Arizona State Office of Rural Health Webinar Series

Today's presentation:

Syphilis 2019: Return of the Great Masquerader

May 16, 2019

Arizona State Office of Rural Health
Monthly Webinar Series

Provides technical assistance to rural stakeholders to disseminate research findings, policy updates, best-practices and other rural health issues to statewide rural partners and stakeholders.

THE UNIVERSITY OF ARIZONA
MEL & ENID ZUCKERMAN COLLEGE OF PUBLIC HEALTH
Center for Rural Health

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ARIZONA TELEMEDICINE PROGRAM

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Today's presentation:

THE UNIVERSITY OF ARIZONA
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Syphilis 2019: Return of the Great Masquerader

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California Prevention Training Center
Assistant Clinical Professor at University of California, San Francisco (UCSF), Family and Community Medicine

SOUTHWEST TELEHEALTH TRC RESOURCE CENTER

The University of Arizona Mel and Enid Zuckerman College of Public Health Center for Rural Health

Syphilis 2019: *Return of the Great Masquerader*

Sharon Adler M.D., M.P.H.
California Prevention Training Center
Assistant Clinical Professor UCSF FCM

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Disclosure

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

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Presentation Overview:

- Epidemiology
- Screening recommendations
- Clinical manifestations and staging
- Diagnostics
- Treatment and follow-up
- Reporting

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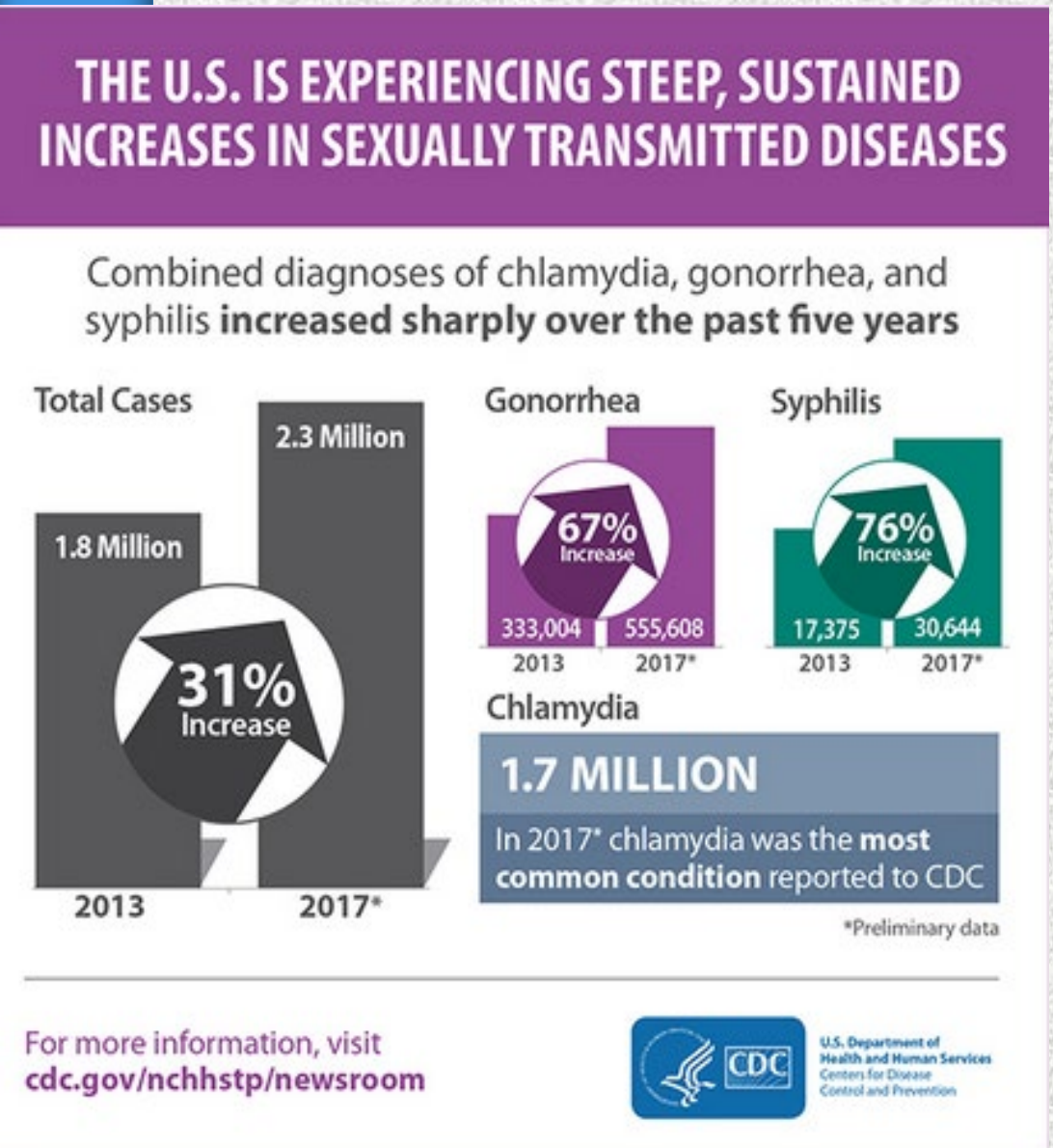
Syphilis Is Back!
Treponema Palladum
causes Syphilis

National STD Snapshot:



Syphilis 2017

- 30,644 Cases
- 76% increase from 2013

Congenital Syphilis

- 918 cases
- 153% increase since 2013
- **64 stillbirths**
- **13 infant death**

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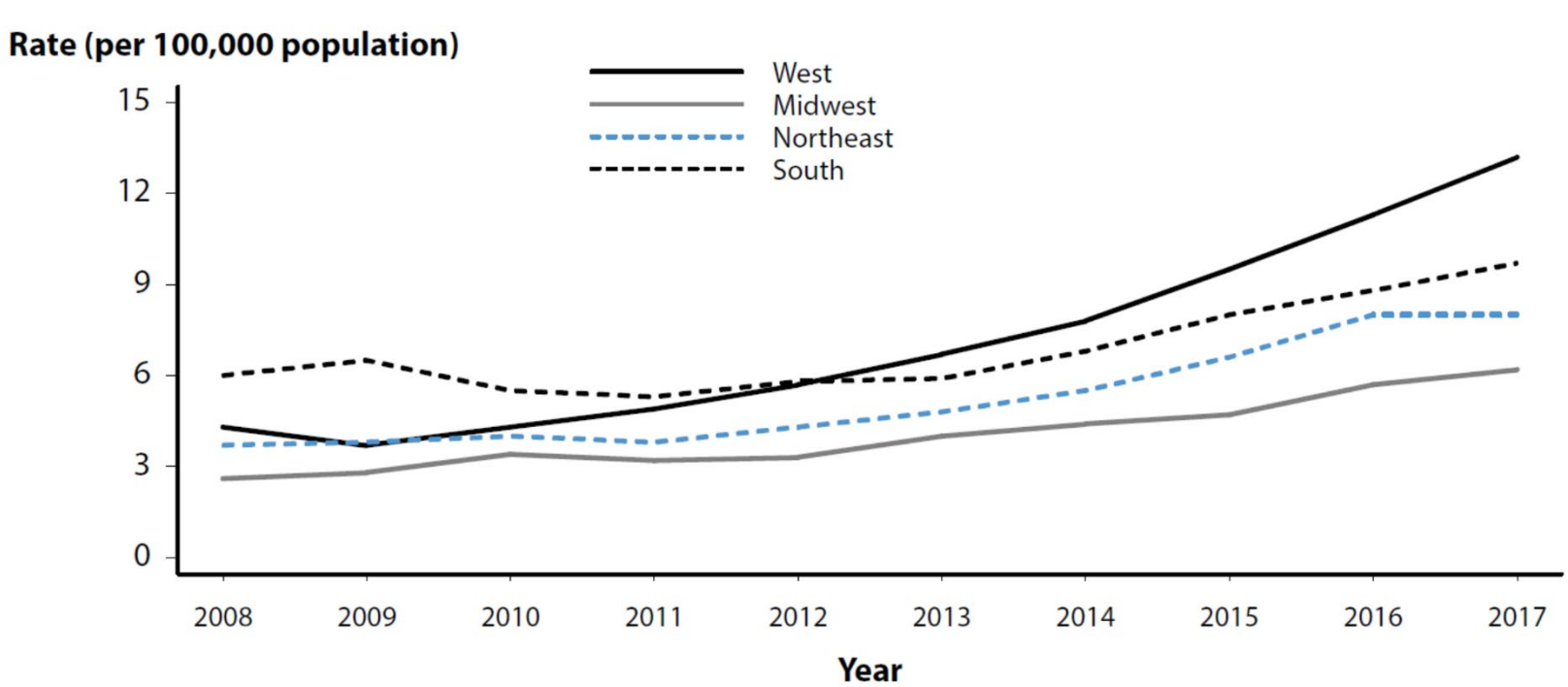
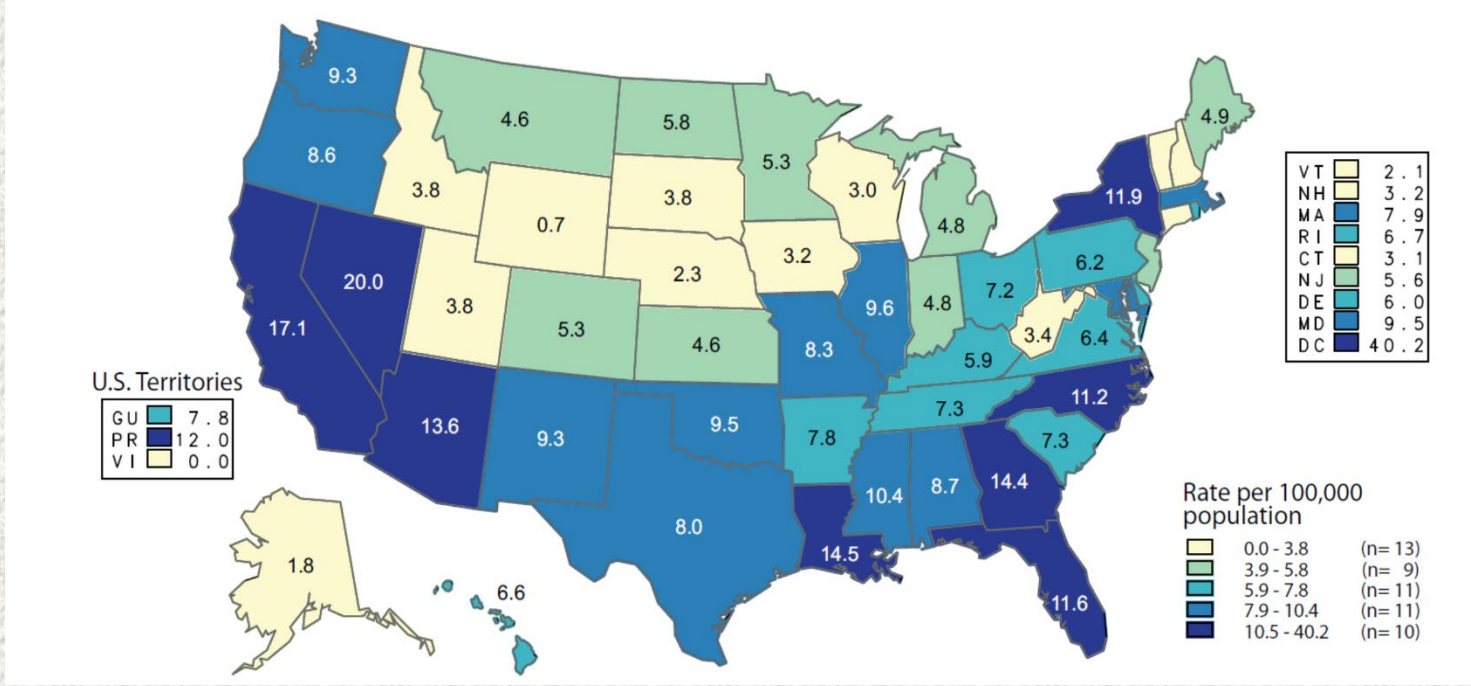
Primary and Secondary Syphilis — Rates of Reported Cases by Region, U.S., 2008–2017



Primary and Secondary Syphilis — Rates of Reported Cases by State, U.S. and Outlying Areas, 2017



NOTE: The total rate of reported cases of primary and secondary syphilis for the United States and outlying areas (including Guam, Puerto Rico, and the Virgin Islands) was 9.5 per 100,000 population. See Section A1.11 in the Appendix for more information on interpreting reported rates in the outlying areas.

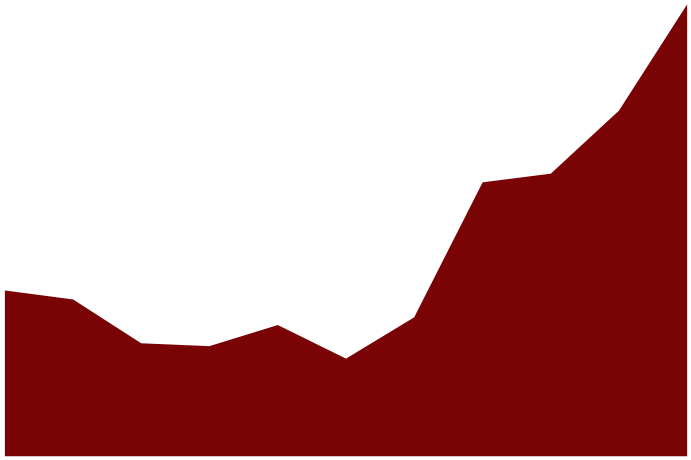
ACRONYMS: GU = Guam; PR = Puerto Rico; VI = Virgin Islands.

What's up with syphilis?

STDs in Arizona

2007 2018

Syphilis in Arizona

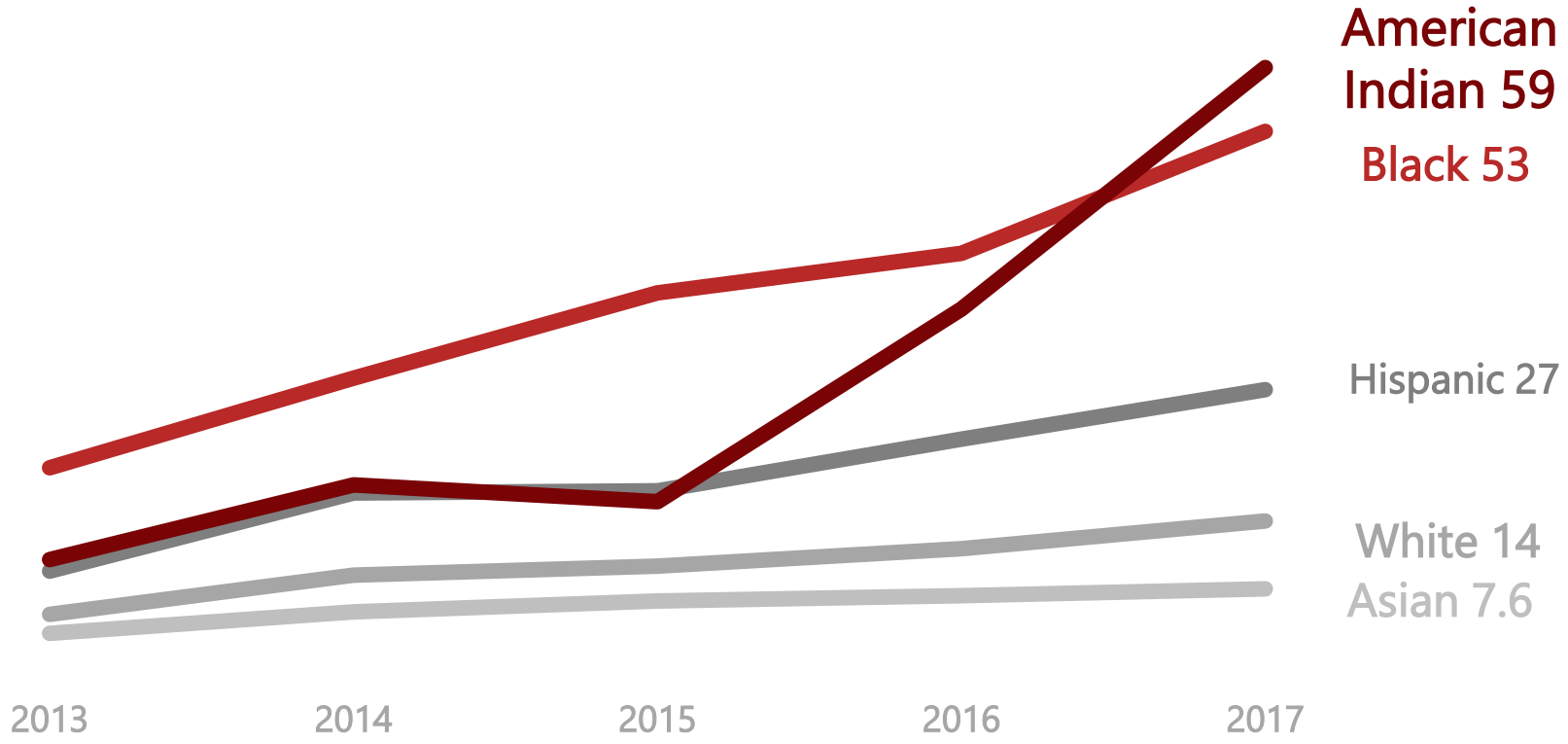


2007 2017

The mean age for an early syphilis is **35 years**.

