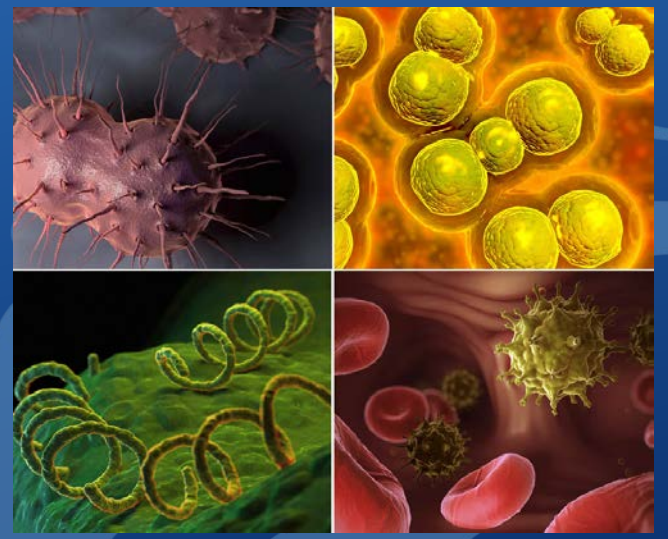
Workshop A:
Clinical Screening and Treatment Core:

1. **Focus on Syphilis**
2. **Focus on Gonorrhea and Chlamydia**
3. **Other Looming STI Big Beasts**



October 30, 2018

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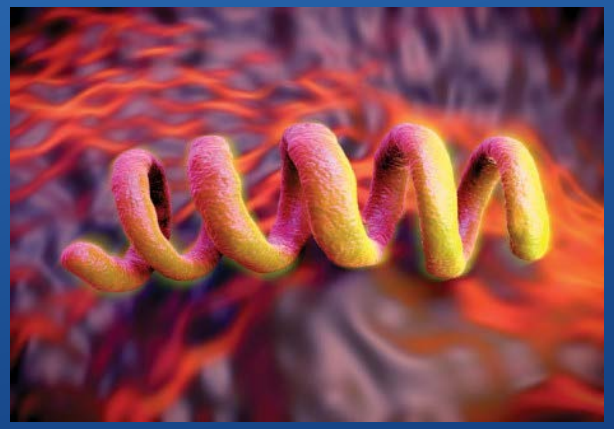
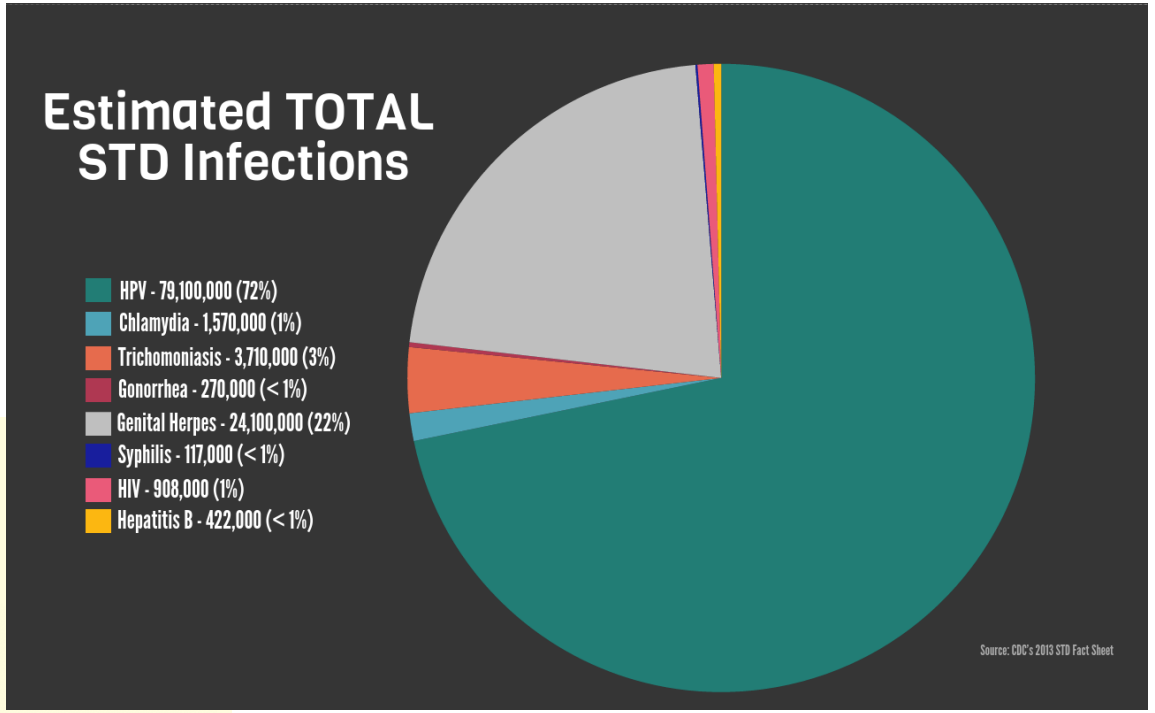
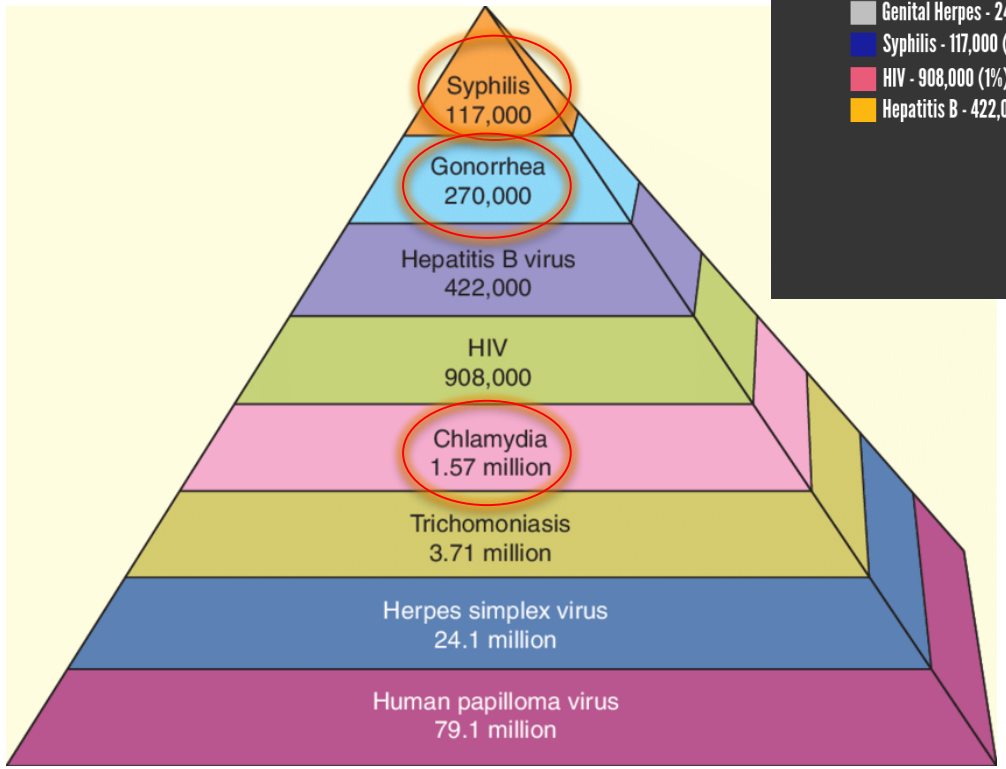
Disclosures: None



County of Los Angeles Public Health



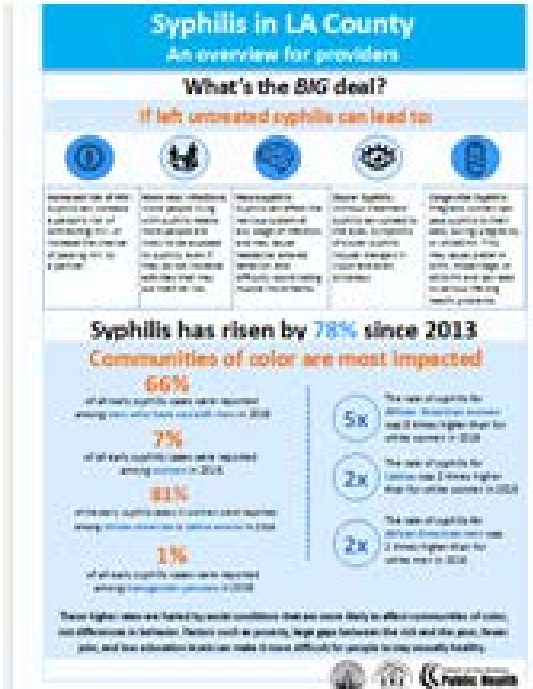


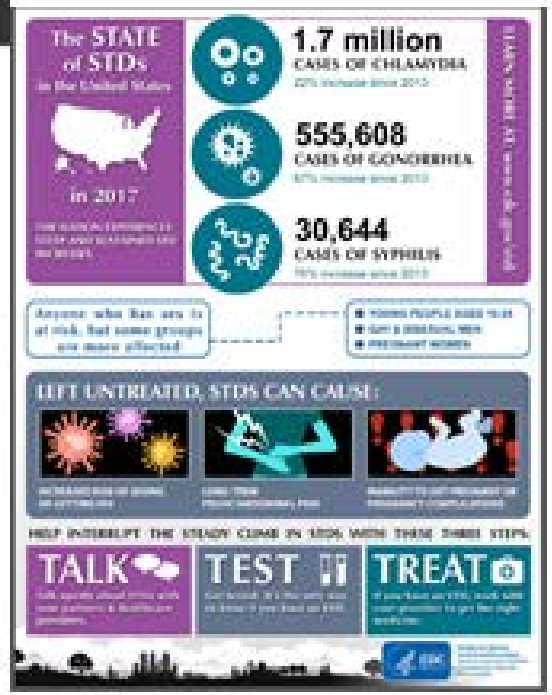
Reference: CDC

Mycoplasma genitalium
Rectal CT- Lymphogranuloma venereum
Trichomonas

Urgent Need for Prevention and Control Efforts

County of Los Angeles Public Health

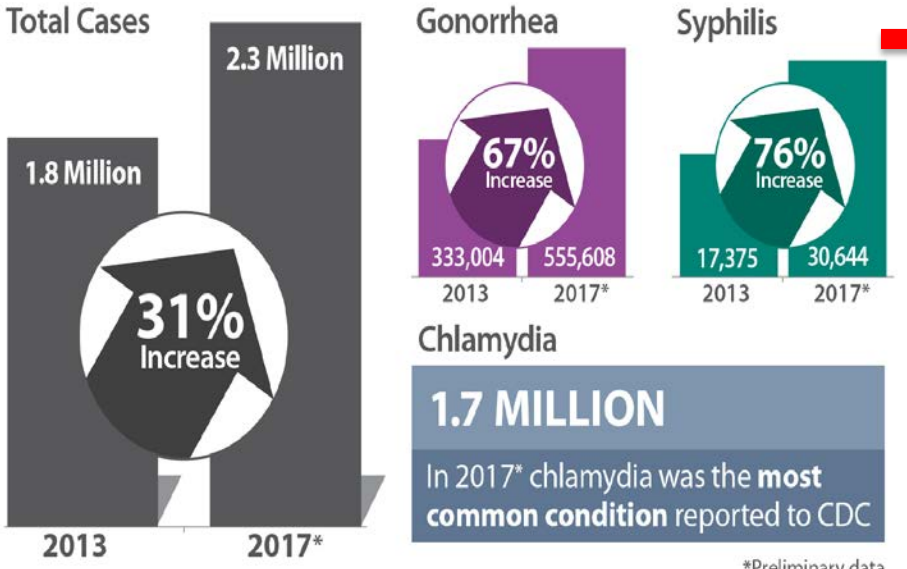




Recent Media hype around STD's

THE U.S. IS EXPERIENCING STEEP, SUSTAINED INCREASES IN SEXUALLY TRANSMITTED DISEASES

Combined diagnoses of chlamydia, gonorrhea, and syphilis **increased sharply over the past five years**



Chlamydia

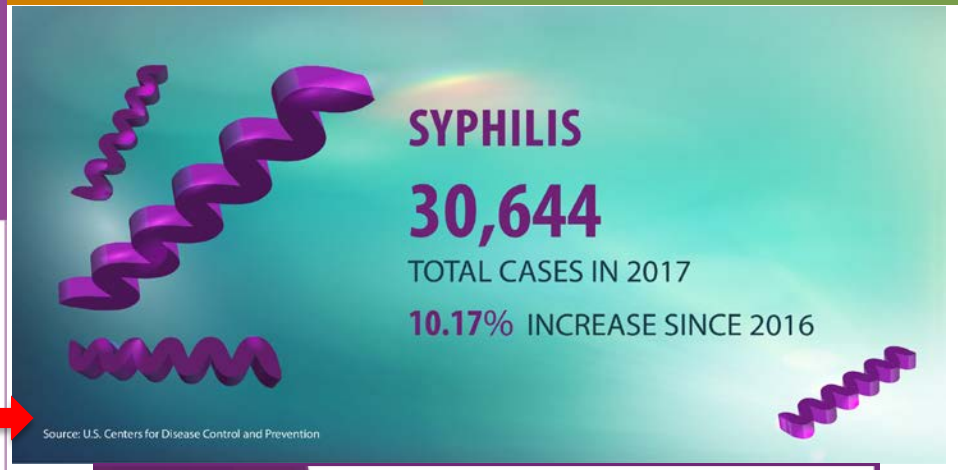
1.7 MILLION

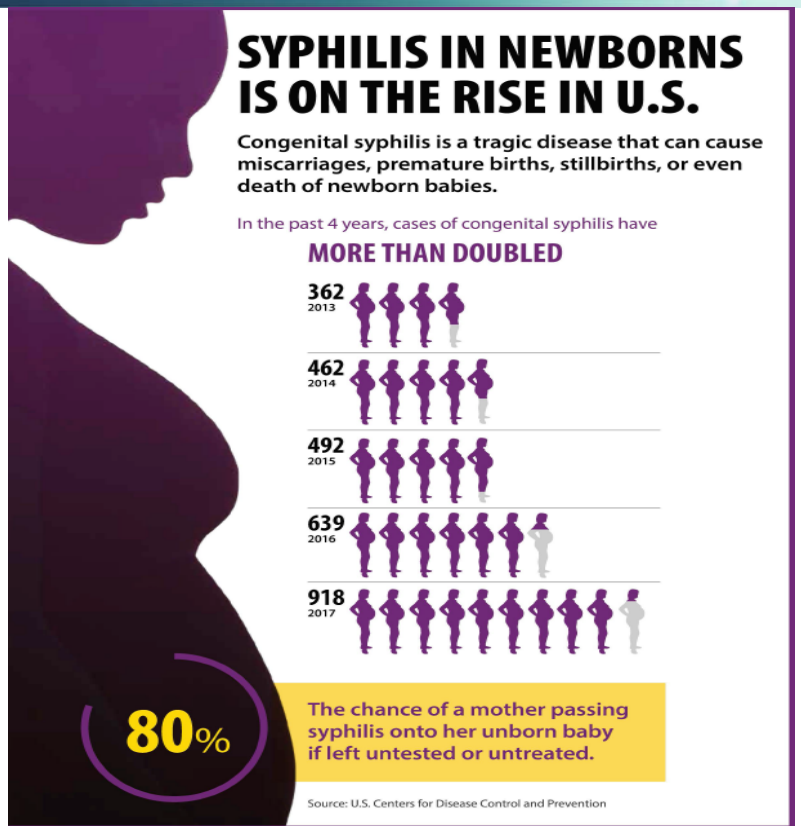
In 2017* chlamydia was the **most common condition** reported to CDC

*Preliminary data

For more information, visit
cdc.gov/nchhstp/newsroom

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

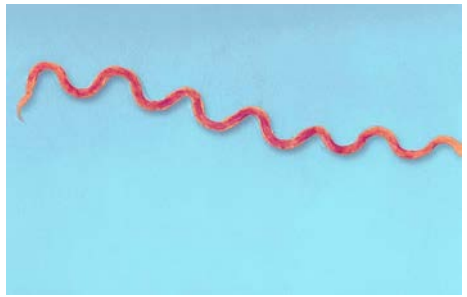




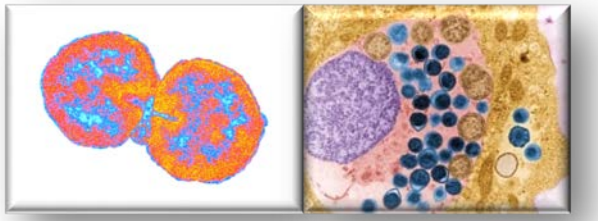
Outline

Workshop A: Clinical Screening and Treatment Core

- **Focus on Syphilis**
  - Clinical highlights, diagnosis and staging
  - Treatment and follow up
  - Epidemiology key points
  - Screening guidelines



- **Focus on Gonorrhea and Chlamydia**
  - Clinical highlights, diagnosis and extragenital testing
  - Treatment, PDPT, retesting and test of cure
  - Epidemiology key points
  - Screening guidelines



Role of the Department of Public Health

Case: Missed Opportunities # 1

Day 0: 40 year old HIV-infected male presents to PCP with rash on forehead. He is virally suppressed on ARTs.

Day 21: He returns with rash over his back. His provider believes the rash to be pityriasis rosea and treats with acyclovir x 1 week.

Day 28: He returns because the rash is not resolving. Having done independent web-based research, patient requests a syphilis test. RPR was 1:128, no treponemal confirmatory test was done.

Day 30: Provider reports positive result to health department within two days but the lab never reported the positive result.

Day 36: Patient returns for treatment and is treated with 3 shots of Benzathine penicillin. RPR is not drawn.

Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Case: Missed Opportunities #2

Day 0: 34 year-old theology student presented to the student health center with reddish, crusted lesions on his penis. He was treated with valacyclovir and anti-fungal cream.

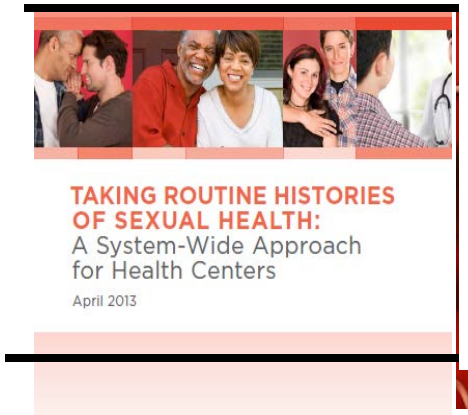
Day 7: He returned because the lesions were not getting better and he was prescribed dicloxacillin.

Day 100: He returned with a rash on his trunk. An RPR test was ordered and he was treated with one shot of Benzathine PCN G. RPR came back 1:32.

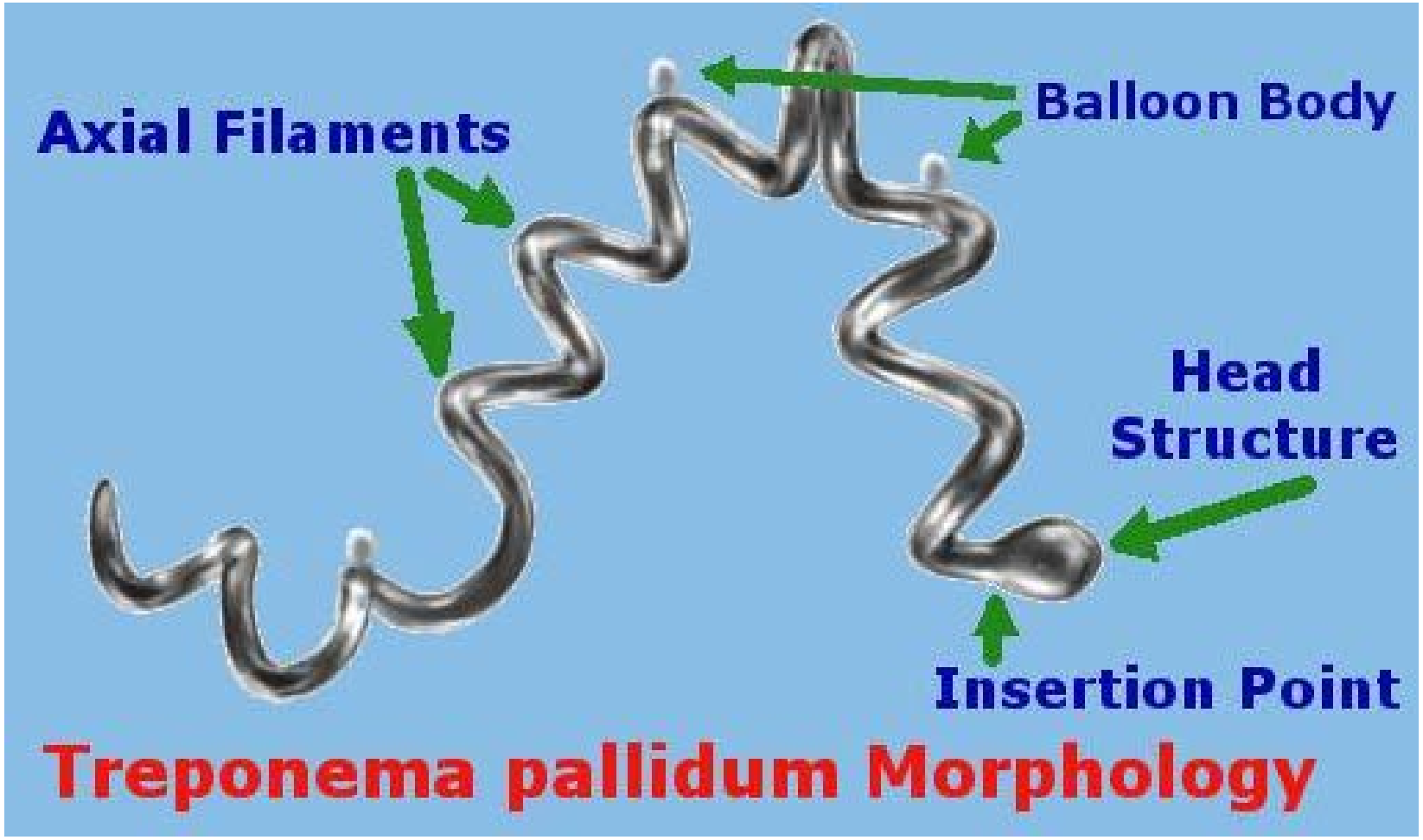
Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Key takeaways

- Take a sexual history: 5 P's (***P***ast STD's, ***P***artners, ***P***ractices, ***P***revention, ***P***regnancy plans and HIV prevention)
- Consider syphilis for rashes, genital lesion (s) or warts
- Low threshold to treat empirically when syphilis is suspected
- Collect a titer on the day of diagnosis
- Report case – health department will reach out and offer partner services and follow-up with sexual contacts



Clinical Highlights

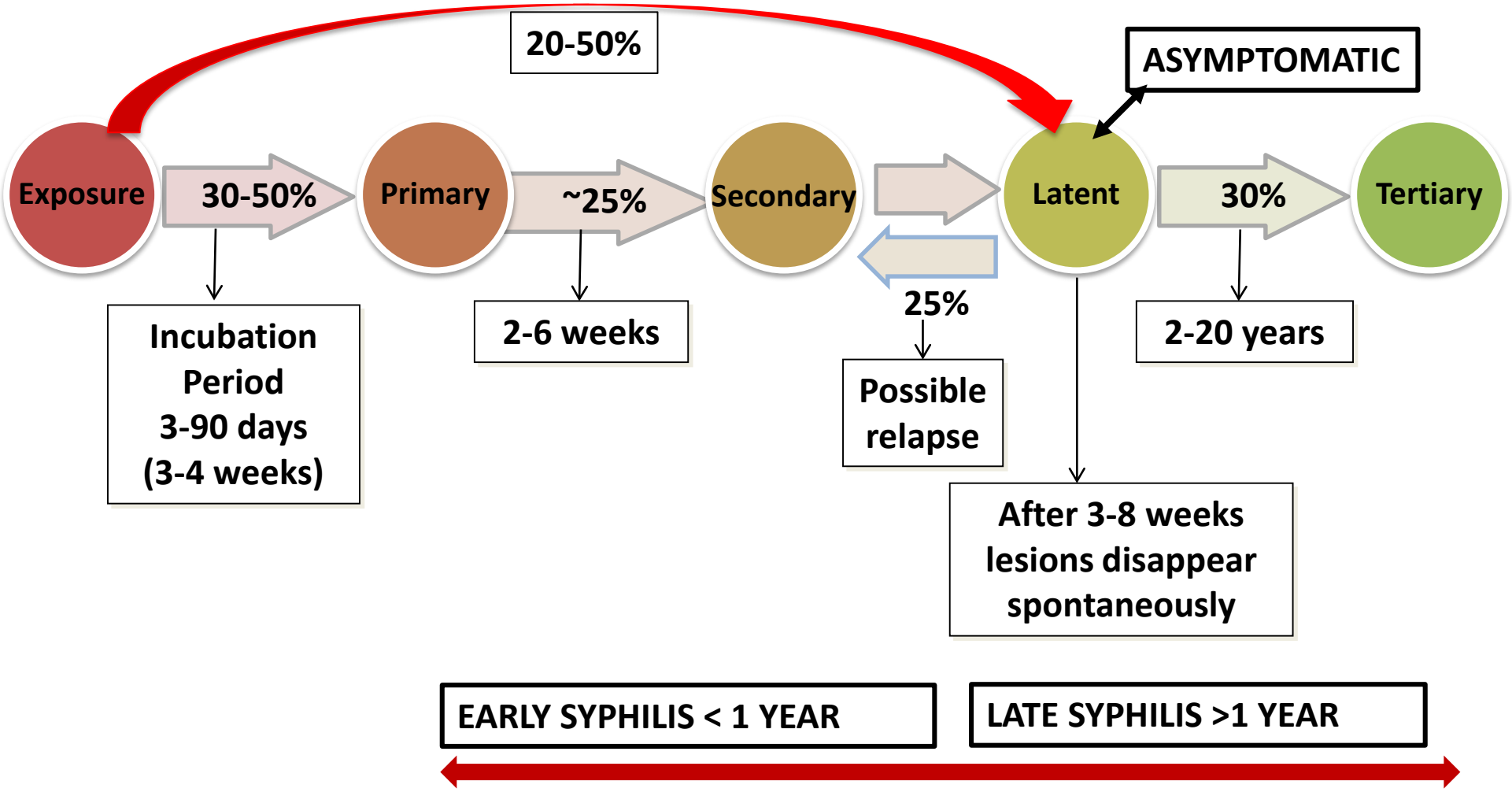


Classical features of human treponematoses

Feature	Yaws	Bejel (endemic syphilis)	Pinta	Venereal syphilis
Causative agent	*T. pallidum* subsp. *pertenue*	*T. pallidum* subsp. *endemicum*	*T. carateum*	*T. pallidum* subsp. *pallidum*
Geographical distribution	Western/Central Africa, Southeast Asia, Pacific Islands	Sahelian Africa, Saudi Arabia	Central and South America	Global
Climatic conditions	Tropical (hot and humid)	Hot and dry (semiarid/arid)	Warm (semiarid)	All
Age group (peak incidence of lesions)	Children (<15 yr)	Children (2–15 yr)	Children and adults	Adults
Common mode of transmission	Skin-to-skin contact	Mucous membrane and skin-to-skin contact (sharing of eating utensils and drinking vessels)	Skin-to-skin contact	Sexual and congenital; occasionally nonsexual contact

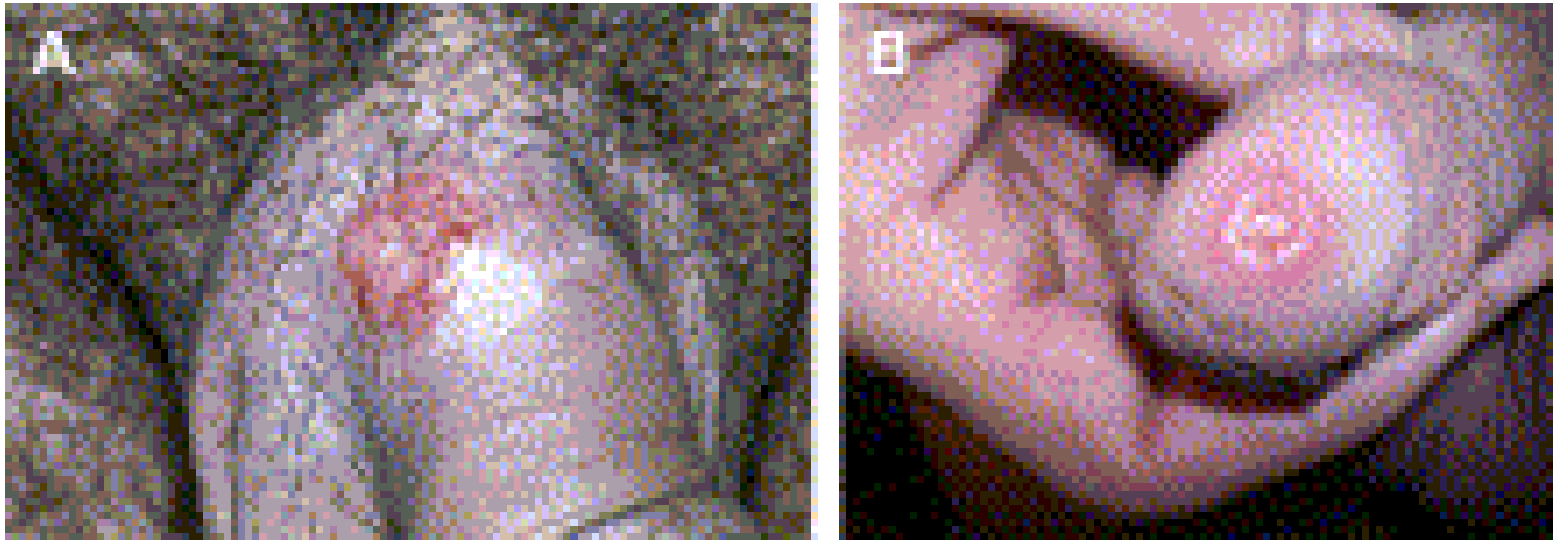
Giocani L, Lukehart S: Clin Microbiol Rev. 2014 Jan; 27(1): 89–115.

