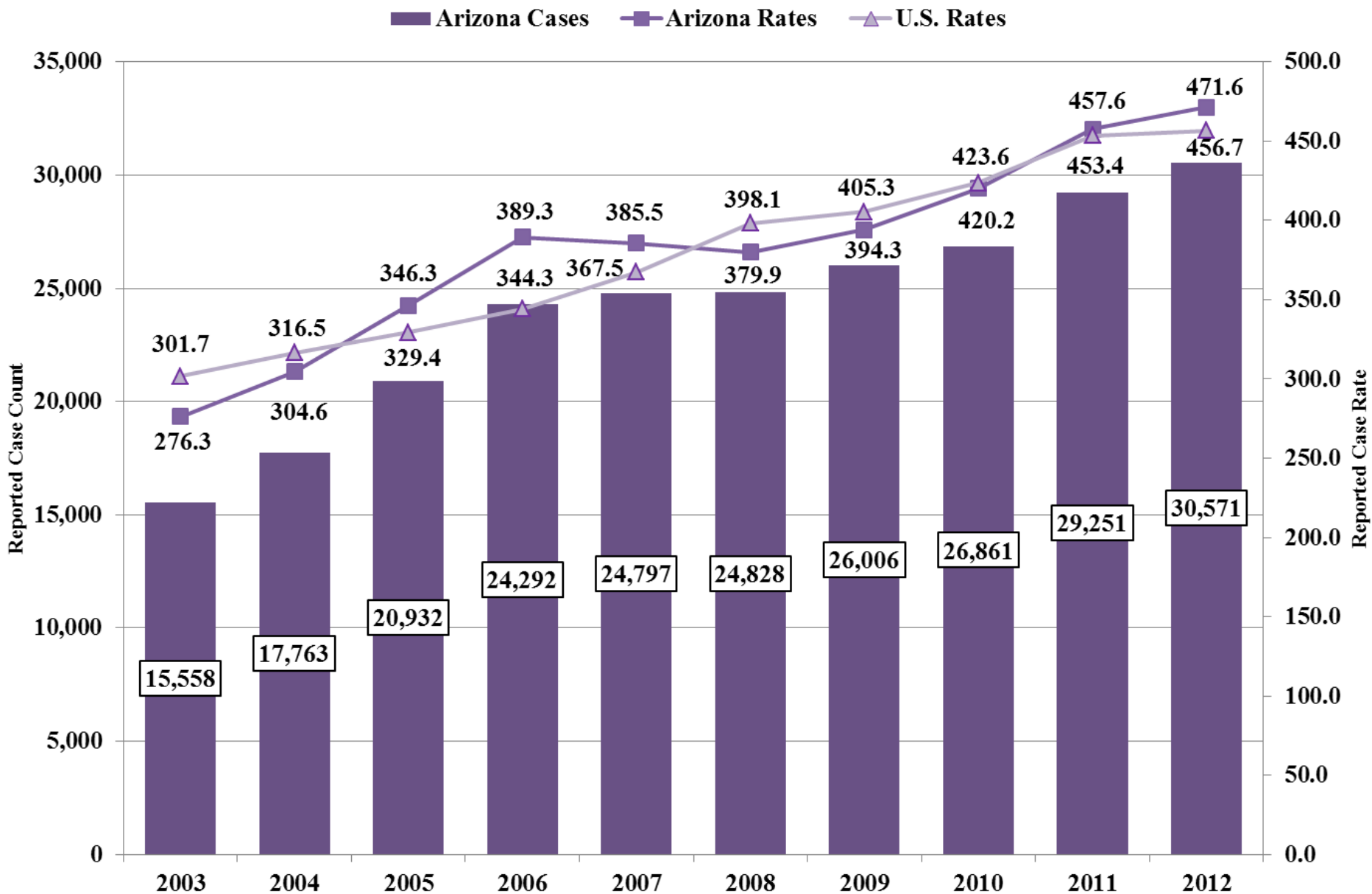
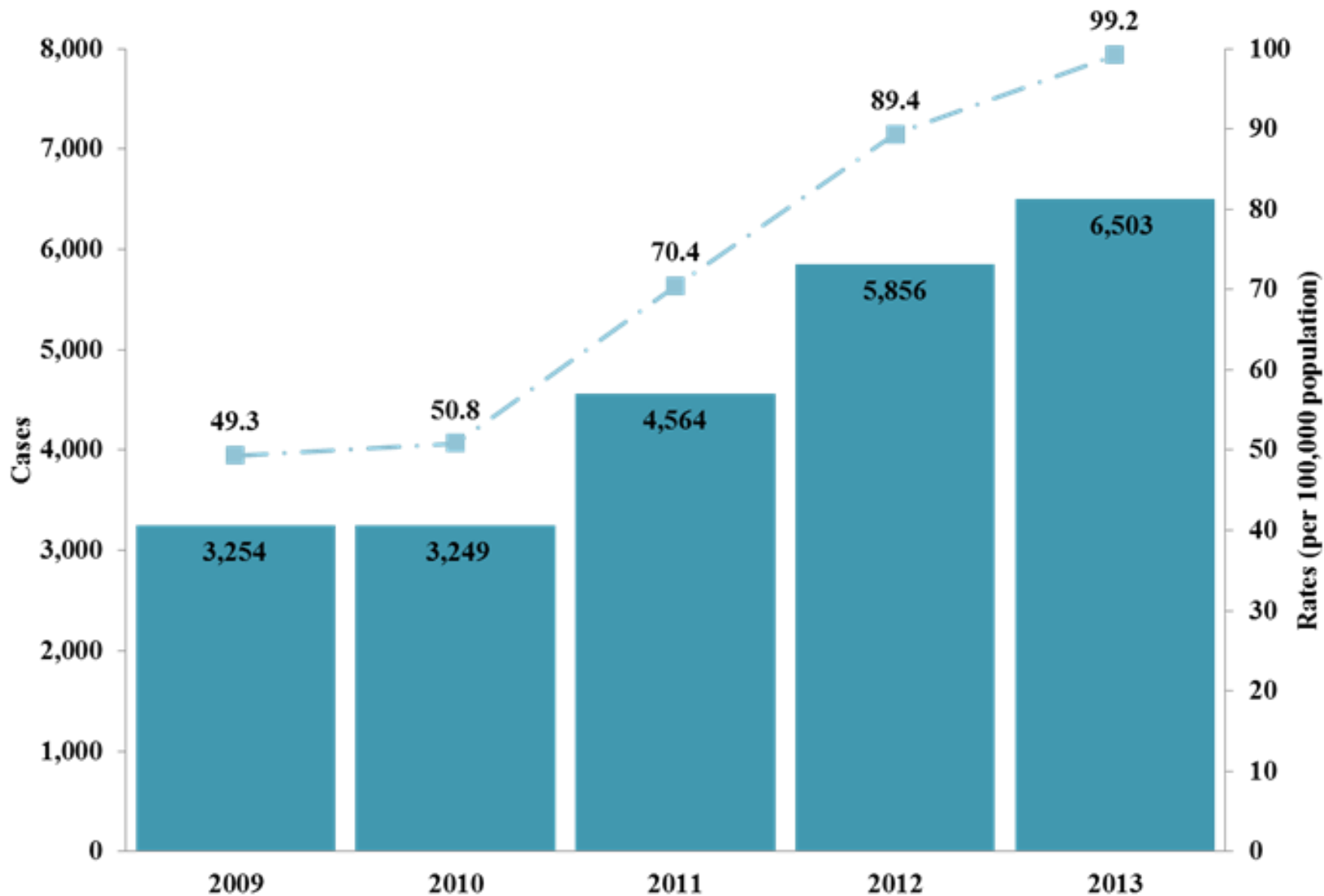


Figure GC 1: Reported Gonorrhea Cases and Rates, Arizona 2009-2013



Data is provisional and subject to changes,
*2012 CDC bridged data used for 2013 case rate population denominators.