Slide courtesy Bree Anderson MPH, AZ DHS

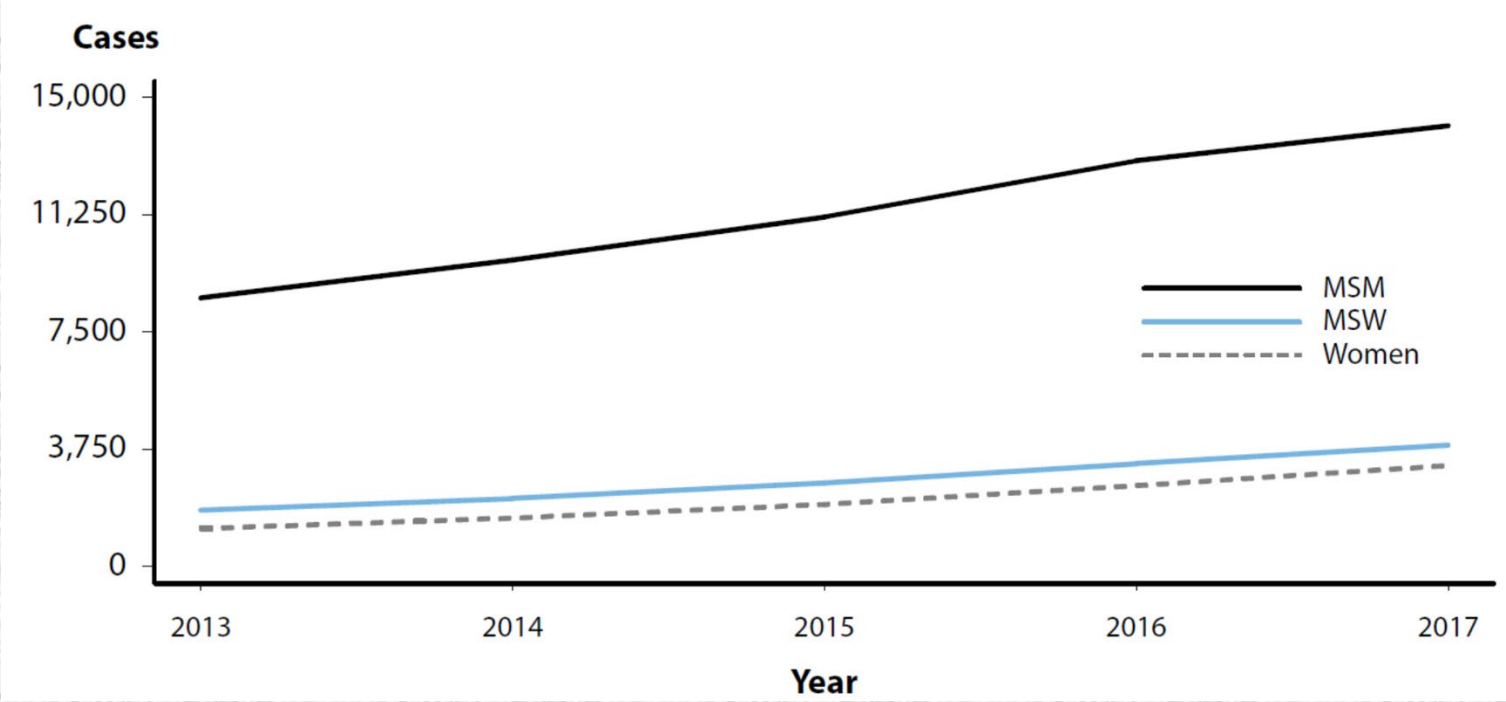
Syphilis Disparities by Race/Ethnicity



American Indian & **Black/African Americans** also have the top two highest rates of **chlamydia** and **gonorrhea** in AZ!

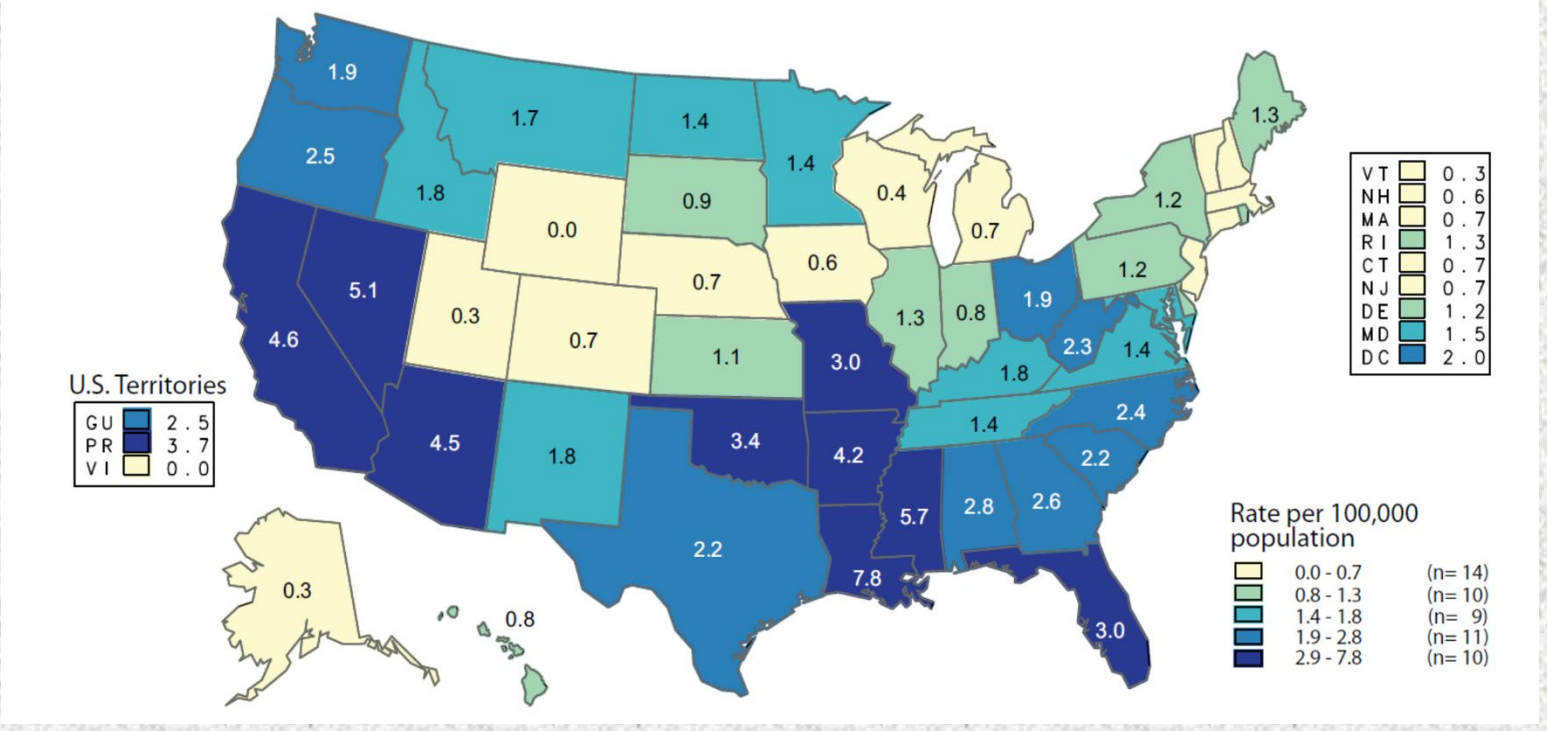
Slide courtesy Bree Anderson MPH, AZ DHS

Primary and Secondary Syphilis — Reported Cases by Sex and Sexual Behavior, 37 States*, 2013–2017



* 37 states were able to classify ≥70% of reported cases of primary and secondary syphilis as either MSM, MSW, or women for each year during 2013–2017.
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

Primary and Secondary Syphilis — Rates of Reported Cases Among Women by State, U.S. and Outlying Areas, 2017



NOTE: The total rate of reported cases of primary and secondary syphilis among women in the United States and outlying areas (including Guam, Puerto Rico, and the Virgin Islands) was 2.3 per 100,000 females. See Section A1.11 in the Appendix for more information on interpreting reported rates in the outlying areas.

ACRONYMS: GU = Guam; PR = Puerto Rico; VI = Virgin Islands.

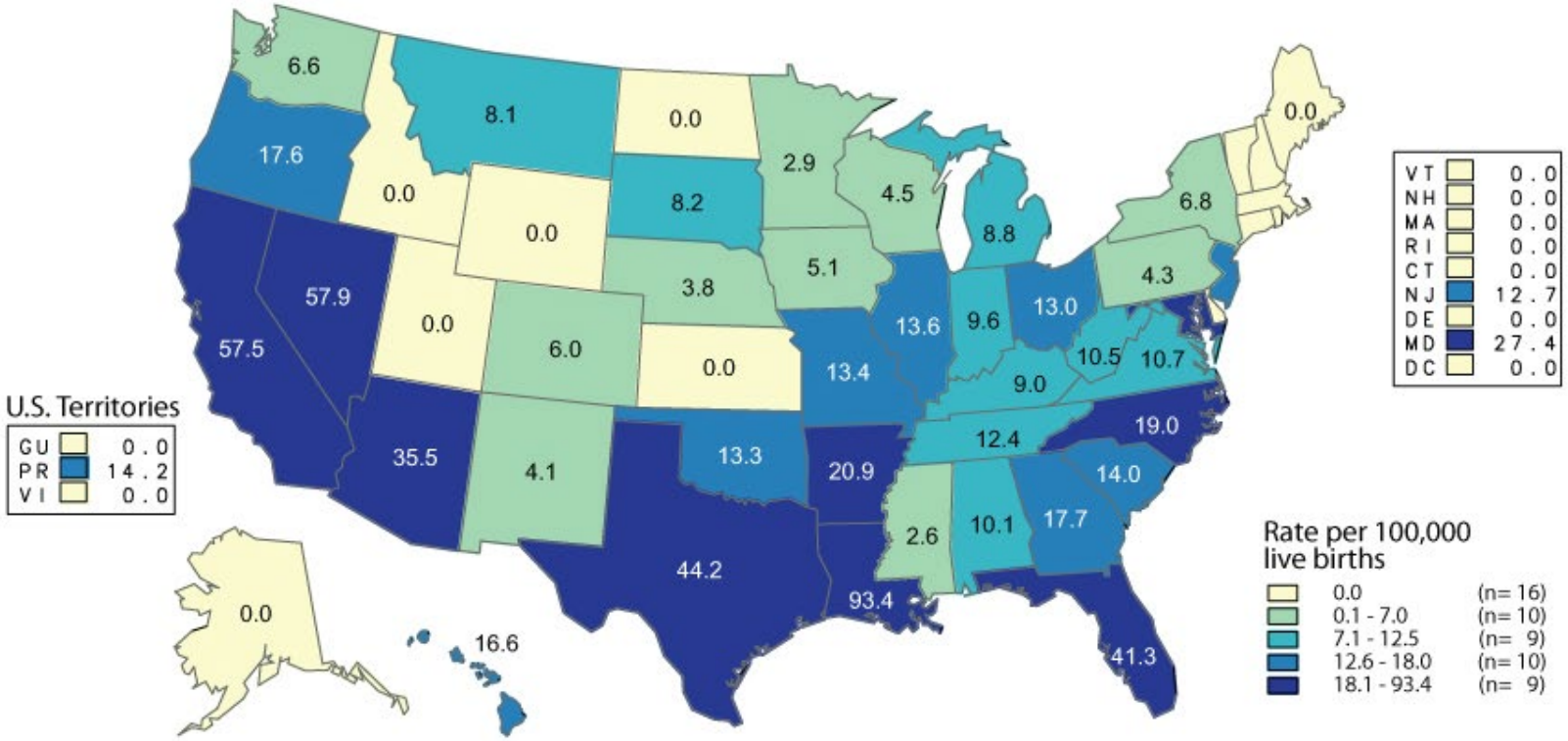
What makes rural Arizona different from urban Arizona?

1 in 5 early syphilis cases are female in Maricopa and Pima County

1 in 3 early syphilis cases are female in rural Arizona

Slide courtesy Bree Anderson MPH, AZ DHS

Congenital Syphilis: Rates of Reported Cases among Infants U.S., 2017



Source CDC

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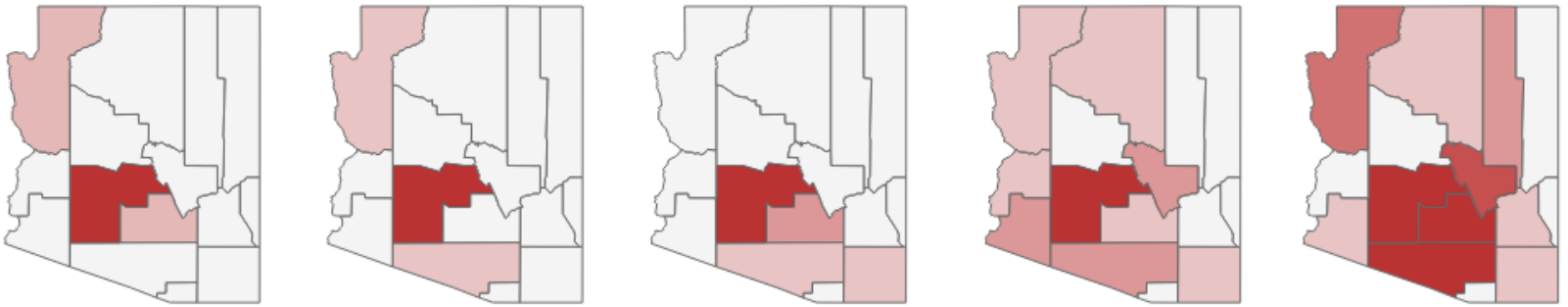
Statewide increase of CS

Congenital Syphilis in Arizona

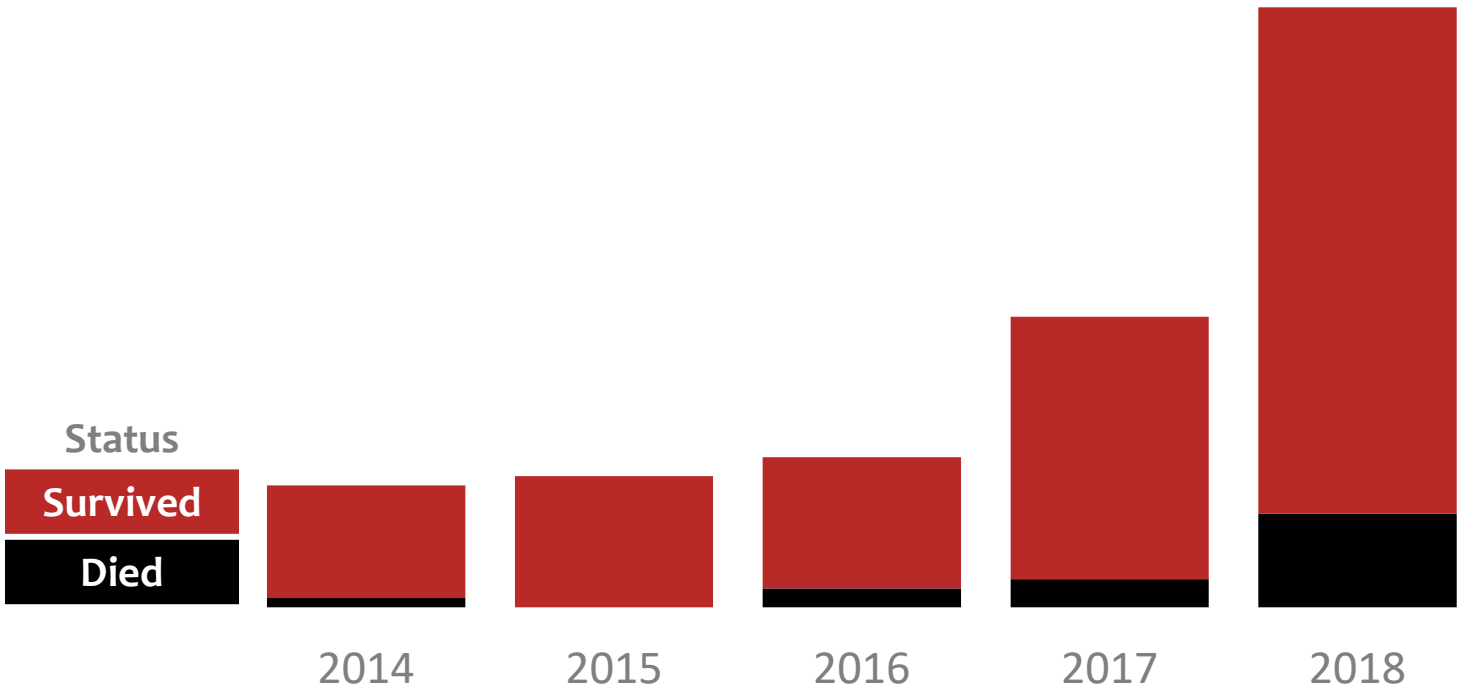


2014 2015 2016 **2017** **2018**

Slide courtesy Bree Anderson MPH, AZ DHS

What about the babies?

Congenital syphilis started to increase in 2017



In 2019, there are 16 cases so far and 18 to be determined, resulting in a 45% increase from this time last year

Slide courtesy Bree Anderson MPH, AZ DHS

Who Should be Screened for Syphilis?