Syphilis Natural History



Primary Syphilis

Single Penile Chancre



SF City Clinic

Most Infectious –Chancres full of bacteria

Person contagious through contact (~30%)

Mosby

STD Atlas, 2010

Primary Syphilis

Multiple Penile Chancres

Courtesy: SF City Clinic

Primary Syphilis

Healing Penile Chancre

Mosby *STD Atlas, 1997*

Primary Syphilis

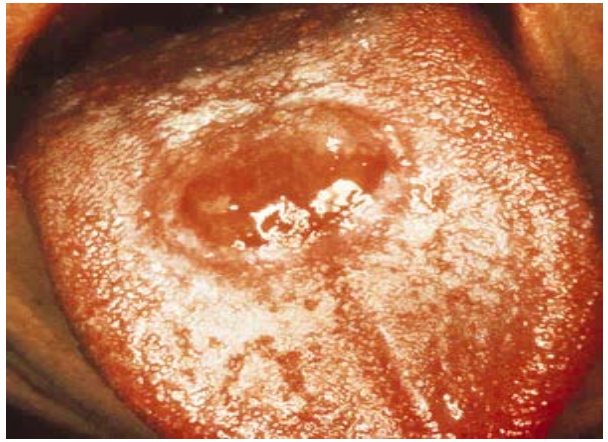
Multiple Vulvar Chancres

SFCC

Mosby *STD Atlas, 1997*

Perinatal transmission possible (70-100%)

Extragenital Primary Syphilis





Clinics in Dermatology, 2016; British Dental Journal, 2000; Raguse et al. Ann Int Med March 2012; Mosby

Secondary Syphilis

- Usually occurs (3-90 days) 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

Secondary Syphilis Body Rash

Mosby *STD Atlas, 1997*

Secondary Syphilis:

Rash on Palms and Soles-characteristic sx/s

Few differentials for rash that involves the hands and feet

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

Secondary Syphilis Genital Rash

Courtesy: SF City Clinic, Mosby

Secondary Syphilis

Condyloma Lata

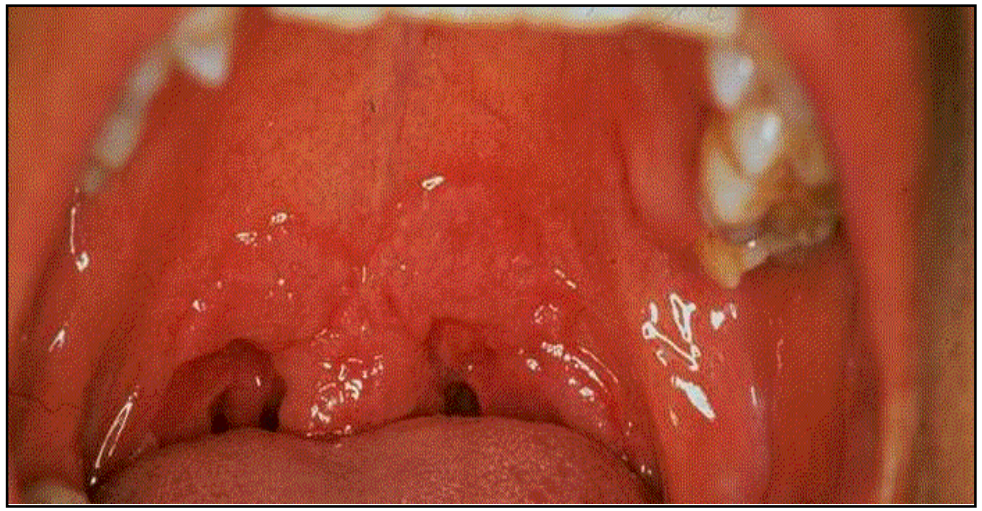
Person contagious through contact (~30%)

Perinatal transmission possible (90-100%)

Courtesy: Gregory Melcher, UC Davis

Susan Philip, SF DPH & UCSF

Secondary Syphilis: Mucous Patches



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

Secondary Syphilis

Patchy Alopecia

Mosby

STD Atlas, 1997

Clinics in Dermatology, 2004

CDC April 2015 Clinical Advisory: Ocular Syphilis Alert- CA, WA, other states

- 24 cases majority HIV-infected MSM
  - Few HIV-uninfected men and women
  - Significant sequelae including blindness
- **Be aware of ocular syphilis:**
  - **Symptoms may include:** loss of vision, floaters, a blue tinge in vision, flashing lights and blurring of vision
- **Careful neurologic exam in syphilis patients**
- **Patients with syphilis and ocular complaints need immediate ophthalmologic evaluation!!!**
- **LP should be performed in patients with syphilis and ocular complaints**
- Prior research has documented neuropathogenic strains
  - ?unknown if oculo-tropic strain role in these cases

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

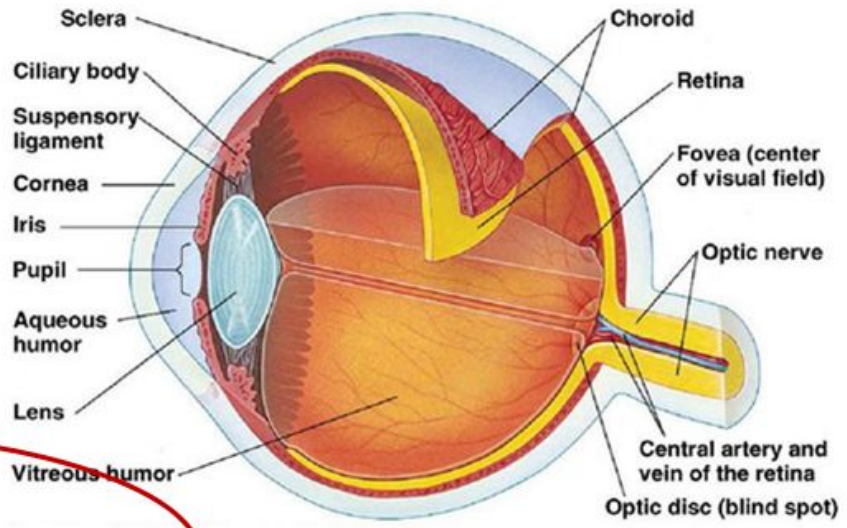
Ocular Syphilis

Manifestations:

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

Symptoms:

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



Diagnosis:

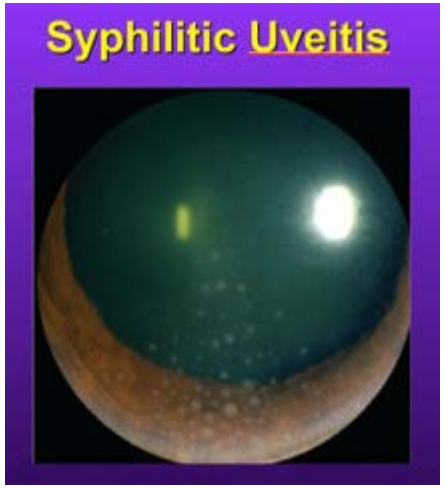
- Ophthalmologic exam
- Serologies: RPR, VDRL, treponemal tests
- Lumbar puncture

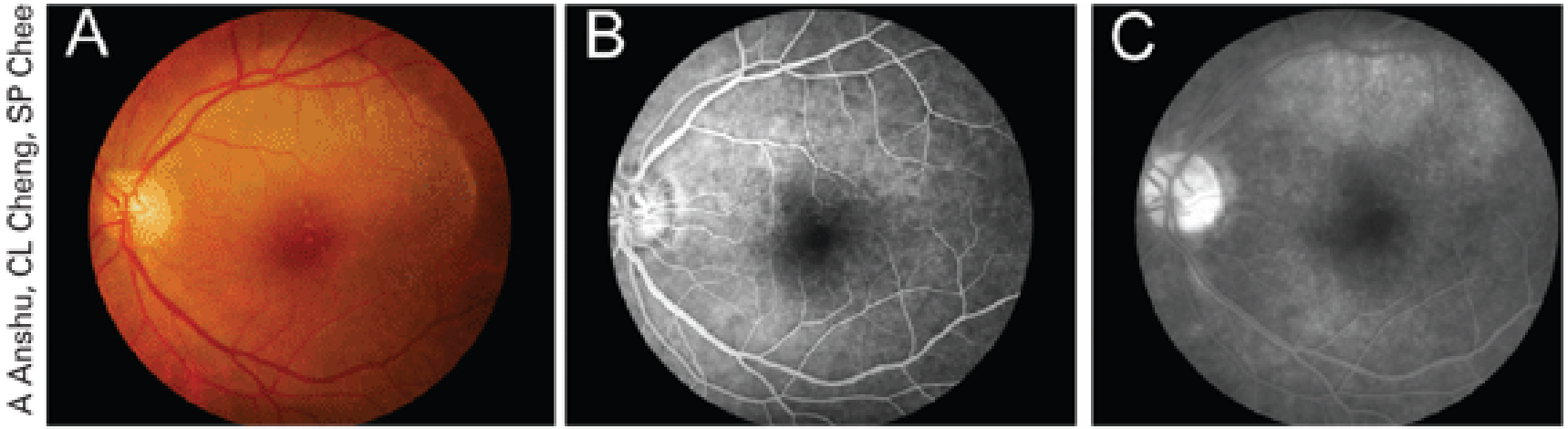
Slide courtesy of Sarah Lewis, MD

Johns Hopkins School of Medicine

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

Clinical images of ocular syphilis

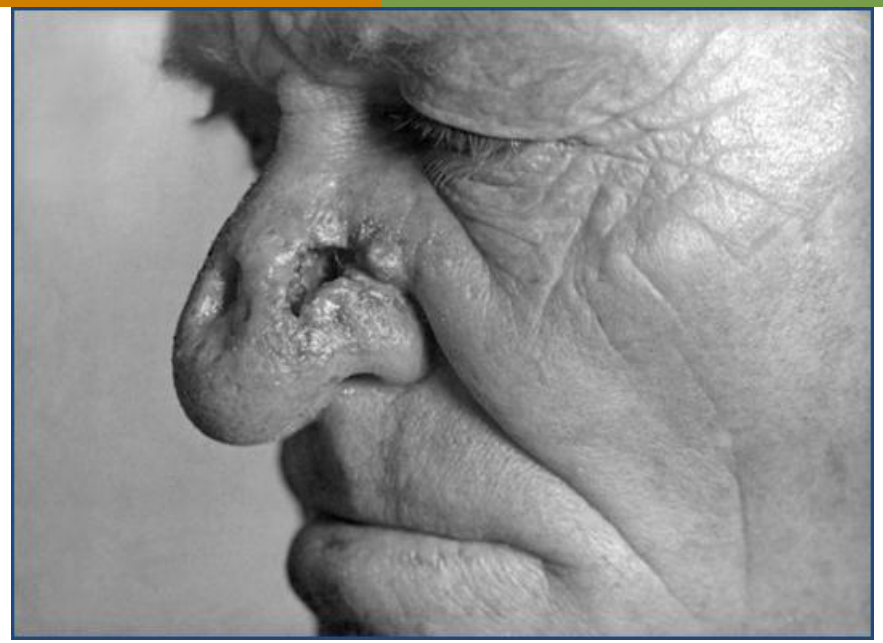


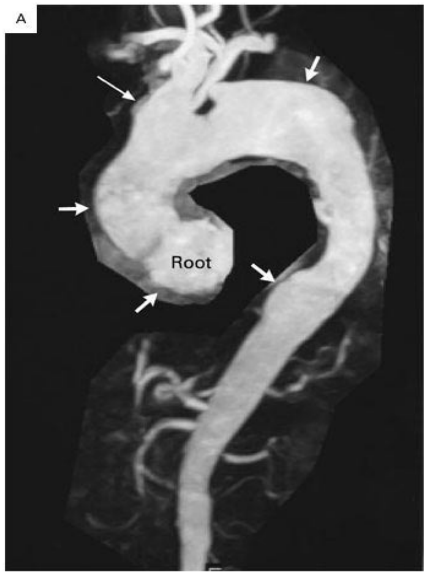


A Anshu, CL Cheng, SP Chee

Figure 5. Color fundus photograph (A) and serial fluorescein angiographic images, (B and C) of acute syphilitic posterior placoid chorioretinopathy (ASPPC) showing a characteristic macular lesion and progressive hyperfluorescence.[33]

Susan Lindsley/CDC





Tertiary Syphilis - Clinical Presentation

- Can appear after 10 – 30 years
- Uncommon and possibly non- infectious
- CNS Involvement (neurosyphilis)
  - **Brain** – headaches, dizziness, blurred vision, mental disturbances, paresis and dementia.
  - **Spinal cord** – unsteady gait, bladder disturbance.
- Solitary granulomatous lesions (gummas) found on skin, in the mouth, throat or in bones - small or larges nodules may persist for years

"When it looks like a duck and quacks like a duck, it must be a zebra!"

Syphilis in Pregnancy and Congenital Syphilis

Syphilis and Pregnancy

- **Infectious at all stages in pregnancy**
- **Untreated syphilis can be transmitted to the fetus the blood stream during any stage**
- Increases in Congenital Syphilis (CS) cases have paralleled the national increase in Primary and Secondary Syphilis among women of reproductive age
  - Estimated 8000 CS cases per year
- Pregnant woman may be more susceptible to infection with syphilis due to cervical ectopy, hyperemia, and friability
- All pregnant females diagnosed with syphilis should also be tested for HIV

Munoz, M. (2017). *Syphilis 101 patho & laboratory interpretation* [PowerPoint slides]. Retrieved from Los Angeles County Division of HIV and STD Program Training.

Complications to Pregnancy

- Spontaneous abortion
- Stillbirth
- Premature delivery
- Low birth weight
- Neonatal death shortly after delivery

(CDC, 2017)

CDC
Centers for Disease Control and Prevention

Early Congenital Syphilis (<2 years old)
Common Presentations

- Lymphadenopathy
- Skin rash (maculopapular, bullous)
- Rhinitis
- Neurologic abnormalities or aseptic meningitis
- Pancreatitis
- Asymptomatic

Congenital Syphilis

- Asymptomatic presentations are common (CDC, 2017)
  - ~2/3 infants born with CS are asymptomatic at birth
  - if untreated will develop symptoms
- In first weeks of life, effects can resemble secondary syphilis including blisters, scaly rash, mucous patches and condyloma lata (highly infectious)
- Deformed and inflamed bones

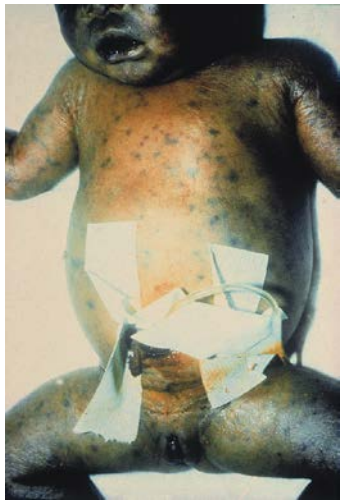
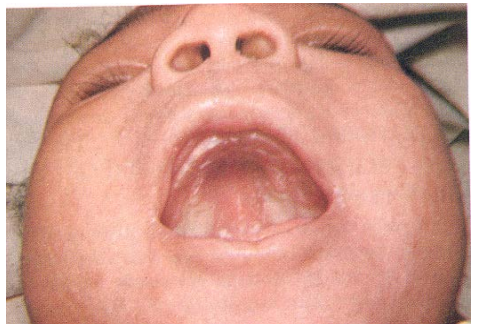
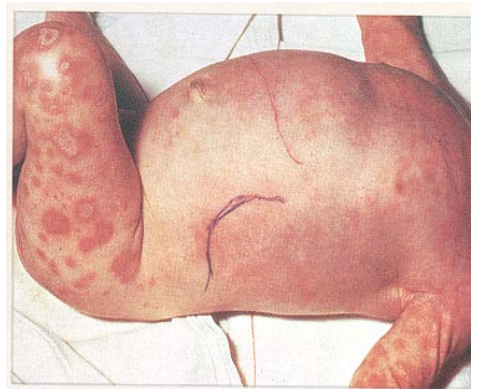


Figure 3:
Figure Source: CDC, 2017
Public Health Image Library by
Robert Sumpler
Osteoperiostitis of the tibia leads "saber shins" congenital syphilis

Figure 1: Source Caserta, M. T. (2015). Merck Manual - vesiculobullous rash on palm, axilla, and face of a newborn with congenital syphilis. http://www.merckmanuals.com/professional/pediatrics/infections-in-neonates/congenital- syphilis
Figure 2: Source: CDC, 2011 Public Health Image Library. Congenital syphilis exhibiting classic skin rash





Congenital Syphilis: Later Manifestations

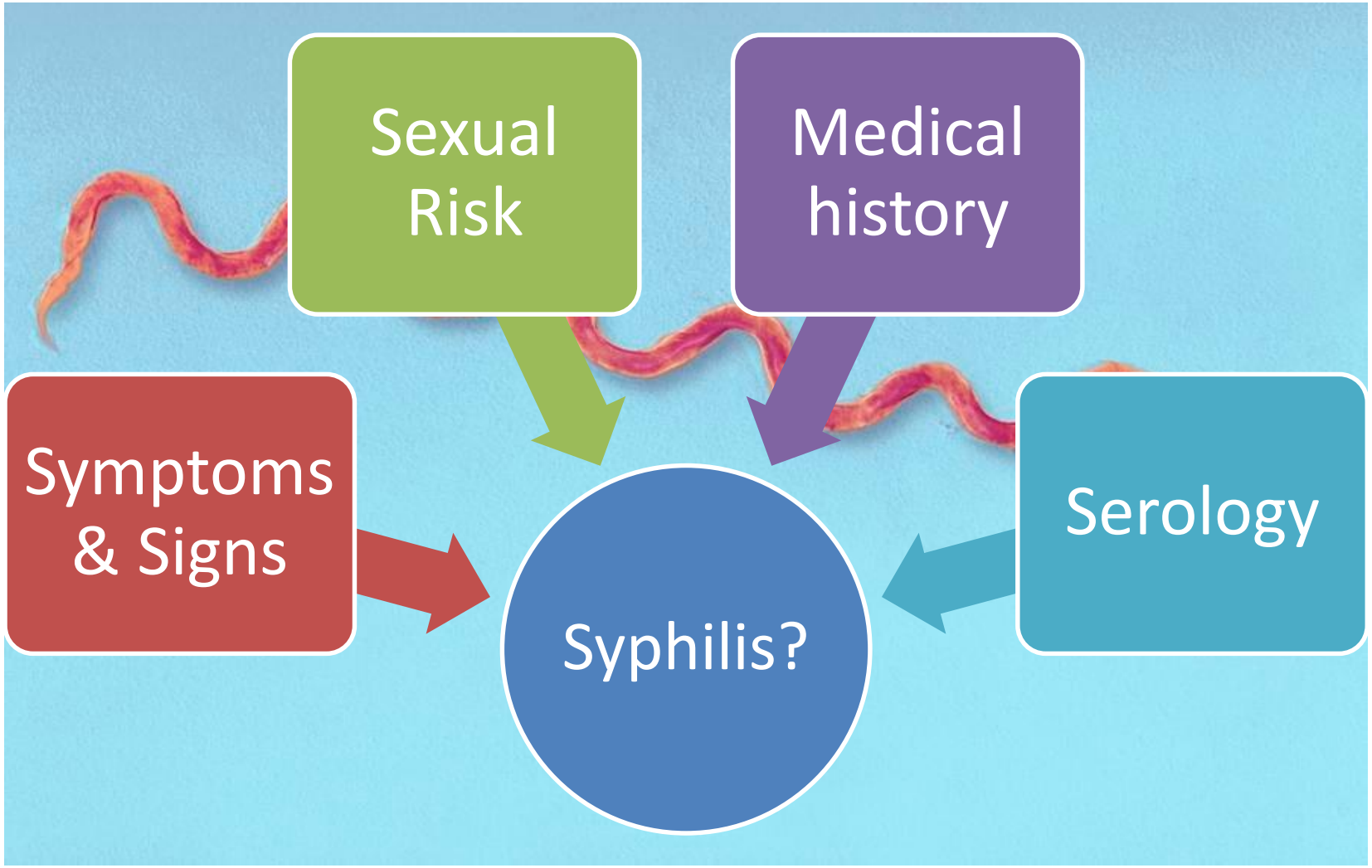
- Signs appear after 2 years of age
- Later signs include:
  - 8th nerve deafness (puberty - adulthood)
  - Interstitial keratitis (5 years old - adulthood)
  - Mucocutaneous lesions (up to age 5)
  - Neurosyphilis: “paresis” or seizures (puberty) or tabes (young adulthood)
  - Bone or tooth abnormalities (saber shins, frontal bossing, Hutchinson’s teeth, etc.)

Late Congenital Syphilis

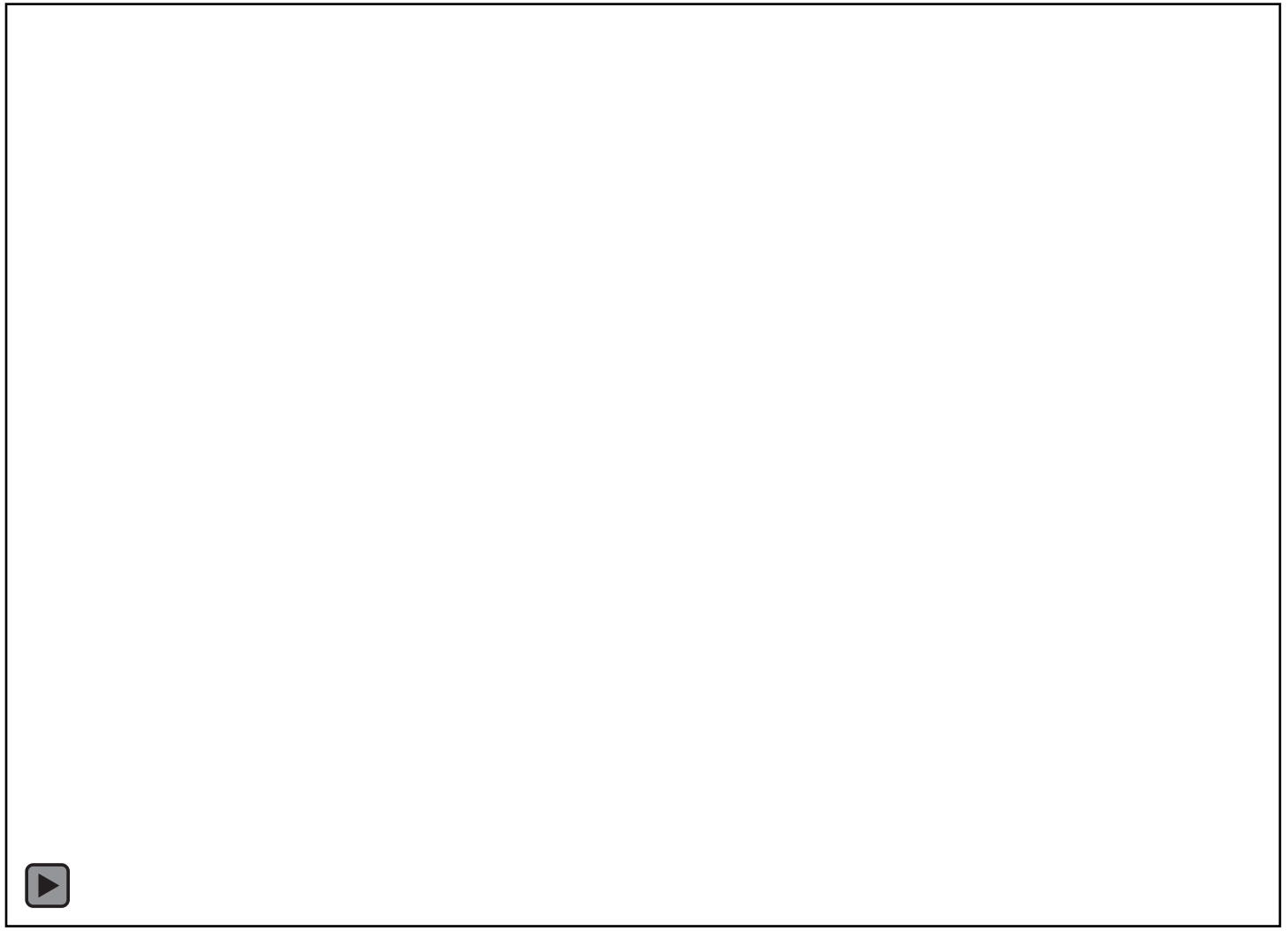
- Hearing loss
- Interstitial keratitis, vision loss
- Bone or tooth abnormalities (Hutchinson's teeth, Sabor shins, Clutton's joints)
- Neurologic abnormalities
- Gummas in the skin or mucous membranes

Photos courtesy of Public Health Image Library, CDC/Susan Lindsley, Robert Sumpter, CDC/J. Pledger

Diagnosing and Staging Syphilis



Treponema pallidum dark field microscopy



Source: CDC and UW STD Prevention Training Center

Serological 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
    - Trep-Sure
  - Chemiluminescence immunoassays (CIAs)
    - LIAISON
    - Architect
  - Microbead immunoassays (MBIA)
    - BioPlex 2200 Syphilis IgM and IgG

Serological Tests for Syphilis

Treponemal tests :

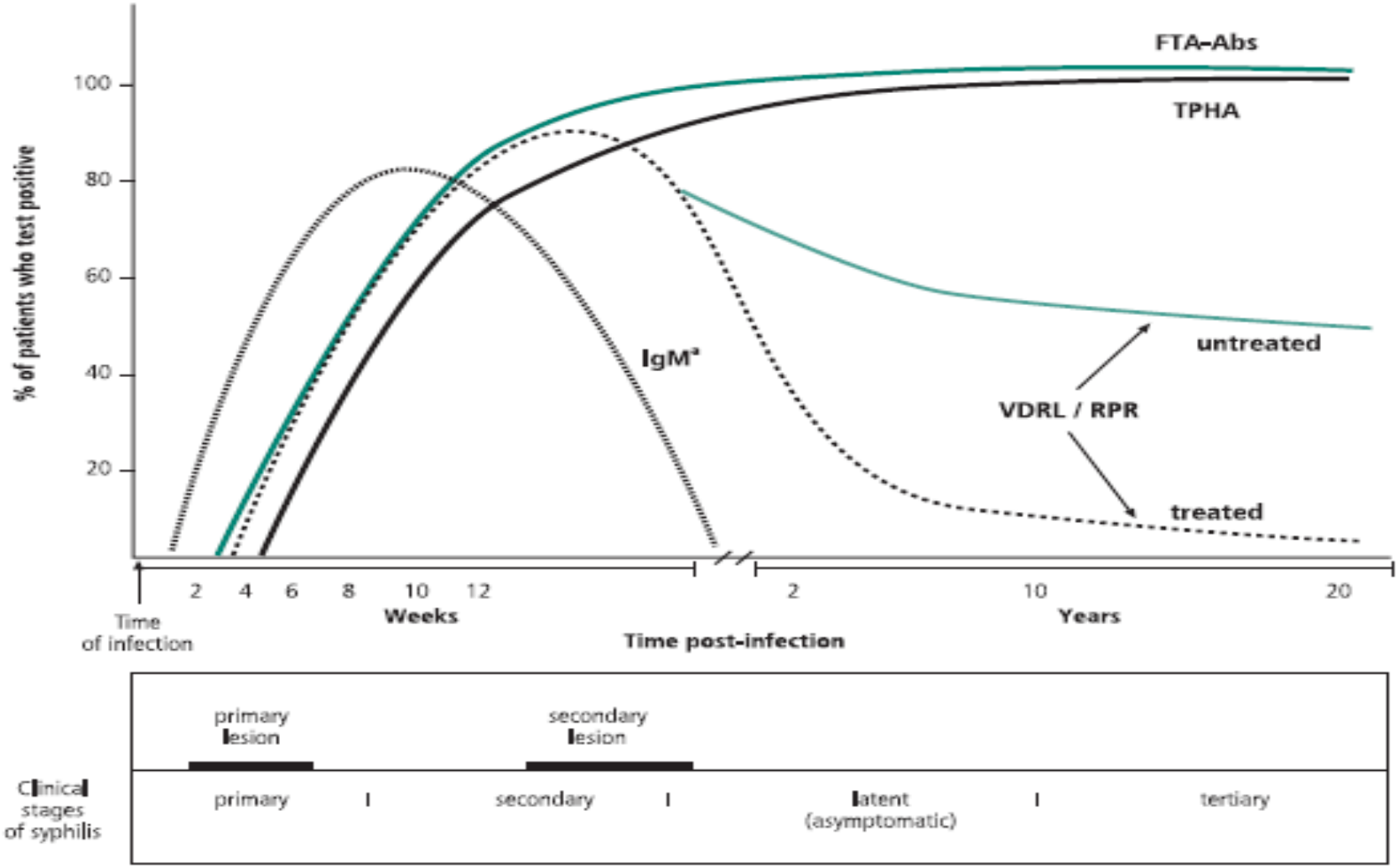
- Test for antibodies (IgM & IgG) directed against *T. pallidum* antigens by particulate agglutination (TP-PA) or immunofluorescence (FTA-abs)
- More specific and typically used to confirm positive non-treponemal tests
- Detects antibody due to past or present infection with *T. pallidum*
- Not used to guide response to therapy or revaluate possible reinfection
- Remain reactive regardless of treatment or disease activity

Ngan, V. & Vanousova, D. (2015). *Syphilis.* Retrieved from https://www.dermnetnz.org/topics/syphilis

Reactive non-treponemal test with a non-reactive treponemal test

- Non-treponemal tests measure antibodies which may be produced in other acute or chronic condition with connective tissue damage
- Common causes of BFP
  - Pregnancy
  - Non-venereal treponemes or spirochetes
  - Viral illnesses (HSV, HIV, Hepatitis)
  - Recent Vaccination
  - Autoimmune/connective tissue diseases
  - Injection drug use
  - Age

Munoz, M. (2017). *Syphilis 101 patho & laboratory interpretation* [PowerPoint slides]. Retrieved from Los Angeles County Division of HIV and STD Program Training.



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

Slide Courtesy of Sarah Lewis, MD, MPH, Santa Clara County

Syphilis Screening Paradigm

REVERSE TRADITIONAL SEQUENCE

Treponemal tests (e.g., EIA, CIA, MBIA)

- *TP*-SPECIFIC ANTIBODIES
- QUALITATIVE
- USUALLY DETECTABLE FOR LIFE
- REACTIVITY DECLINES WITH TIME

reflex to

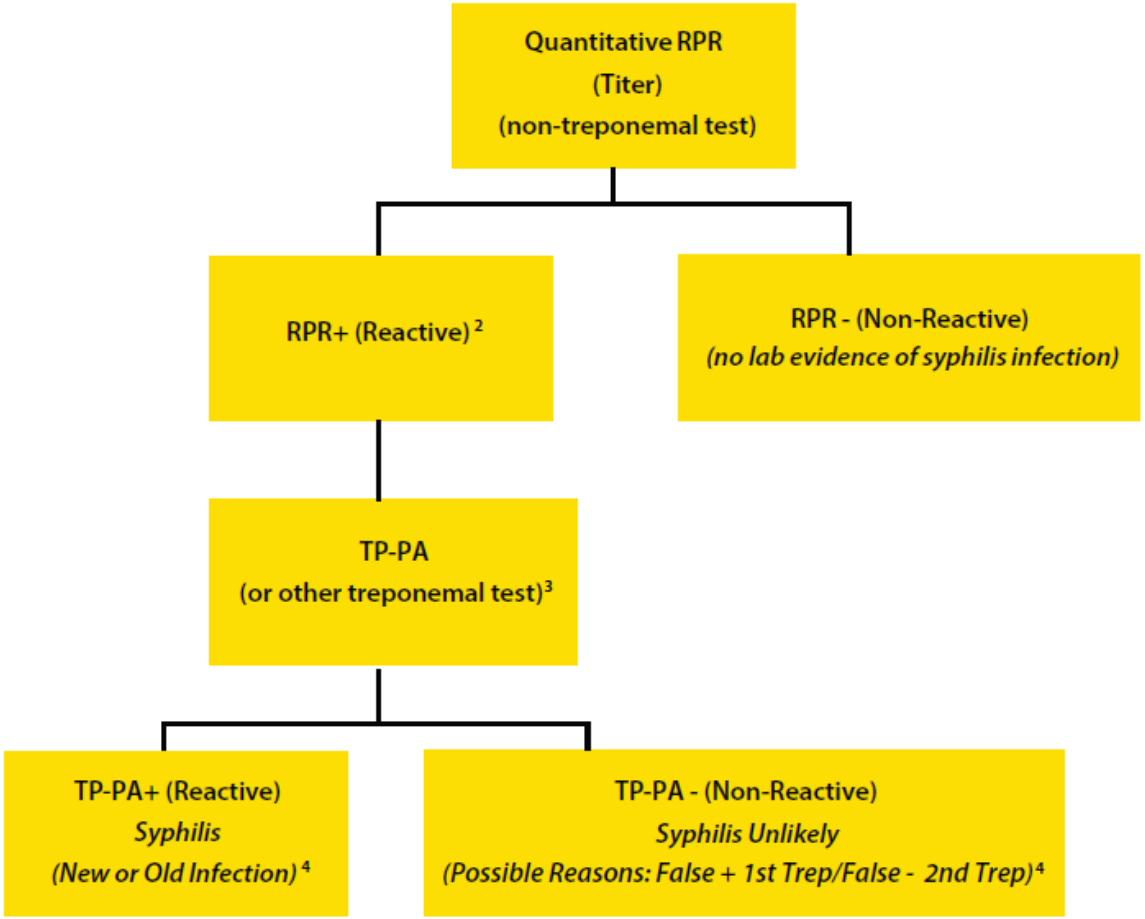
Non-treponemal tests (e.g., RPR, VDRL)

- NON-SPECIFIC ANTIBODIES TO LIPOIDAL ANTIGENS
- QUANTITATIVE
- REACTIVITY DECLINES WITH TIME

Need both types of serologic tests to make syphilis diagnosis;
Use of only one type of test is insufficient.