Figure GC 3: Gonorrhea Rates by County, Arizona 2013

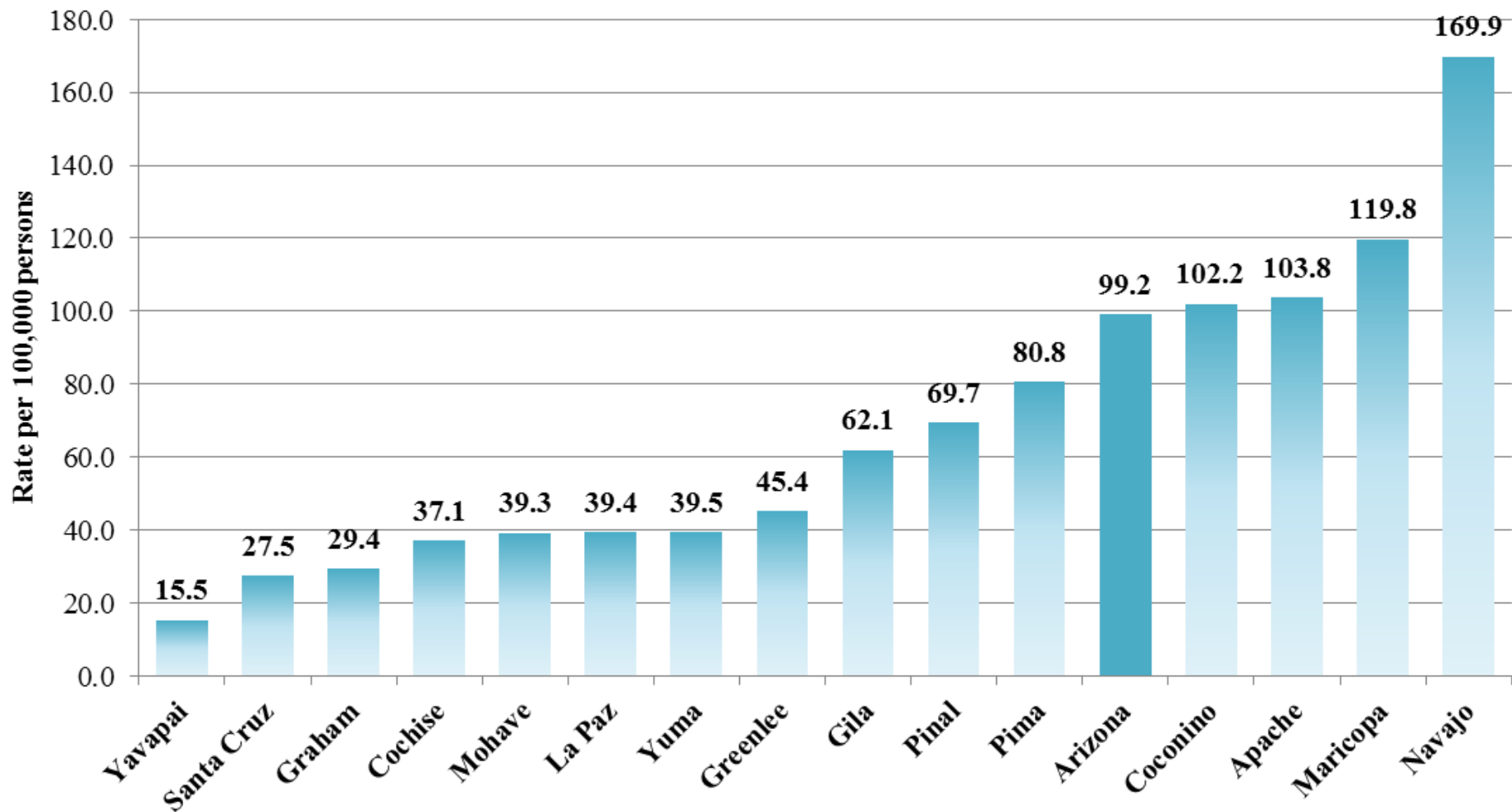


Figure S1. Reported Primary and Secondary Syphilis Cases and Case Rate, Arizona 2009-2013



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 (HPV and HBV)
- 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 Number of Sex Partners
- Male Condoms
- Female Condoms
- Male Circumcision
- PEP and PrEP for HIV
- Expedited Partner Therapy



You mean you're not
CIRCUMCISED!
Stand Proud. Get Circumcised.

 The Republic of Uganda
Ministry of Health

For more information about Safe Male Circumcision visit the nearest health facility where you see the SMC sign or call the National Health Hotline on 031 2 500 600 or 0800-200 600 OR Type SMC (leave a space) your question and send to 8198.

 **SMC**
SAFE MALE CIRCUMCISION

Ministry of Health Advisory: Even with circumcision, having sex without condoms puts you at great risk of contracting HIV/AIDS.

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 ARV with an undetectable viral load
- He reports no history of genital herpes
- **What is the differential diagnosis?**

Differential Diagnosis

- Herpes simplex virus (HSV)
- *Haemophilus ducreyi* (Chancroid)
- *Treponema pallidum* (Syphilis)
- *Klebsiella granulomatis* (Granuloma inguinale)
- *Chlamydia trachomatis* serovars L1-3 Lymphogranuloma venereum (LGV)
- Behcet's syndrome
- Squamous cell carcinoma
- Reactive arthritis
- Contact Dermatitis
- Balanitis

What tests would you order?

Laboratory Testing

STD	Direct Tests	Serology
Syphilis	Darkfield micro	Stat RPR
	<i>T. pallidum</i> PCR	POC EIA
	DFA <i>T. pallidum</i>	Non-trep (RPR, VDRL)
		Trep (TP-PA, FTA-ABS, EIA, CLIA)
Herpes	Culture	Type-specific HSV serology
	HSV PCR	POC type-specific HSV serology
Chancroid	Culture	