Pregnancy	• At first prenatal visit • Again in the third trimester and at delivery (if at high risk, or residing in area with high syphilis morbidity)
MSM	• Including those on PrEP • **Annually, or more frequently, 3-6 months if at high risk (multiple, anonymous partners, meth use)**
Corrections	• Universal screening based on local area or institutional incidence
HIV+	• At least annually
STD Clinics	• Regardless of symptoms • Client with other STDs

CDC 2015 STD Treatment Guidelines

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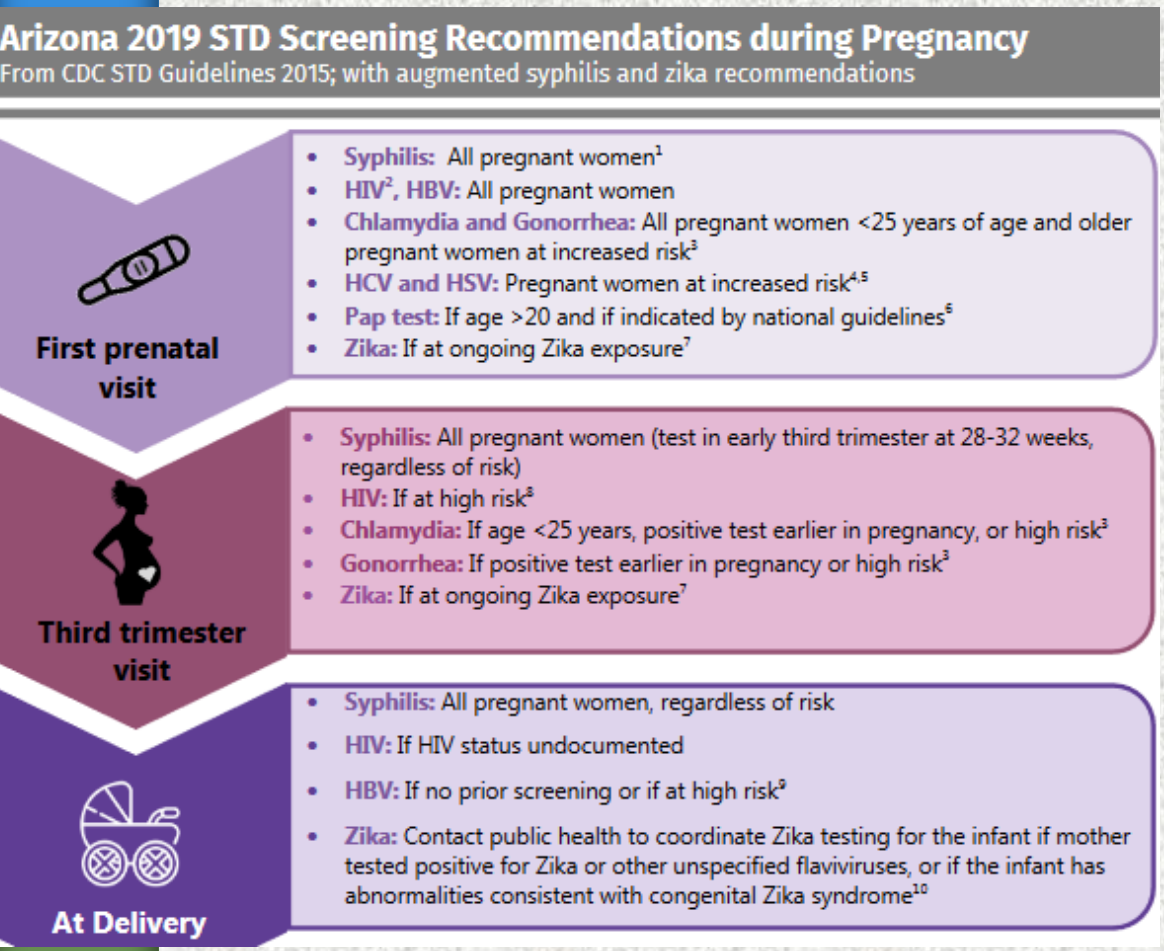
Arizona 2019 STD Screening Recommendations in Pregnancy



Syphilis Screening:

- First Prenatal Visit
- Third Trimester

And

- At Delivery for All Women Regardless of Risk

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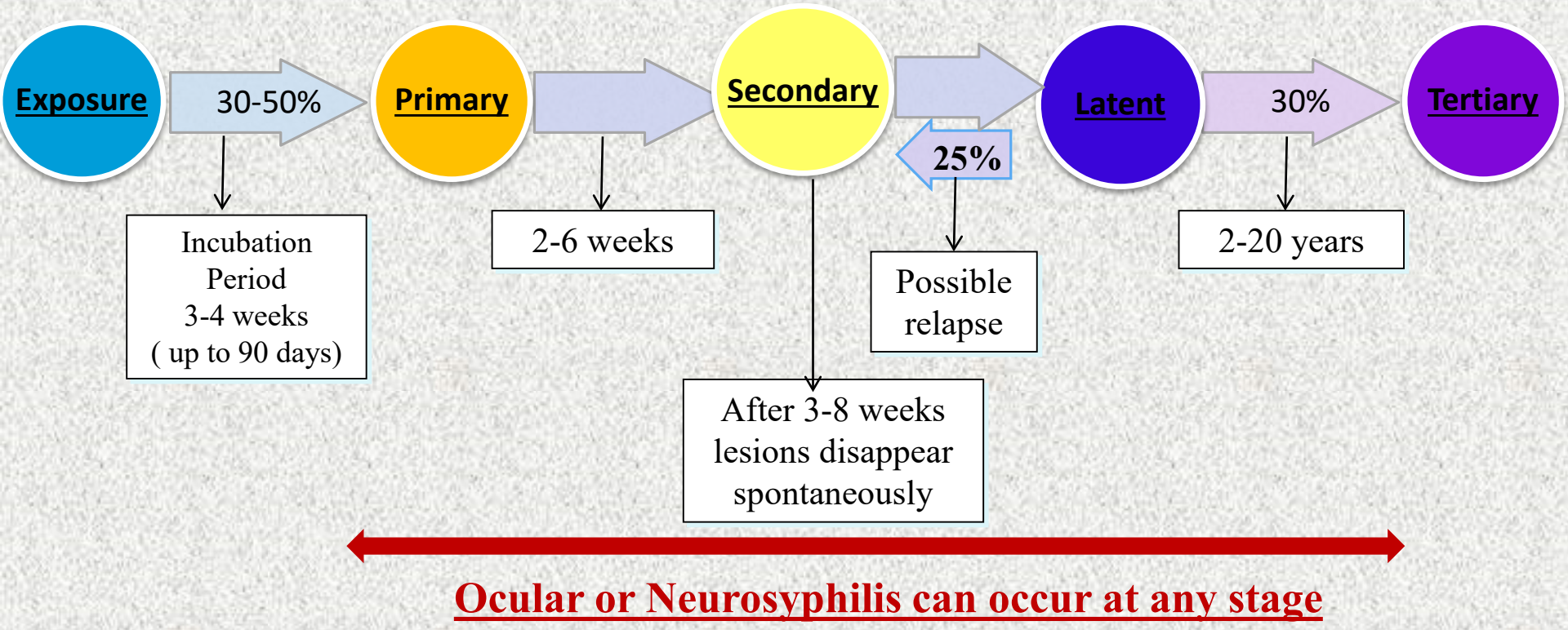
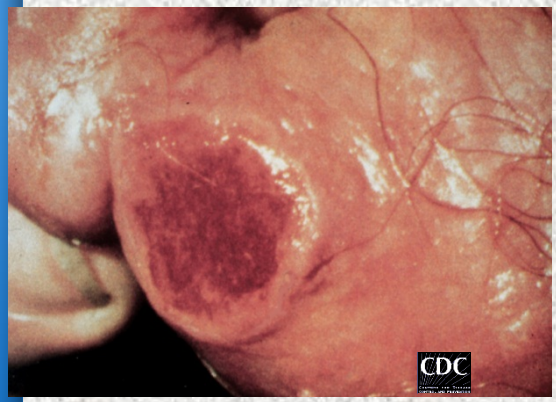
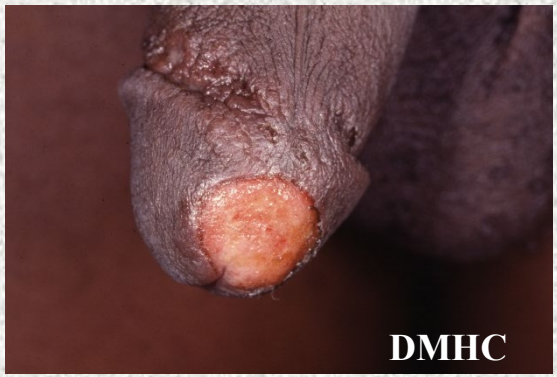
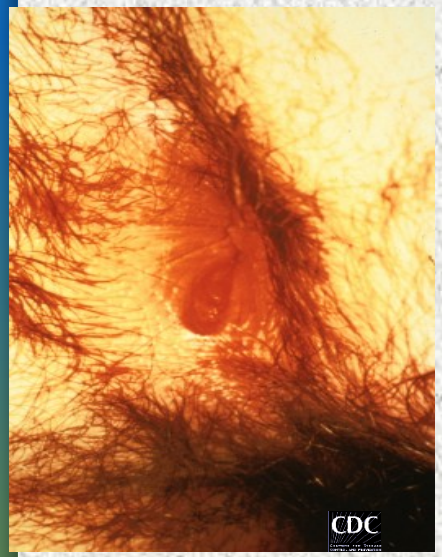
Syphilis Natural History

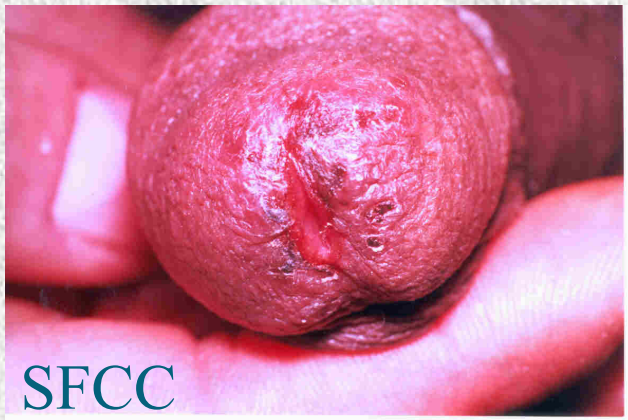


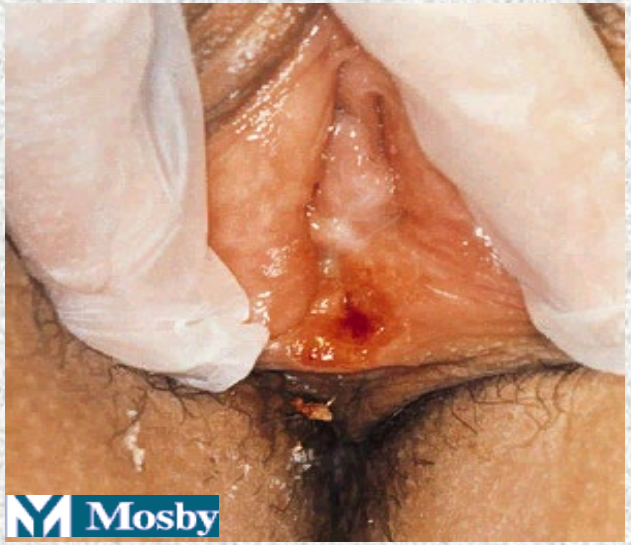
Primary Syphilis











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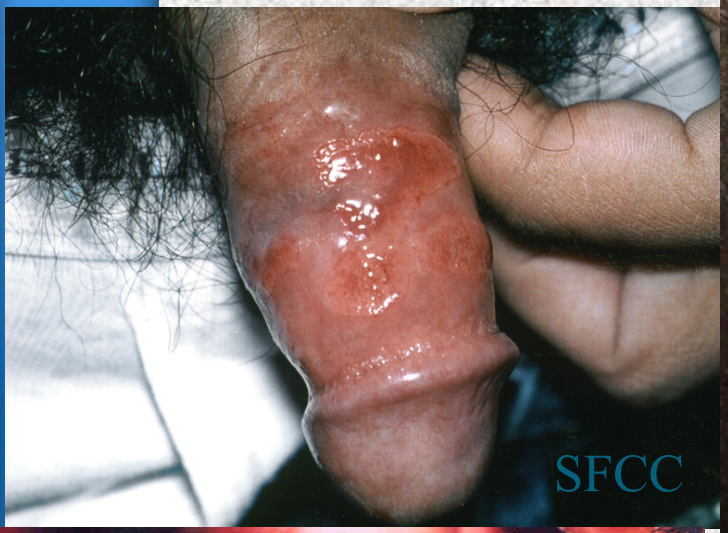
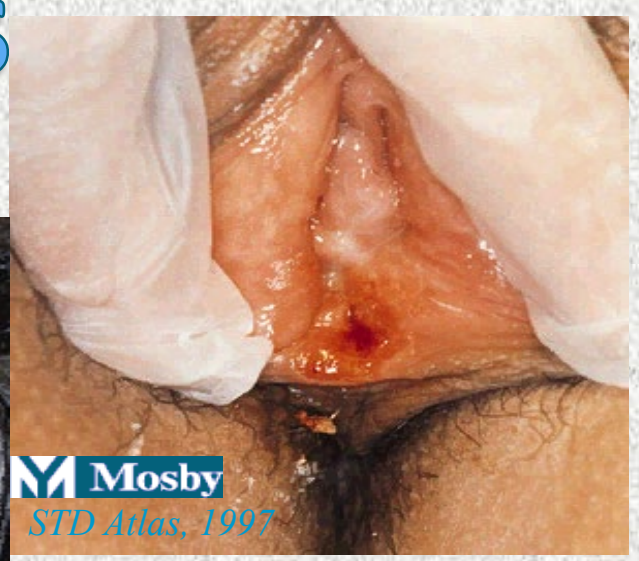
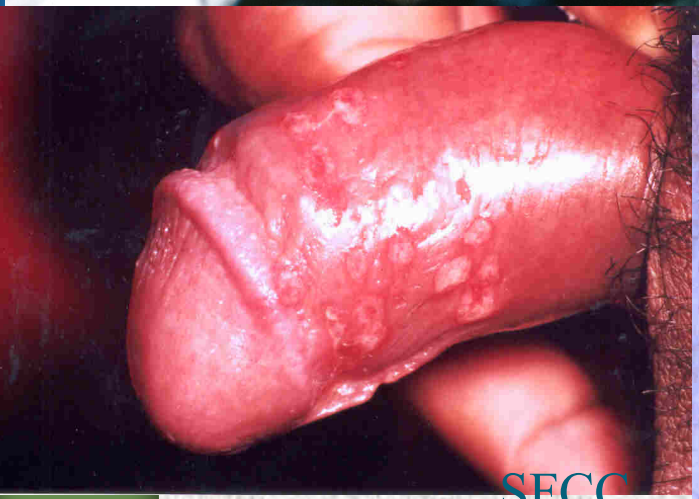
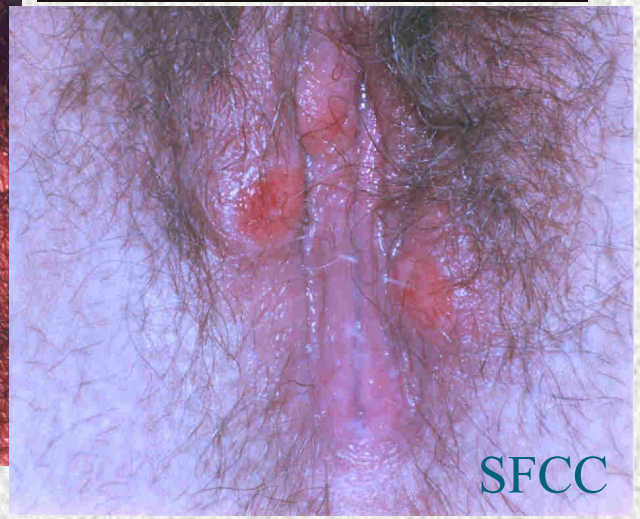
Primary Syphilis

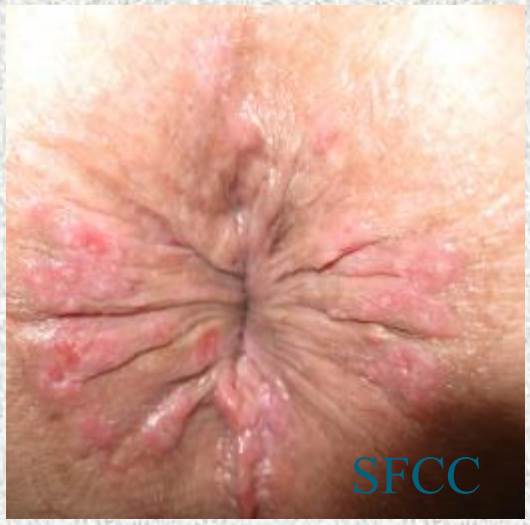
Multiple and Atypical Ulcers











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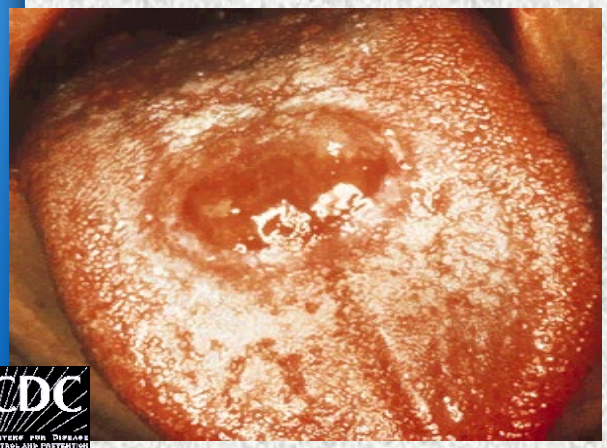
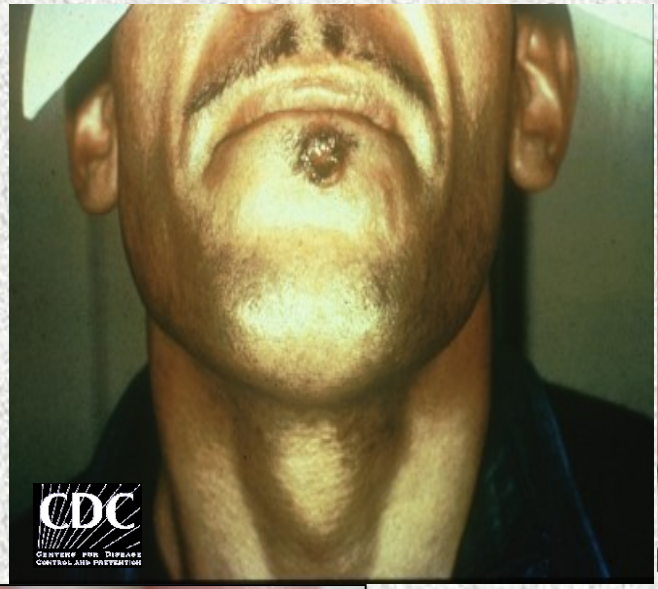
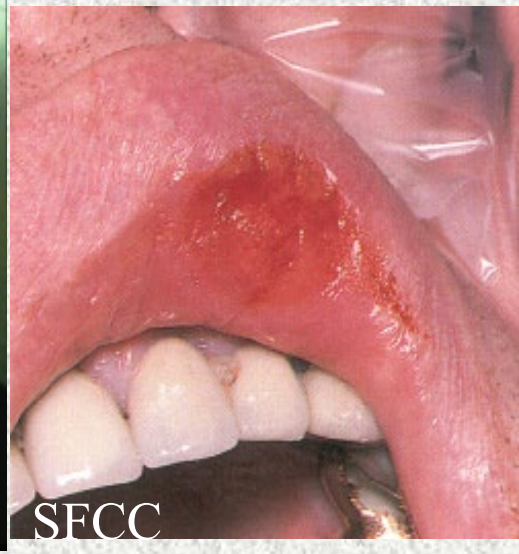
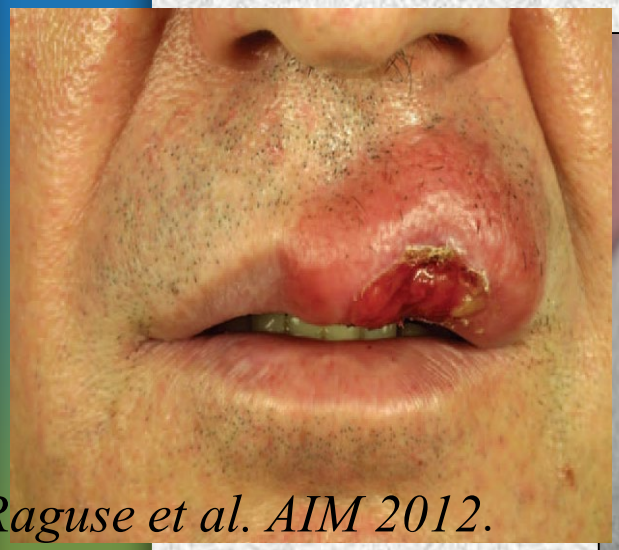
Primary Syphilis Chancres: Extragenital sites