Slide Courtesy of Sarah Lewis, MD, MPH, Santa Clara County

Traditional Syphilis Serologic Screening Algorithm [1]

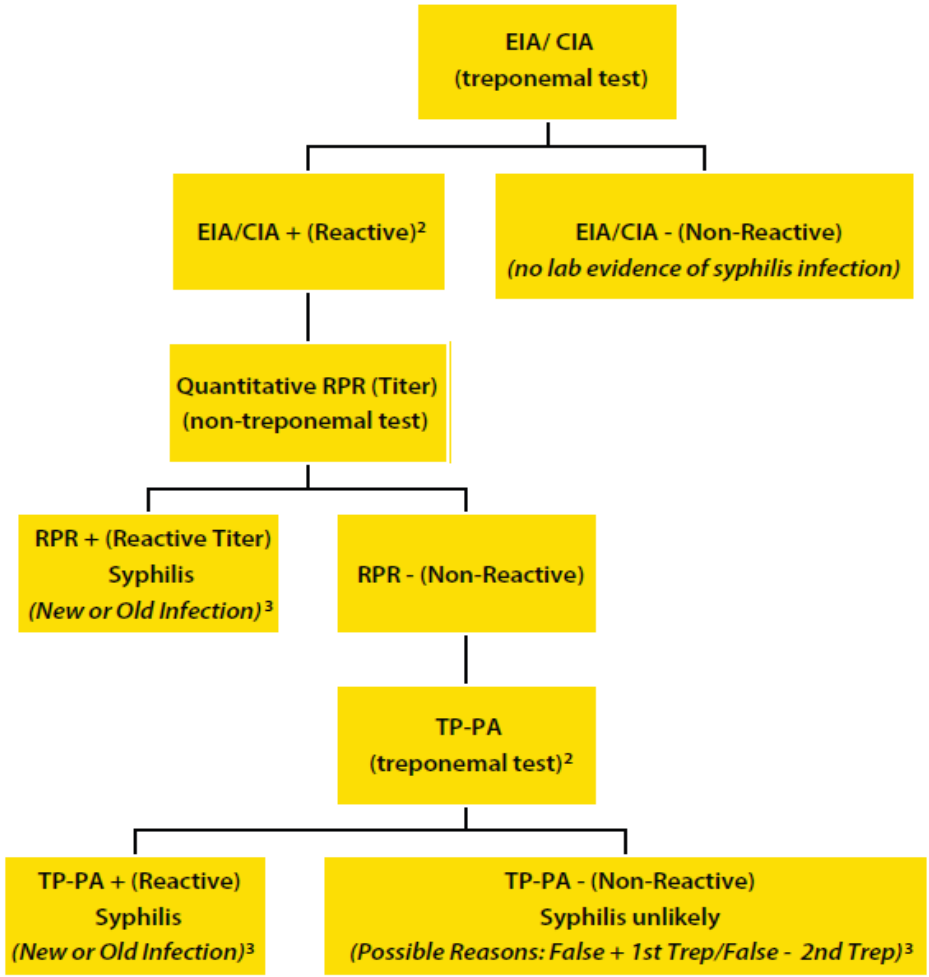


MMWR / February 11, 2011 / Vol. 60 / No. 5

Interpreting Traditional Algorithm

- Need a positive treponemal test to confirm diagnosis
- If RPR is >=4 fold higher than previous RPR, then it is most likely a new infection
- RPR can be non reactive when the titer is higher than the dilution is able to test (prozone phenomenon)
- If RPR reactive and trep test negative ~ BFP test
- Causes of BFP
  - Viral illnesses (HSV, HIV, Hepatitis)
  - Recent vaccination
  - Autoimmune/connective tissue diseases
  - Injection drug use
  - Aging and pregnancy

Reverse Sequence Syphilis Serologic Screening Algorithm [1]



MMWR / February 11, 2011 / Vol. 60 / No. 5

New Point-of-Care Syphilis Tests

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

- Syphilis Health Check (Trinity Biotech)
- Treponemal only (3rd gen EIA format, detects IgG and IgM)
- Results in 10 min
- FDA approved, recently CLIA waived

- DPP Syphilis Screen and Confirm (ChemBio)
- Combined treponemal and non-treponemal results
- Results in 15 min
- Not yet available in US

Syphilis Serology may be NEGATIVE in Primary Syphilis

Testing Approach	Overall	Sensitivity: HIV–	Sensitivity: HIV+	P Value
VDRL with reflex to TPPA				.05
TPPA as first-line test	86%	88%	83%	.53

Bottom line:
Order BOTH Non-trep and Trep tests if primary syphilis is suspected

Creegan et al. STD 2007: 34: 1016-8.

Slide Courtesy of Sarah Lewis, MD, MPH, Santa Clara County

Sensitivity and Specificity of Treponemal Assays for Detection of Syphilis, by Stage and Overall

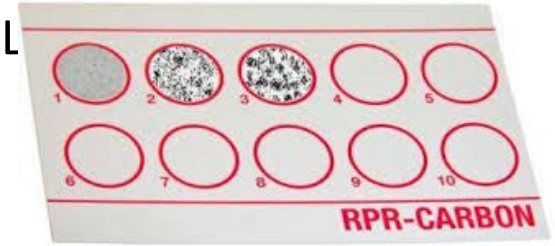
Assay	Sensitivity by Stage				Overall Sensitivity (n = 262)	Overall Specificity (n = 403)
	Primary (n = 55)	Secondary (n = 98)	Early Latent (n = 41)	Late Latent (n = 68)		
FTA-ABS	**78.2** [a] (65.0–88.2)	**92.8** [a] (85.7–97.0)	100 (90.7–100)	92.6 (83.7–97.6)	**90.8** [a] (86.7–94.0)	98.0 (96.1–99.1)
TPPA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	**86.8** [b] (76.4–93.8)	95.4 (92.1–97.6)	100 (99.0–100)
Centaur CIA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	94.1 (85.6–98.4)	97.3 (94.6–98.9)	95.5 (93.0–97.3)
Trep-Sure EIA	94.5 (84.9–98.9)	100 (96.2–100)	100 (90.7–100)	98.5 (92.1–99.9)	98.5 (96.1–99.6)	**82.6** [c] (78.4–86.1)
LIAISON CIA	96.4 (94.5–98.2)	100 (96.2–100)	97.6 (87.4–99.9)	92.6 (83.7–97.6)	96.9 (94.1–98.7)	94.5 (91.8–96.5)
Bioplex MBIA	96.4 (94.5–98.2)	100 (96.2–100)	95.1 (83.8–99.4)	94.1 (85.6–98.4)	96.9 (94.1–98.7)	96.7 (94.4–98.2)
INNO-LIA	96.4 (94.5–98.2)	100 (96.2–100)	100 (90.7–100)	91.1 (81.7–96.7)	96.9 (94.1–98.7)	98.5 (96.8–99.5)

Park IU, Fakile YF, Chow JM, et al. Performance of treponemal tests for the diagnosis of syphilis. [published online July 9, 2018]. *Clin Infect Dis, 2018*

Diagnostic Challenges

False negatives

- Early primary and late latent stages
  - Serology may be negative in up to 25% of primary syphilis cases
- Prozone reaction (RPR/VDRL



Discordant serology

(EIA or CIA + and RPR –)

- Untreated late latent
- Non-syphilis treponemal infection

Biologic False Positives

- Non-treponemal test positive with confirmatory Treponemal test negative
- Viral illnesses including HIV, recent immunizations, autoimmune and chronic diseases

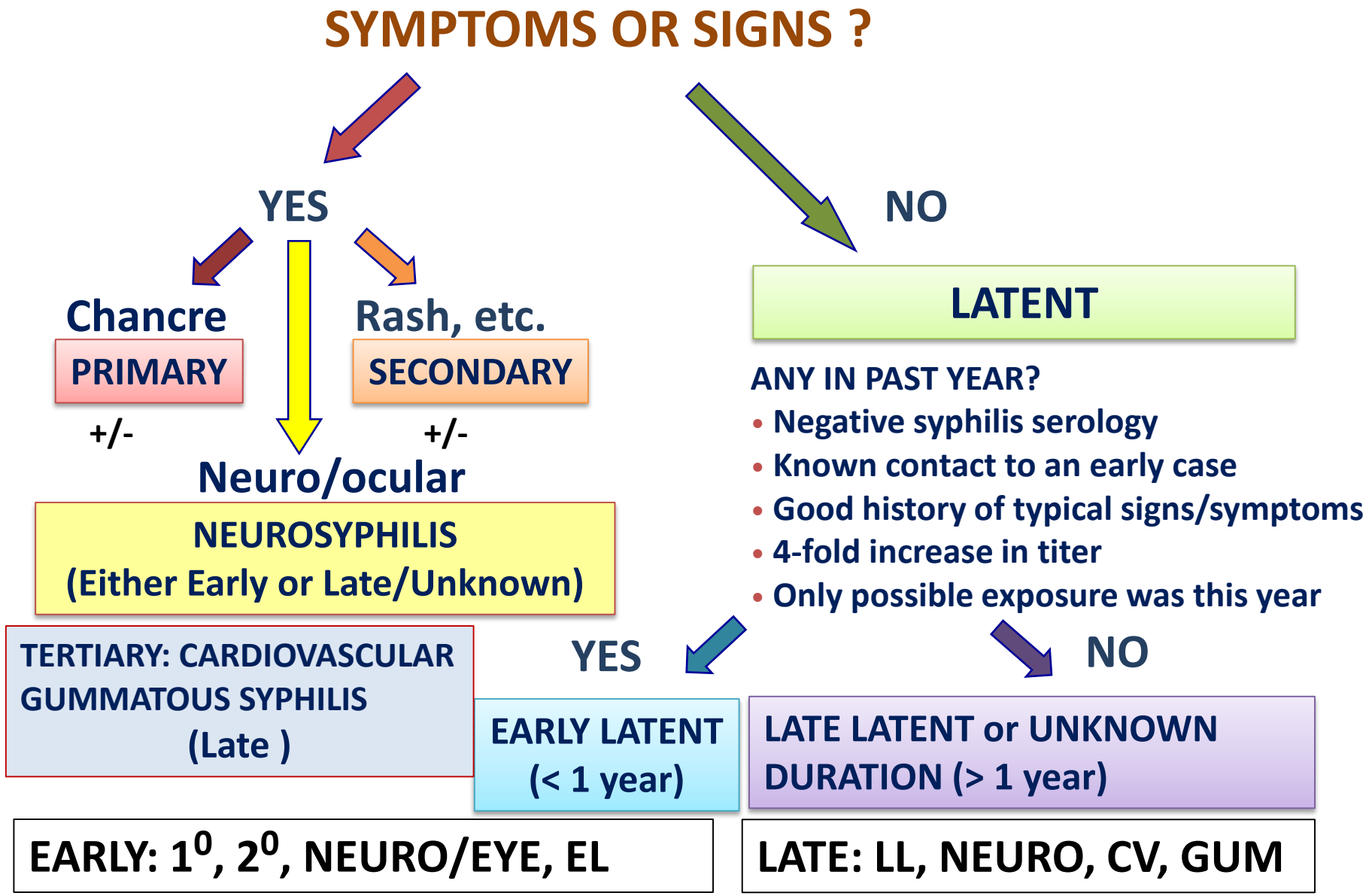
Reinfection vs. Treatment Failure

- Four-fold rise in RPR/VDRL
- Positive non-trep test after resolution
- Failure to fall four-fold after 1-2 years

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

Slide Courtesy of Sarah Lewis, MD, MPH, Santa Clara County

Syphilis Staging Flowchart



Syphilis Staging → Treatment

County of Los Angeles Public Health

CDC 2015 STD Treatment Guidelines
www.cdc.gov/std/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/unknown 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 (>1 year)

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!**

Treatment of Syphilis in Pregnancy

- The only treatment for syphilis in pregnancy is penicillin. There are no available alternatives.
- Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection.
- Pregnant women with penicillin allergy should be desensitized.
  - Desensitization occurs in a hospital setting because of the risk for serious IgE –mediated hypersensitivity reactions (CDC, 2015).

Syphilis in Pregnancy:
Time Between Doses for Latent Syphilis

Adherence to 7 day interval between doses in pregnancy is necessary

- 40% of pregnant woman are below treponemicidal levels after 9 days
- Restart entire series (3 weekly doses) if dose is missed (interval >7 days) (LADPH-DHSP, 2017).

Los Angeles County STD Treatment Guidelines for Adults & Adolescents, 2017

California STD Treatment Recommendations in Pregnancy 2017

These treatment regimens reflect recent updates in the 2015 CDC STD Treatment Guidelines and are specific to PREGNANT WOMEN. Non-pregnant women and men may have different recommended regimens. See CDC 2015 STD Treatment Guidelines (www.cdc.gov/std/treatment) for comprehensive recommendations. Call the local health department for assistance with management of pregnant women with syphilis and confidential notification of sexual partners of patients with syphilis, gonorrhea, chlamydia, or HIV infection. For STD clinical management consultation, submit your question online to the STD Clinical Consultation Network at www.stdccn.org.

DISEASE	RECOMMENDED REGIMENS	DOSE / ROUTE	ALTERNATIVE REGIMENS: To be used if medical contraindication to recommended regimen
CHLAMYDIA (CT) [3]	Azithromycin	1 g po once	Amoxicillin 500 mg po tid x 7 d **or** Erythromycin base 500 mg po qid x 7 d **or** Erythromycin base 250 mg po qid x 14 d **or** Erythromycin ethylsuccinate 800 mg po qid x 7 d **or** Erythromycin ethylsuccinate 400 mg po qid x 14 d
GONORRHEA (GC) [1,2,3]	***Dual therapy with:*** Ceftriaxone **PLUS** Azithromycin	250 mg IM once 1 g po once	Cefixime [4] 400 mg po **PLUS** Azithromycin 1 g po If cephalosporin allergy or IgE mediated penicillin allergy, consult with specialist, see footnotes. [1]
CERVICITIS [5,6,7]	Azithromycin	1 g po once	
PELVIC INFLAMMATORY DISEASE [5,8]	Clindamycin **PLUS** Gentamicin	900 mg IV q 8 hours 2 mg/kg IM or IV loading dose followed by 1.5 mg/kg IM or IV q 8 hours Discontinue parenteral therapy 24 hours after patient improves clinically and continue with oral clindamycin 450 mg po qid for a total of 14 d	
SYPHILIS [9,10]			
Primary, Secondary, Early Latent [11]	Benzathine penicillin G	2.4 million units IM once	NONE
Late Latent and Unknown Duration	Benzathine penicillin G	7.2 million units, administered as 3 doses of 2.4 million units IM each, at 1-week intervals	NONE
Neurosyphilis and Ocular Syphilis [12]	Aqueous crystalline penicillin G	18-24 million units daily, administered as 3-4 million units IV q 4 hours x 10-14 d	Procaine penicillin G 2.4 million units IM qd for 10-14 d **PLUS** Probenecid 500 mg po qid for 10-14 d
CHANCROID	Azithromycin **or** Ceftriaxone **or** Erythromycin	1 g orally once 250 mg IM once 500 mg po tid x 7 d	
LYMPHOGRANULOMA VENEREUM [13]	Erythromycin base	500 mg po qid x 21 d	
TRICHOMONIASIS [14,15]	Metronidazole	2 g po once	
BACTERIAL VAGINOSIS	Metronidazole **or** Metronidazole gel **or** Clindamycin cream [16]	500 mg po bid x 7 d 0.75%, one full applicator (5 g) intravaginally qd x 5 d 2%, one full applicator (5 g) intravaginally qhs x 7 d	Clindamycin 300 mg po bid x 7 d **or** Clindamycin ovules [16] 100 mg intravaginally qhs x 3 d
ANOGENITAL HERPES [17]			
First Clinical Episode	Acyclovir **or** Acyclovir **or**	400 mg po tid x 7-10 d [18] 200 mg po five times daily x 7-10 d	
Episodic Therapy for Recurrent Episode	Acyclovir **or** Acyclovir **or** Acyclovir	400 mg po tid x 5 d 800 mg po bid x 5 d 800 mg po tid x 2 d	
Suppressive Therapy (from 36 weeks gestation until delivery)	Acyclovir **or** Valacyclovir	400 mg po tid 500 mg bid	
ANOGENITAL WARTS [19]			
External Genital/Perianal	Cryotherapy **or** Trichloroacetic acid (TCA) 80%-90% **or** Bichloroacetic acid (BCA) 80%-90% **or** Surgical removal	Apply once q 1-2 weeks Apply once q 1-2 weeks Apply once q 1-2 weeks	
Mucosal Genital Warts [20]	Cryotherapy **or** Surgical removal **or** TCA or BCA 80%-90%	Vaginal, vulvar, anal Vaginal, vulvar, anal Vaginal, vulvar, anal	

Evaluation of Infants Born to Mothers with Syphilis

- CDC has provided detailed guidance on treatment of infants born to mothers with syphilis :

- Treatment decisions are based on:
  - Identification of syphilis in the mother
  - Adequate maternal treatment
  - Clinical, lab, x-ray evidence of syphilis in neonate
  - Comparison of maternal (at delivery) and neonatal **non treponemal** titers (same test-preferably same lab)
  - Umbilical cord blood **is not recommended**
  - Treponemal tests are not recommended
    - Maternal non-trep and trep IgG antibodies can transfer via placenta thus complicating interpretation of neonatal serologies

(CDC, 2015).

Scenario	Definition	Minimum Evaluation	Treatment
Proven or Highly Probable CS	1. Exam c/w CS, *OR* 2. Infant RPR 4x Maternal RPR *OR* 3. Darkfield or PCR+ lesion	1. Serum RPR 2. LP: VDRL, cell ct, protein 3. CBC with diff 4. Long bone x-rays 5. Neuroimaging, ophtho, auditory, CXR, LFTs	Aqueous PCN G 100K-150K U/kg/day divided q12h until 7d old then then q8h for 10 days total.
Possible CS	1. Maternal Tx not done, not documented, not recommended regimen, or inadequate *OR* 2. Maternal Tx <4weeks before delivery	1. Serum RPR 2. LP: VDRL, cell ct, protein 3. CBC with diff 4. Long bone x-rays	1. Aqueous PCN G 100K-150K U/kg/day divided q12h until 7d old then then q8h for 10 days total, *OR* 2. Bicillin 50K U/kg IM once (if all eval normal/negative)
CS Less Likely	1. Full maternal Tx documented >4 weeks before delivery *AND* 2. No evidence maternal relapse/reinfection	1. Serum RPR 2. Normal neonatal eval	1. Bicillin 50K U/kg IM once, OR 2. Infant RPR q2-3mo x6mo (if documented maternal response to treatment)
CS Unlikely	1. Documented full maternal Tx *before* pregnancy *AND* 2. Maternal RPR remained low and stable	1. Serum RPR 2. Normal neonatal eval	No Tx recommended (If infant RPR+, monitor until NR, and can consider Bicillin 50K U/kg IM once)

Syphilis Treatment Alternatives for Penicillin Allergic Non-Pregnant Adults

Primary, Secondary, and Early Latent Syphilis

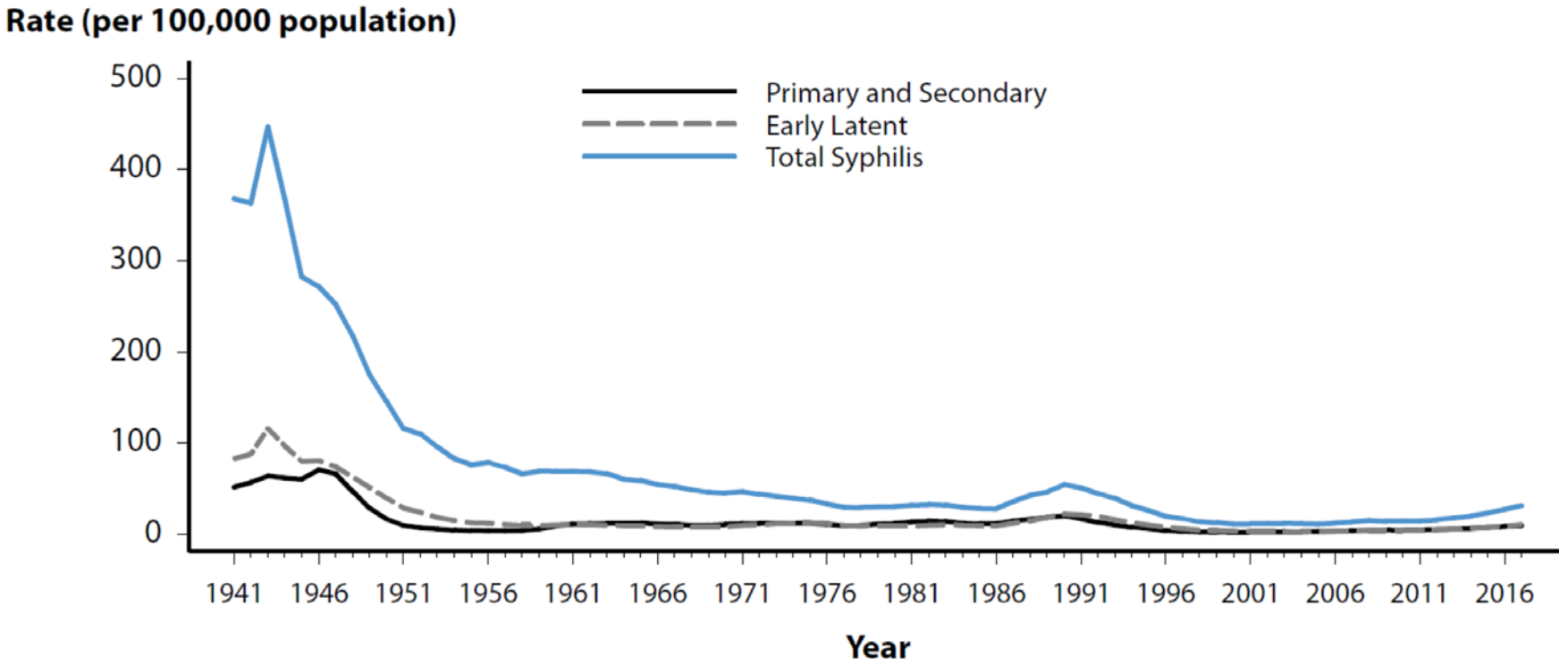
- Doxycyline 100 mg po twice a day x 14 days
- Tetracyline 500 mg po twice a day x 14 days
- Ceftriaxone 1 gm IV (or IM) daily x 10-14 days

Late Latent Syphilis

- Doxycyline 100 mg po twice a day x 28 days
- Tetracyline 500 mg po twice a day x 28 days

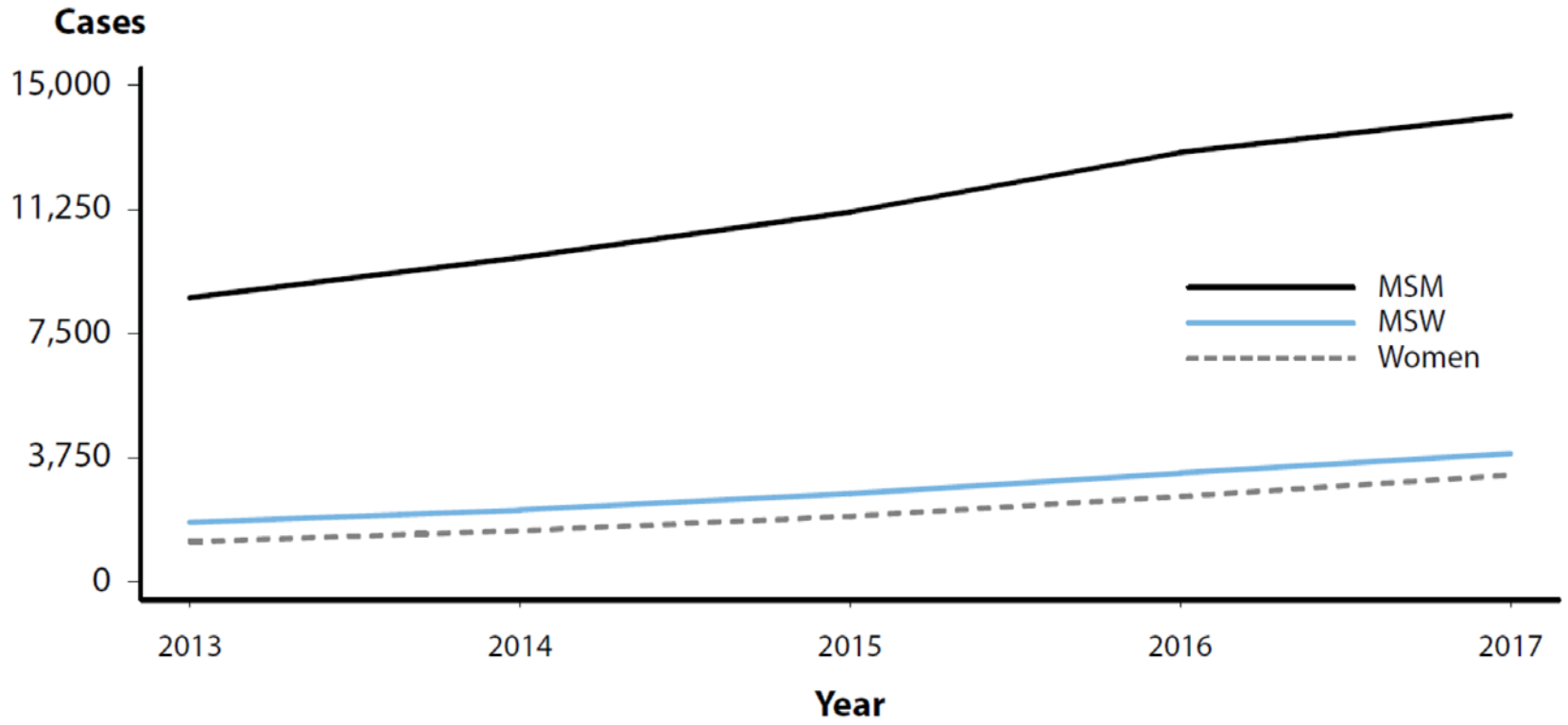
(**Los Angeles County STD Treatment Guidelines for Adults & Adolescents, 2017**

Syphilis Rates of Reported Cases by Stage of Infection, United States, 1941–2017



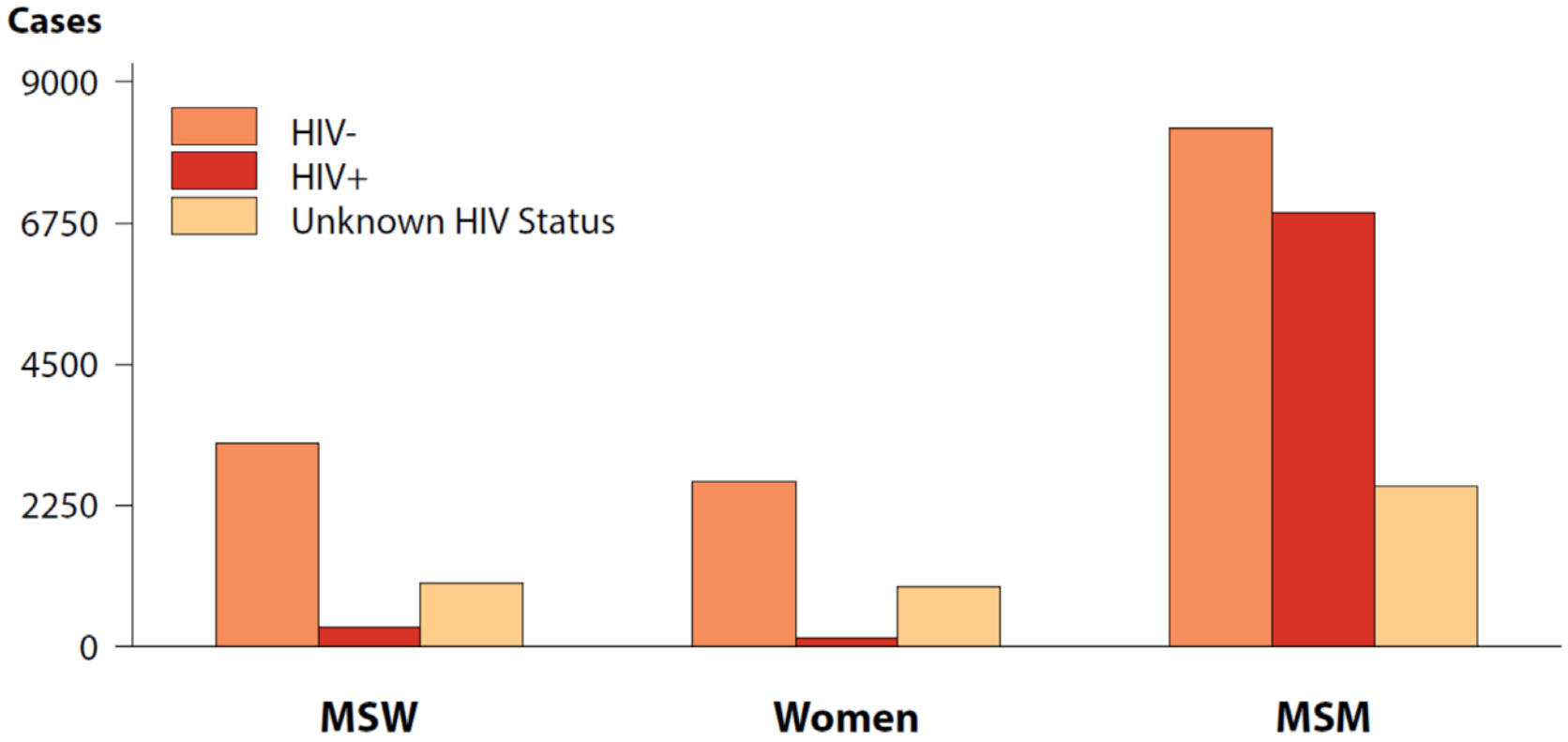
NOTE: Data collection for syphilis began in 1941; however, syphilis became nationally notifiable in 1944. Refer to the National Notifiable Disease Surveillance System (NNDSS) website for more information: https://wwwn.cdc.gov/nndss/conditions/syphilis/.