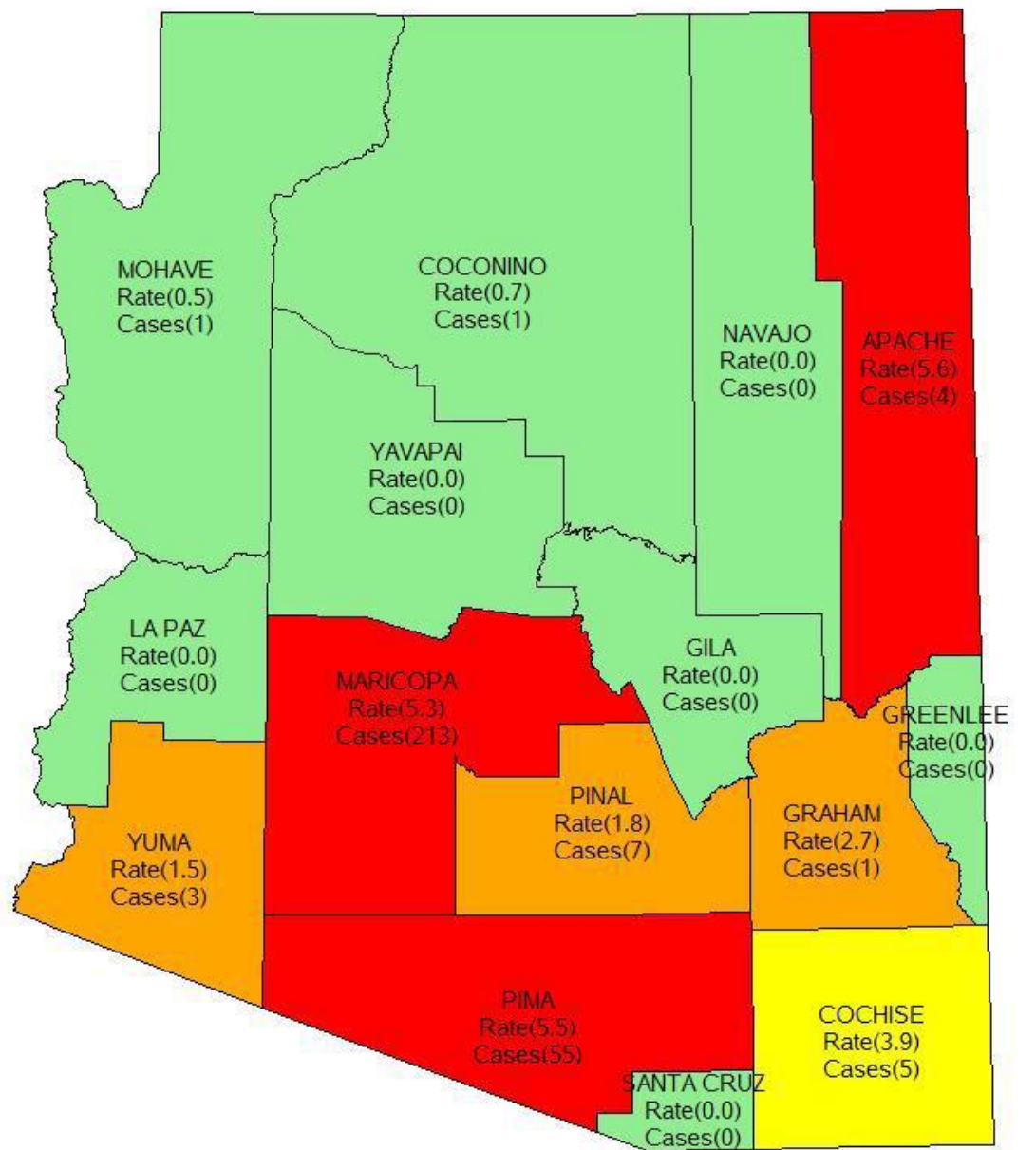
Case 1

- 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

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

Figure S2: Rate of Primary and Secondary Syphilis by County, Arizona 2013



Rate per 100,000 persons

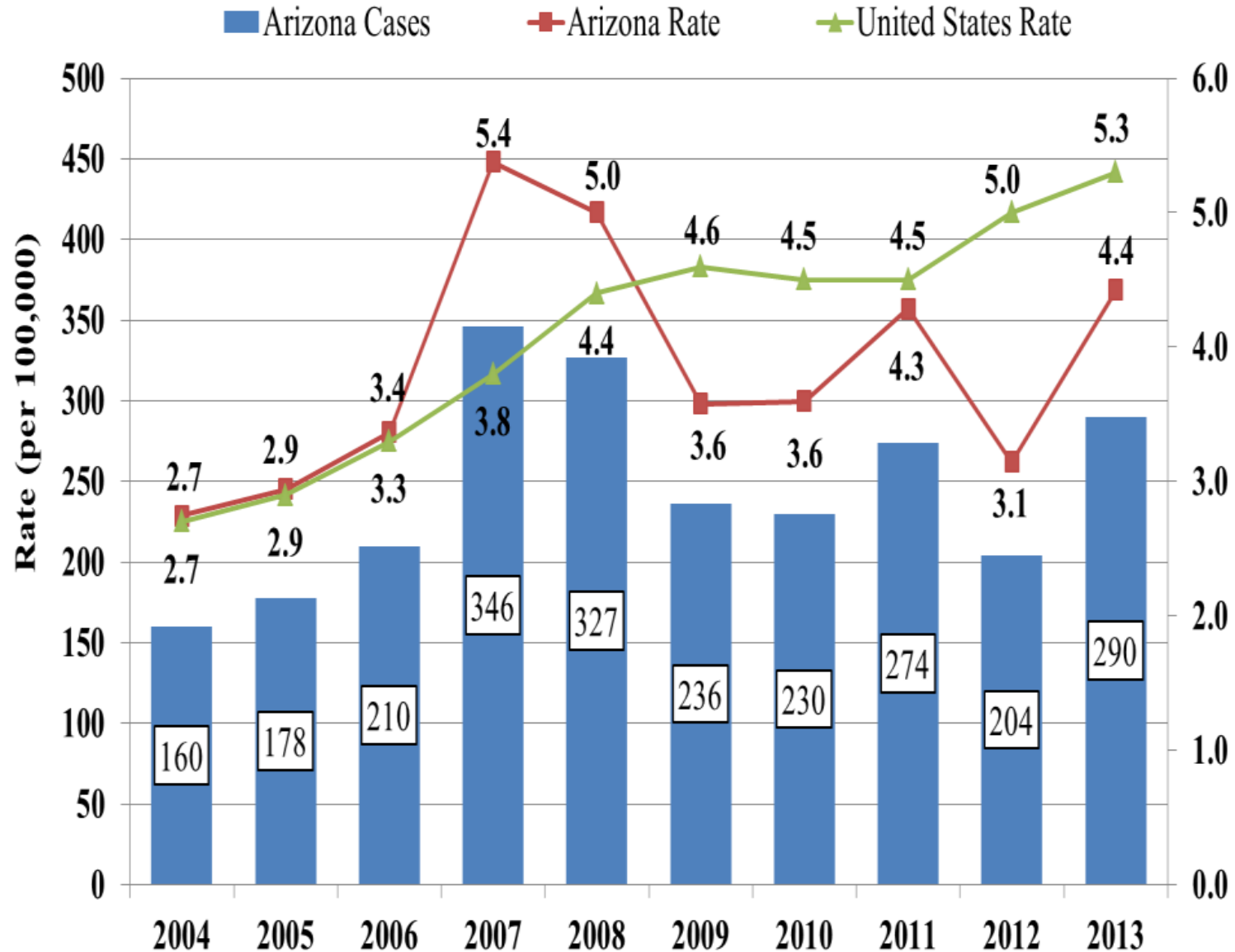
Less than 1

Between 1 and 3

Between 3 and 4

Greater than 5

Figure S3: Reported Primary and Secondary Syphilis Case Rate United States and Arizona 2004 - 2013