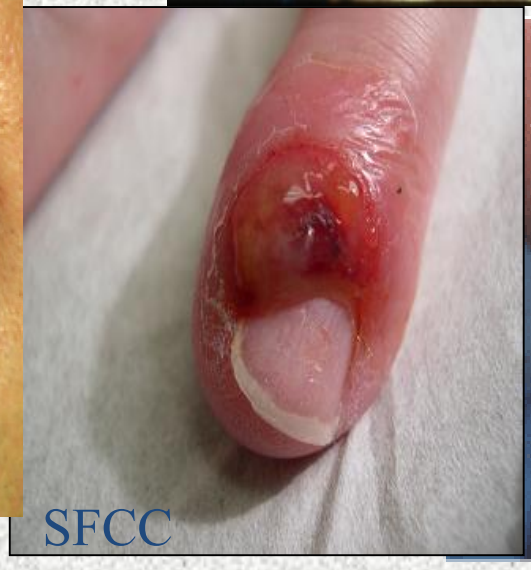


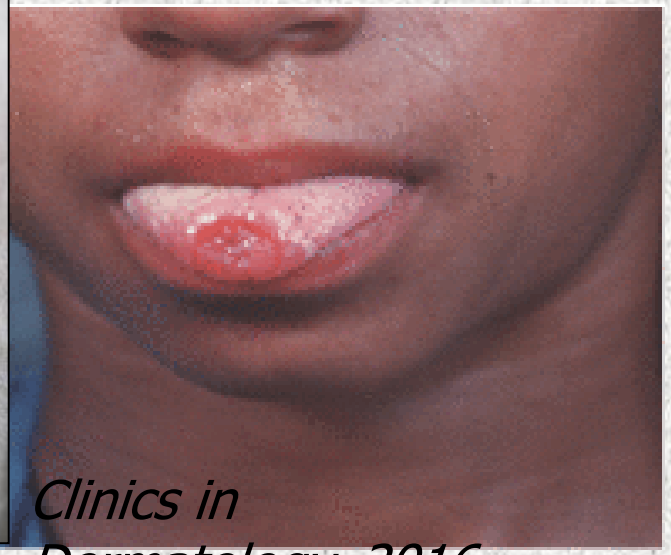






Raguse et al. AIM 2012.





Clinics in Dermatology, 2016

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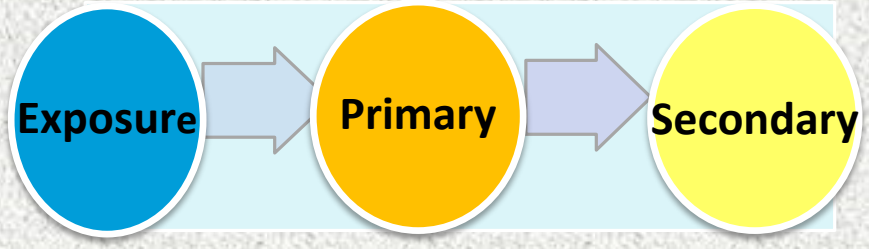
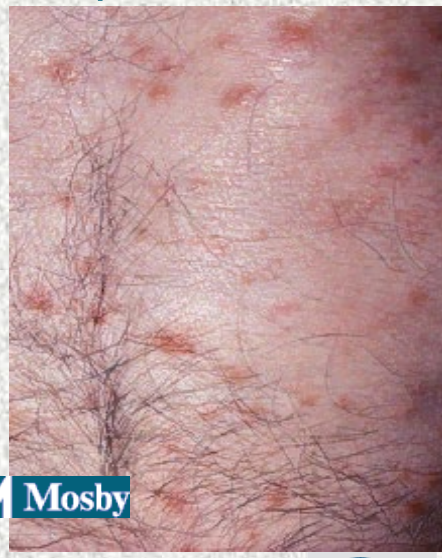
Secondary Syphilis



- Usually occurs 3-6 weeks after primary chancre
- Rash (75-90%), involving palms/soles (60%)
- Generalized lymphadenopathy (70-90%)
- Constitutional symptoms (50-80%)
- Mucous patches (5-30%)
- Condyloma lata (5-25%)
- Patchy alopecia (10-15%)
- Symptoms of neurosyphilis (1-2%)
- Less common: meningitis, hepatitis, arthritis, nephritis



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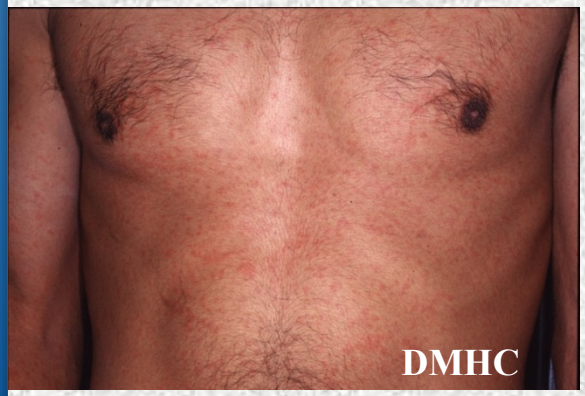
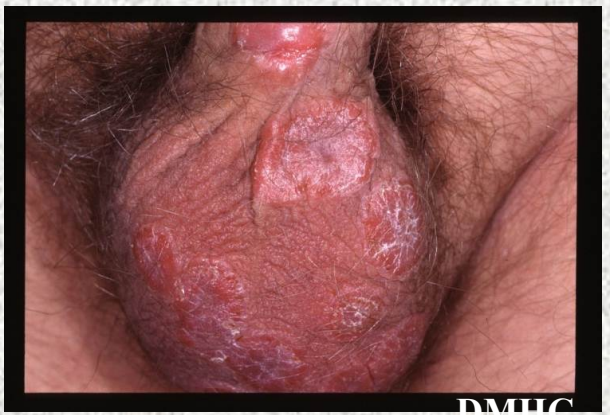
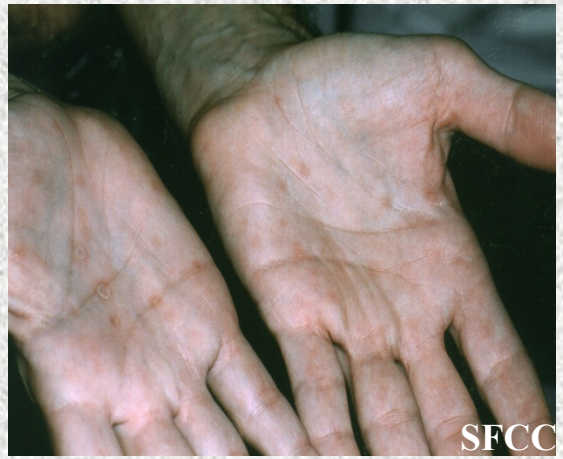
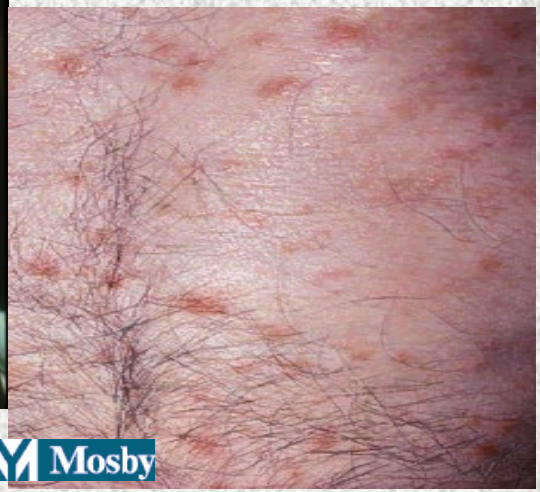
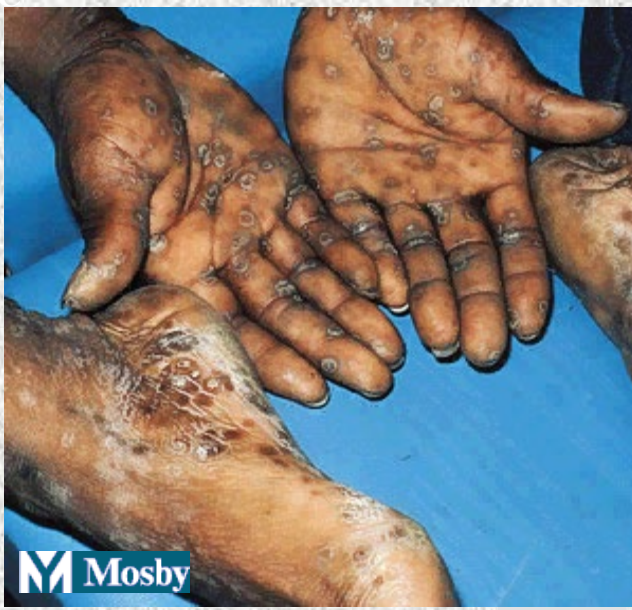
Secondary Syphilis











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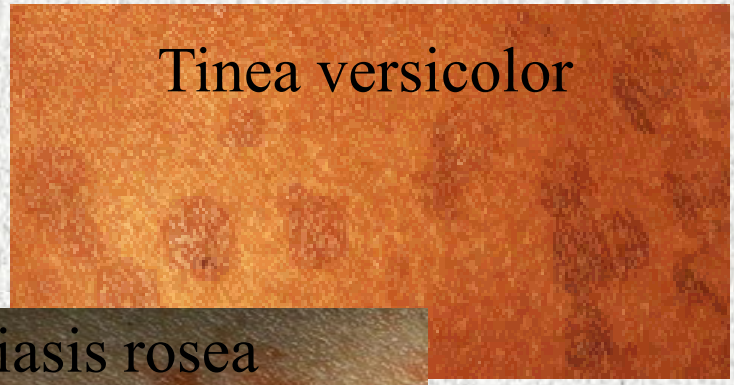
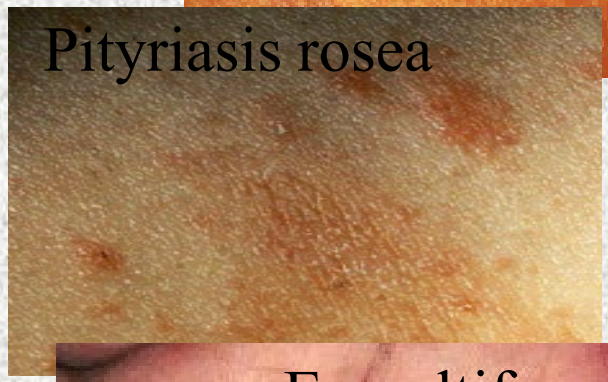
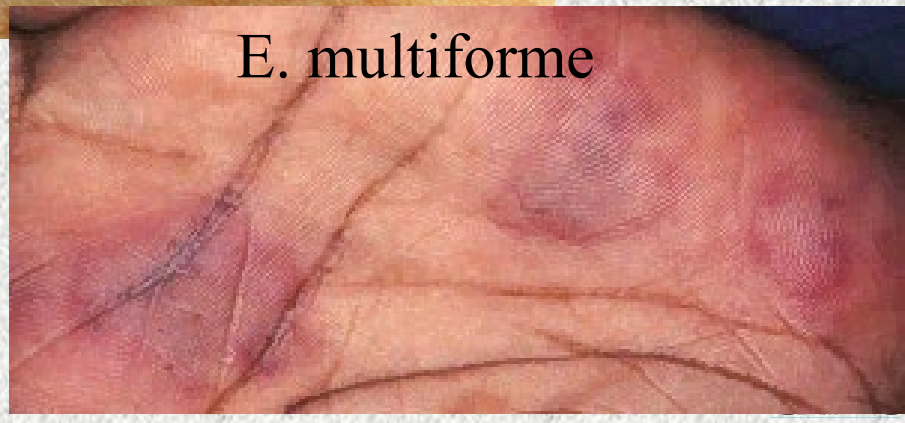
Differential Diagnosis of Secondary Syphilis Rash

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



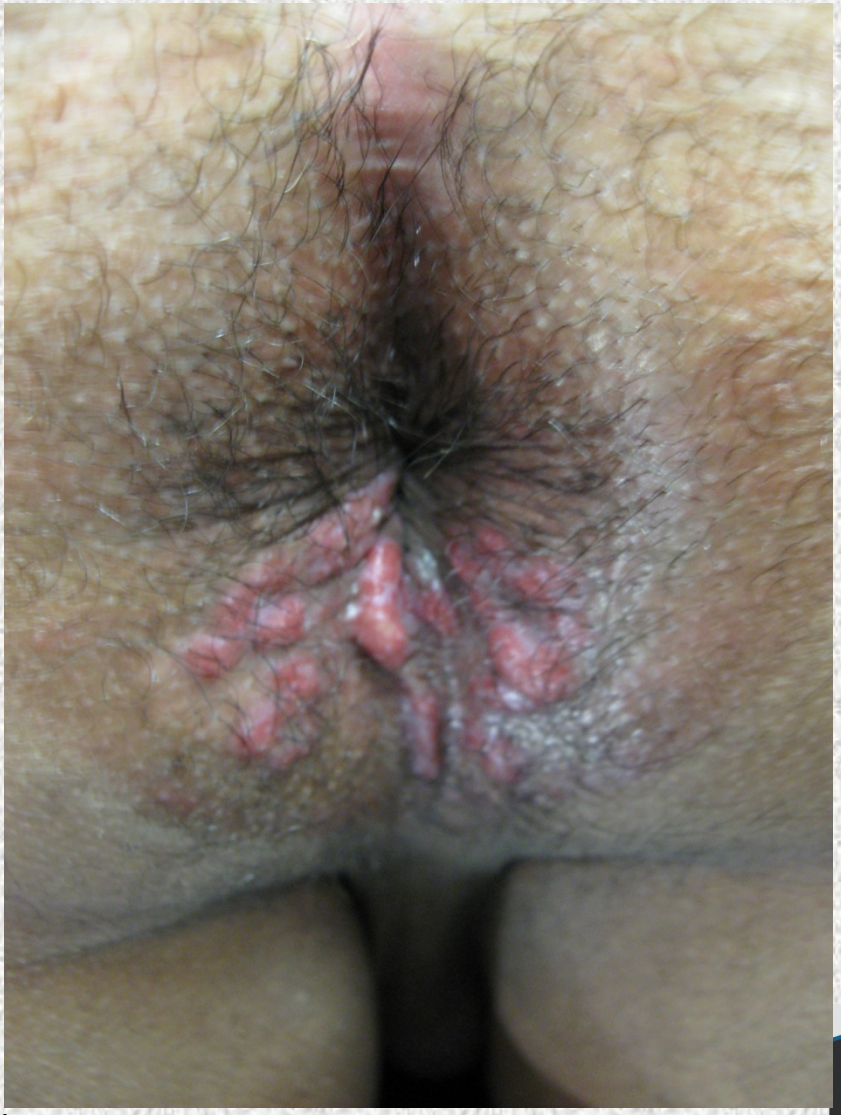




Suspected Genital Warts

46 yo HIV+ man presents with peri-anal lesions

Treated with liquid nitrogen for presumed genital warts.