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



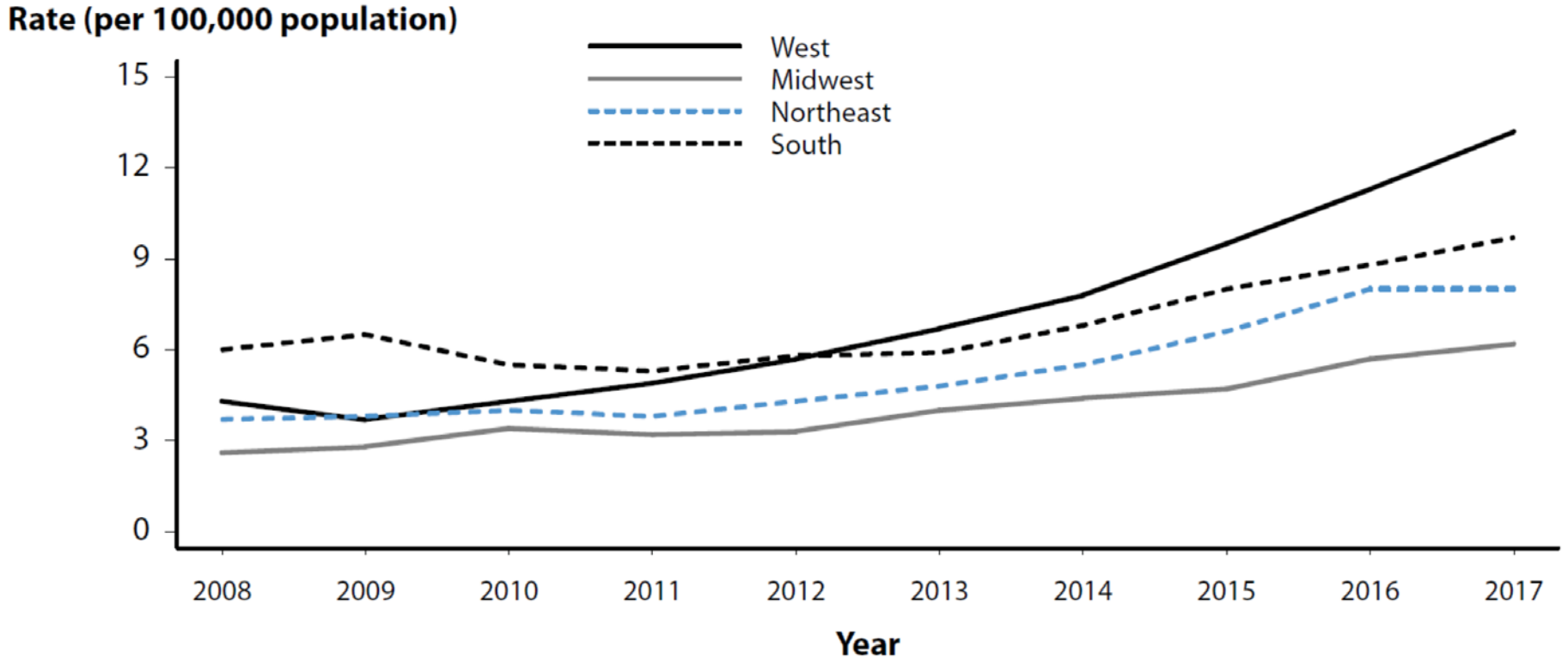
* 37 states were able to classify ≥70% of reported cases of primary and secondary syphilis as either MSM, MSW, or women for each year during 2013–2017.
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

Primary and Secondary Syphilis — Reported Cases by Sex, Sexual Behavior, and HIV Status, United States, 2017



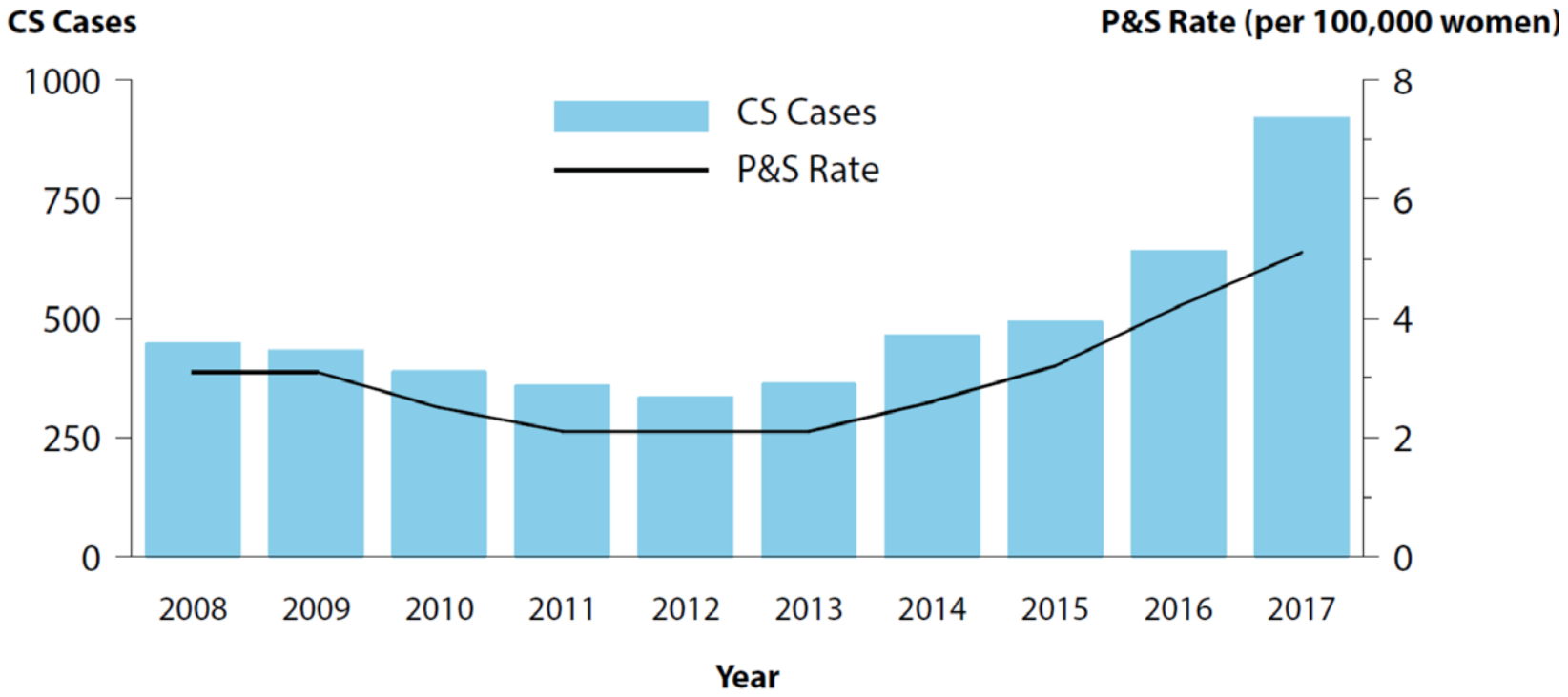
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men (collectively referred to as MSM); MSW = Men who have sex with women only.

Primary and Secondary Syphilis — Rates of Reported Cases by Region, United States, 2008–2017



Source: CDC.gov

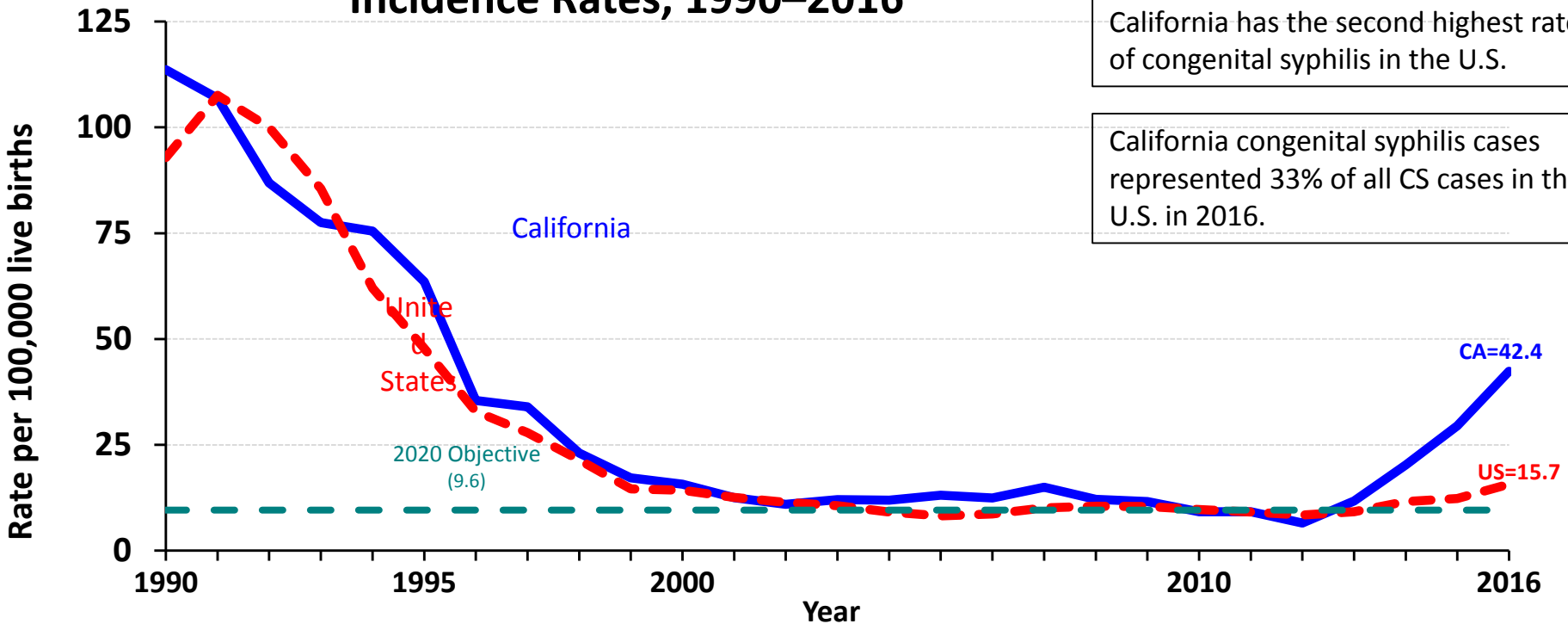
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2008–2017



States with the highest overall case rates of congenital syphilis are Louisiana, California and Texas- CDC 2017 data

ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.

Congenital Syphilis, California versus United States Incidence Rates, 1990–2016



California has the second highest rate of congenital syphilis in the U.S.

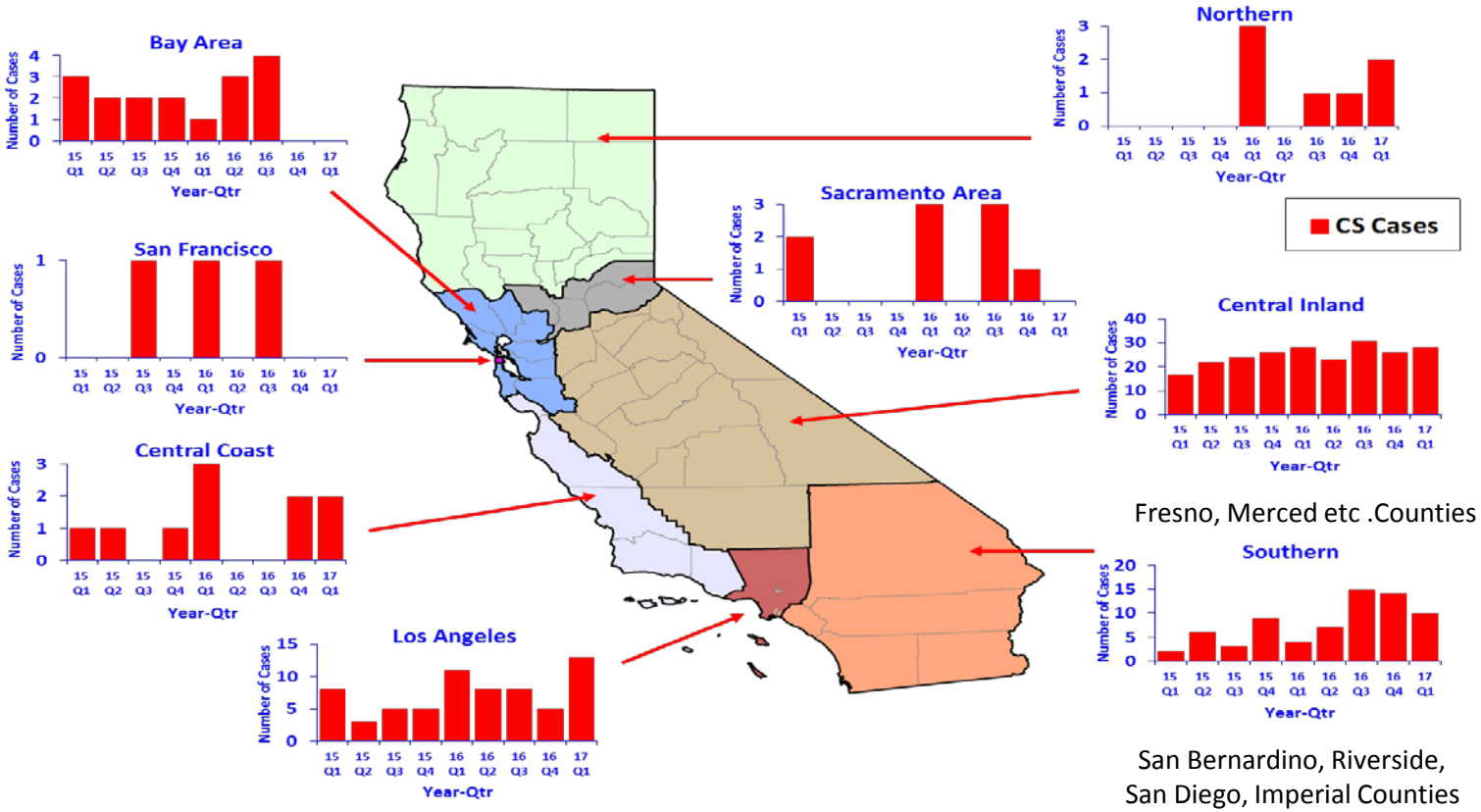
California congenital syphilis cases represented 33% of all CS cases in the U.S. in 2016.

Note: The Modified Kaufman Criteria were used through 1989. The CDC Case Definition (MMWR 1989; 48: 828) was used effective January 1, 1990. California data prior to 1985 include all cases of congenital syphilis, regardless of age.

Rev. 6/2017

Courtesy of Heidi Bauer, MD, MS, MPH, Chief, STD Control Branch, CDPH

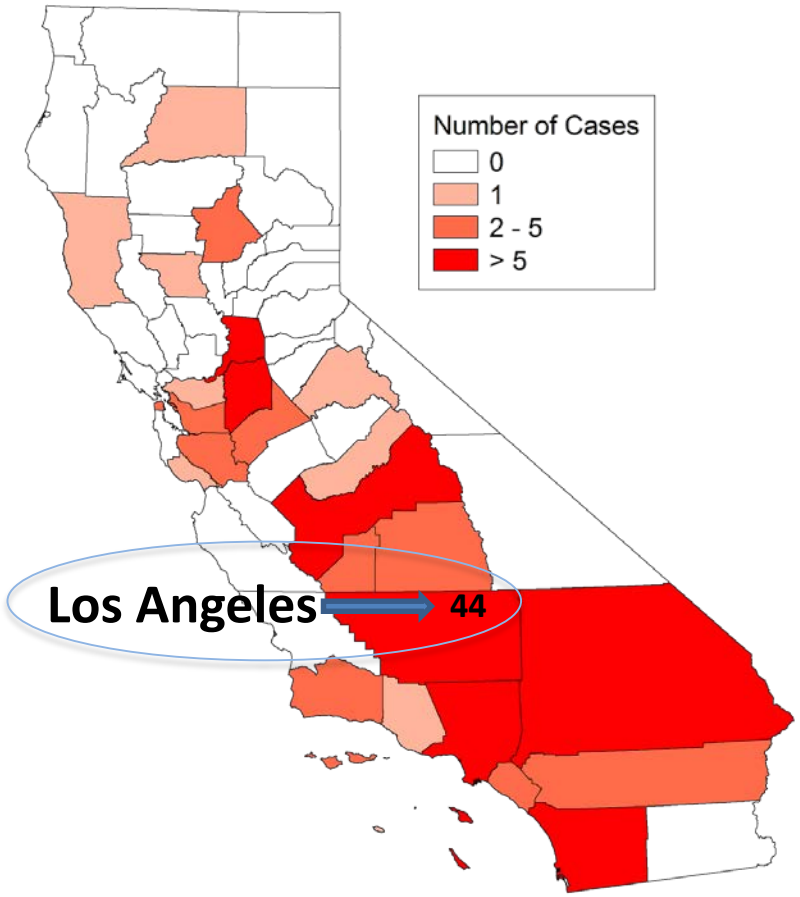
Number of Congenital Syphilis Cases by Region and Year-Quarter of Birth



Source: CDPH, 2017
https://archive.cdph.ca.gov/data/statistics/Pages/STDData.aspx

Congenital Syphilis

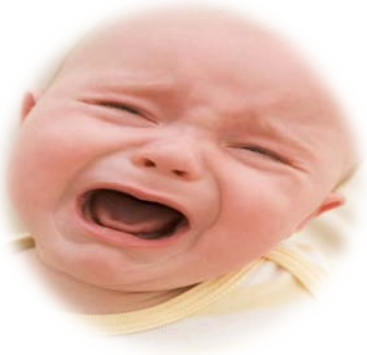
Number of Cases – Los Angeles County 2017



Alarming rise of Congenital Syphilis in Los Angeles County

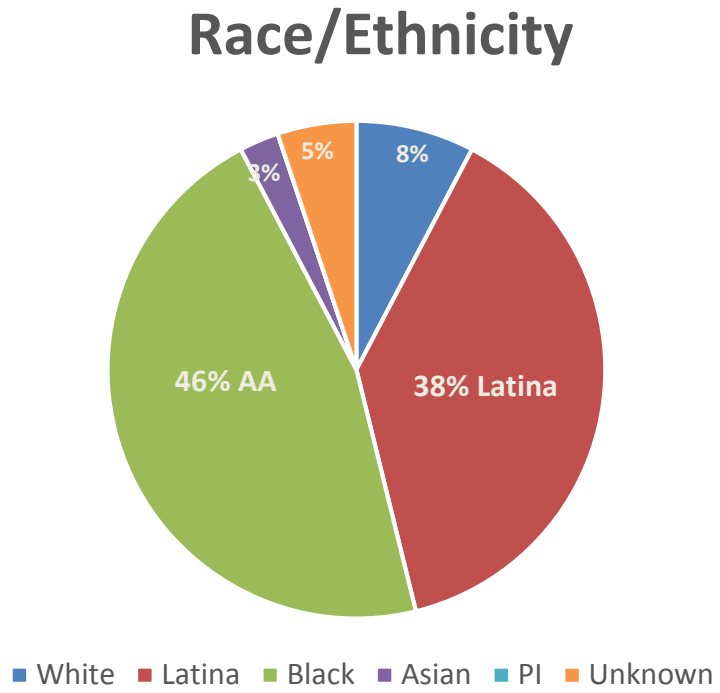
- **733%** Increase of CS Cases in 2017 compared to numbers reported in 2012

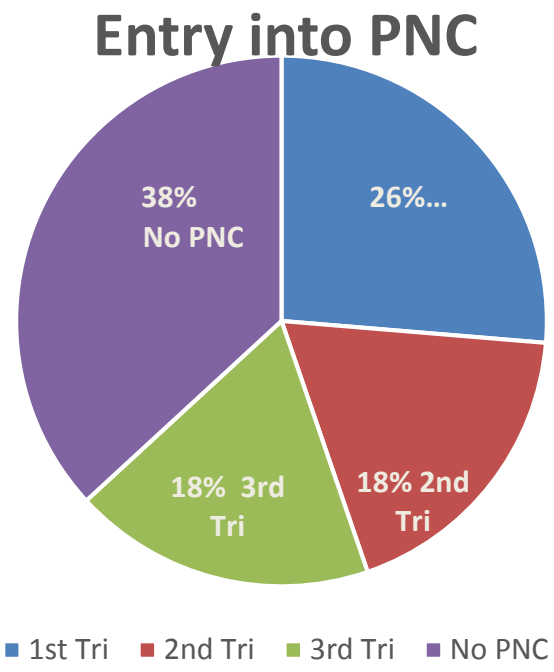
- **600%** Increase of early syphilis among females of childbearing age 2017 compared to numbers reported in 2012



Courtesy of M. Munoz, NM, LAC, DHSP

2017 Maternal Characteristics (n=40)
Median Age: 29.2 years (range 16-38)

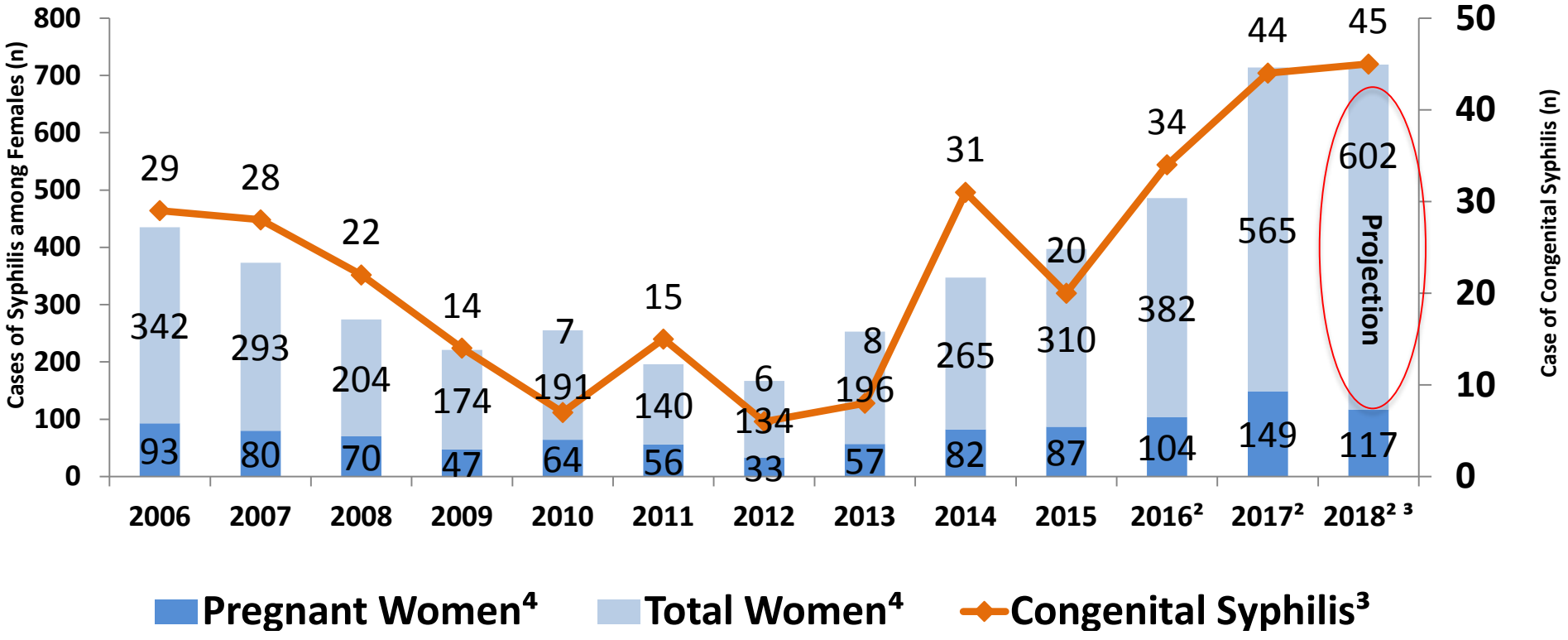




Contributing factors: drug use, incarceration, displacement

Courtesy of M. Munoz, NM, LAC, DHSP

Number of Female Syphilis and Congenital Syphilis (CS) Cases, LAC, 2006-2018[1]



Source: Division of HIV and STD Programs

[1] Data are from STD Casewatch as of 07/17/2018 and excludes cases from Long Beach and Pasadena

[2] 2016-2018 data are provisional due to reporting delay. 2018 projections are based on provisional data. As of 7/31/18, 26 congenital syphilis cases have been reported.

[3] Congenital Syphilis includes syphilitic stillbirths

[4] Syphilis among females of childbearing age (ages 15-44) including all cases staged as primary, secondary, early latent and late latent

Possible causes for Increasing syphilis infection rates among-WOMEN

- Multiple partners or partner(s) with multiple partners
- Reinfection during pregnancy
- Lack of or late access to prenatal care
- Inadequate or delayed treatment during before or pregnancy
- Exchange sex for money/shelter/other things of value
- Displacement
- Serious mental illness
- Drug abuse
- Emerging birth tourism (2014)

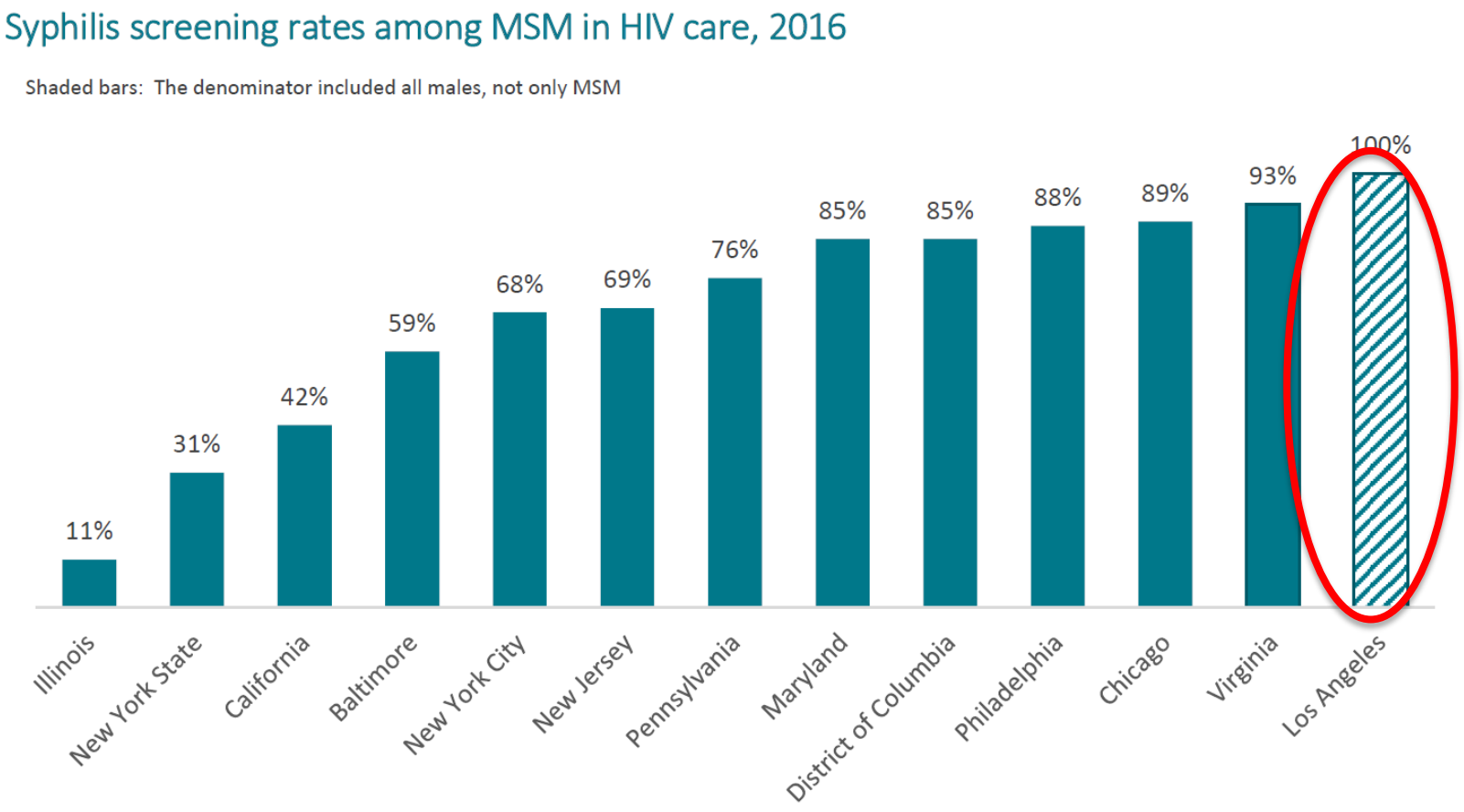
Munoz, M. (2017). *Role of public health nurses in controlling prenatal & congenital syphilis in los Angeles county* [PowerPoint slides]. Retrieved from http://publichealth.lacounty.gov/dhsp/PresentationsSypilisConf2017.htm

Possible causes for Increasing syphilis infection rates among-MEN

- Missed syphilis screening opportunities
- Having multiple partners
- No treatment or inadequate treatment
- Exchanging sex for money or other things of value to a person
- Drug Use
- Using internet and mobile hook up apps.

Bauer, H. M. (2017). *Stemming the rising tide of syphilis in California* [PowerPoint slides]. Retrieved from http://publichealth.lacounty.gov/dhsp/PresentationsSyphilisConf2017.htm

Syphilis screening among MSM in HIV care



Source: STD AAPPS Program Outcome Measures 2016 | Syphilis screening among MSM in HIV care

Mobile Hook-up Apps

Pictures Source: Bauer, H. M. (2017). *Stemming the rising tide of syphilis in california* [PowerPoint slides]. Retrieved from http://publichealth.lacounty.gov/dhsp/PresentationsSyphilisConf2017.htm

Rotblatt, H. & Wohlfeiler, D. (2017). *MSM and syphilis: what's the message?* [PowerPoint slides]. Retrieved from http://publichealth.lacounty.gov/dhsp/PresentationsSyphilisConf2017.htm

JAMA Network
County of Los Angeles Public Health

From: **Screening for Syphilis Infection in Pregnant WomenUS Preventive Services Task Force Reaffirmation Recommendation Statement**

JAMA. 2018;320(9):911-917. doi:10.1001/jama.2018.11785

Population	Pregnant women
Recommendation	Screen early for syphilis infection in all pregnant women. Grade: A

Risk Assessment	All pregnant women are at risk. All pregnant women should be tested for syphilis as early as possible when they first present to care. If a woman has not received prenatal care before delivery, she should be tested at the time she presents for delivery.
Screening Tests	Screening for syphilis infection is a 2-step process. The traditional approach is to perform an initial "nontreponemal" antibody test (ie, Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR] test), followed by a confirmatory "treponemal" antibody detection test (ie, fluorescent treponemal antibody absorption or Treponema pallidum particle agglutination test). A newer alternative is the reverse sequence screening algorithm: an automated treponemal antibody test (eg, enzyme-linked, chemiluminescence, or multiplex flow immunoassay) is performed first, followed by a nontreponemal VDRL or RPR test. If the test results are discordant, a second treponemal test is performed.
Treatments and Interventions	The Centers for Disease Control and Prevention recommend parenteral benzathine penicillin G for the treatment of syphilis in pregnant women.
Relevant USPSTF Recommendations	The USPSTF has made recommendations on screening for other sexually transmitted infections, including chlamydia and gonorrhea, hepatitis B virus, genital herpes, and HIV.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to https://www.uspreventiveservicestaskforce.org.

U.S. Preventive Services TASK FORCE

JAMA

Figure Legend:

Clinical Summary: Screening for Syphilis Infection in Pregnant Women USPSTF indicates US Preventive Services Task Force.

Date of download: 10/28/2018

Syphilis Screening Guidelines

Syphilis	
Pregnant Women	• All pregnant women at the first prenatal visit[11] • Retest early in the third trimester and at delivery if at high risk[12]
Men Who have Sex With Men (MSM)	• At least annually for sexually active MSM[13] • Every 3 to 6 months if at increased risk[7]
Persons with HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter[14,15,16] • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology[13]

SOURCE: CDC.gov

Recommendations in Pregnancy 2017

First prenatal visit

- HIV
- Syphilis
- Chlamydia[1]
- Gonorrhea[1]
- Hepatitis B surface antigen (HBsAg)
- Hepatitis C antibody if risk[2]
- Type-specific HSV serology can be considered if high risk[3]
- Pap test if age ≥ 21 years and indicated by national guidelines[4]

Third trimester

- HIV if high risk[5]
- Syphilis if living in an area with high syphilis prevalence or high risk[6] (test in early third trimester at 28-32 weeks)
- Chlamydia if age <25 years, positive test earlier in pregnancy, or high risk[1]
- Gonorrhea if positive test earlier in pregnancy or high risk[1]

During labor & delivery

- HIV rapid testing if HIV status undocumented
- Syphilis (stat RPR) if no prior prenatal care
- Syphilis if living in an area with high syphilis prevalence or high risk[6]
- HBsAg on admission if no prior screening or if high risk[7]

1. CDC recommends screening for chlamydia and gonorrhea if age <25 years or high risk. Risk factors for chlamydia or gonorrhea: prior chlamydia or gonorrhea infection, particularly in past 24 months; new or multiple partners; suspicion that a recent partner may have had concurrent partners; sex partner diagnosed with an STD; commercial sex; drug use; African American women up to age 30; and local factors such as community prevalence of infection.
2. The primary risk factor for Hepatitis C is past or current injection drug use. Additional risk factors include: history of blood transfusion or organ transplantation before July 1992; receipt of an unregulated tattoo; long-term hemodialysis; and intranasal drug use.
3. Risk factors for genital HSV: exposure to partner with genital herpes; recurrent genital symptoms or atypical symptoms with negative HSV cultures; clinical diagnosis of genital herpes without laboratory confirmation; or HIV-infected status.
4. Cervical cancer screening guidelines: http://www.cdc.gov/cancer/cervical/pdf/guidelines.pdf
5. Risk factors for HIV: illicit drug use; new STD diagnosis during pregnancy; new or multiple partners; living in an area with high HIV prevalence; or HIV-infected partner.
6. Risk factors for syphilis among pregnant women: receiving late or limited prenatal care; new or multiple partners; suspicion that a recent partner may have had concurrent partners; partner with male partners; new STD diagnosis in pregnancy; sex partner diagnosed with an STD; commercial sex; drug use; and living in an area with high syphilis prevalence among women.
7. Risk factors for hepatitis B: injection drug use; new STD diagnosis in pregnancy; new or multiple partners; or HBsAg-positive partner.