Syphilis Diagnosis

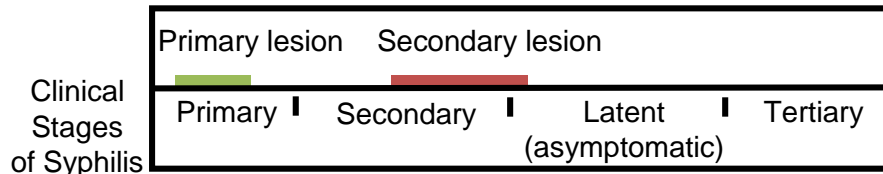
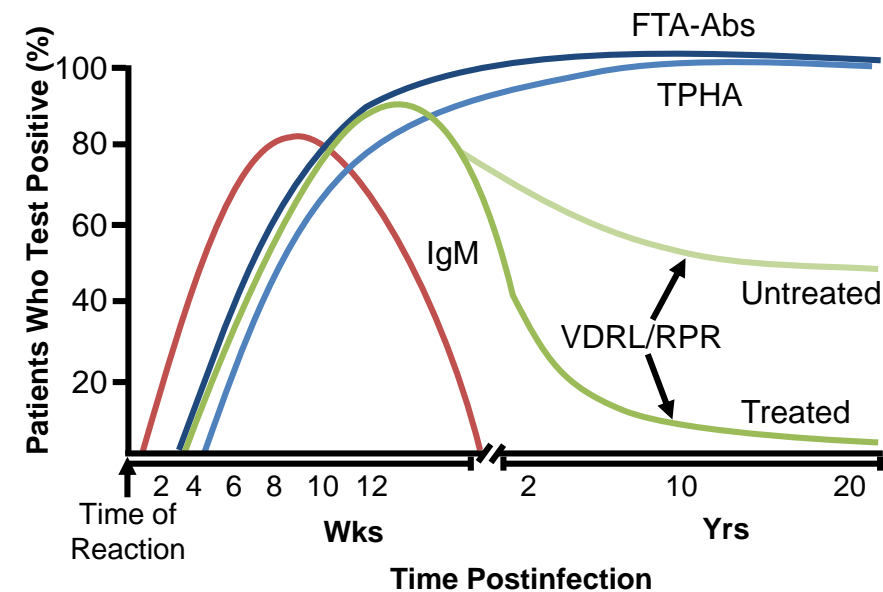
- A presumptive diagnosis of syphilis requires use of two tests:
 - A nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or Rapid Plasma Reagin [RPR]) and
 - A treponemal test (i.e., fluorescent treponemal antibody absorbed [FTA-ABS] tests, the *T. pallidum* passive particle agglutination [TP-PA] assay, various enzyme immunoassays [EIAs], chemiluminescence immunoassays, immunoblots, or rapid treponemal assays)

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

Screening for Syphilis: Serological Tests

Common Patterns of Serological Reactivity in Syphilis Patients^[1]



Serological Tests For Syphilis^[1,2]

Nontreponemal Tests

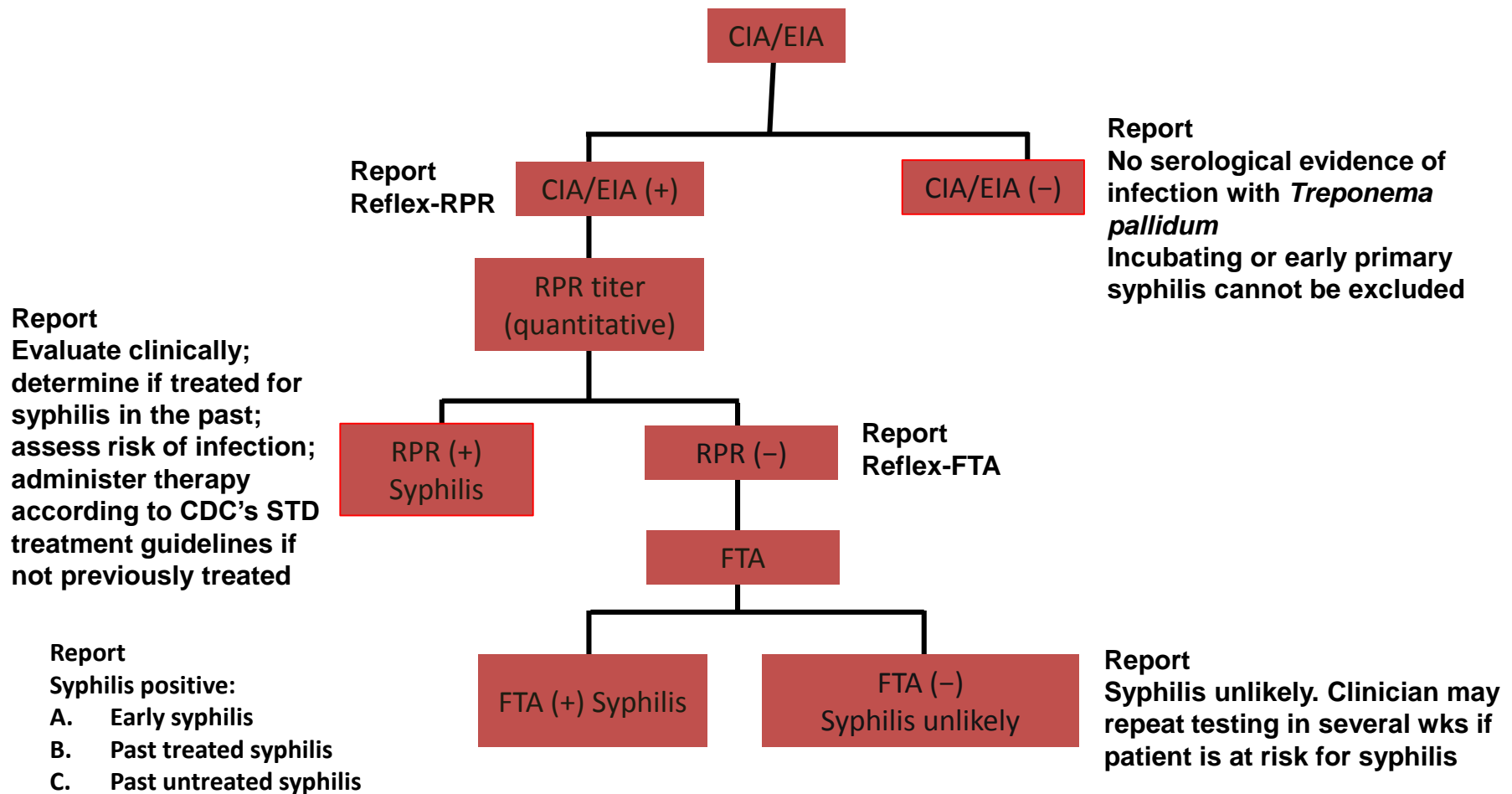
- Complement fixation tests
 - Wasserman reaction
- Flocculation tests
 - RPR
 - VDRL
 - TRUST