Images courtesy of Joe Engelman City Clinic

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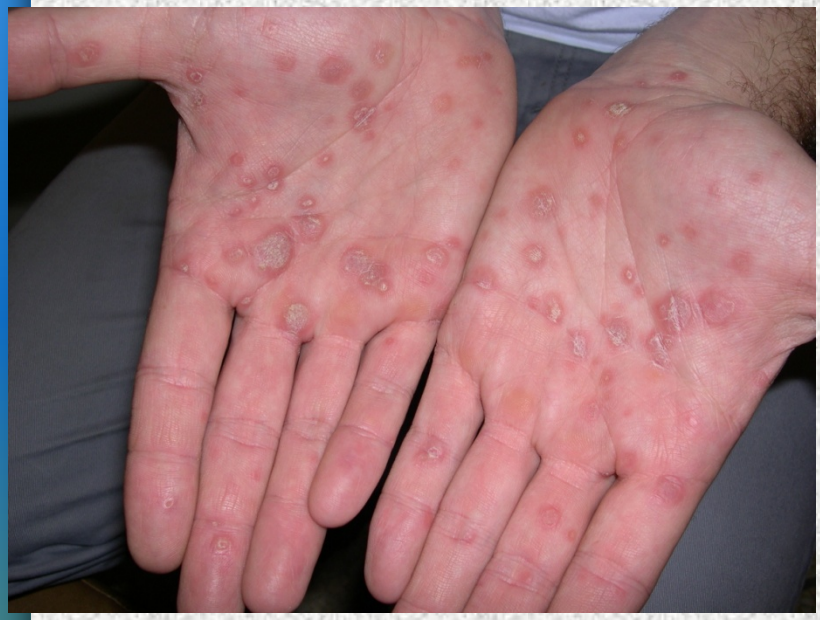
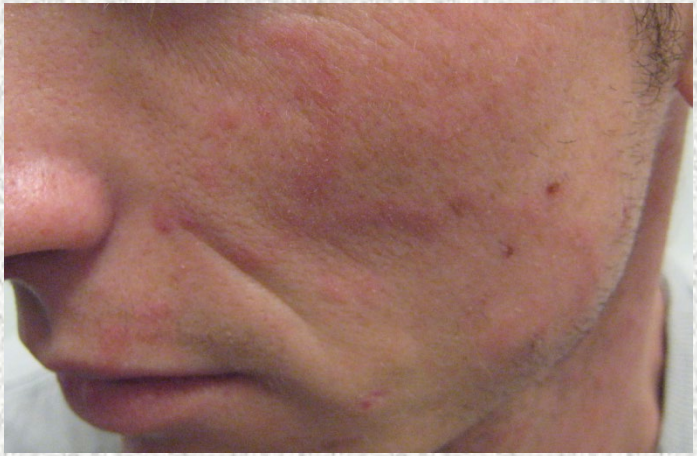
A few days later new rash





Also has macular/papular rash on trunk

Images courtesy of Joe Engelman City Clinic

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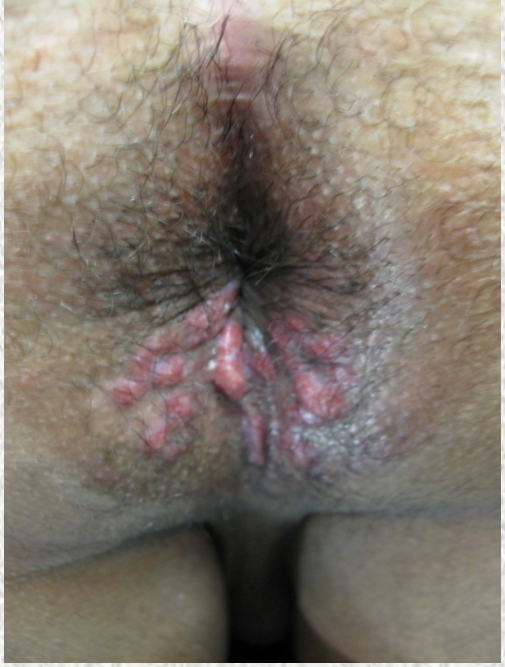
Condyloma Lata Mimic genital warts



- RPR 1:256
- Don't forget to think about syphilis (*condylomata lata*) when you see something that looks like anogenital warts!

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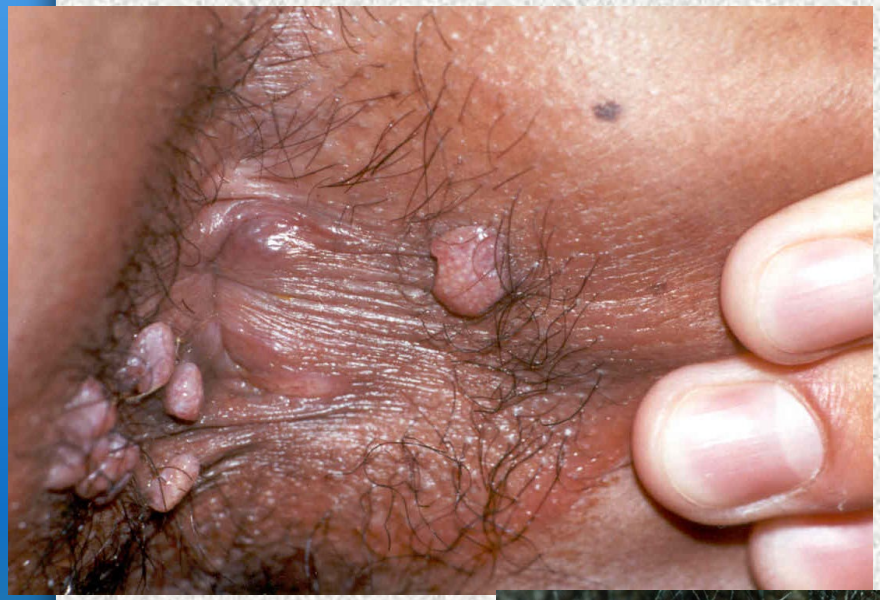
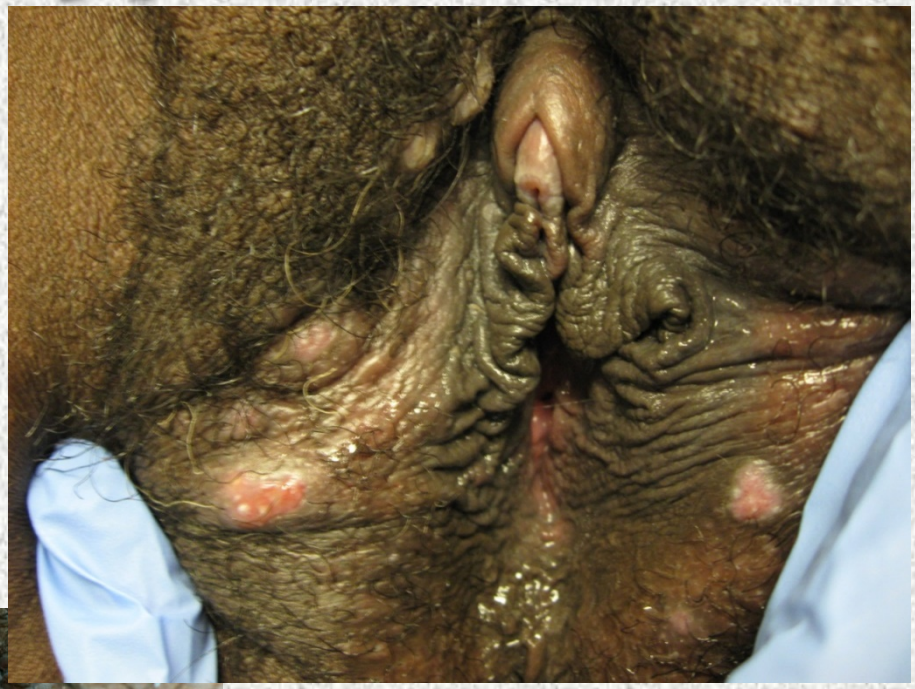
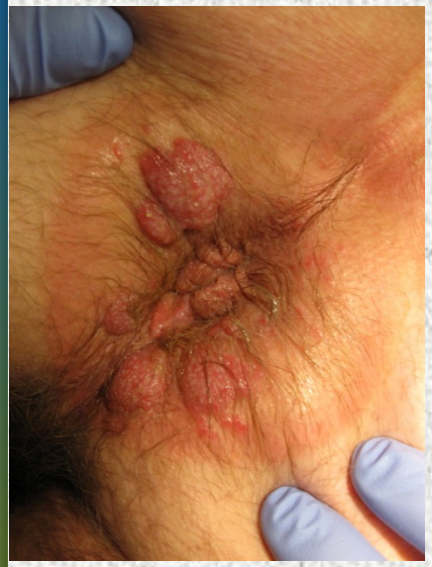
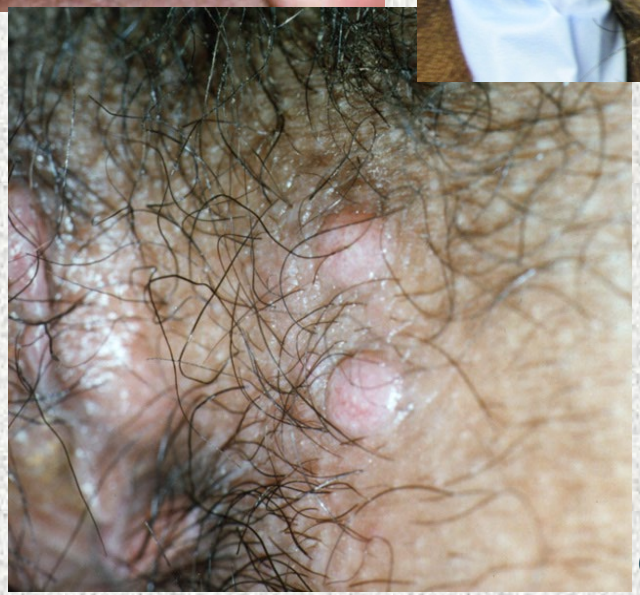
Secondary Syphilis: Lata









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

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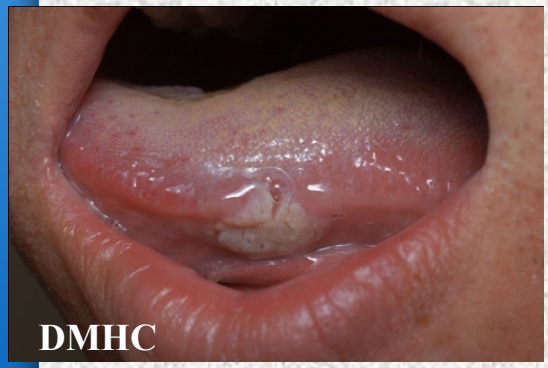
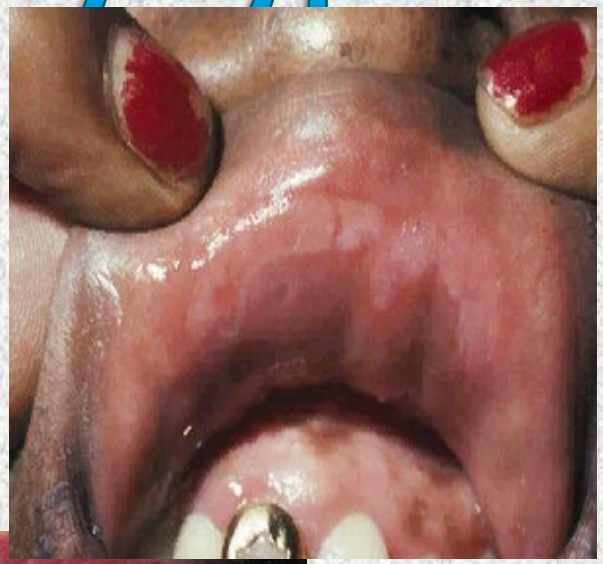
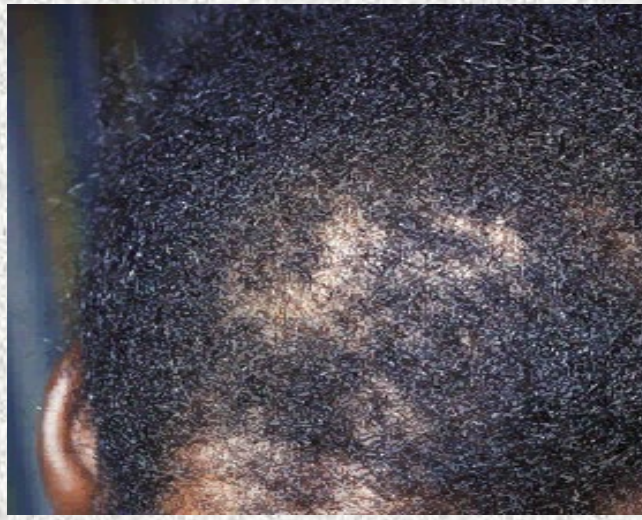
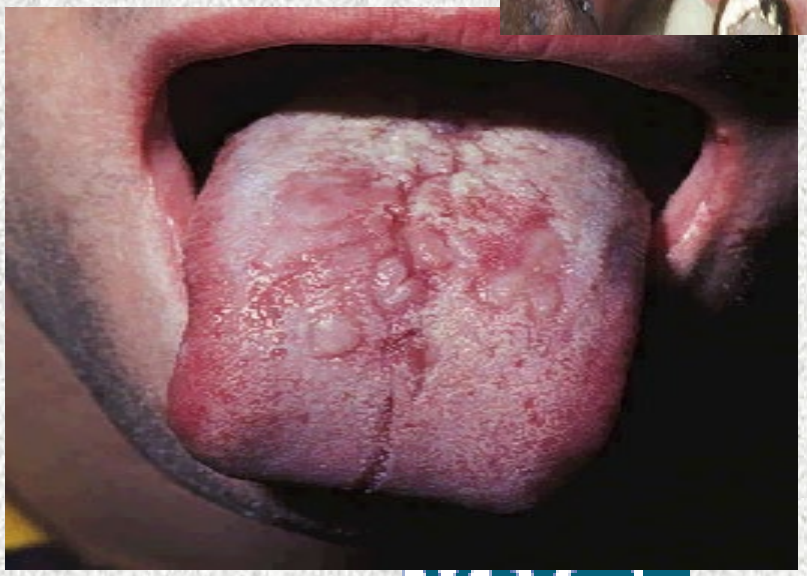
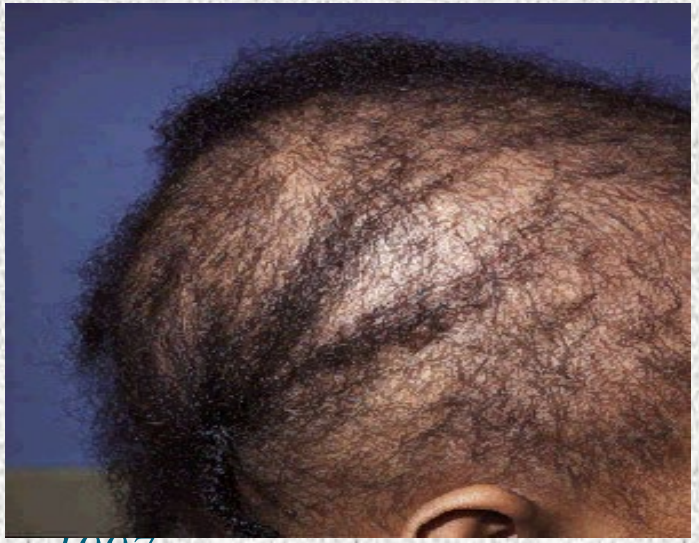
Mucous Patches & Alopecia Secondary Syphilis











Mosby *STD Atlas, 1997*

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Neurosyphilis:

Can Occur at Any Stage of Syphilis

- All patients with syphilis should be evaluated for neurologic symptoms and signs
- Asymptomatic CNS invasion common in early syphilis
- Early symptomatic forms (months to a few years):
  - Acute syphilitic meningitis (CN VI, VII, VIII)
  - Hearing loss
  - Ocular syphilis
  - Meningovascular (stuttering stroke)
  - Altered mental status
- Late symptomatic forms (> 2 years):
  - General paresis and tabes dorsalis

cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/NeurosyphilisGuide.pdf

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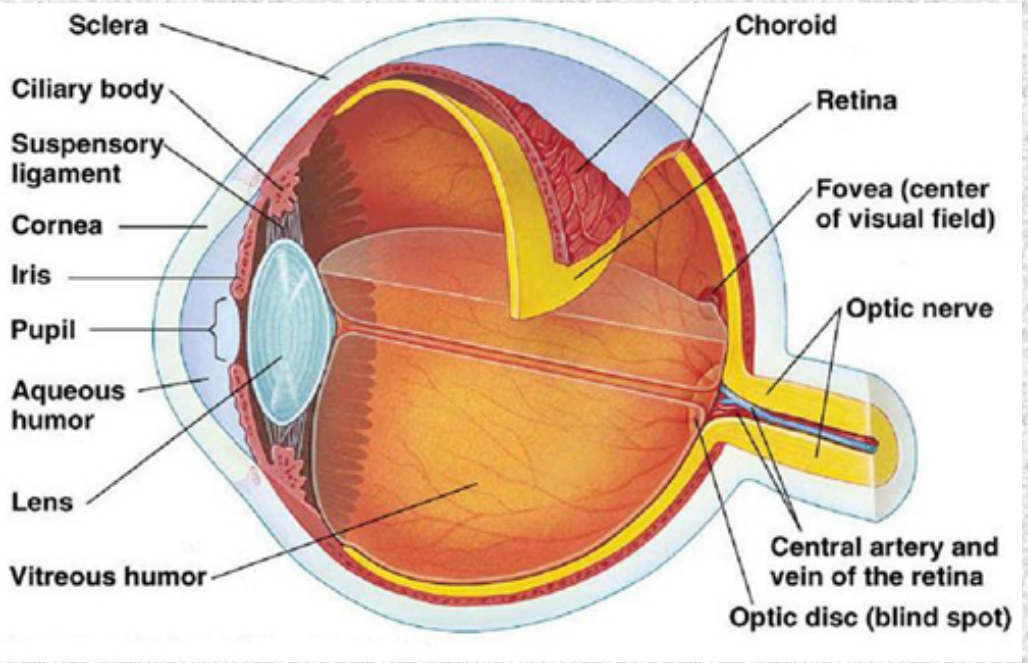
Ocular Syphilis