Recommended vaccinations during pregnancy: Tdap and influenza.

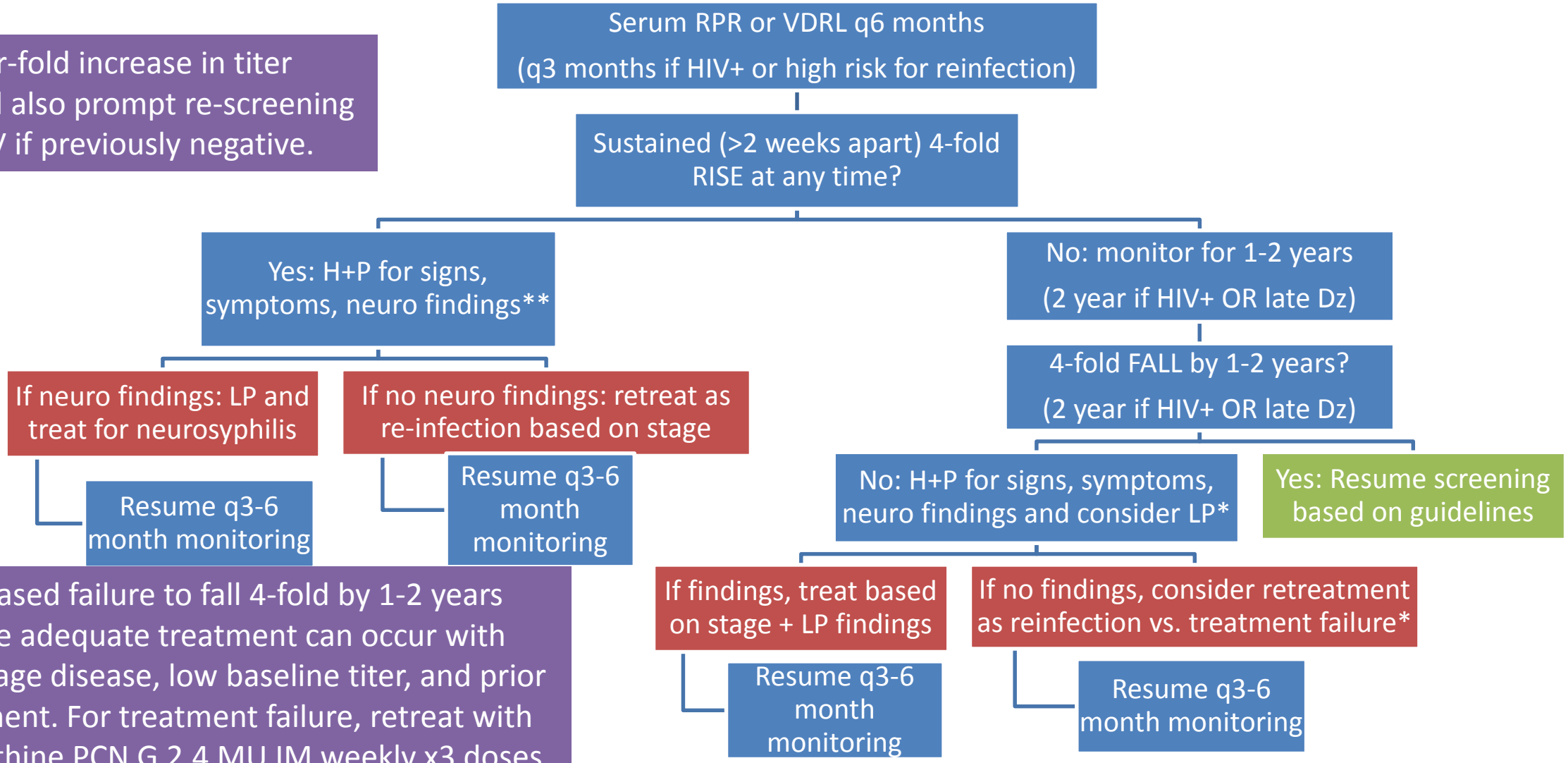
Developed by the California Prevention Training Center and California Department of Public Health STD Control Branch
Updated June 2017

Syphilis Follow-up and Serologic Response

- Patients with lesions should be re-examined within 1 week and 1 month to assess clinical response
- 1^{o} and 2^{o} and EL - recheck non-treponemal serology at 6 and 12 months; adequate response is fourfold decrease in serology within 6-12 months
- Titers should be compared to the non-treponemal titer obtained on day of treatment
- Latent - recheck non-treponemal serology at 6, 12 and 24 months; adequate response is fourfold decrease in serology in 12-24 months (if titer initially $\geq$1:32)
- Pregnant women: Serologies should be re-checked at 28-32 weeks of gestation, at delivery, and following recommendations for stage of disease.
  - May follow titers monthly in high-risk women.

Monitoring after treatment

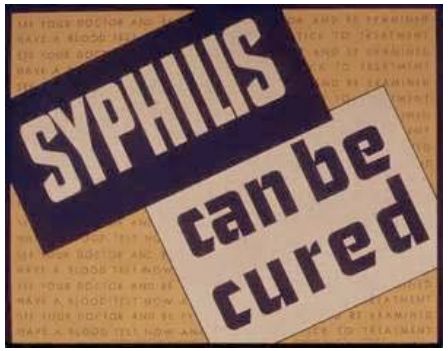
**Four-fold increase in titer should also prompt re-screening for HIV if previously negative.



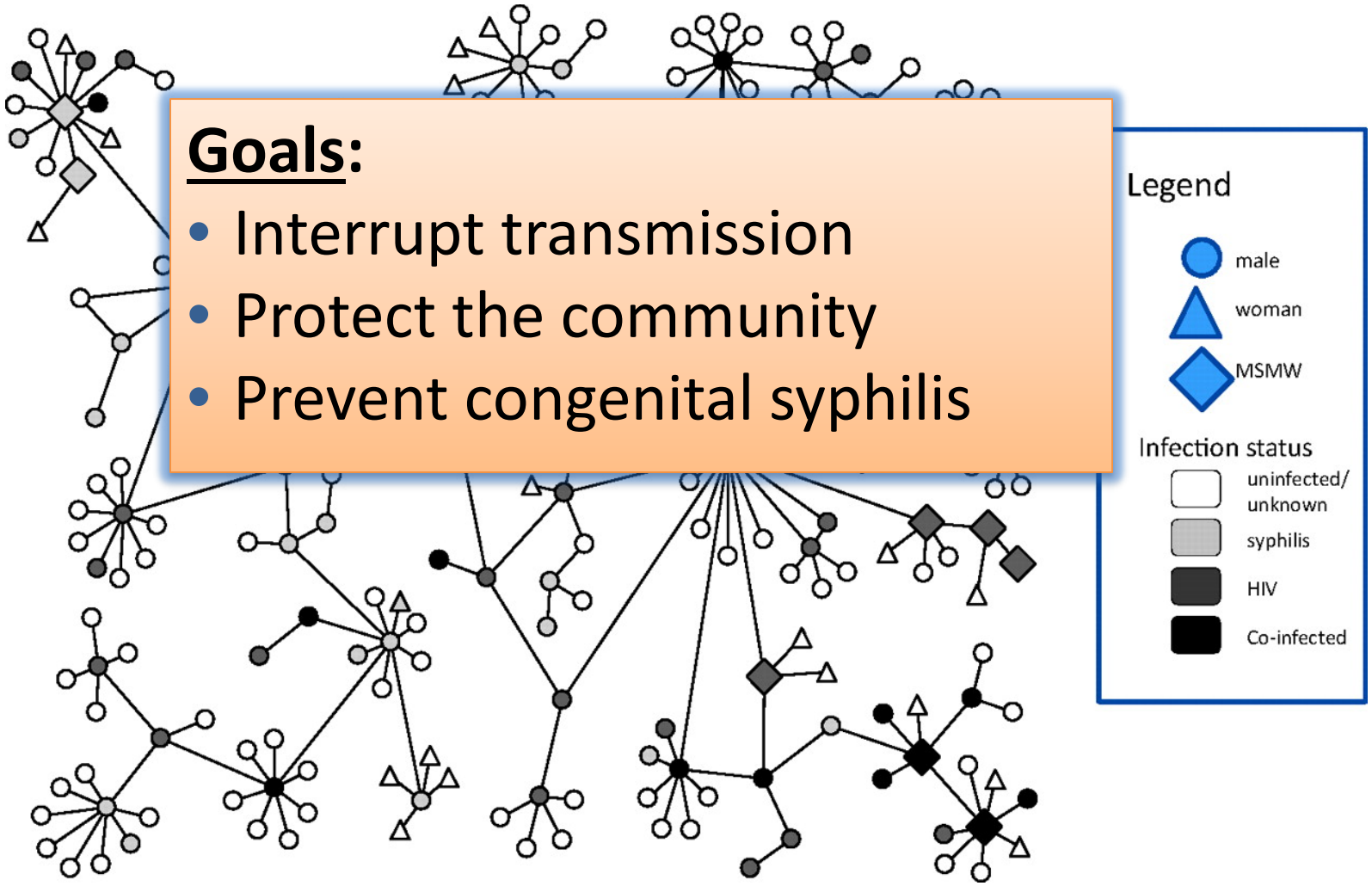
*Increased failure to fall 4-fold by 1-2 years despite adequate treatment can occur with late stage disease, low baseline titer, and prior treatment. For treatment failure, retreat with Benzathine PCN G 2.4 MU IM weekly x3 doses.

Key Take Home Points: Syphilis

- Rates are increasing (MSM, MSW and women)
- Congenital syphilis is preventable
- Recognize symptoms and signs
  - Evaluate for neuro/ocular symptoms/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
- Report to local health department



Case Investigation and Contact Tracing



Goals:

- Interrupt transmission
- Protect the community
- Prevent congenital syphilis

Role of Public Health

1. Strategic planning for prevention and control
2. Mandatory reporting
3. Clinical consultations via the warm line
4. Assistance with partner follow up
5. Prevention through education

Addressing Rising Congenital Syphilis rates in LAC

- Social media platforms to enhance CDC STD messaging;
- Broad mass marketing about rising rates of syphilis with focus on women

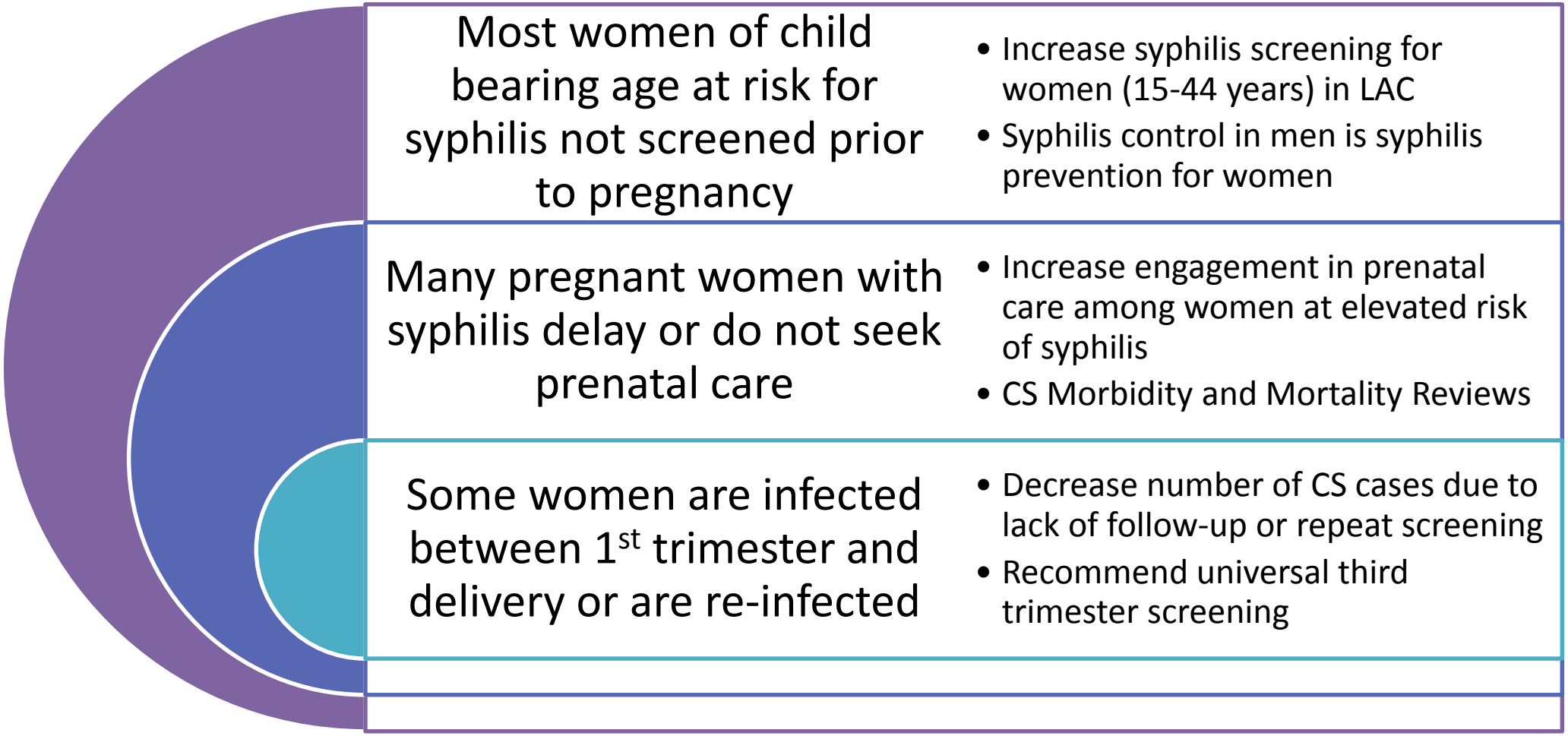
- Enhanced Partner Services for female cases conducted by Public Health Nurses;
- Training of Public Health Nurses and Public Health Investigators

- Regular CS morbidity and mortality review

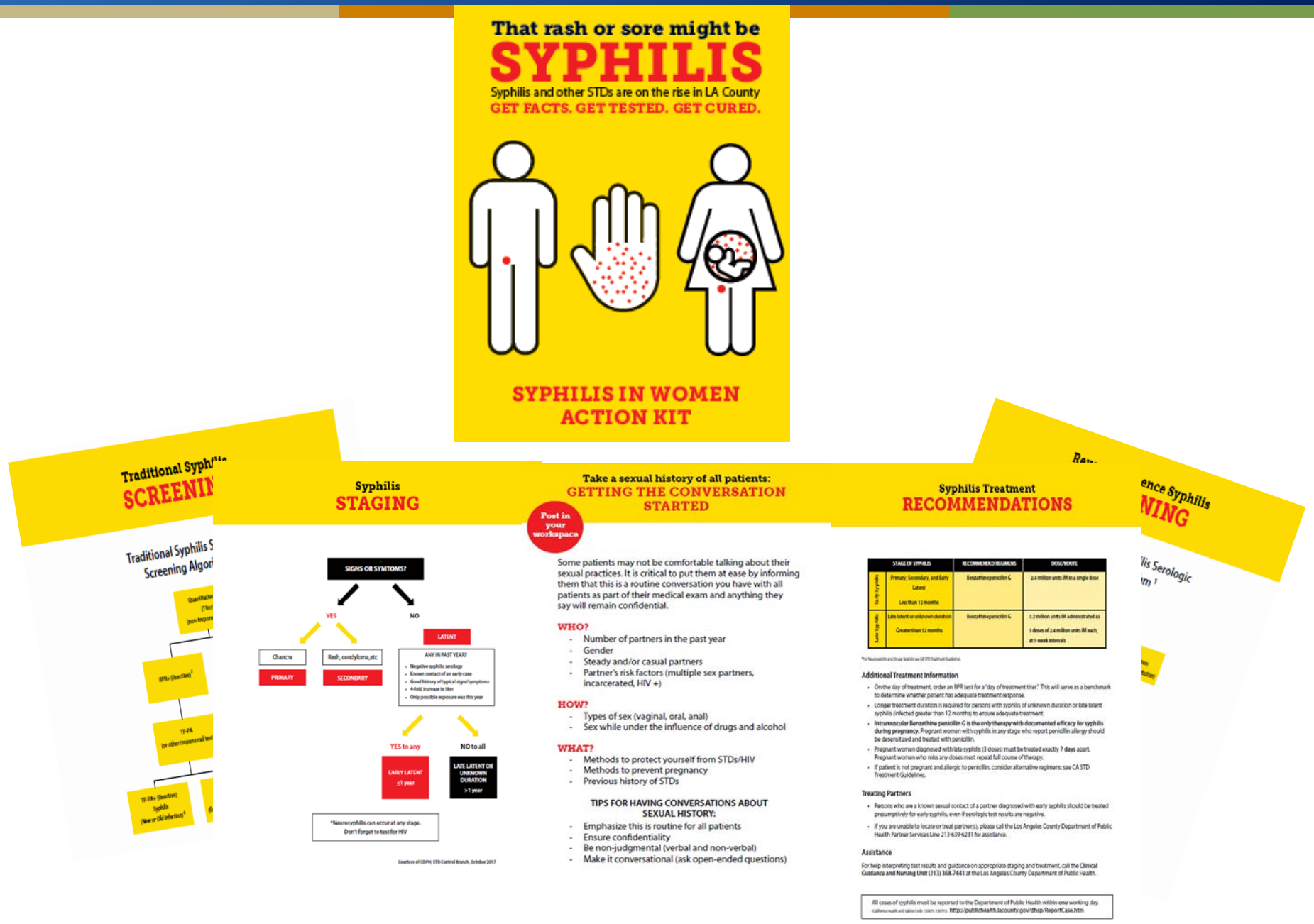
- Nurse Family Partnership (MCAH) program to promote third trimester screening;
- CS trainings at LAC perinatal health programs;
- Implementation of rapid syphilis testing in women's jail with DHS

- Public Health Provider Detailing to engage over 500 medical providers to increase syphilis detection and proper treatment
- Includes comprehensive STD and DPH resources and CME

Congenital Syphilis Trends and Interventions



Public Health Detailing with Syphilis in Women Action Kit



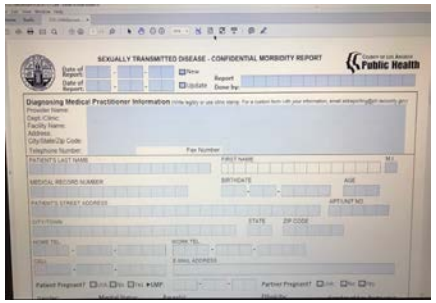
State Law Mandate for 5 reportable STI's

- **Required to report:**
  - Medical Doctors, Osteopaths, Coroners, Podiatrists, Dentists, Nurse Practitioners, Infection Control Practitioners, Health Facility/School Administrators knowing of or suspecting a case of a communicable disease.
- **Reportable STI's:**
  - Chlamydia (including LGV)
  - Chancroid
  - Gonorrhea
  - Syphilis
  - HIV

- **Reporting STD cases does not require patient consent and does not contradict the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule.**
- **The privacy rule allows covered entities to disclose protected health information to public health authorizes when required by federal, tribal, state, or local laws[45 CFR 164.512(a)].**

Reporting of STI's

1. The laboratory reports all positive reportable STI's
2. The clinician **<u>also</u>** reports and completes a confidential morbidity report (CMR) which includes:
   - Clinical Diagnosis
   - Demographics
   - Pregnancy status
   - Treatment
   - Any partner treatment



www.publichealth.lacounty.gov/dhsp/Reportcase.htm

STD Reporting Call (213) 368-7441

HIV Reporting Call (213) 351 - 8516

3. Timeline for reporting:
   - Laboratory confirmed **chlamydia and gonorrhea cases within 7 calendar days** of diagnosis
   - **Syphilis** within **1 working day** of diagnosis

Clinical Nursing and Guidance Unit Warm Line

The Division of HIV and STD Programs is here to help you

Available Mon-Fri 8:00 am-5:00 pm

- **Record Searches**
- **Respond to CMR-related questions**
- **Verify patient previous history (diagnosis and/or treatment)**
- **Provide guidance for clinical questions**
- **Process consultations for the Office of Clinical and Quality Management's Nursing and Guidance Unit/STD Clinical Chief**

The Los Angeles County Department of Public Health is here to help you.

Call the Clinical Nursing and Guidance Unit for:

- Clinical Consultations
- Assistance with mandatory case reporting
- Countywide record searches: syphilis test results and treatment

Mon-Fri 8am-5pm. Messages returned by the next business day. **213-368-7441**

publichealth.lacounty.gov/dhsp/InfoForProviders.htm

Prevention through Education

Patient Education Sheet on Congenital Syphilis

Preguntas más frecuentes

Sífilis Congénita (Sífilis de madre a hijo)

1. ¿Qué es la sífilis congénita?
La sífilis es una enfermedad de transmisión sexual (ETS) causada por bacterias (gérmenes). La sífilis es fácil de curar. Sin tratamiento, puede hacerle daño a los órganos de su cuerpo. La sífilis congénita es cuando una mujer embarazada le pasa la sífilis a su bebé durante el embarazo o el parto. Puede causar que mujeres tengan a su bebé demasiado temprano o un aborto espontáneo o el bebé nacido muerto. También puede causar defectos de nacimiento graves en los bebés.

2. ¿Cómo se propaga esta enfermedad?
Usted puede contraer sífilis mediante el contacto directo con una llaga de sífilis durante las relaciones sexuales anales, vaginales u orales. Las llagas se pueden encontrar en el pene, la vagina, el ano, el recto o los labios y la boca. Puede que no pueda ver las llagas y no causan dolor. La sífilis congénita se propaga de una madre infectada a su bebé durante el embarazo o durante el parto.

3. ¿Cuáles son los síntomas de esta enfermedad?
A menudo las personas no presentan síntomas, por lo que ellos no saben que están infectadas. Señales de la sífilis pueden incluir una llaga cerca del área donde el germen entro a el cuerpo (vagina, ano, labios o boca) o salpullido en una o más áreas del cuerpo. La única manera de saber con seguridad es hacerse una prueba. Una prueba de detección de la sífilis es parte del cuidado prenatal (atención médica durante el embarazo).

4. ¿Cómo debo hacerme la prueba?
Las mujeres embarazadas deben hacerse la prueba para la sífilis durante su primera visita prenatal. Algunas mujeres también deben hacerse la prueba una vez más, más adelante en el embarazo. Asegúrese de obtener los resultados de su prueba para la sífilis y siga el consejo médico de su médico.

5. ¿Cuál es el tratamiento para esta enfermedad?
La sífilis puede ser tratada y curada, incluso durante el embarazo, con una inyección de antibióticos (medicamento que mata los gérmenes). Asegúrese de que su(s) pareja(s) sexual(es) se hagan una prueba y reciban tratamiento también. Esto les ayudará a mantenerse saludable y evitar contagiar a otras personas, y evitar infectarse de nuevo.

6. ¿Cómo se previene esta enfermedad?
- Use condones
- Vaya a sus visitas prenatales para las pruebas y el tratamiento lo antes posible. Si no tiene un médico, llame gratis al teléfono de asistencia para ETS **(800) 758-0880** para encontrar dónde puede hacerse un análisis y recibir tratamiento gratis.

Puntos clave:
- La sífilis congénita es cuando una mujer embarazada pasa la sífilis a su bebé durante embarazo o parto.
- Los síntomas comunes de la sífilis incluyen una llaga o salpullido, pero muchas personas no ven señales de la enfermedad.
- La sífilis es tratada y curada con antibióticos.
- El cuidado prenatal es muy importante para detectar y tratar la sífilis.

Para más información:

Centros para el Control y la Prevención de Enfermedades (CDC por sus siglas en inglés)
http://www.cdc.gov/std/pregnancy/stdfact-pregnancy.htm
http://www.cdc.gov/std/syphilis/stdfact-syphilis.htm

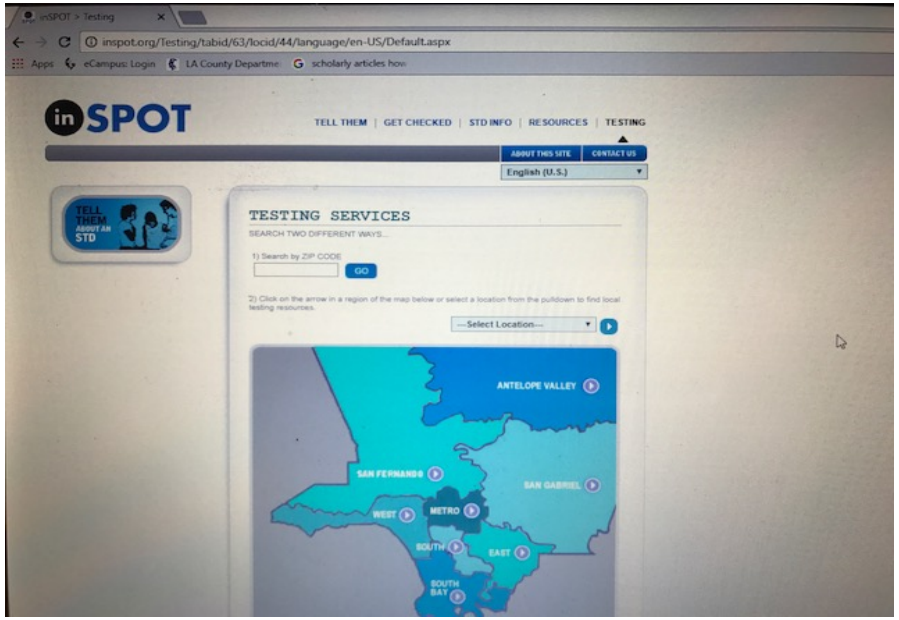
Oficina de la Salud de la Mujer de los EE.UU.
https://www.womenshealth.gov/publications/our-publications/fact-sheet/syphilis.html

DHSP-STD-0023-02 9/08/15)

Departamento de Salud Pública del Condado de Los Ángeles
http://www.publichealth.lacounty.gov

Salud Pública

Anonymous Partner Notification via Internet through an electronic postcard



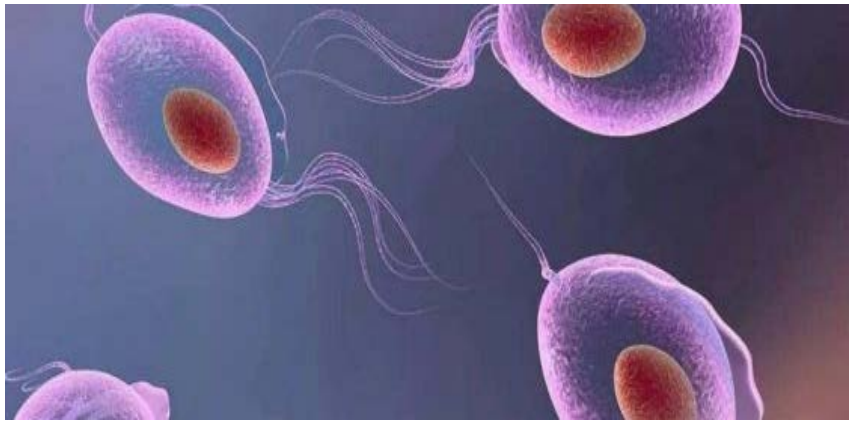
http://inspot.org/Testing/tabid/63/locid/44/language/en-US/Default.aspx

Los Angeles County Department of Public Division of HIV and STD Programs, (LADPH, DHSP), 2015). http://publichealth.lacounty.gov/dhsp/Syphilis.htm

Focus on Gonorrhea and Chlamydia: Overview

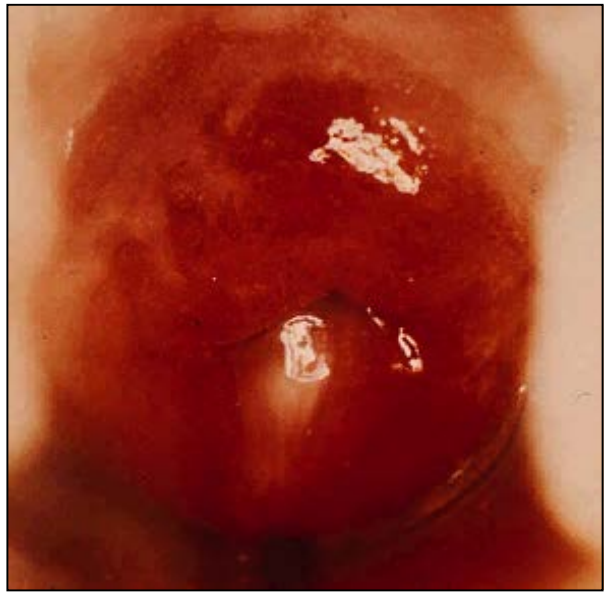
- Clinical highlights, diagnosis and extragenital testing
- Treatment, PDPT, retesting and test of cure
- Epidemiological key points
- Screening guidelines

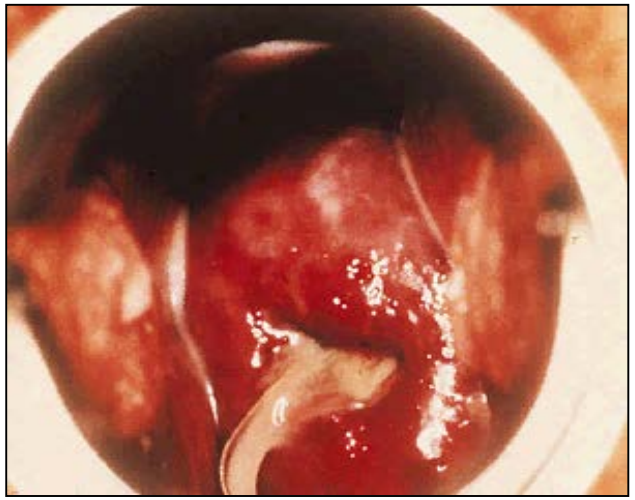
Antibiotic Resistance
Vaccine ?