Treponemal Tests

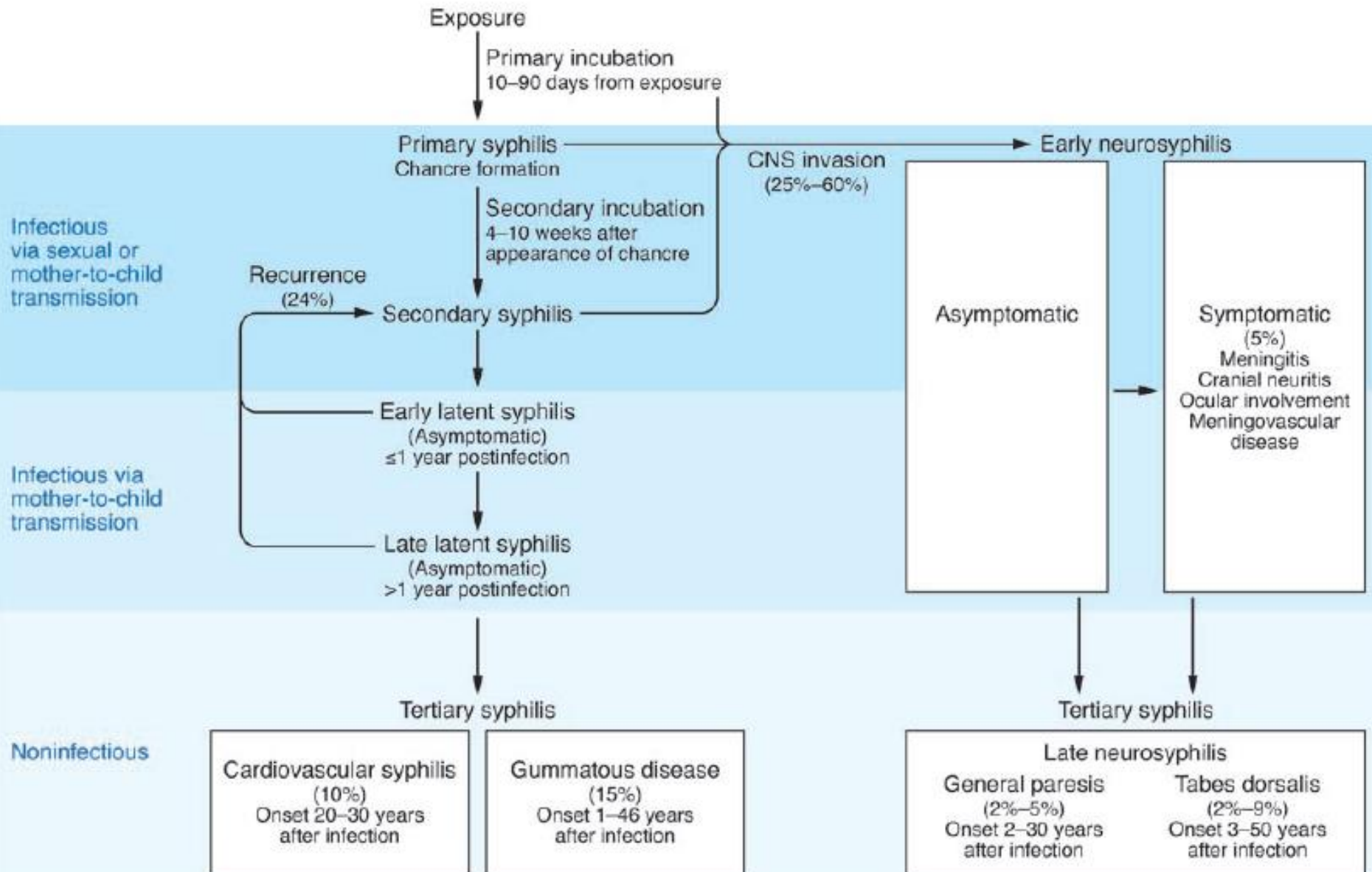
- TPI
- FTA-Abs
- TPHA
- TPPA
- EIA
- WB and pseudoblots
- Automated chemi-luminescence platforms
- Chromatographic POC tests
- Microsphere Immunoassay

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

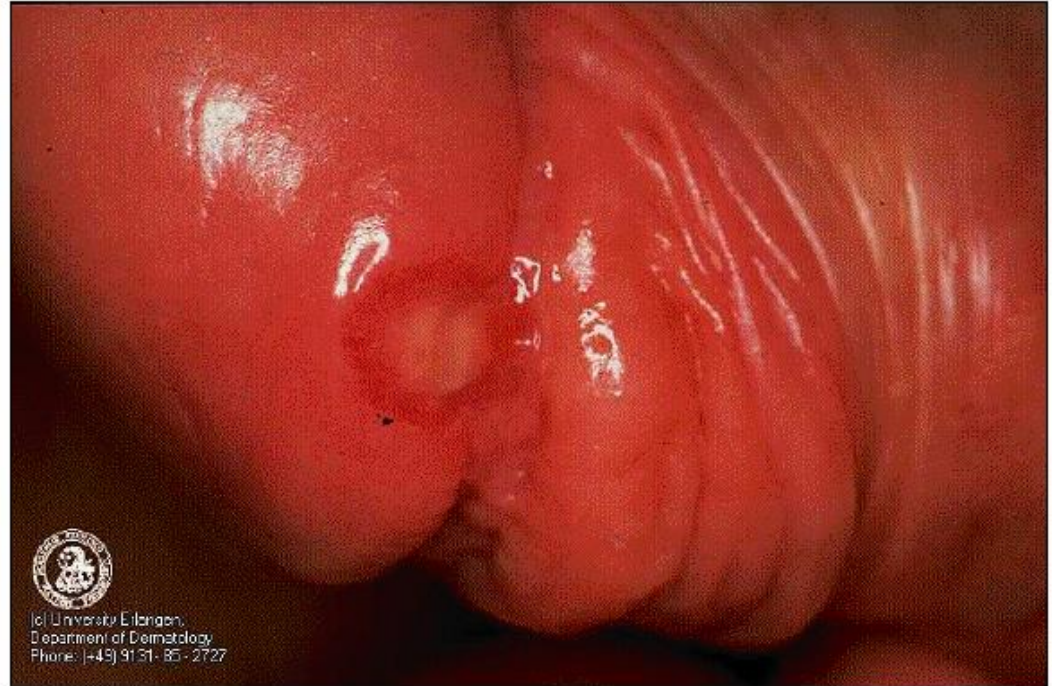
Screening for Syphilis: Interpretation of Reverse Sequence Algorithm



Natural History of Syphilis



Primary Syphilis Penile Chancre



*DOIA
Website,
2000*

Primary Syphilis

Multiple Vulvar Chancres



 **Mosby** *STD Atlas, 1997*

Primary Syphilis

Less Common Locations



Secondary Syphilis

Condyloma Lata



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

Rash of Secondary Syphilis



IMAGES IN CLINICAL MEDICINE

Papulonodular Syphilis



Annular Secondary Syphilis



Secondary Syphilis: Mucous Patches



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

Alopecia

Moth-Eaten



Diffuse



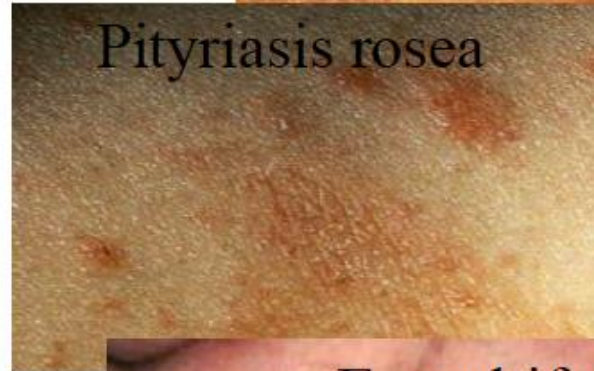
Differential Diagnosis of Secondary Syphilis Rash