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

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

Criteria for CSF Examination*

- Neurologic or **ophthalmic** symptoms/signs
  - Auditory disease, cranial nerve dysfunction, meningitis, stroke, altered mental status, loss of vibration sense, iritis, uveitis
- Evidence of tertiary disease
  - aortitis, gumma
- Serologic Treatment failure

In HIV infection, unless neurologic symptoms, there is no evidence that CSF exam is associated with improved outcomes, so not recommended

*CDC 2015 STD Treatment Guidelines
Guidelines for Prevention and Treatment of OI in HIV+ 2013

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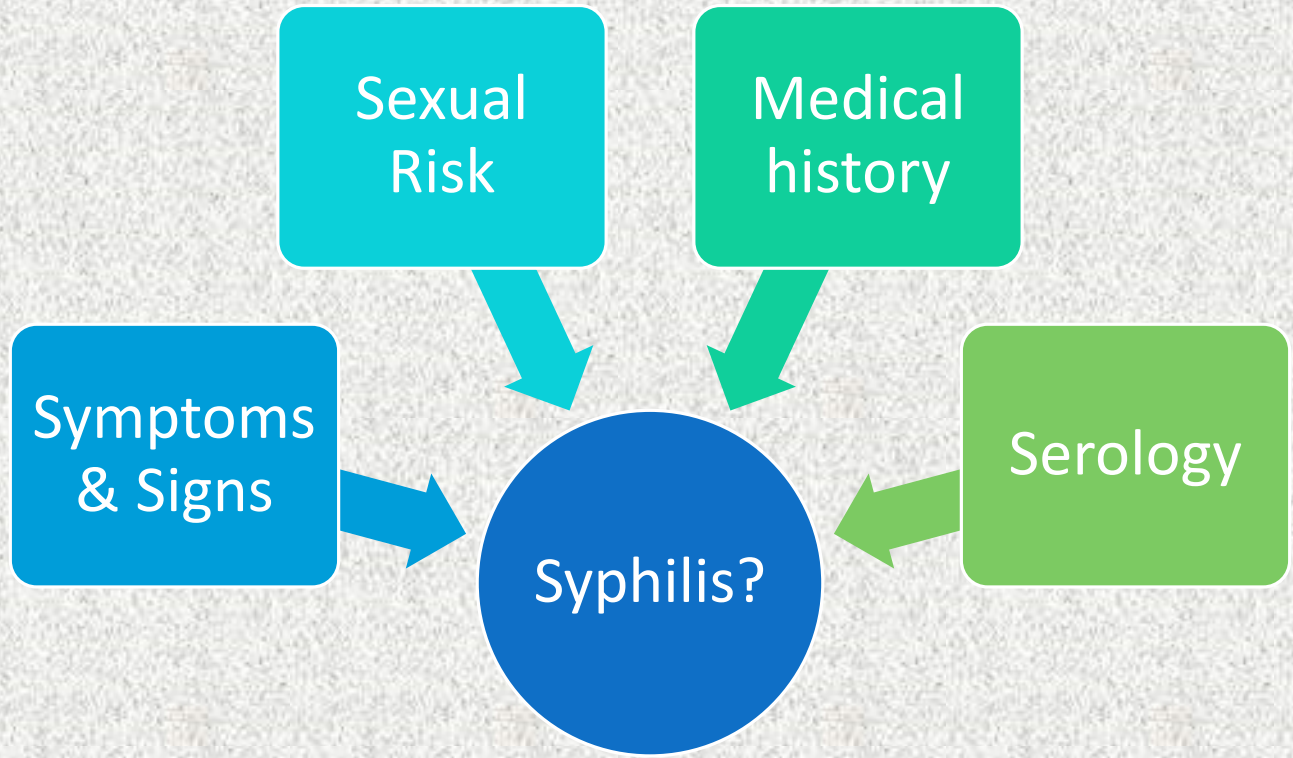

Diagnosing Syphilis

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Syphilis Diagnosis

Treponema pallidum cannot be cultured

- Direct detection methods
  - Darkfield microscopy
    - Not widely available
    - Sensitivity declines with age of lesion & use of topical agents
  - Polymerase chain reaction (PCR) NAAT
    - None FDA approved for commercial use (some labs have done internal validation studies)
    - **Ulcer/Lesion exudate Sensitivity range: 60-95%**
      - Useful if positive to confirm dx; negative NAAT does not rule out dx
    - Not useful in TP identification in blood, serum, plasma
      - CSF NAAT can support dx, negative does not rule out dx

Serology

- Non-treponemal test
- Treponemal tests

CDC 2015 STD Treatment Guidelines
APHL 2018 Syphilis Meeting Report

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Serologic Tests for Syphilis

- **Nontreponemal tests**
  - Rapid plasma reagin (RPR) test
  - Venereal Disease Research Laboratory (VDRL) test
  - Toluidine red unheated serum test (TRUST)
- **Treponemal tests**
  - Fluorescent treponemal antibody absorbed (FTA-ABS) test
  - Treponema pallidum particle agglutination (TP-PA) test
  - Enzyme immunoassays (EIAs)
    - Trep-Check and Trep-Sure
  - Chemiluminescence immunoassays (CIAs)
    - LIAISON and Architect
  - Microbead immunoassays (MBIA)
    - BioPlex 2200 Syphilis IgM and IgG

Need both types of serologic tests to make syphilis diagnosis: use of only one type of test is insufficient

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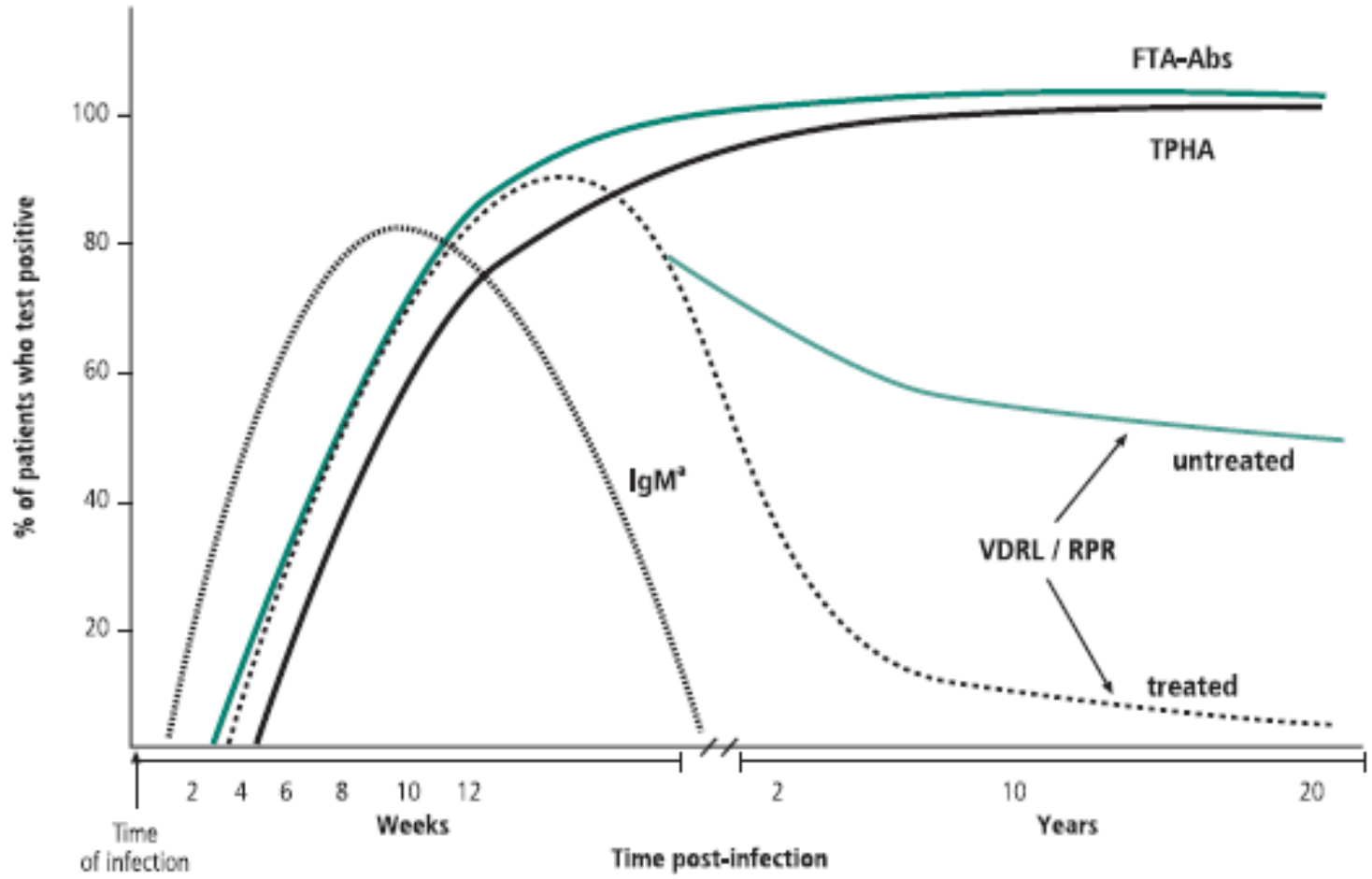
Common Patterns of Syphilis Serologic Reactivity



Peeling et al. / Bulletin of the World Health Organization / 2004 / Vol. 82 / No. 6

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Performance of Syphilis Serologic Tests

Test	Sensitivity during stage of infection, % (range)				Specificity, % (range)
	Primary	Secondary	Latent	Late	
Nontreponemal tests					
VDRL [14]	78 (74–87)	100	96 (88–100)	71 (37–94)	98 (96–99)
TRUST [14]	85 (77–86)	100	98 (95–100)	NA	99 (98–99)
RPR [14]	86 (77–99)	100	98 (95–100)	73	98 (93–99)
Early treponemal tests					
MHA-TP [15]	76 (69–90)	100	97 (97–100)	94	99 (98–100)
TPPA [16]	88 (86–100)	100	100	NA	96 (95–100)
TPHA [17]	86	100	100	99	96
Enzyme immunoassays					
IgG-ELISA [18]	100	100	100	NA	100
IgM-EIA [19]	93	85	64	NA	NA
ICE [20]	77	100	100	100	99
Immunochemiluminescence assays					
CLIA [21]	98	100	100	100	99

Rare Caveat: Prozone, False Negative in HIV+, Secondary

NOTE. CLIA, chemiluminescence assay; ELISA, enzyme-linked immunosorbent assay; EIA, enzyme immunoassay; FTA-ABS, fluorescent treponemal antibody absorption assay; ICE, immune-capture EIA; MHA-TP, microhemagglutination assay for *Treponema pallidum*; NA, not available; TPHA, *T. pallidum* hemagglutination assay; TPPA, *T. pallidum* particle agglutination; TRUST, toluidine red unheated serum test.

Sena, CID 2010

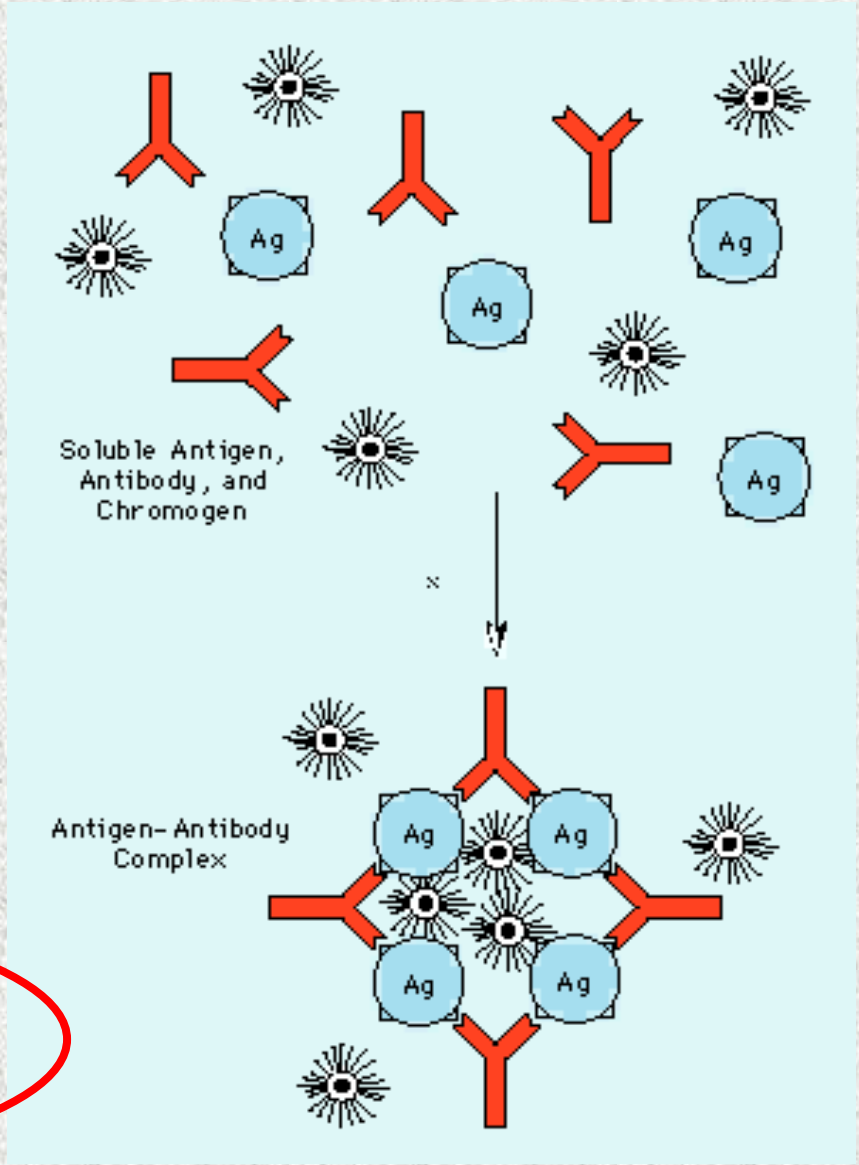
Prozone Phenomenon

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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Interpreting RPR/VDRL Titers: What Do They Mean?

- Higher numbers correspond to higher level of antibodies in patient's serum
- Number determined by progressive dilution of serum until it becomes non-reactive
- Two-fold change
  - Generally considered within margin of test error
- Sustained four-fold change
  - Considered to be significant

1:1024
1:512
1:256
1:128
1:64
1:32 } 2-fold change
1:16 }
1:8 } 4-fold change
1:4 }
1:2 }
1:1

Compare titer using same serologic test

- RPR often higher than VDRL

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Diagnostic Challenges

False negatives

- Early primary -*Serology negative in up to 25% primary case*
- Prozone Reaction(RPR/VDRL)
- Untreated late latent

Biologic False Positives

Non-trep test positive with confirmatory trep test negative

- Viral illnesses including HIV
- Recent immunizations,
- IDU
- autoimmune and chronic diseases

Treponemal Tests

- Can remain positive for life
- Specificity issues- FTA-ABS

Discordant serology

- EIA or CIA + and RPR –
- Non-syphilis trep infection

Jurado RL et al. *Arch Intern Med* 1993, **153:**2496–2498.
Geisler MG. *South Med Jour* 2004, **97**: 327-328.

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Interpreting Syphilis Screening Results

- Asymptomatic 30 y/o Female
- Syphilis screening results are:
  - Trep IgM/IgG Antibody Positive
  - RPR Non-Reactive
  - TP-PA Reactive

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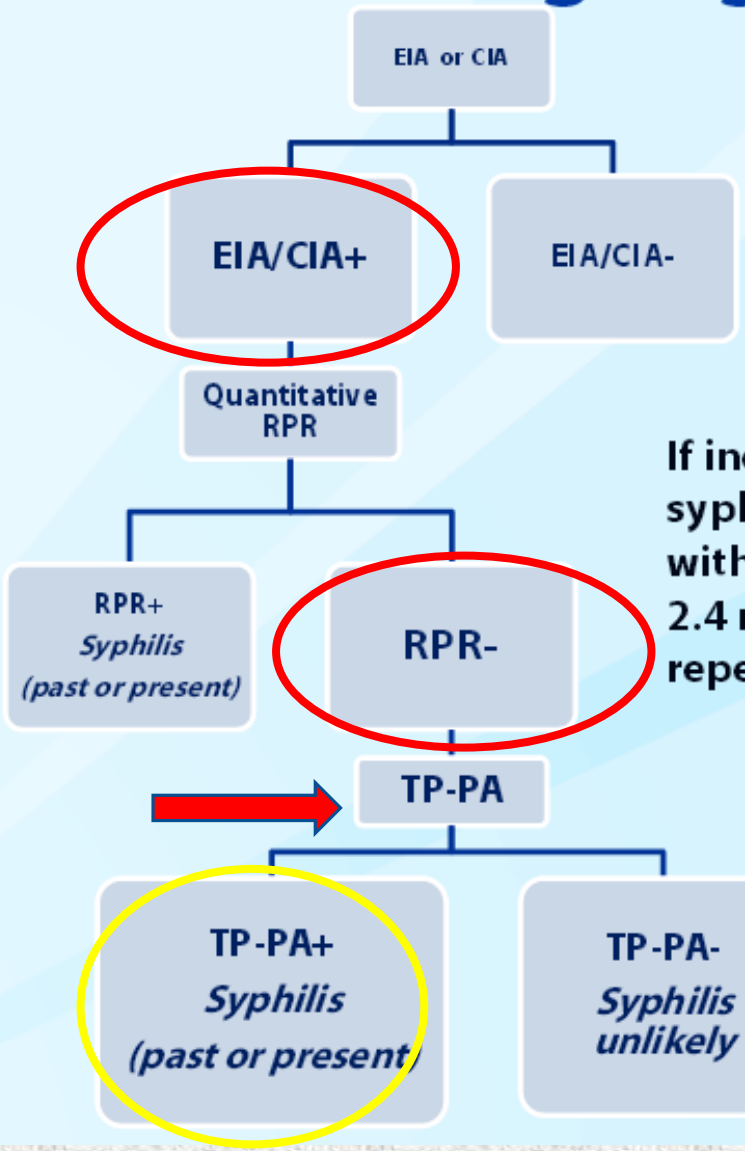
Reverse Screening Algorithm



Evaluate clinically, determine if treated for syphilis in the past, assess risk of infection, and administer therapy according to guidelines if not previously treated.