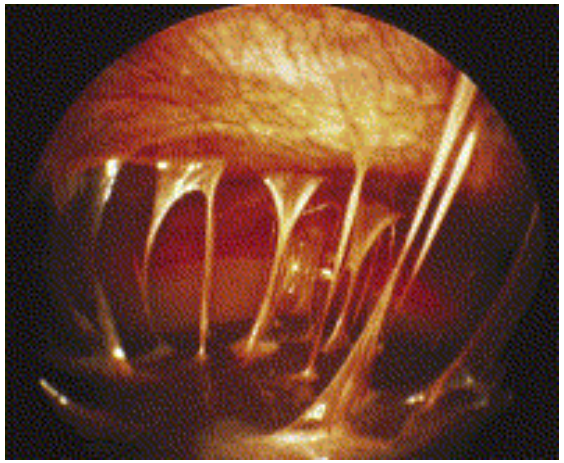
LGV Proctitis

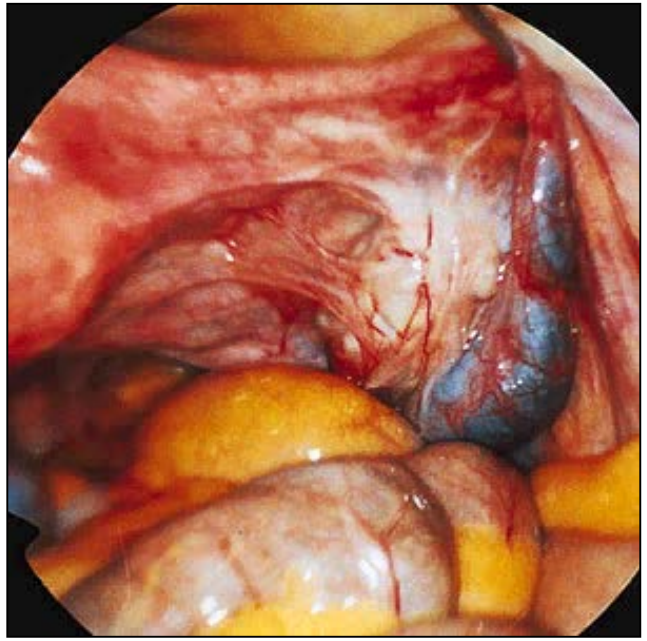
Clinical Manifestations: Cervicitis





PID





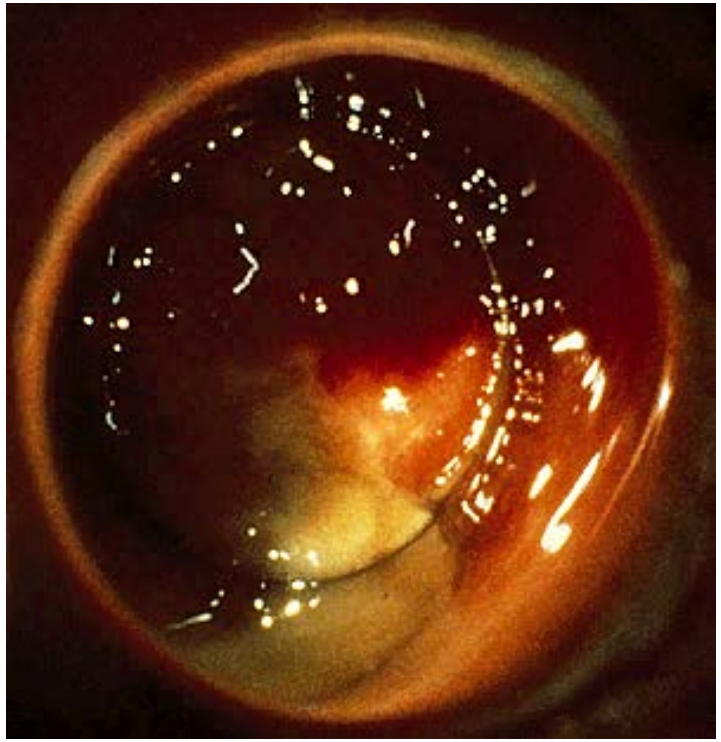
Mosby **STD Atlas**

Clinical Manifestations: Urethritis

Epididymitis

Pharyngitis

Proctitis



Conjunctivitis

STD Atlas, 1997

Mosby

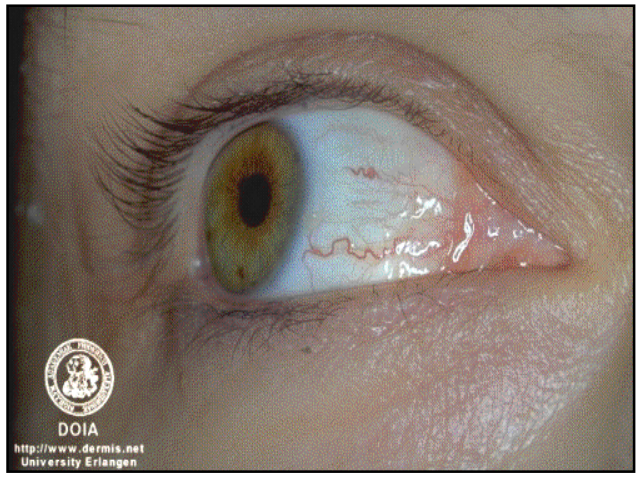
Disseminated Gonococcal Infection

STD Atlas, 1997

Mosby

Reactive Arthritis

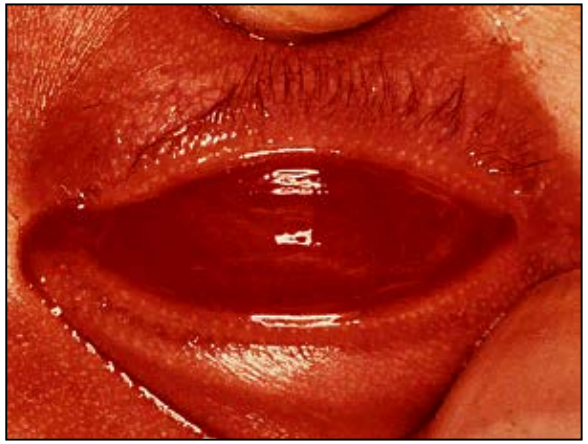
Conjunctivitis, Keratoderma Blennorhagica, Circinate Balanitis, Oligoarthritis

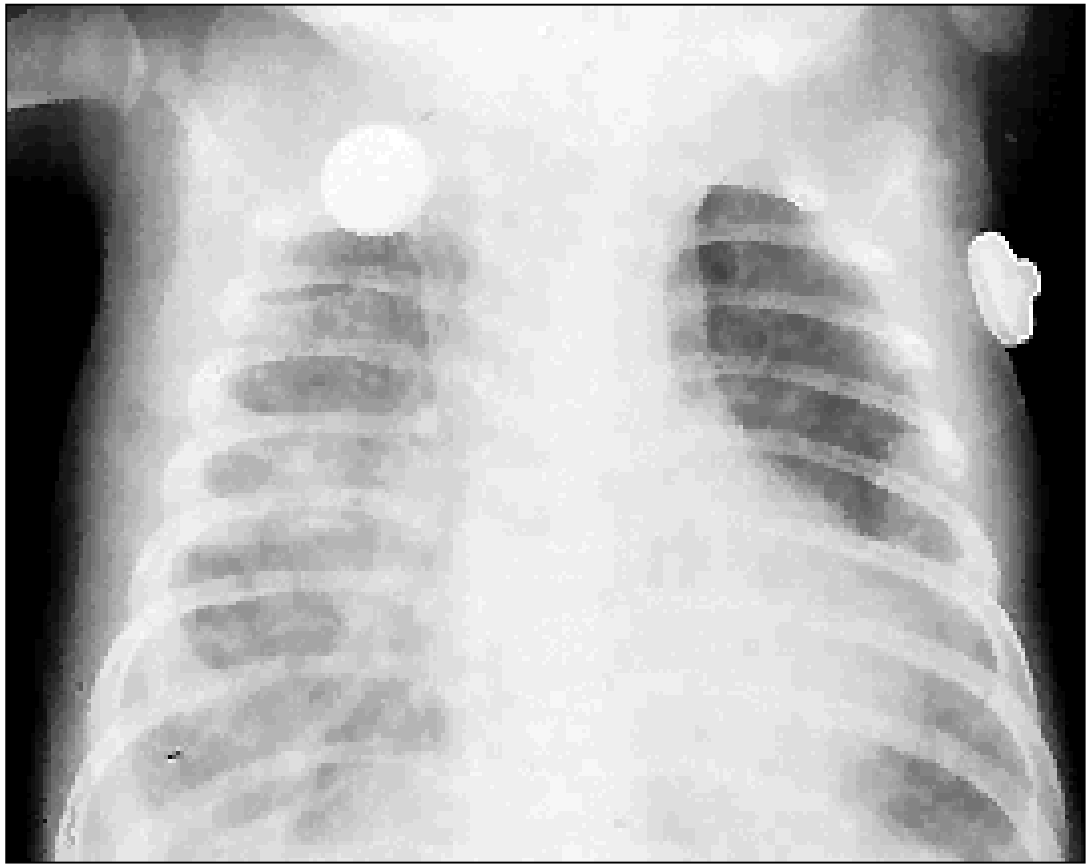


DOIA Website, 2000

Clinics in Dermatology, 2014

Neonatal Conjunctivitis and Pneumonitis





STD Atlas, 1997

Mosby

Chlamydia and *Gonorrhea* NAAT:

- Nucleic Acid Amplification tests have not been cleared by FDA for the rectum and pharynx
- Several commercial laboratories have undergone validation procedures to use them off label
- Similar validation steps apply for self-collected swabs
- CDPH can assist with lab protocols, billing codes
  - https://www.cdph.ca.gov/programs/std/Documents/MSMToolkit.pdf

MMWR. Mar 14 2014;63(No RR-12):1-19.

NAAT Laboratory Ordering and Billing Codes

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

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

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

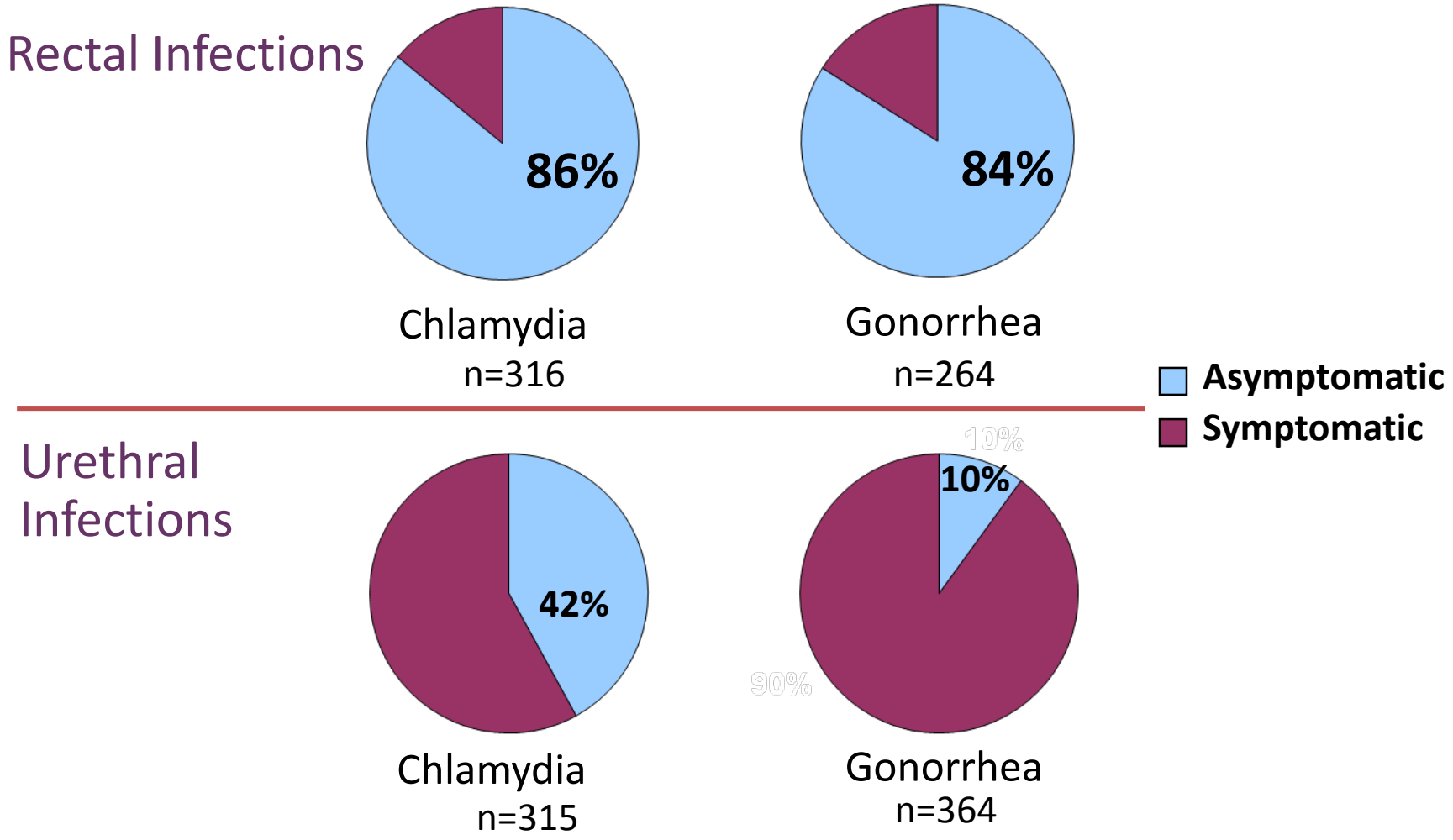
*CDC does not endorse these laboratories, however, they represent the largest laboratories nationally. There may be other private laboratories that have verified rectal and pharyngeal testing with NAATs. Many PHLs have also verified rectal and pharyngeal testing.

Vaginal Swabs versus Urine for Women

- Nucleic acid amplification tests are recommended
- Sample type: self- or clinician-collected vaginal swab
- A first catch urine specimen is acceptable but might detect 10% fewer infections when compared with vaginal and endocervical swab samples.

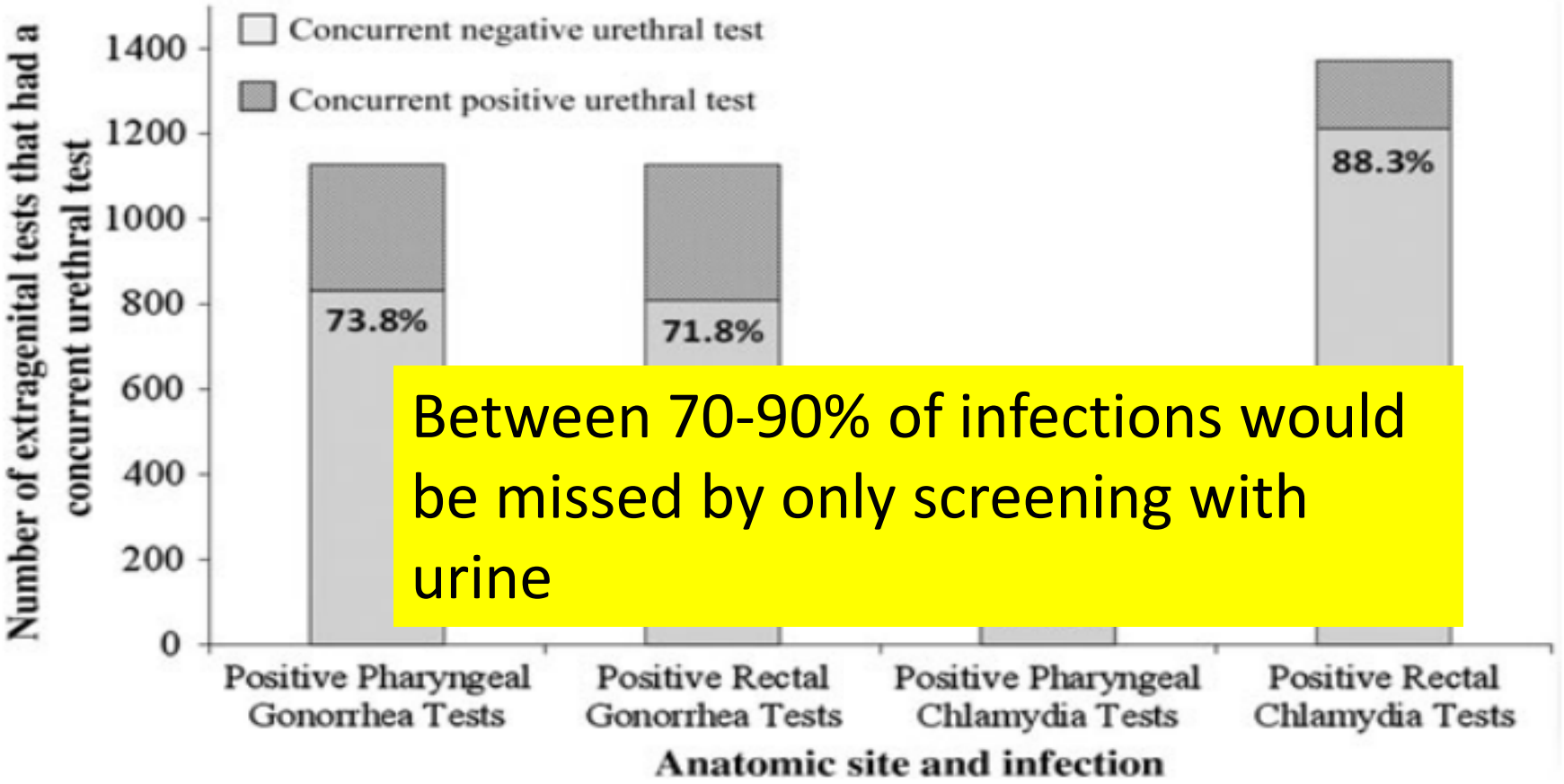
CDC. MMWR 2014 / 63(RR02);1-19

Majority of Rectal Infections in MSM are Asymptomatic



Kent, CK et al, Clin Infect Dis July 2005

High % of Pharyngeal and Rectal CT/GC Associated with Negative Urine test, STD Surveillance Network (n=21994)



Between 70-90% of infections would be missed by only screening with urine

Patton et al CID 2014

What About Extra Genital CT/GC Screening in Women?

- No clear recommendations for women
  - No studies to see if reduces adverse reproductive health outcomes
  - Few studies on burden of infection
  - No FDA approved NAATs
  - Some providers are using a hierarchy to guide extra genital screening based on sexual practices
    - Cervical then rectal then pharyngeal

Family PACT Update:

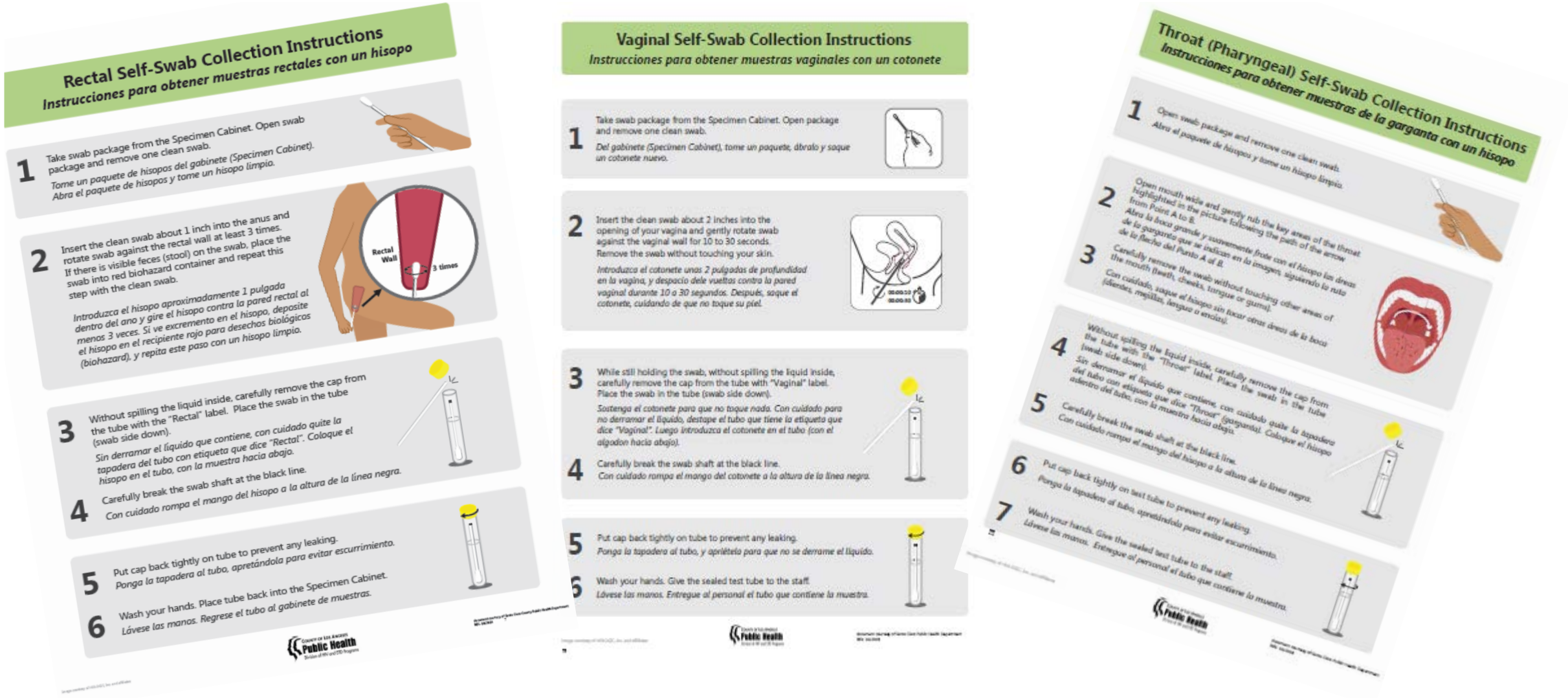
- Frequency limits for chlamydia and gonorrhea nucleic acid amplification testing (NAAT) laboratory billing codes have been updated to 3 units/day as of September 1, 2018. Prior to this update, only one test (i.e. one anatomical site) was allowed per day. Under this new update, more than one anatomical site can be tested for chlamydia and gonorrhea on the same day. For billing codes and more information, see the August 2018 Family PACT Update.
- As of May 1, 2018, Family PACT also covers trichomonas vaginalis NAAT testing

Self-collected rectal/pharyngeal STI testing

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

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

SELF-SWAB INSTRUCTION SHEETS



Rectal Self-Swab Collection Instructions
Instrucciones para obtener muestras rectales con un hisopo

1 Take swab package from the Specimen Cabinet. Open swab package and remove one clean swab.
Tome un paquete de hisopos del gabinete (Specimen Cabinet). Abra el paquete de hisopos y tome un hisopo limpio.

2 Insert the clean swab about 1 inch into the anus and rotate swab against the rectal wall at least 3 times. If there is visible feces (stool) on the swab, place the swab into red biohazard container and repeat this step with the clean swab.
Introduzca el hisopo aproximadamente 1 pulgada dentro del ano y gire el hisopo contra la pared rectal al menos 3 veces. Si ve excremento en el hisopo, deposite el hisopo en el recipiente rojo para desechos biológicos (biohazard), y repita este paso con un hisopo limpio.

Rectal Wall
3 times

3 Without spilling the liquid inside, carefully remove the cap from the tube with the "Rectal" label. Place the swab in the tube (swab side down).
Sin derramar el líquido que contiene, con cuidado quite la tapadera del tubo con etiqueta que dice "Rectal". Coloque el hisopo en el tubo, con la muestra hacia abajo.

4 Carefully break the swab shaft at the black line.
Con cuidado rompa el mango del hisopo a la altura de la línea negra.

5 Put cap back tightly on tube to prevent any leaking.
Ponga la tapadera al tubo, apretándola para evitar escurrimiento.

6 Wash your hands. Place tube back into the Specimen Cabinet.
Lávese las manos. Regrese el tubo al gabinete de muestras.

Public Health

Vaginal Self-Swab Collection Instructions
Instrucciones para obtener muestras vaginales con un cotonete

1 Take swab package from the Specimen Cabinet. Open package and remove one clean swab.
Del gabinete (Specimen Cabinet), tome un paquete, ábralo y saque un cotonete nuevo.

2 Insert the clean swab about 2 inches into the opening of your vagina and gently rotate swab against the vaginal wall for 10 to 30 seconds. Remove the swab without touching your skin.
Introduzca el cotonete unas 2 pulgadas de profundidad en la vagina, y despacio dele vueltas contra la pared vaginal durante 10 a 30 segundos. Después, saque el cotonete, cuidando de que no toque su piel.

3 While still holding the swab, without spilling the liquid inside, carefully remove the cap from the tube with "Vaginal" label. Place the swab in the tube (swab side down).
Sostenga el cotonete para que no toque nada. Con cuidado para no derramar el líquido, destape el tubo que tiene la etiqueta que dice "Vaginal". Luego introduzca el cotonete en el tubo (con el algodon hacia abajo).

4 Carefully break the swab shaft at the black line.
Con cuidado rompa el mango del cotonete a la altura de la línea negra.

5 Put cap back tightly on tube to prevent any leaking.
Ponga la tapadera al tubo, y apriétela para que no se derrame el líquido.

6 Wash your hands. Give the sealed test tube to the staff.
Lávese las manos. Entregue al personal el tubo que contiene la muestra.

Public Health

Throat (Pharyngeal) Self-Swab Collection Instructions
Instrucciones para obtener muestras de la garganta con un hisopo

1 Open swab package and remove one clean swab.
Abra el paquete de hisopos y tome un hisopo limpio.

2 Open mouth wide and gently rub the key areas of the throat highlighted in the picture following the path of the arrow from Point A to B.
Abra la boca grande y suavemente frote con el hisopo las áreas de la garganta que se indican en la imagen, siguiendo la ruta de la flecha del Punto A al B.

3 Carefully remove the swab without touching other areas of the mouth (teeth, cheeks, tongue or gums).
Con cuidado, saque el hisopo sin tocar otras áreas de la boca (dientes, mejillas, lengua o encías).

4 Without spilling the liquid inside, carefully remove the cap from the tube with the "Throat" label. Place the swab in the tube (swab side down).
Sin derramar el líquido que contiene, con cuidado quite la tapadera del tubo con etiqueta que dice "Throat" (garganta). Coloque el hisopo adentro del tubo, con la muestra hacia abajo.

5 Carefully break the swab shaft at the black line.
Con cuidado rompa el mango del hisopo a la altura de la línea negra.

6 Put cap back tightly on test tube to prevent any leaking.
Ponga la tapadera al tubo, apretándolo para evitar escurrimiento.

7 Wash your hands. Give the sealed test tube to the staff.
Lávese las manos. Entregue al personal el tubo que contiene la muestra.

Public Health

Source: Santa Clara County Department of Public Health

Case Scenario: Tony

- 19 yo male presents for STD screening
- He reports exclusively male partners, 3 in past 6 months, oral sex, insertive and receptive anal sex ‘sometimes’, 1 anonymous partner
- Good health, no complaints, h/o GC last year

What STD testing is indicated?

Which vaccines are important to provide?

STD Screening for MSM

- HIV
- Syphilis
- Urethral GC and CT
- Rectal GC and CT (if RAI)
- Pharyngeal GC (if oral sex)

*

- HSV-2 serology (consider)
- Hepatitis B (HBsAg)
- Hepatitis C (if high risk)
- Anal Pap (consider for HIV+)

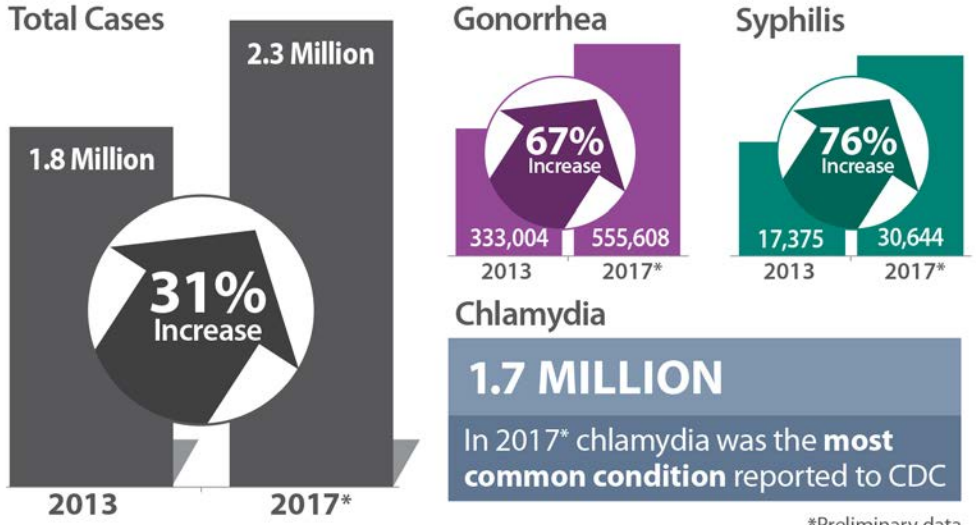
* At least annually, more frequent (3-6 months) if at high risk (multiple/anonymous partners, drug use, high risk partners)

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

Epidemiology key points

THE U.S. IS EXPERIENCING STEEP, SUSTAINED INCREASES IN SEXUALLY TRANSMITTED DISEASES

Combined diagnoses of chlamydia, gonorrhea, and syphilis **increased sharply over the past five years**



Chlamydia

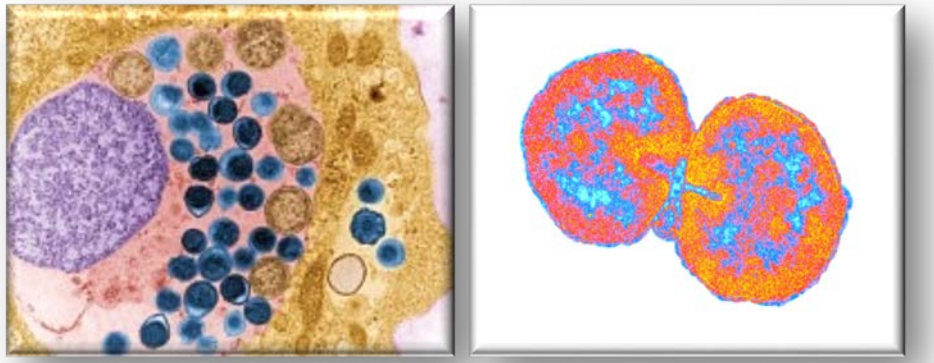
1.7 MILLION

In 2017* chlamydia was the **most common condition** reported to CDC

*Preliminary data

For more information, visit
cdc.gov/nchhstp/newsroom

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



CONTINUED CONCERNS ABOUT ANTIBIOTIC RESISTANT GONORRHEA

Gonorrhea is expected to eventually wear down our last highly effective antibiotic

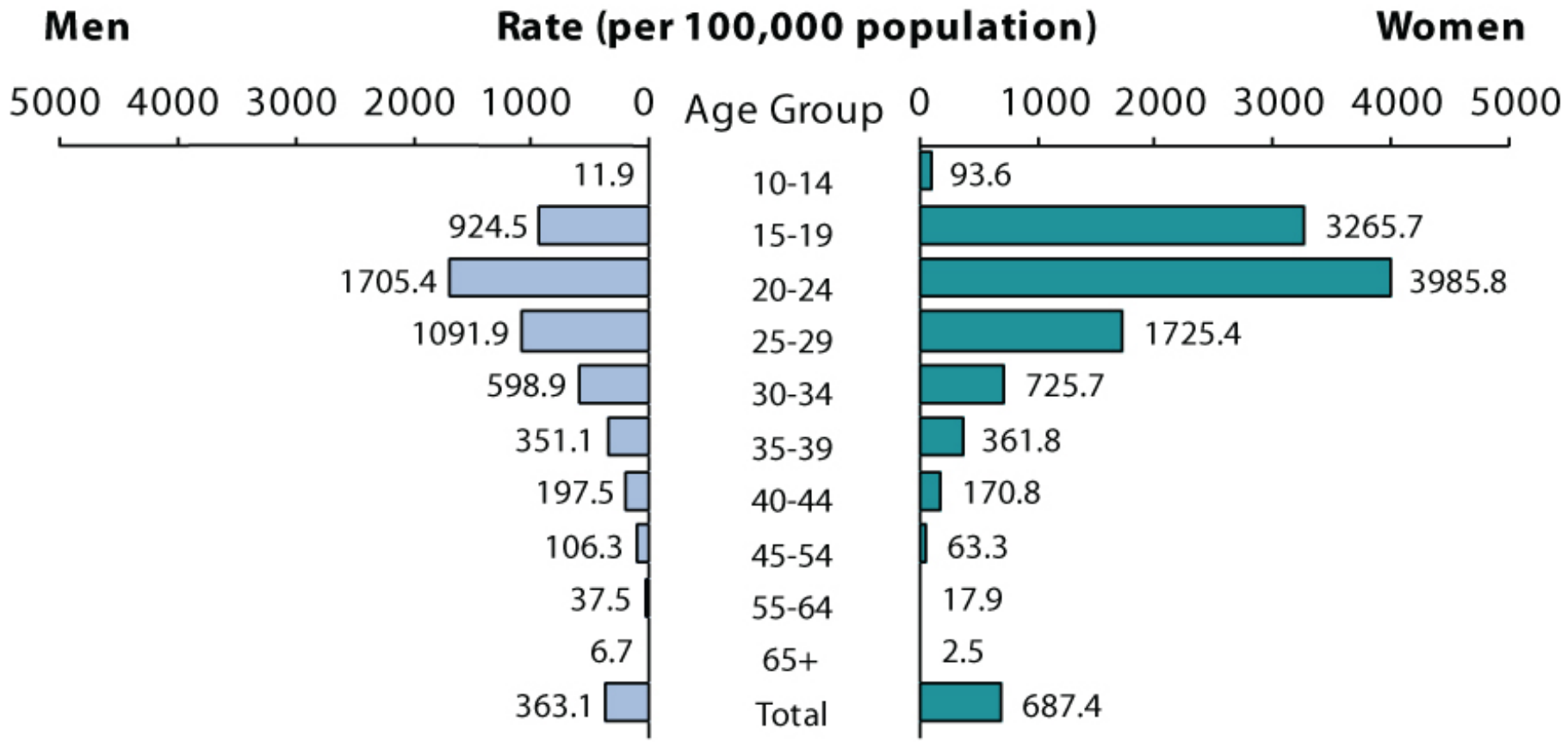
Lab tests show a small but growing fraction of gonorrhea samples have **signs of emerging antibiotic resistance**