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

Tinea versicolor



Pityriasis rosea

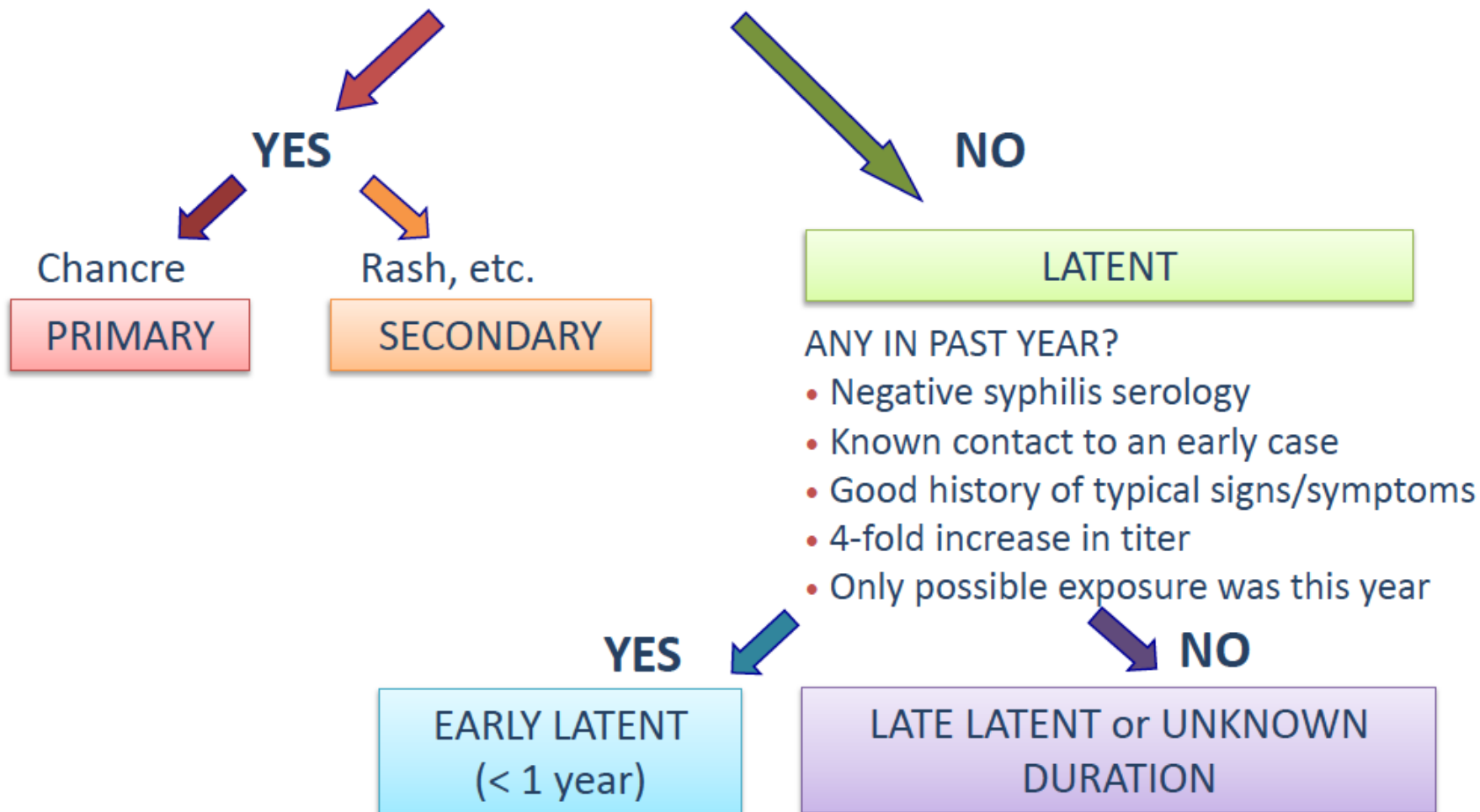


E. multiforme



Syphilis Staging Flowchart

SIGNS OR SYMPTOMS?



Case 1

- Test Results:
 - RPR 1:256, TP-PA Reactive
- Health Department notified
- Patient denied history of Penicillin allergy
 - Treated with PCN x 1
- Scheduled for follow-up

Treatment

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).

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 nontreponemal 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 (>2 weeks) fourfold increase or greater in titer is observed
 - An initially high titer ($\geq 1:32$) 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