If incubating or primary syphilis is suspected, treat with benzathine penicillin G 2.4 million units IM x 1 and/or repeat in 2-4 weeks.

If at risk for syphilis, repeat RPR in 2 to 4 weeks.

CDC 2015 STD Treatment Guidelines

Sensitivity and Specificity of Treponemal Tests

Assay	Overall Sensitivity (n = 262)	Overall Specificity (n = 403)
FTA-ABS	**90.8**[a] (86.7–94.0)	98.0 (96.1–99.1)
TPPA	95.4 (92.1–97.6)	100 (99.0–100)
Centaur CIA	97.3 (94.6–98.9)	95.5 (93.0–97.3)
Trep-Sure EIA	98.5 (96.1–99.6)	**82.6**[c] (78.4–86.1)
LIAISON CIA	96.9 (94.1–98.7)	94.5 (91.8–96.5)
Bioplex MBIA	96.9 (94.1–98.7)	96.7 (94.4–98.2)
INNO-LIA	96.9 (94.1–98.7)	98.5 (96.8–99.5)

Park IU et al. 2018, Clin Infect Dis

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Neurosyphilis Diagnosis

- CSF VDRL has limitations
  - Very specific but not very sensitive
  - Only test approved for CSF specimen
  - CSF VDRL negative patients consider neurosyphilis treatment if no other etiology identified and
    - CSF WBCs >5 in HIV negative patients
    - CSF WBCs >20 in HIV infected patients*
- CSF FTA-abs not specific , a negative test result may help rule out neurosyphilis (not if clinical suspicion is high**)
- CSF- TP-PA limited data but may support diagnosis

*CDC 2010 STD Treatment Guidelines

**Harding, Ghanem. STD 2012; 39, (4) 291-97.

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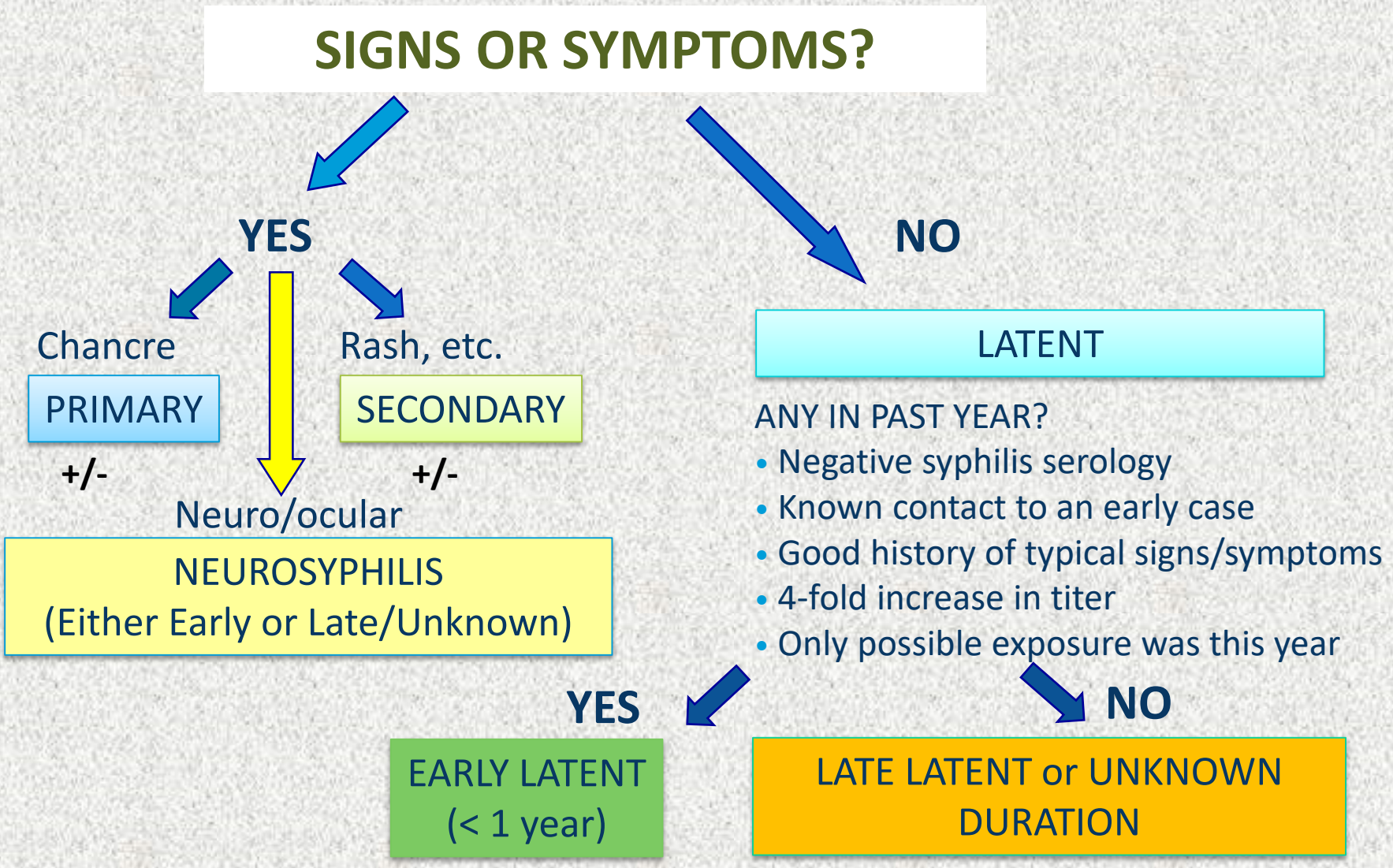
Syphilis Staging Flowchart



Syphilis Treatment

Primary, Secondary & Early Latent

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

* Bicillin L-A is the trade name. DO NOT USE Bicillin C-R!

** No enhanced efficacy of additional doses of BPG, amoxicillin or other antibiotics even if HIV infected

Alternatives (non-pregnant penicillin-allergic adults):

- Doxycycline 100 mg po bid x 2 weeks
- Tetracycline 500 mg po qid x 2 weeks
- Ceftriaxone 1 g IV or IM qd x 10-14 d

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

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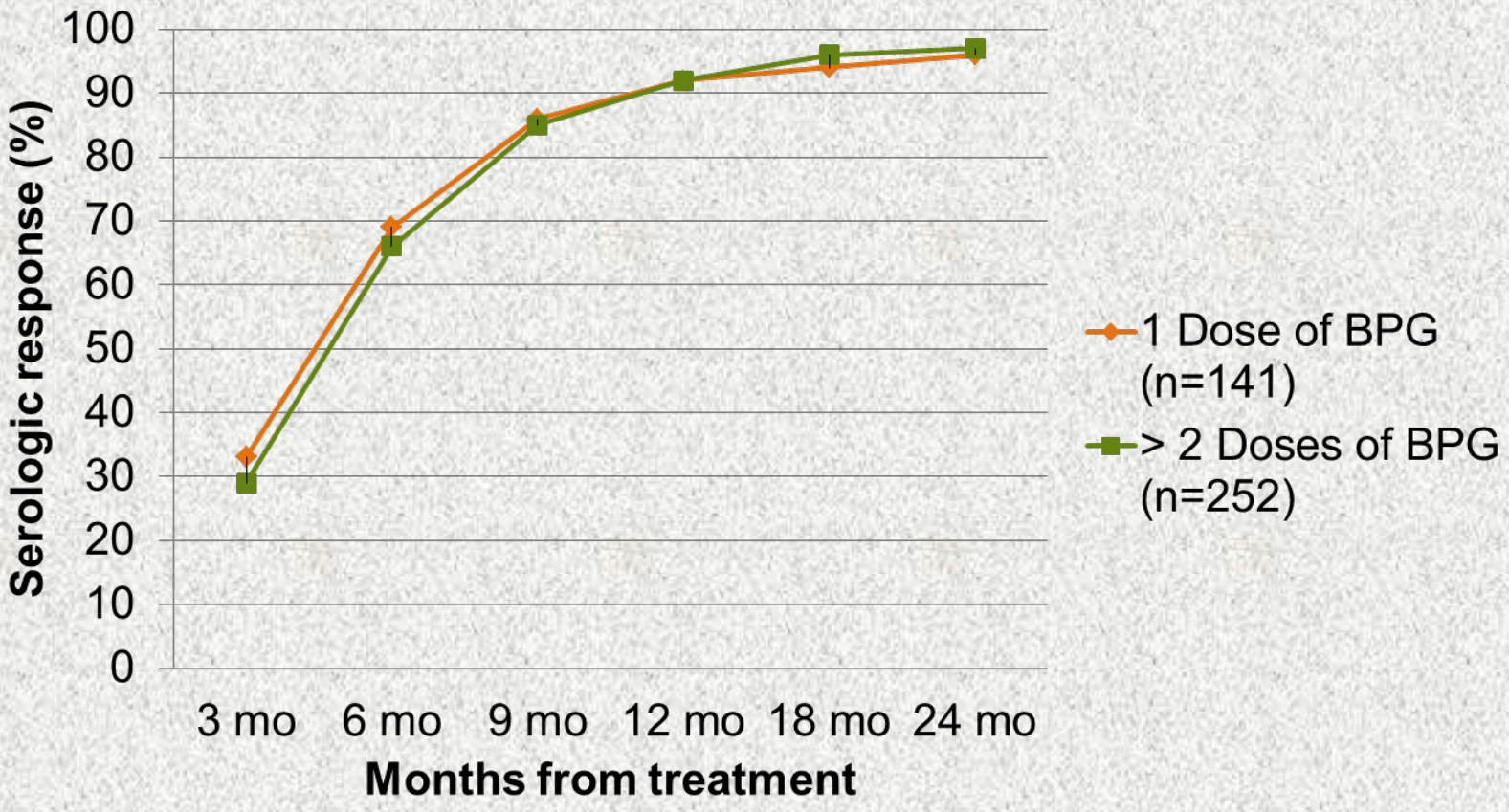
Serologic Response to Therapy: HIV + Early Syphilis



Source: Ganesan A, et al. A single dose of benzathine penicillin G is as effective as multiple doses of benzathine penicillin G for the treatment of HIV-infected persons with early syphilis. Clin Infect Dis. 2015. 60(4): 653-660.

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Syphilis Treatment

Late Latent or Latent of Unknown Duration

Benzathine penicillin G* 7.2 million units IM total in 3 doses of 2.4 MU each at one week* intervals

- Maximum 10-14 day interval (7-9 day ideal)
- 7 day interval in pregnancy (6-8 day may be ok)

Alternatives (non-pregnant penicillin-allergic adults):

- ❖ Doxycycline 100 mg po bid x 4 weeks
- ❖ Tetracycline 500 mg po qid x 4 weeks

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

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Syphilis Treatment Issues

Jarisch-Herxheimer Reaction

- Acute febrile reaction that may occur within 24 hours (usually 2-8 hours) of syphilis treatment
- Headache,myalgias and exacerbation of cutaneous lesions (rash)
- Most common in primary, secondary
- Uncommon in latent
- Does not indicate drug hypersensitivity

CDC 2015 STD Treatment Guidelines

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Neurosyphilis/Ocular Syphilis Treatment

Aqueous crystalline penicillin G 18-24 million units IV daily administered as 3-4 million units IV q 4 hr for 10-14 days

* Consider: BIC 2.4 million units IM once per week up to 3 weeks after completion of 10-14 day course for late syphilis

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

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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*

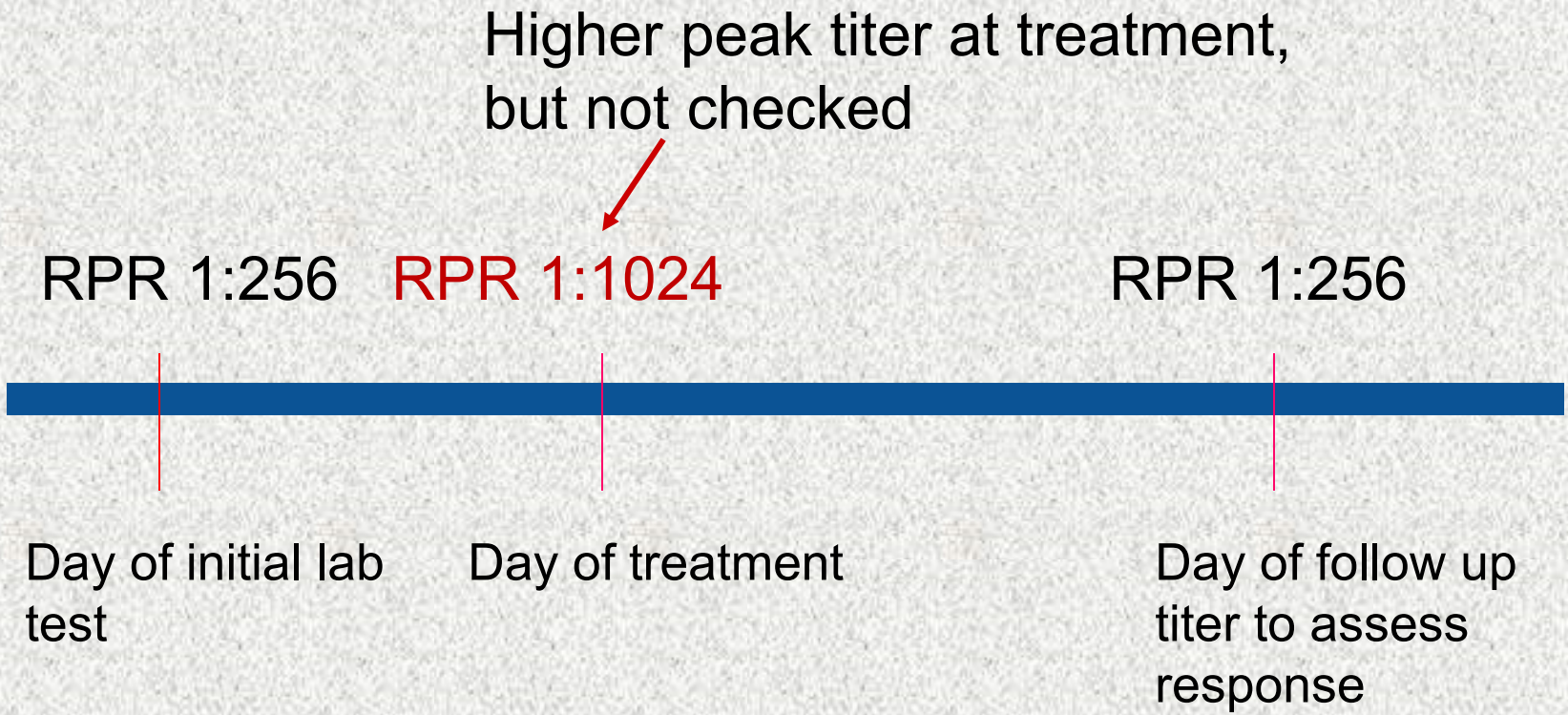
LATE LATENT or UNKNOWN DURATION

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!