CDC recommends a two-drug combination to preserve our **last highly effective antibiotic**

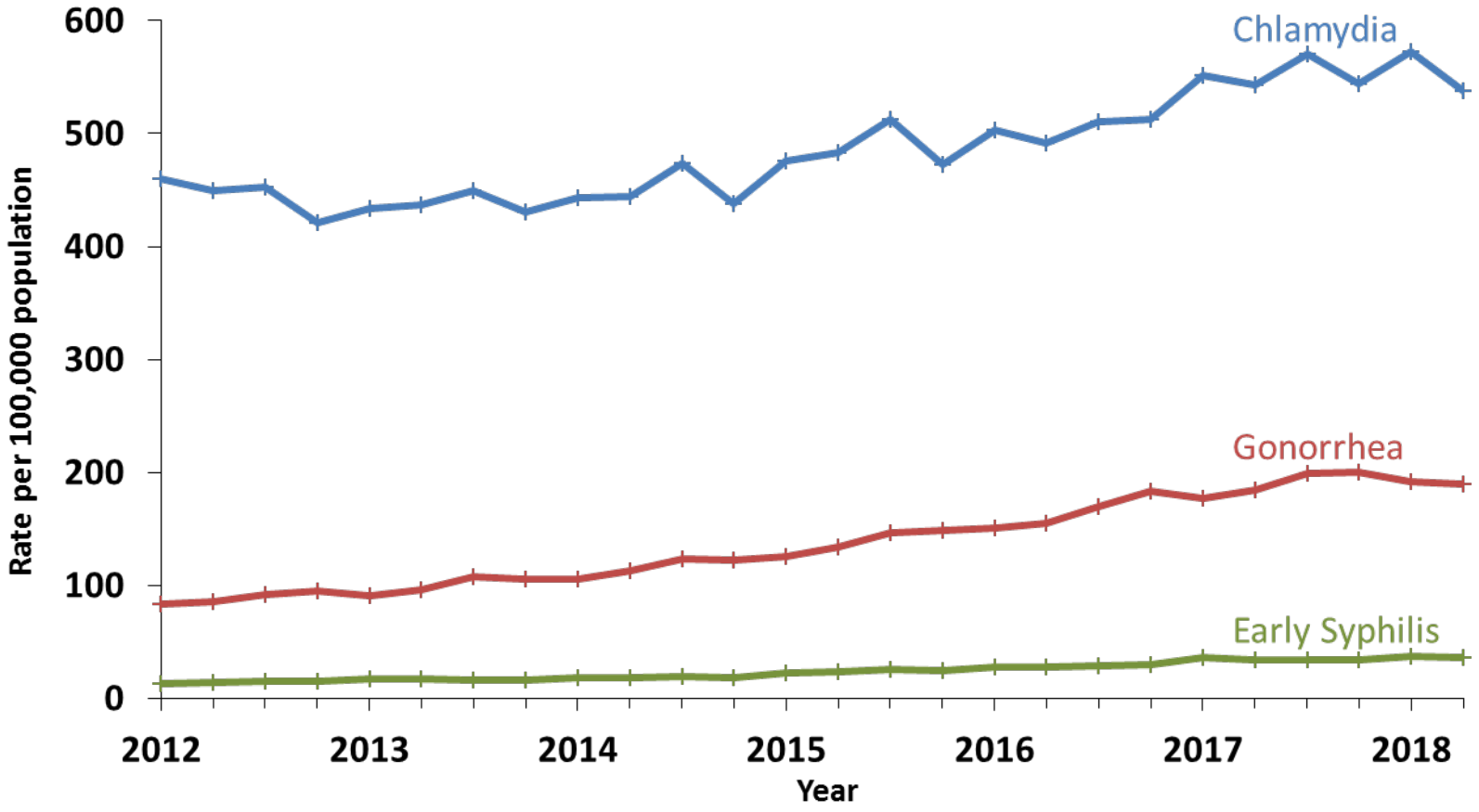
For more information, visit
cdc.gov/nchhstp/newsroom

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

Chlamydia — Rates of Reported Cases by Age Group and Sex, United States, 2017



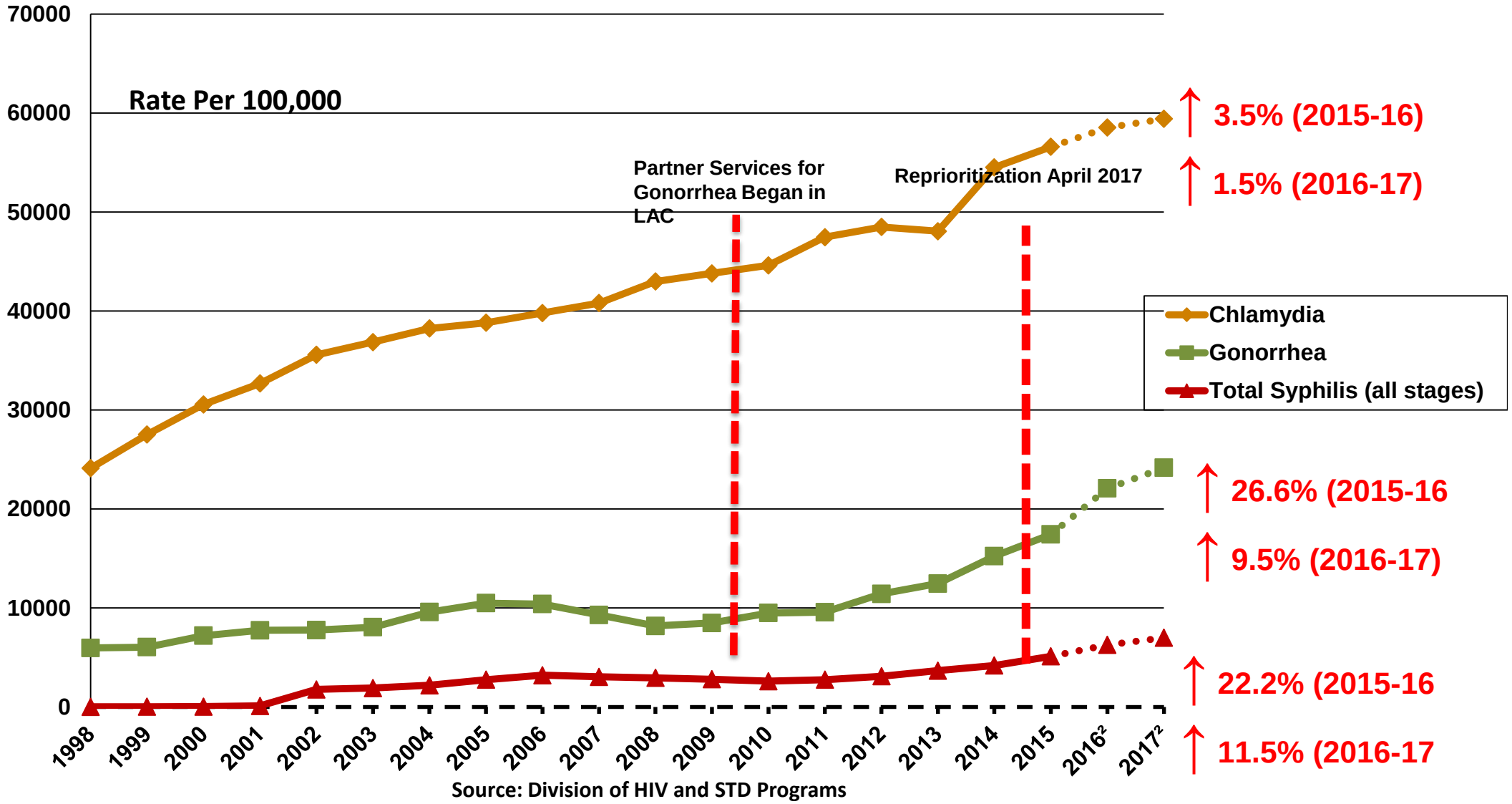
Chlamydia, Gonorrhea, and Early Syphilis† California Rates by Year-Quarter, 2012–2018*



† Early syphilis includes primary, secondary and early latent syphilis

Source CDPH

Number of Reported Cases of Syphilis (all stages), Gonorrhea, and Chlamydia, Los Angeles County, 1998-2017[1]



Source: Division of HIV and STD Programs

1. Does not include cases reported in the cities of Long Beach and Pasadena; total syphilis includes all cases staged as primary, secondary, early latent, late latent, and unknown duration 2. 2016 and 2017 data are provisional due to reporting delay.

Pop Quiz

Which of the following patients does NOT need a screening test for CT and GC?

a) Amanda, asymptomatic cisgender woman with male and female sex partners. She screened positive for chlamydia and negative for GC and HIV, 3 months ago.

b) Jeff, a cisgender man who has receptive and insertive anal sex with exclusively male sex partners. He had a negative urine, throat, and rectal screen for CT, GC, syphilis, and HIV, 3 months ago.

c) Dave, a cisgender man with exclusively female partners. He screened negative for CT, GC, and HIV, 3 months ago. He has had no new partners, no symptoms, and no high risk exposure such as contact with sex workers.

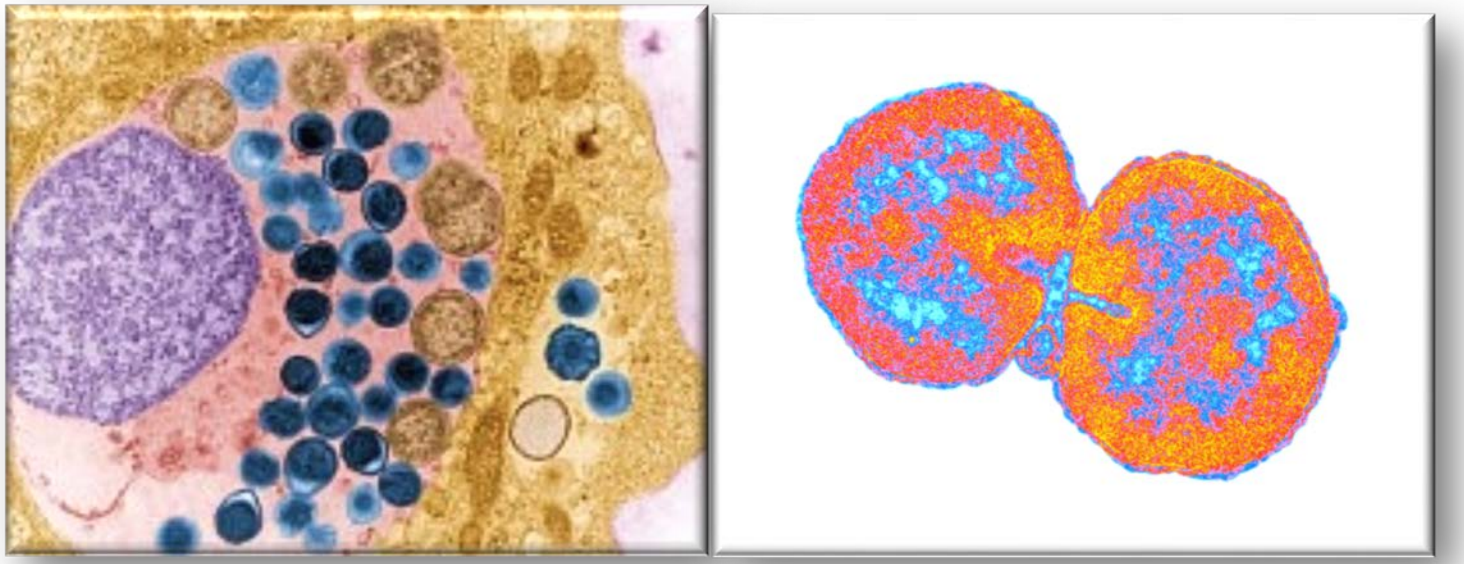
d) Martha, a transgender woman with exclusively male partners. She is on PrEP for HIV prevention and screened negative for CT, GC, syphilis, and HIV, 3 months ago. She has had no new partners and no symptoms.

Who Should be Screened for CT/GC?

County of Los Angeles Public Health

Females	• < 25 annually, 25+ if at risk • Pregnant (first trimester)
MSM	• At least annually • Exposed sites: genital, rectal, throat
Hetero males	• High prevalence settings (corrections, STD clinics)
HIV +	• At least annually • All exposed sites
Patients on PrEP	• Every 3 months
Post-Tx	• All patients, 3 months after treatment

CDC 2015 STD Tx Guidelines www.cdc.gov/std/treatment
Plus: Guidelines for HIV care and PrEP



CT/GC Treatment

Chlamydia Treatment

Adolescents and Adults

	Recommended	Alternatives (new)
Non-pregnant	Azithromycin 1 g orally in a single dose Doxycycline 100 mg orally twice daily for 7 days	Doxycycline (delayed release) 200 mg QD x 7 d
Pregnant*	Azithromycin 1 g orally in a single dose	Amoxicillin 500 mg po TID x 7 days

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

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

Case: When it Rains it Pours

- 52 yo HIV+ MSM, not in care and not on ART, presents with complaints of rectal discharge and bleeding and abdominal pain

- Physical exam: Bloody rectal discharge; resolving patchy hair loss; No rash or anogenital lesions.

<u>10 weeks prior:</u>

- Contact to Gonorrhea (GC)
- Patchy alopecia
- Treated empirically for secondary syphilis with Benzathine penicillin G (BPG) 2.4 mu IM x 1 *and* GC with ceftriaxone 250 mg IM x 1 and azithromycin 1 g PO x 1
- RPR 1:128, TP-PA positive, and rectal NAAT positive for GC (negative for CT)

Source: Bolan-Cohen Meet the Professor Session ID Week 2018

How would you manage this patient?

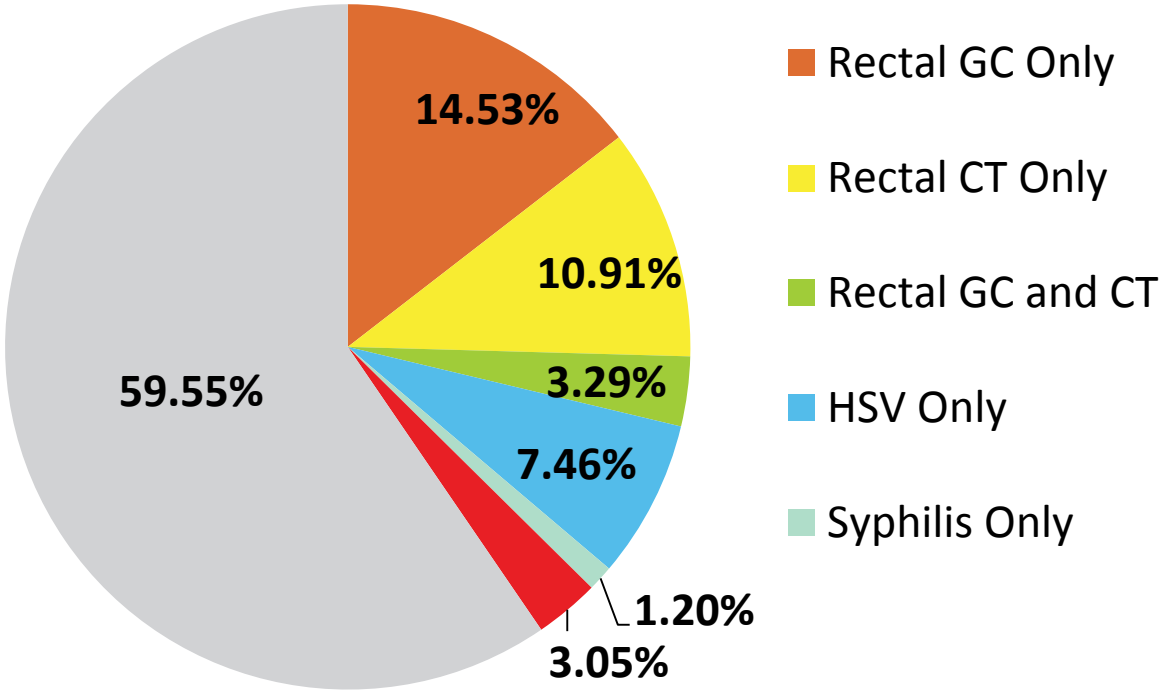
Order lab studies, including RPR and rectal GC and CT NAAT, and:

1) Wait for results
2) Treat with ceftriaxone 250 mg IM x 1 and azithromycin 1 g po x1
3) Treat with ceftriaxone 250 mg IM x 1 and doxycycline 100 mg PO BID x 7 days
4) Treat with ceftriaxone 250 mg IM x 1 and doxycycline 100 mg PO BID x 21 days
5) Treat with ceftriaxone 250 mg IM x 1, doxycycline 100 mg PO BID x 21 days and benzathine penicillin G 2.4 mu IM x 1

Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Clinical Issue #1: Evaluation and Management of Proctitis

Microbiologic Etiology of Proctitis Cases, 2004-2012 (n=1246)[1]



[1]Cohen SE, ISSTDR 2013

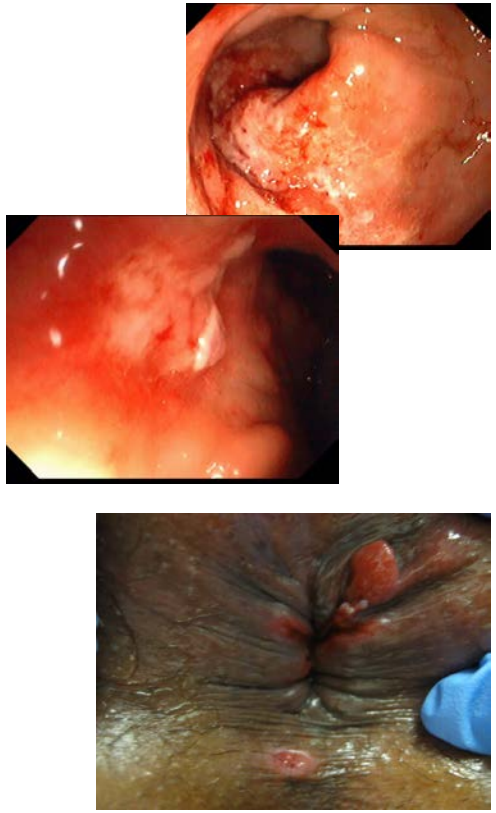
- Diagnosis:
  - Anoscopy
  - RPR
  - Rectal GC and CT NAAT
  - Rectal HSV PCR
  - If possible: LGV PCR

Red: multiple diagnoses; Grey: No diagnosis

Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Evaluation of and Management LGV Proctitis

- Caused by L-serovars (L1, L2, L3) of *Chlamydia trachomatis (CT)*
- Anorectal syndrome: Asymptomatic to hemorrhagic proctocolitis
- Rectal CT NAAT will be positive – does not further specify whether LGV serovars are the cause
- ***MSM with acute proctitis and bloody rectal discharge, perianal ulcers or mucosal ulcers, and either a positive rectal chlamydia NAAT or HIV infection should be offered presumptive treatment for LGV with doxycycline 100 mg PO BID for 21 days.***



Photos: J Engelman, SFCC; de Vrieze Expert Review Anti-infective therapy 2014.
Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Clinical Controversies and LGV

- % of rectal CT that is caused by LGV varies by jurisdiction and region (8-18%)[1]
- No RCT data to guide treatment of LGV
- Unclear if *asymptomatic* LGV requires a prolonged course of treatment[2]
- *BASHH guidelines recommend that all positive rectal Chlamydia be reflex tested for LGV, and if positive, treated with 3 weeks of doxycycline regardless of symptoms

[1]Schillinger Nat'l STD Prev Conf 2018; Saxon Emerg Infect Dis 2016; de Vrieze STI 2013; Leeyaphan STD 2017.
[2]Simons STD 2018; Handsfield STD 2018.
*** BASHH British Association for Sexual Health and HIV**

Azithromycin versus Doxycycline for Treatment of Urogenital CT

- RCT comparing azithromycin with doxycycline
- Directly observed treatment of CT among teens in correctional facilities
- Measured treatment failure at 28 days after treatment initiation
  - Treatment failure determined on basis of NAAT, sexual history, and genotyping of CT strains
- Results: (N=155 in each group)
  - Azithromycin 97% effective
  - Doxycycline 100% effective

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

Is azithro adequate treatment for rectal CT infection?

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

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

Case Continued

- Treated for proctitis with ceftriaxone 250 mg IM x 1 and doxycycline 100 mg PO BID x 21 days
- Referred to HIV navigator for assistance with re-linkage to care
- Results:
  - **Rectal NAAT positive for GC and CT**
  - **Rectal LGV PCR positive**
  - Rectal HSV PCR negative
  - RPR 1:64

Clinical Issue #2:
Optimal management of concurrent rectal LGV+GC

LGV treatment differs from recommended rectal GC treatment

- First-line treatment for rectal GC is:
  Ceftriaxone 250 mg IM x1 *plus* Azithromycin 1 g PO x1
- CTX *plus* doxycycline 100 mg PO BID x 7 days
  downgraded to alternative due to high prevalence of tetracycline resistant GC

Source: Bolan-Cohen Meet the Professor Session ID Week 2018

Gonorrhea Dual Therapy
Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose

PLUS

Azithromycin 1 g orally

- Azithro recommended regardless of CT test result
- Dual treatment = ceftriaxone and azithromycin administered on the same day preferably simultaneously and under direct observation

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

Gonorrhea Treatment Alternatives

Anogenital Infections

ALTERNATIVE ORAL TREATMENT:

Cefixime 400 mg ***PLUS*** Azithromycin 1 g

IN CASE OF SEVERE ALLERGY:

- Gentamicin 240 mg IM + azithromycin 2 g PO

OR

- Gemifloxacin 320 mg orally + azithromycin 2 g PO

Per-protocol efficacy in RCT of adults with urethral or cervical gonorrhea:

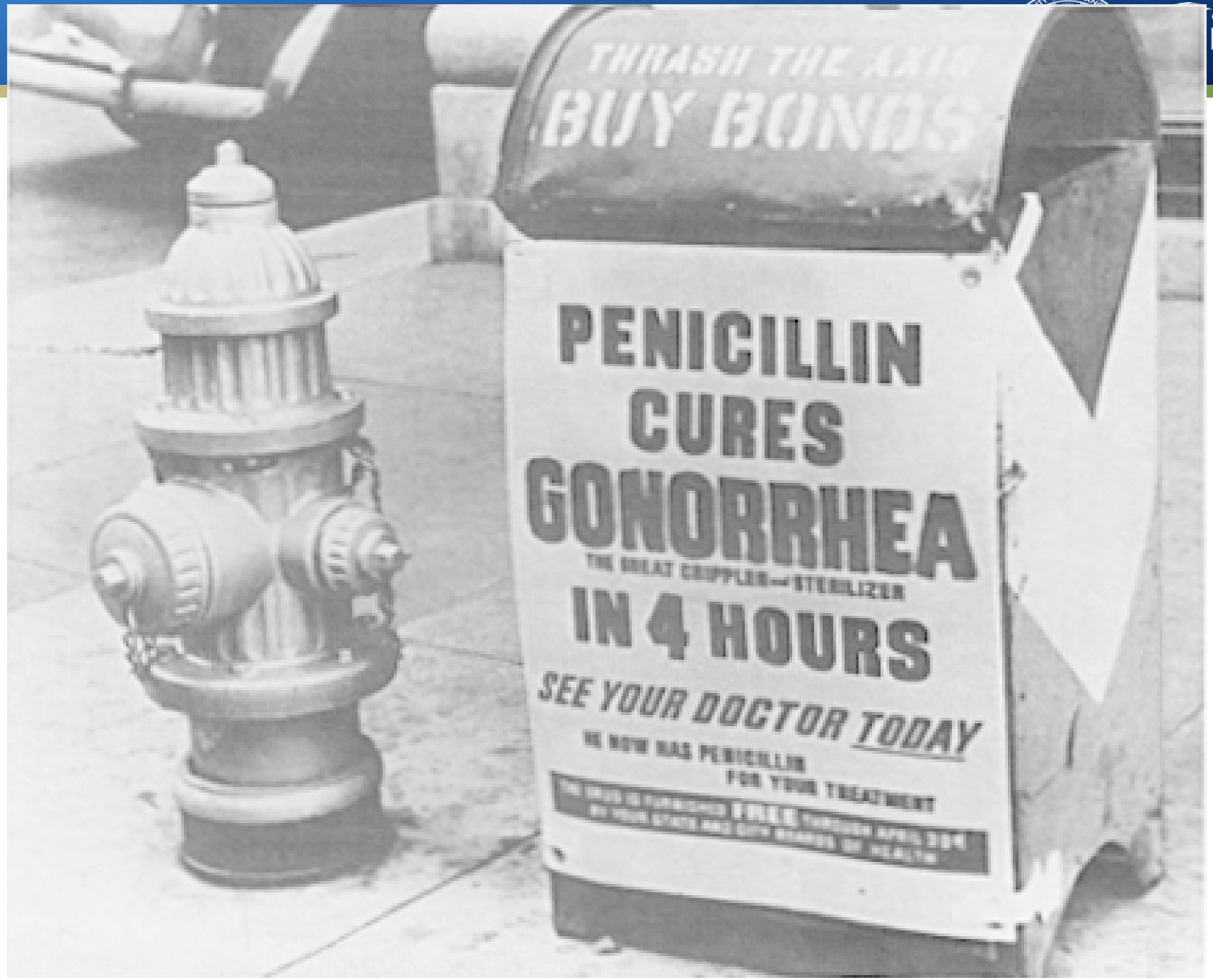
- gentamicin + azithromycin = 100% (202/202)
- gemifloxacin + azithromycin = 99.5% (198/199)

Kirkcaldy, CID 2014;59:1083-91

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

Any downside to the alternative regimens?

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


BUY BONDS
PENICILLIN
CURES
GONORRHEA
IN 4 HOURS
SEE YOUR DOCTOR TODAY
FOR YOUR TREATMENT

DRUG-RESISTANT NEISSERIA GONORRHOEAE

THREAT LEVEL URGENT

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

246,000 DRUG-RESISTANT GONORRHEA INFECTIONS

- **188,600** RESISTANCE TO TETRACYCLINE
- **11,480** REDUCED SUSCEPTIBILITY TO CEFIXIME
- **3,280** REDUCED SUSCEPTIBILITY TO CEFTRIAXONE
- **2,460** REDUCED SUSCEPTIBILITY TO AZITHROMYCIN

820,000 GONOCOCCAL INFECTIONS PER YEAR

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

RESISTANCE OF CONCERN

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

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

PUBLIC HEALTH THREAT

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

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

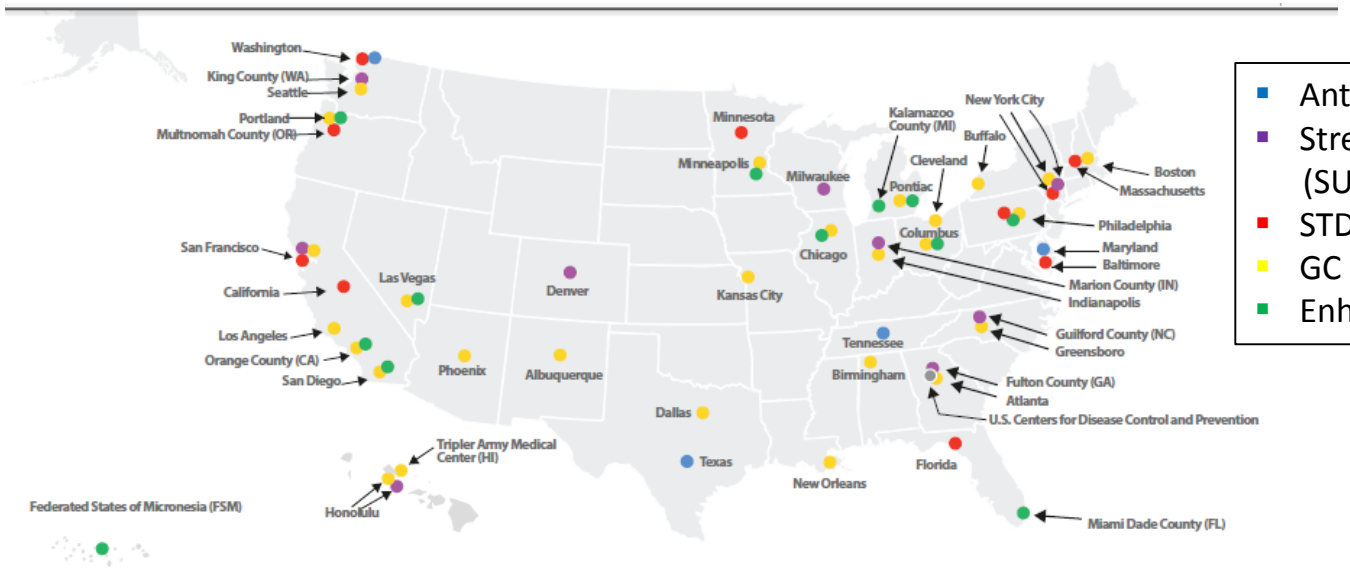
	Percentage	Estimated number of cases
Gonorrhea		820,000
Resistance to any antibiotic	30%	246,000
Reduced susceptibility to cefixime	<1%	11,480
Reduced susceptibility to ceftriaxone	<1%	3,280
Reduced susceptibility to azithromycin	<1%	2,460
Resistance to tetracycline	23%	188,600

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

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

N. gonorrheae is "naturally competent"

Places Working to Combat Drug-Resistant Gonorrhea



- Antimicr. Regional Lab Network (ARLN)
- Strengthening US Response to Res. GC (SURRG)
- STD Surveillance Network (SSuN)
- GC Isolate Surveillance Project (GISP)
- Enhanced GISP (eGISP)

ARLN*
- Maryland
- Texas
- Tennessee
- Washington

SURRG† Sites
- Denver
- Fulton County (GA)
- Guilford County (NC)
- Honolulu
- King County (WA)
- Marion County (IN)
- Milwaukee
- New York City
- San Francisco

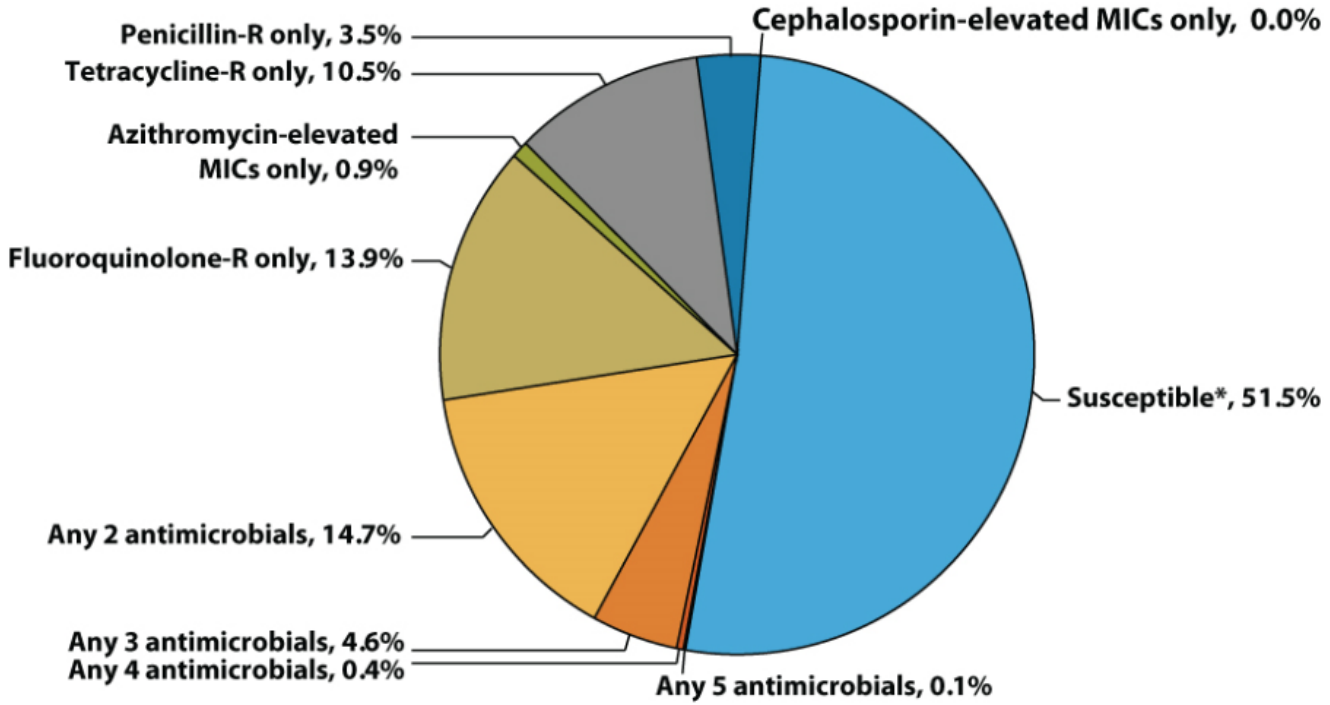
SSuN* Sites
- Baltimore
- California
- Florida
- Massachusetts
- Minnesota
- Multnomah County (OR)
- New York City
- Philadelphia
- San Francisco
- Washington