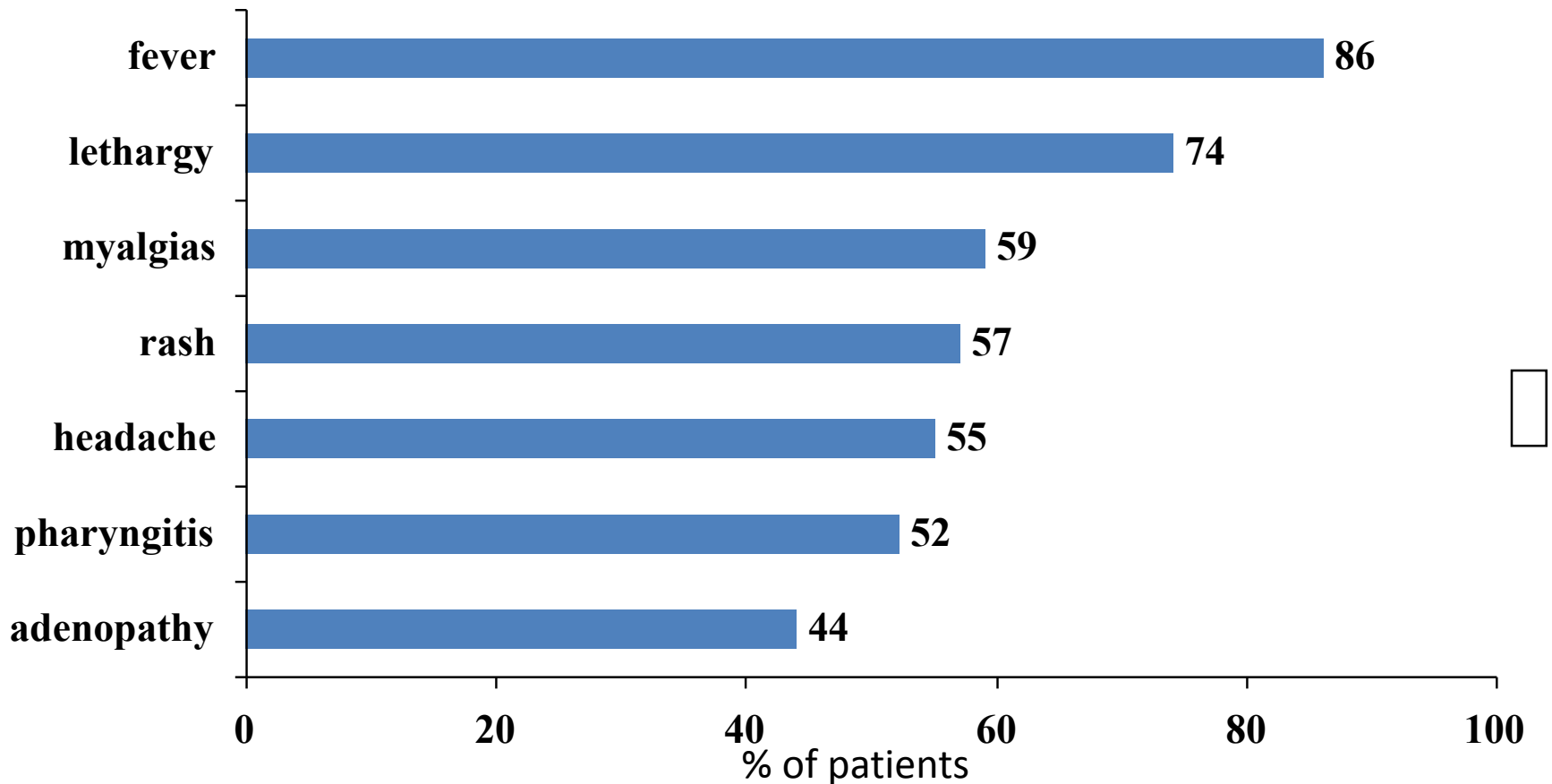
Neurosyphilis Follow-up

- 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

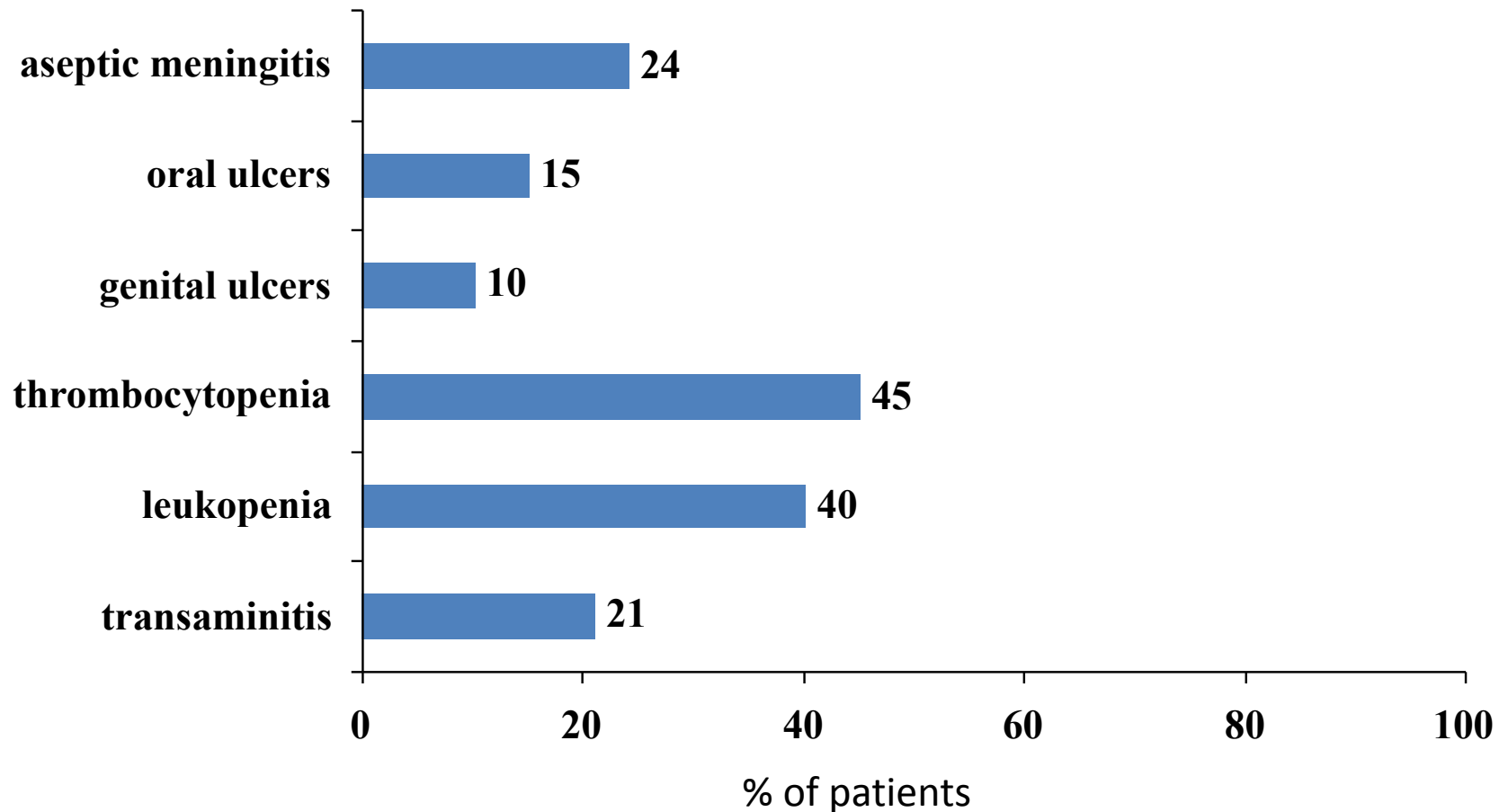
Primary HIV Infection: Signs and Symptoms

- About 40-90% of patients will be symptomatic
- A mononucleosis-like illness of non-specific signs and symptoms
- Signs and symptoms typically begin 1-4 weeks post-exposure
- High index of suspicion is critical

Primary HIV Infection: Common Signs and Symptoms



Primary HIV Infection: Other Signs and Symptoms



Primary HIV Infection

Rash



Trunk and face > limbs
Small pink macules

Mucosal Lesions



Oral ulcers, thrush

(Kahn, NEJM, 1998)

**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



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

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

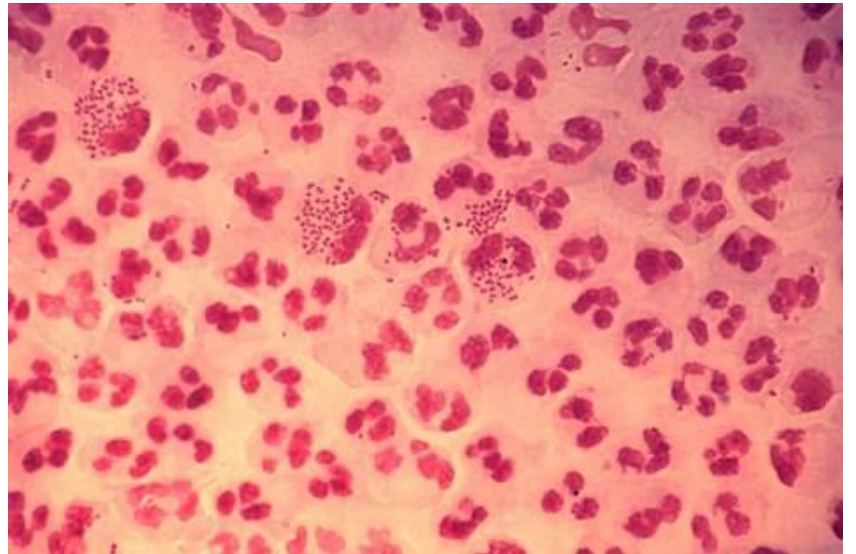
Chlamydia Follow-up

- Test-of-cure to detect therapeutic failure (i.e., repeat testing 3-4 weeks after completing therapy) is not advised
- Men and women who have been treated for chlamydia should be retested approximately 3 months after treatment

Gonococcal Infections

- In the United States, 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 infection 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. gonorrhoea*
- Culture is available for detection of rectal, oropharyngeal, and conjunctival gonococcal infection, but NAAT is not FDA-cleared for use with these specimens

Antimicrobial-Resistant *N. gonorrhoeae*

- In 2007, emergence of fluoroquinolone-resistant *N. gonorrhoeae* in the United States prompted CDC to cease recommending fluoroquinolones for treatment of gonorrhea
- CDC's 2010 STD treatment guidelines recommended dual therapy
- In addition, treatment failures with cefixime or other oral cephalosporins have been reported in Asia, Europe, South Africa, and Canada

- The CDC no longer recommends cefixime at any dose as a first-line regimen for treatment of gonococcal infections. If cefixime is used as an alternative agent, then the patient should return in what period of time for a test-of-cure (culture) or with a NAAT at the site of infection?
- A. 1 week
- B. 2 weeks
- C. 4 weeks
- D. 6 months
- E. 1 Year

Updated CDC GC Treatment Recommendations

- Firstline
 - 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 orally twice a day for 7 days) can be used as an alternative second antimicrobial when used in combination with ceftriaxone or cefixime