Importance of Day of Treatment Titer



- Establishes baseline to compare response post treatment
- Frequently forgotten and without baseline makes assessment of titer response difficult

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Follow-up and Serologic Response

» Primary and Secondary Syphilis

- > Examine at ~1 week to confirm improvement of symptoms (1^{o} and 2^{o})
- > Repeat titers at 6 and 12 months (3, 6, 9, 12, and 24 for HIV+)
- > Expect fourfold decrease in serology in 6-12 months

(12-24 months for HIV+)

» Latent Syphilis

- > Re-examine at 6, 12, and 24 months (6, 12, 18 and 24 for HIV+)
- > Expect fourfold decrease in serology in 12-24 months (if titer initially >1:16) (24 months for HIV+)

CDC 2015 STD Treatment Guidelines

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Syphilis Treatment Failures

Clinical Failure: Slow resolution or relapse of mucocutaneous signs

Serologic Failure:

- Sustained (> 2 weeks) fourfold increase in nontreponemal titers
  - Reinfection may be difficult to rule out

Serologic Non-response: Failure of initially high nontrep titers to decrease four-fold

- ? Possible treatment failure“
- Estimate ~15-20%* don’t have 4- fold drop
  - Earlier stage/higher titer more likely to decline 4-fold

* Seña AC, et al. CID 2011

*Rolfs RT, et al. NEJM 1997 CDC 2015 STD Treatment Guidelines

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Treatment Failure: Management Options

- HIV test and CSF evaluation
  - Treat based on CSF findings
  - If LP normal retreat with Benzathine Penicillin G 7.2 million units (2.4 MU weekly x 3)
- Optimal management unclear for primary/secondary syphilis w/o 4-fold drop in titer
  - Additional serologic/clinical follow-up necessary and HIV test
  - If follow-up uncertain retreat with Benzathine Penicillin G 7.2 million units (2.4 MU weekly x 3)
  - Consider LP

Follow titers annually- need for further treatment/LP unclear

CDC 2015 STD Treatment Guidelines

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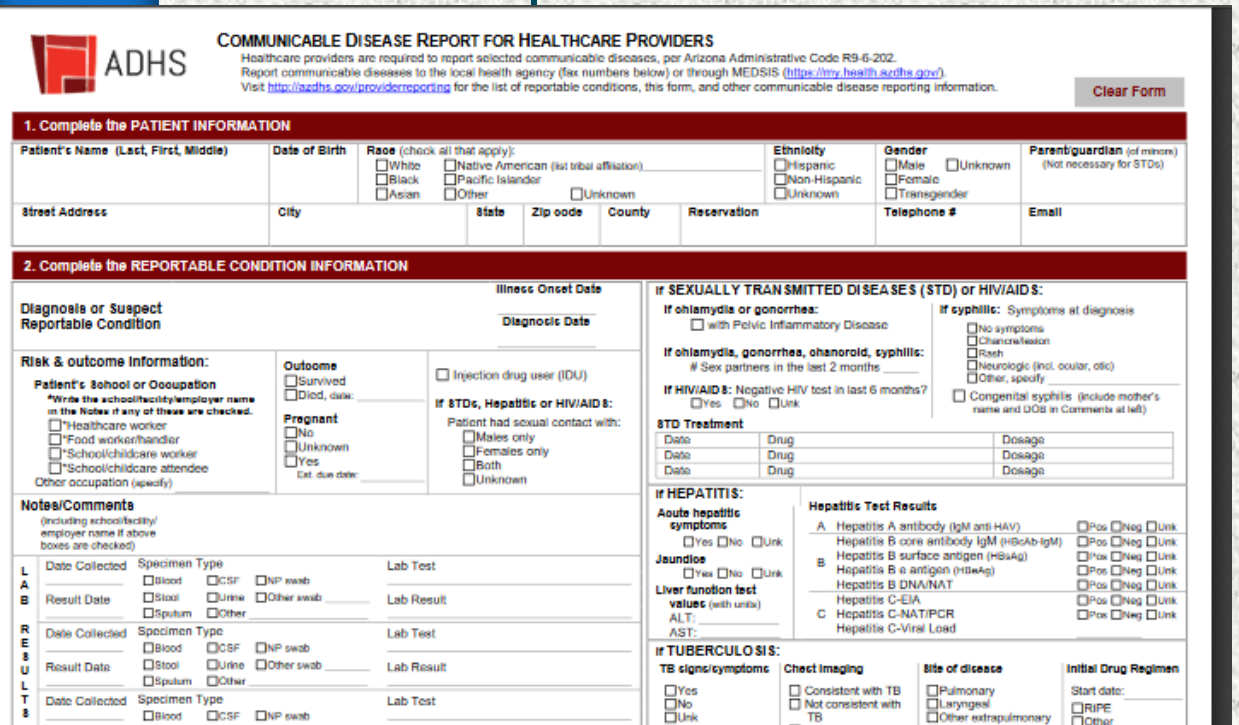
Reporting: Syphilis Cases

- Report all syphilis cases to Local Health Department
  - Report within 5 days
  - Report within 1 day if pregnant female case/ suspect case



ADHS

COMMUNICABLE DISEASE REPORT FOR HEALTHCARE PROVIDERS

Healthcare providers are required to report selected communicable diseases, per Arizona Administrative Code R9-6-202.
Report communicable diseases to the local health agency (fax numbers below) or through MEDSIS (https://my.health.azdhs.gov/).
Visit http://azdhs.gov/providerreporting for the list of reportable conditions, this form, and other communicable disease reporting information.

Clear Form

1. Complete the PATIENT INFORMATION

Patient's Name (Last, First, Middle) | Date of Birth | Race (check all that apply): White, Black, Asian, Native American (list tribal affiliation), Pacific Islander, Other, Unknown | Ethnicity: Hispanic, Non-Hispanic, Unknown | Gender: Male, Female, Transgender, Unknown | Parent/guardian (of minors) (Not necessary for STDs)

Street Address | City | State | Zip code | County | Reservation | Telephone # | Email

2. Complete the REPORTABLE CONDITION INFORMATION

Diagnosis or Suspect Reportable Condition | Illness Onset Date | Diagnosis Date

Risk & outcome information:
Patient's School or Occupation
*Write the school/facility/employer name in the Notes if any of these are checked.
*Healthcare worker
*Food worker/handler
*School/childcare worker
*School/childcare attendee
Other occupation (specify)

Outcome: Survived, Died, date:
Pregnant: No, Unknown, Yes, Est. due date:
Injection drug user (IDU)
If STDs, Hepatitis or HIV/AIDS: Patient had sexual contact with: Males only, Females only, Both, Unknown

Notes/Comments (including school/facility/employer name if above boxes are checked)

LAB RESULTS
Date Collected | Specimen Type: Blood, CSF, NP swab, Stool, Urine, Other swab, Sputum, Other | Lab Test
Result Date | Lab Result

If SEXUALLY TRANSMITTED DISEASES (STD) or HIV/AIDS:
If chlamydia or gonorrhea: with Pelvic Inflammatory Disease
If chlamydia, gonorrhea, chancroid, syphilis: # Sex partners in the last 2 months
If HIV/AIDS: Negative HIV test in last 6 months? Yes No Unk
If syphilis: Symptoms at diagnosis: No symptoms, Chancre/lesion, Rash, Neurologic (incl. ocular, otic), Other, specify
Congenital syphilis (include mother's name and DOB in Comments at left)

STD Treatment

Date	Drug	Dosage
Date	Drug	Dosage
Date	Drug	Dosage

If HEPATITIS:
Acute hepatitis symptoms: Yes No Unk
Jaundice: Yes No Unk
Liver function test values (with units): ALT: AST:

Hepatitis Test Results

A	Hepatitis A antibody (IgM anti-HAV)	Pos Neg Unk	
B	Hepatitis B core antibody IgM (HBcAb-IgM)	Pos Neg Unk	
	Hepatitis B surface antigen (HBsAg)	Pos Neg Unk	
	Hepatitis B e antigen (HBeAg)	Pos Neg Unk	
	Hepatitis B DNA/NAT	Pos Neg Unk	
C	Hepatitis C-EIA	Pos Neg Unk	
	Hepatitis C-NAT/PCR	Pos Neg Unk	
	Hepatitis C-Viral Load		

If TUBERCULOSIS:
TB signs/symptoms: Yes, No, Unk
Chest imaging: Consistent with TB, Not consistent with TB
Site of disease: Pulmonary, Laryngeal, Other extrapulmonary
Initial Drug Regimen: Start date: RIPE, Other

www.azdhs.gov/preparedness/epidemiology-disease-control/index.php#reporting-providers

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Syphilis Partner management

- 45 male presents as contact to early case of syphilis.
- Asymptomatic, no syphilis findings on exam.
- RPR is non reactive.
- Does this contact need treatment?

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Management of Contacts to Infectious Syphilis

- Contacts to primary, secondary or early latent
  - Exposed ≤ 90 days before diagnosis
    - Might be infected even if seronegative (can take up to 90 days for serology to convert); treat presumptively
  - Exposed >90 days before diagnosis
    - serologic tests are negative, no treatment is needed
      - If follow-up uncertain or serology unavailable then treat presumptively

CDC 2015 STD Treatment Guidelines

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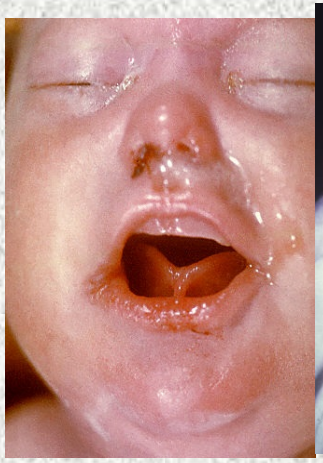
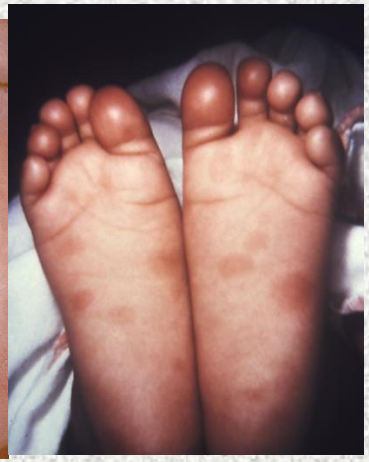
Congenital Syphilis

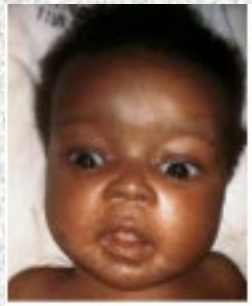
- Infection of the fetus or newborn at any stage during pregnancy
- Manifestations can be early or late including:
  - > Stillbirth, miscarriage, neurologic abnormalities, bony abnormalities, hearing loss, visual loss



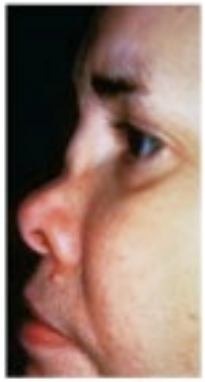
Syphilitic Rhinitis



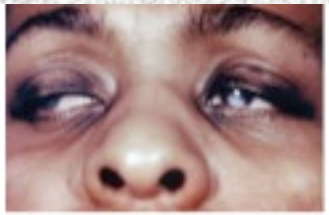
Syphilitic Rash



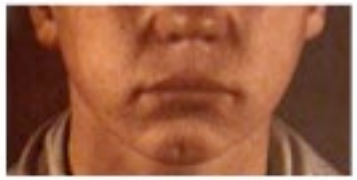
Frontal bossing; Saddle nose



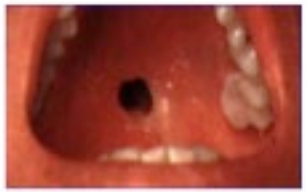
Saddle nose



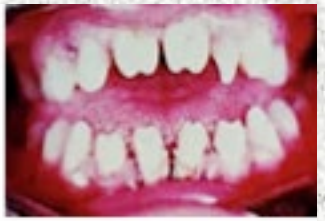
Interstitial keratitis



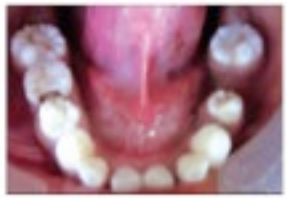
Rhagades



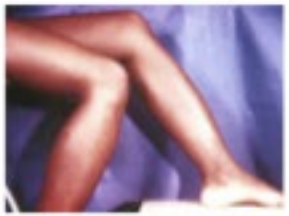
Perforated hard palate



Hutchinson teeth



Mulberry molar



Saber shins

Photos courtesy of Public Health Image Library, CDC and Dr. Norman Cole

Prevention of Congenital Syphilis

1) Screen for syphilis in the 1st trimester
2) Repeat screening at 28 weeks and again at delivery – AZ guidance 2019 (Do not D/C mom and baby without documenting a negative serology)
3) Timely treatment of syphilis during pregnancy
    - At least 4 weeks prior to delivery
    - Benzathine PCN is the only treatment option, no alternatives

CDC 2015 STD Treatment Guidelines

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Take home points

- Syphilis Rates are increasing among MSM and women
- Congenital syphilis is devastating and preventable
- Recognize symptoms and signs
  - Evaluate for neuro/ocular signs
  - Empiric treatment if high suspicion
- Assess risk and screen
- Determine stage of disease to guide treatment
  - Get day-of-treatment titer
  - Follow titers to assess treatment
  - Use Bicillin L-A as first line
- Report to local health department

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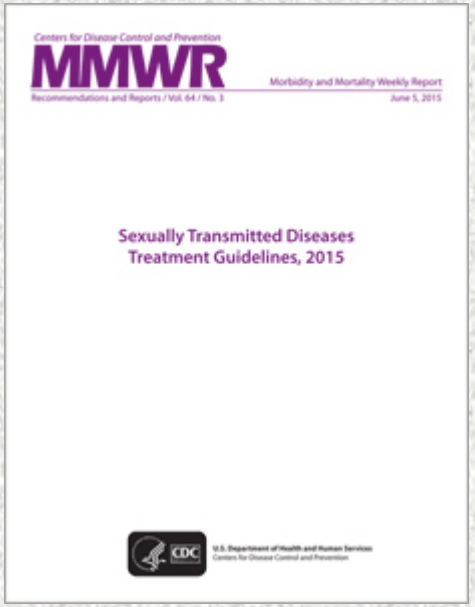
Clinical Guidelines and Consultation



STD Clinical Consultation Network

stdccn.org

CDC STD Treatment Guidelines App
Available now, free
Search for "STD TX"

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

National Network of STD Clinical Prevention Training Centers

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Thank You

Questions?

Questions and Discussion

Please type your questions and comments into the Zoom Webinar Platform Chat box.

THE UNIVERSITY OF ARIZONA
MEL & ENID ZUCKERMAN COLLEGE OF PUBLIC HEALTH
Center for Rural Health

Syphilis 2019: Return of the Great Masquerader

Sharon Adler, MD, MPH
California Prevention Training Center
Assistant Clinical Professor at University of California, San Francisco (UCSF), Family and Community Medicine

Thank you!

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http://www.crh.arizona.edu/programs/sorh/webinars

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» Extra Slides

Titer rise early after treatment

- Cases of primary/secondary/early latent syphilis (N=470)
- RPR titer day 0,7,14 post Rx
- 20% had titer rise 14 day after Rx (88% 2-fold rise, 12% 4-fold rise)
- Primary cases had greatest titer rise
- Early rise in titer not indicative of increased risk of Rx failure

Holman et al. STD 2012

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Syphilis in Pregnancy: Follow-up

- Titers at 28-32 weeks of gestation, delivery, and following recommendations for stage of disease
- Serologic titers can be checked monthly in high-risk women
- Clinical and serologic response should be appropriate for stage
  - Most women will deliver before serologic response to treatment can be assessed

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Neurosyphilis

» Neurosyphilis can be characterized as early/acute or late disease. Early neurosyphilis can be symptomatic or asymptomatic and can occur at any stage of syphilis, including concurrently with primary or secondary disease. Early symptomatic neurosyphilis consists of syphilitic meningitis, ocular syphilis and/or otosyphilis. Rarely, vascular complications can result from syphilitic meningitis and lead to an ischemic stroke; vascular complications are more commonly associated with late disease.

Early Neurosyphilis: Review of Systems *(pertinent positive symptoms)*

GENERAL/CONSTITUTIONAL: headache, fever, fatigue, weakness, dizziness

HEAD, EYES, EARS, NOSE AND THROAT:
- Eyes- pain, redness, loss of vision, double or blurred vision, photophobia, flashing lights or spots
- Ears- ringing in the ears, loss of hearing

GASTROINTESTINAL: nausea, vomiting

MUSCULOSKELETAL: neck pain/stiffness, muscle weakness

NEUROLOGIC: headache, dizziness, muscle weakness, confusion, loss of consciousness, seizures, difficulty speaking

PSYCHIATRIC: confusion

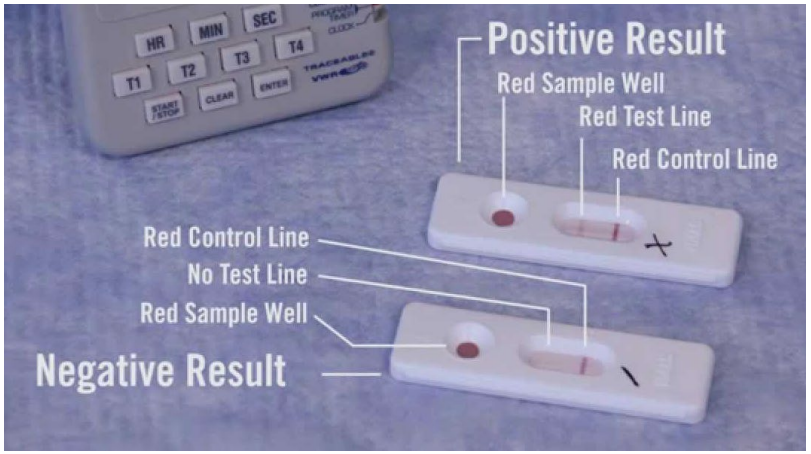
Early Neurosyphilis: Focused Neurologic Exam

- **Cranial Nerve Exam**: assess for cranial nerve palsies (key maneuvers in **bold**)

Available at: http://www.cdph.ca.gov/programs/std/Documents/NeurosyphilisGuide.pdf

New Point-of-Care Syphilis Tests

Rapid Immunochromatographic Assays: lateral flow immunoassays (e.g. rapid HIV-antibody tests, urine HCG)



Syphilis Health Check

Treponemal only

Results in 10 min

FDA approved, CLIA waived

US $8 per test

DPP Syphilis Screen and Confirm

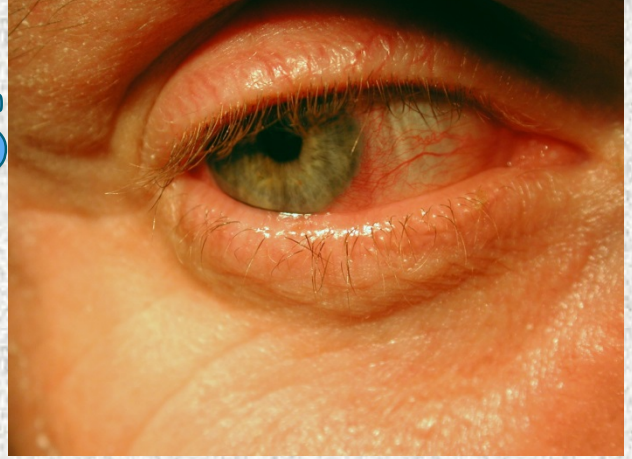
Combined treponemal and non-treponemal results

Results in 15 min

Seeking FDA, eligible for CLIA waiver

US 1.50-$2 per test

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

CDC 2015 STD Treatment Guidelines

Photo Courtesy: Dr. Kees Rietmeijer, Denver PHD

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Syphilis: Management of Contacts: Late Syphilis

- Long term sex partners of patients who have late syphilis should be evaluated clinically and serologically for syphilis and treated on the basis of findings

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