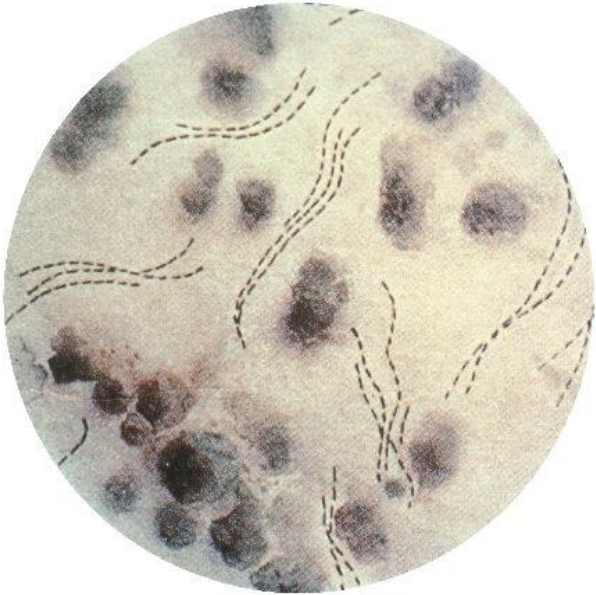
Other Antimicrobial Options

- 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

- 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

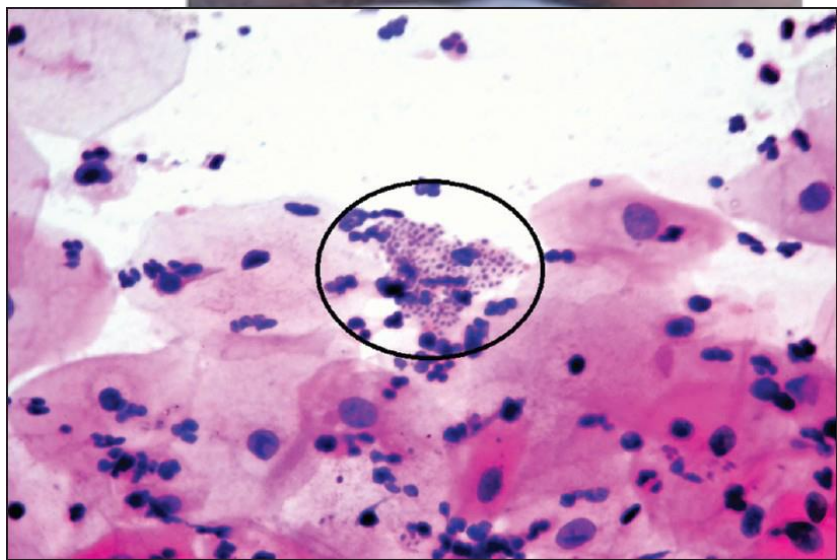
Erythromycin base 500 mg orally three times a day for 7 days

* 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

Granuloma Inguinale (Donovanosis)

- A genital ulcerative disease caused by the *Klebsiella granulomatis* (formerly known as *Calymmatobacterium granulomatis*)
- Painless, slowly progressive ulcerative lesions without regional lymphadenopathy; subcutaneous granulomas (pseudobuboes). Lesions are highly vascular (i.e., beefy red appearance) and bleed easily on contact
- Extragenital infection can occur with extension of infection to the pelvis, or it can disseminate to intraabdominal organs, bones, or the mouth



Granuloma Inguinale (Donovanosis)

Recommended Regimen

- **Azithromycin** 1 g orally once per week or 500 mg daily for at least 3 weeks and until all lesions have completely healed

Alternative Regimens

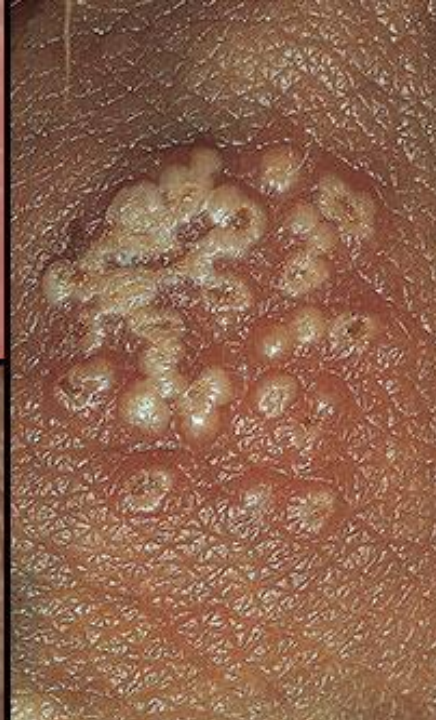
- **Doxycycline** 100 mg orally twice a day for at least 3 weeks and until all lesions have completely healed
- **Ciprofloxacin** 750 mg orally twice a day for at least 3 weeks and until all lesions have completely healed
- **Erythromycin** base 500 mg orally four times a day for at least 3 weeks and until all lesions have completely healed
- **Trimethoprim-sulfamethoxazole** one double-strength (160 mg/800 mg) tablet orally twice a day for at least 3 weeks and until all lesions have completely healed

Genital Herpes Simplex Infections

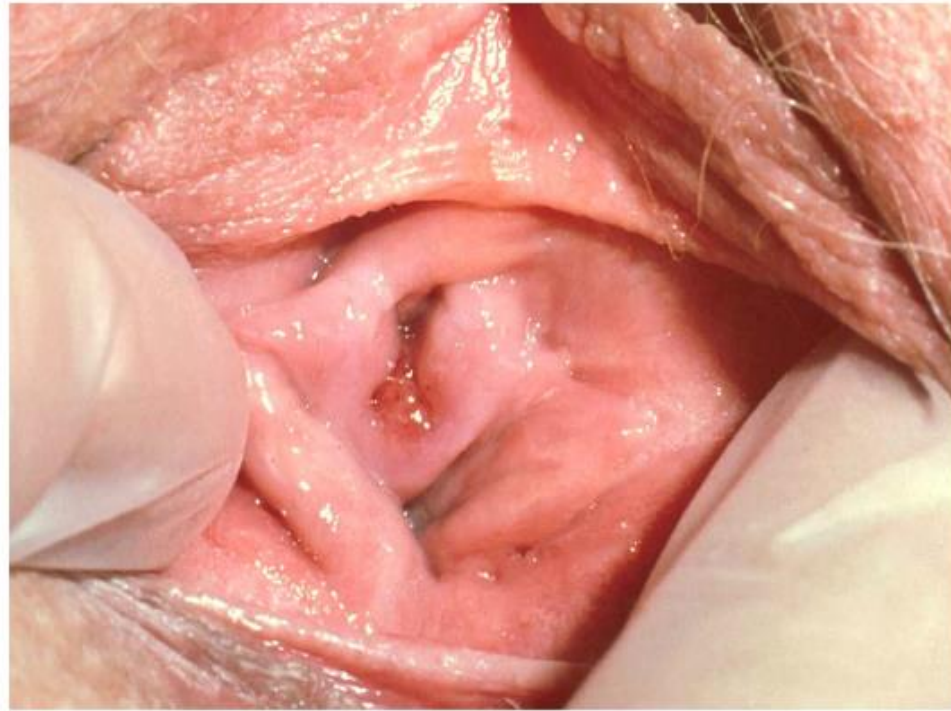
- Both HSV-1 and HSV-2 can cause genital herpes
- Most recurrent cases are caused by HSV-2, and approximately 50 million persons in the US are infected with HSV-2
- However, acquisition of genital HSV-1 is increasing, and genital HSV-1 also can be asymptomatic

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 or 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 Serologic Tests

- The most commonly used test, HerpeSelect HSV-2 Elisa might be falsely positive and should be confirmed with another test, such as Biokit or the Western blot
- IgM testing for HSV 1 or HSV-2 is not useful, because IgM tests are not type-specific and might be positive during recurrent genital or oral episodes of herpes

Type-Specific gG-Based HSV Serology: Commercial Kits, 2011

	<u>Sensitivity</u>	<u>Specificity</u>
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



Type-Specific Serologic Tests

- Utility in the following scenarios:
 - Recurrent genital symptoms or atypical symptoms with negative HSV PCR or culture
 - Clinical diagnosis of genital herpes without laboratory confirmation
 - A patient whose partner has genital herpes
 - Serologic testing should be considered for persons presenting for an STD evaluation, HIV infection, and MSM at increased risk for HIV acquisition.
- Screening for HSV-1 and HSV-2 in the general population is not indicated.

Treatment

- Even persons with first-episode herpes who have mild clinical manifestations initially can develop severe or prolonged symptoms
- Therefore, 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
Famciclovir 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

Spring
breakers →

It's gonna
be a busy
week guys.

Hello:
My name is
Gonorrhea