GISP‡ Sites
- Albuquerque
- Atlanta
- Birmingham
- Boston
- Buffalo
- Chicago
- Cleveland
- Columbus
- Dallas
- Greensboro
- Honolulu
- Indianapolis
- Kansas City
- Las Vegas
- Los Angeles
- Minneapolis
- New Orleans
- New York City
- Orange County (CA)
- Philadelphia
- Phoenix
- Pontiac
- Portland
- San Diego
- San Francisco
- Seattle
- Tripler Army Medical Center

eGISP§ Sites
- Chicago
- Columbus
- Federated States of Micronesia (FSM)
- Kalamazoo County (MI)
- Las Vegas
- Miami Dade County (FL)
- Minneapolis
- Orange County (CA)
- Philadelphia
- Pontiac
- Portland
- San Diego

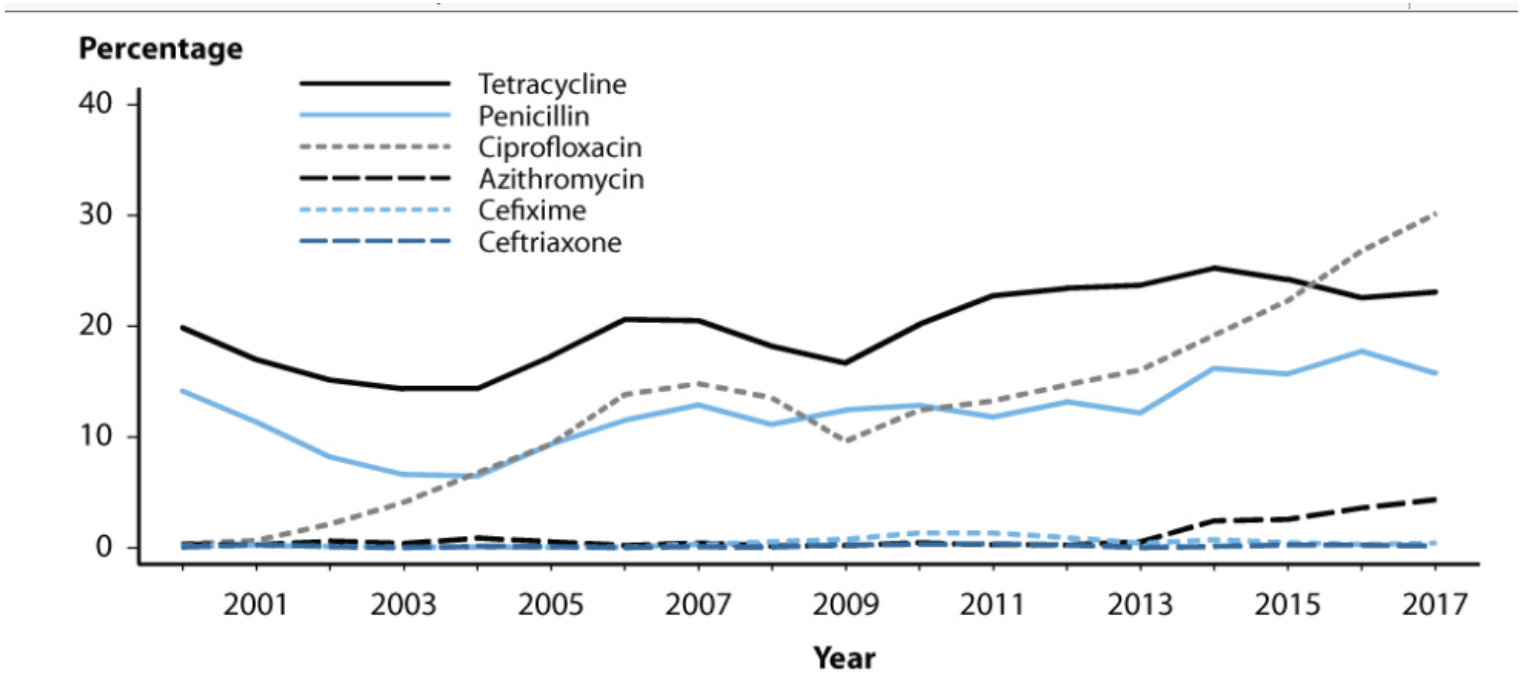
CDC.gov: Revised August 9, 2017

Susceptibility Patterns of *Neisseria gonorrhoeae* Isolates to Antimicrobials, Gonococcal Isolate Surveillance Project (GISP), 2017



CDC.gov

Neisseria gonorrhoeae — Prevalence of Tetracycline, Penicillin, or Fluoroquinolone Resistance* or Elevated Cefixime, Ceftriaxone, or Azithromycin Minimum Inhibitory Concentrations (MICs)†, by Year — Gonococcal Isolate Surveillance Project (GISP), 2000–2017

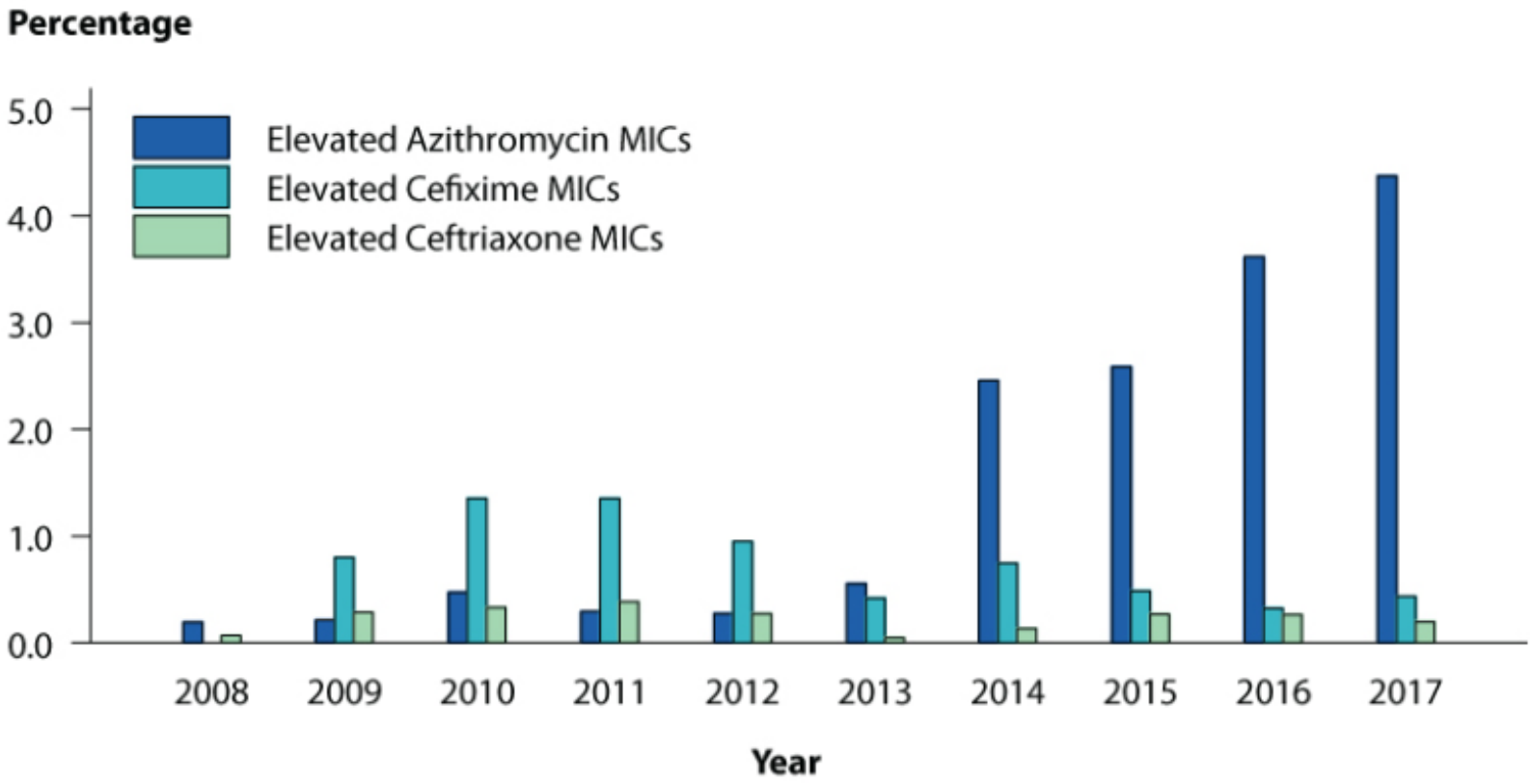


* Resistance: Fluoroquinolone (ciprofloxacin) = MIC ≥1.0 µg/mL; Penicillin = MIC ≥2.0 µg/mL or B-lactamase positive; Tetracycline = MIC ≥2.0 µg/mL.

† Elevated MICs: Azithromycin = MIC ≥1.0 µg/mL (2000–2004); ≥2.0 µg/mL (2005–2017); Ceftriaxone = MIC ≥0.125 µg/mL; Cefixime = MIC ≥0.25 µg/mL.

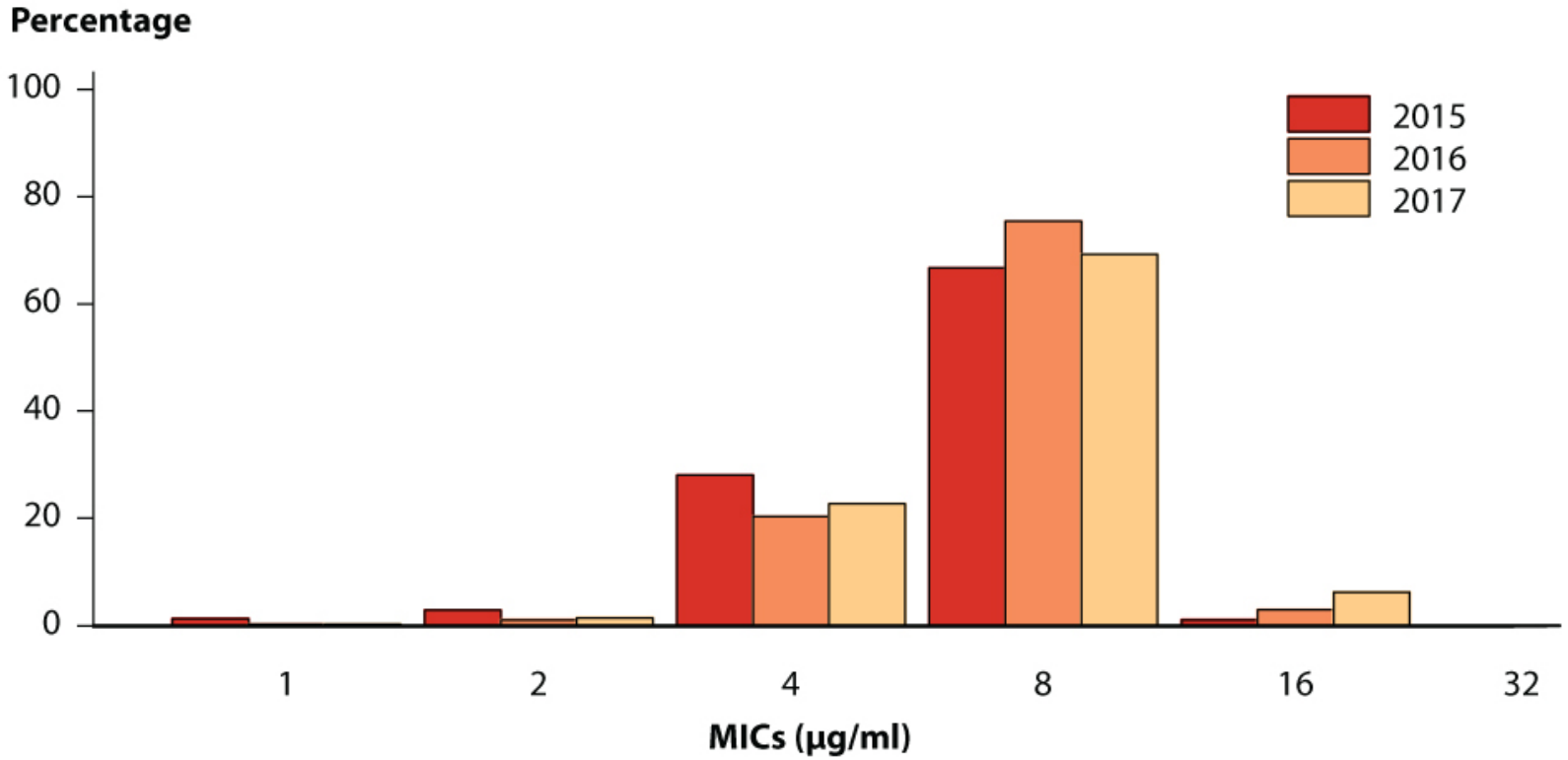
NOTE: Cefixime susceptibility was not tested in 2007 and 2008.

Neisseria gonorrhoeae — Percentage of Isolates with Elevated Azithromycin Minimum Inhibitory Concentrations (MICs) (≥2.0 µg/ml), Elevated Ceftriaxone MICs (≥0.125 µg/ml), and Elevated Cefixime MICs (≥0.25 µg/ml), Gonococcal Isolate Surveillance Project (GISP), 2008–2017 (CDC.gov)



NOTE: Isolates not tested for cefixime susceptibility in 2008.

Neisseria gonorrhoeae — Distribution of Gentamicin Minimum Inhibitory Concentrations (MICs) by Year, Gonococcal Isolate Surveillance Project (GISP), 2015–2017



CDC.gov

Gonorrhea outbreak in Hawaii shows increased antibiotic resistance

By Susan Scutti, CNN

Updated 10:50 AM ET, Thu September 22, 2016

Epi-X The Epidemic Information Exchange

Cluster of Hawaii Gonorrhea Isolates with Diminished Susceptibility to Multiple Antibiotics, Including Very High Azithromycin MIC and Alert-Value Ceftriaxone MIC -- April-May, 2016

The Hawaii DOH has identified 7 cases of gonorrhea infection yielding isolates with uncommon antimicrobial susceptibility testing (AST) profiles, including very high azithromycin minimum inhibitory concentrations (MICs), alert-value ceftriaxone MICs, and elevated MICs for 5 other antibiotics.

Minimum Inhibitory Concentrations, µg/mL

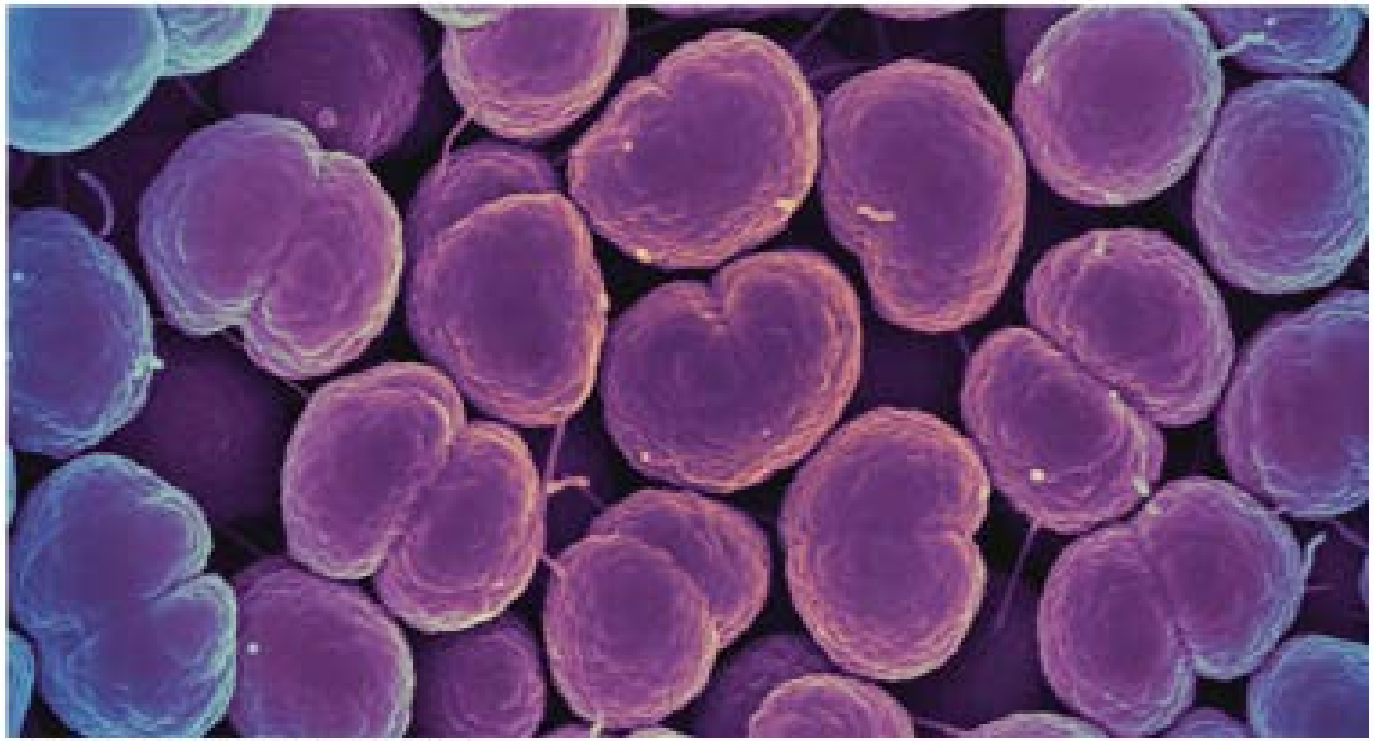
	azithromycin*	ceftriaxone*	cefixime*	penicillin**	tetracycline**	gentamicin**	ciprofloxacin**
1	> 256	0.125	0.094	> 4	4	8	8
2	> 256	0.125	0.094	> 4	4	8	16
3	> 256	0.190	0.190	> 4	4	8	16
4	> 256	0.125	0.125	pending	pending	pending	pending
5	> 256	0.094	0.094	pending	pending	pending	pending
6	> 256	0.125	0.125	pending	pending	pending	pending
7	> 256	0.125	0.094	pending	pending	pending	pending

June 17, 2016

HEALTH

Rare strain of gonorrhea identified in Canada, compounding fears of drug resistance

By HELEN BRANSWELL / NOVEMBER 16, 2017



Neisseria gonorrhoeae bacteria, which cause gonorrhea.

Emerging Infectious Diseases, Vol 24 (2), February 2018

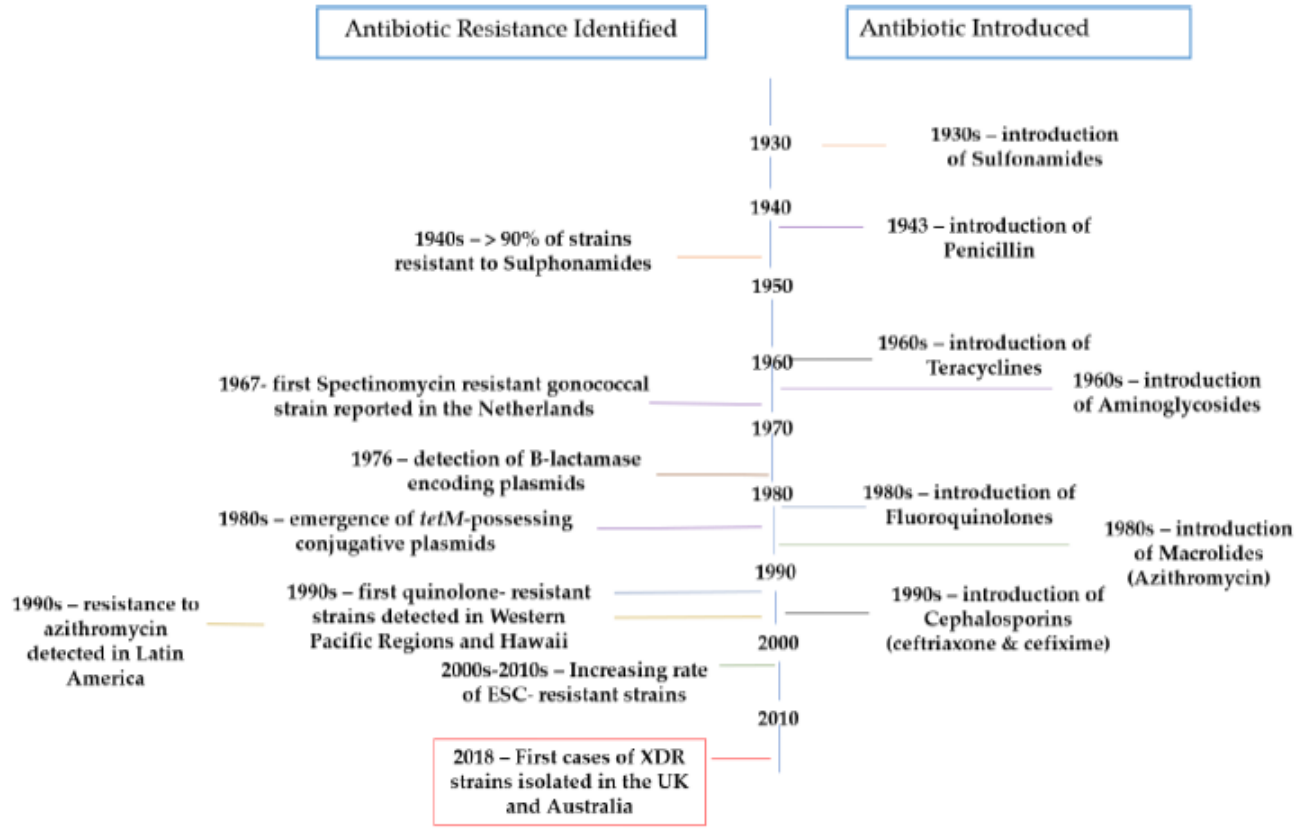
Drug-Resistant *Neisseria gonorrheae*

"This report is one more confirmation of our greatest fear: drug-resistant gonorrhea spreading around the globe," David Harvey, executive director of the National Coalition of STD Directors, told CNN.

- In early 2018, a heterosexual man who reported one regular female sexual partner in the U.K., and one in Southeast Asia about a month before symptom onset — was reported with the world's first confirmed case of gonorrhea that is resistant to both azithromycin and ceftriaxone. He was treated with spectinomycin and subsequently with an intravenous course of ertapenem according to the National Institutes of Health.
- Two other cases of multi-drug resistant gonorrhea was reported by the Australian Government Dept of Health in April 2018. One case from Western Australia and a second from Queensland

European Centre for Disease Prevention and Control. Extensively drug-resistant (XDR) *Neisseria gonorrhoeae* in the United Kingdom and Australia – 7 May 2018. Stockholm: ECDC; 2018

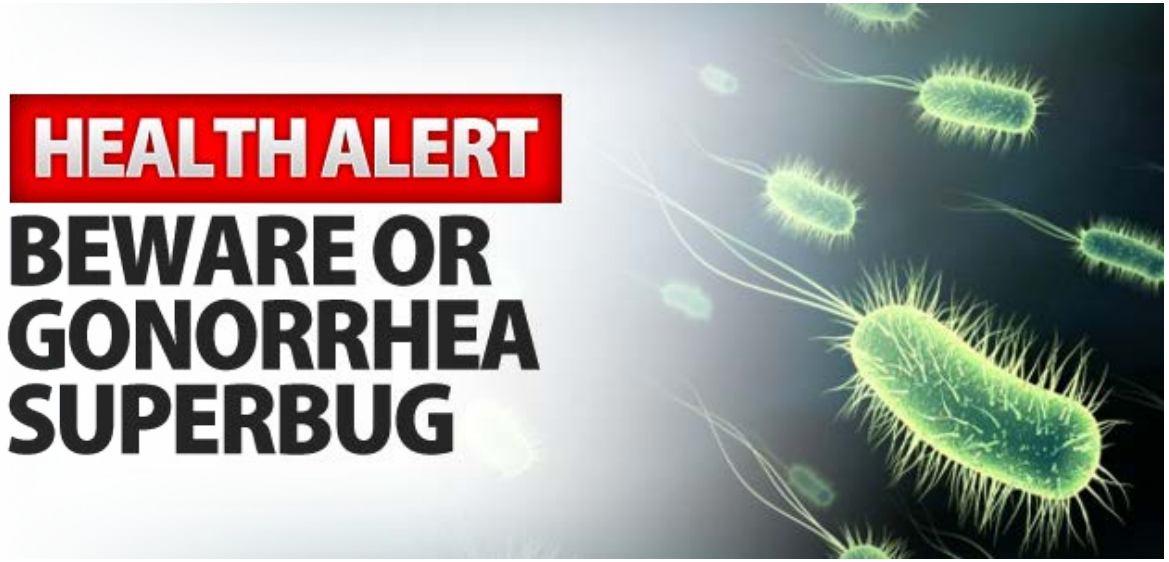
Timeline representing the introduction of treatments used against gonorrhea (right) and the first reports of resistance (left)



Suay-Garcia B: Antibiotics 2018, 7, 49

Cephalosporin treatment failures

- Oral cephalosporin treatment failures reported worldwide
  - Japan, Hong Kong, England, Austria, Norway, France, South Africa, Canada
- Ceftriaxone treatment failures in pharyngeal gonorrhea and a few isolates with high-level ceftriaxone resistance reported



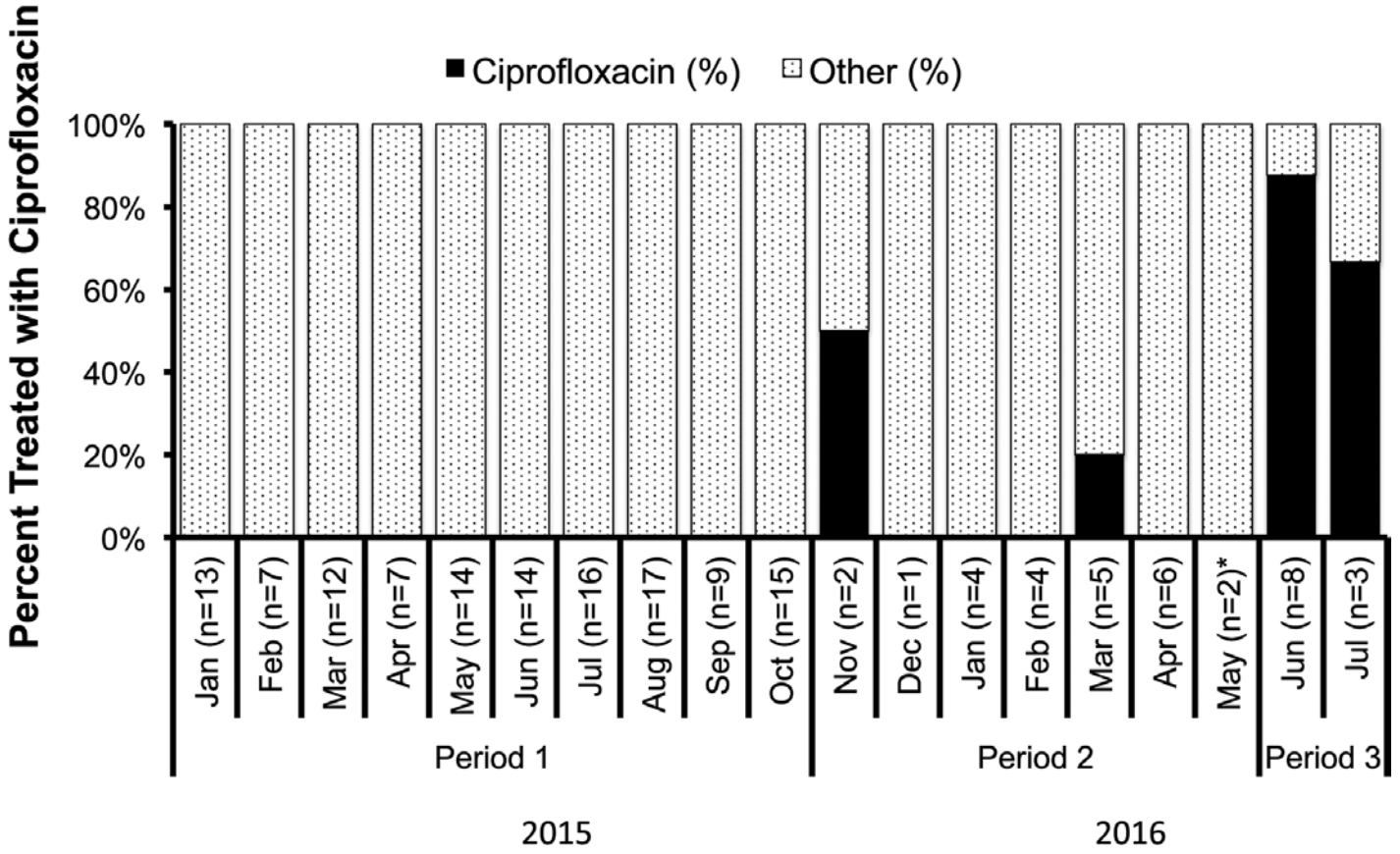
Single dose treatment guidelines for gonorrhea worldwide

WHO * [11]	Australasia [12]	Canada [13]	USA [14]	UK [15]	EU [16]	New Zealand [17]
Ceftriaxone 250 mg IM + Azithromycin 1 g PO Or ** Cefixime 400 mg PO + Azithromycin 1 g PO	Cetriaxone 500 mg IM + Azithromycin 1 g PO	Ceftriaxone 250 mg IM + Azithromycin 1 g PO	Ceftriaxone 250 mg IM + Azithromycin 1 g PO	Ceftriaxone 500 mg IM + Azithromycin 1 g PO	Ceftriaxone 500 mg IM + Azithromycin 1 g PO	Ceftriaxone 250 mg IM + Azithromycin 1 g PO
Ceftriaxone 500 mg IM + Azithromycin 2 g PO Or ** Cefixime 800 mg PO + Azithromycin 2 g PO Or ** Gentamicin 240 mg IM + Azithromycin 2 g PO Or ** Spectinomycin 2 g IM + Azithromycin 2 g PO		Cefixime 800 mg PO + Azithromycin 1 g PO Or ** Spectinomycin 2 g IM + Azithromycin 1 g PO	Cefixime 400 mg PO + Azithromycin 1 g PO	Cefixime 400 mg PO + Azithromycin 1 g PO Or ** Spectinomycin 2 g IM + Azithromycin 1 g PO Or ** Cefotaxime 500 mg IM + Azithromycin 1 g PO	Cefixime 400 mg PO + Azithromycin 2 g PO Or ** Spectinomycin 2 g IM + Azithromycin 2 g PO	Spectinomycin 2 g IM + Azithromycin 1 g PO Or ** Gentamicin 240 mg IM + Azithromycin 2 g PO

* WHO (World Health Organization); IM (Intramuscular); PO (Per os-oral) ** An "or" between combinations means that any of those combinations may be prescribed.

Suay-Garcia B: Antibiotics 2018, 7, 49

Use of Ciprofloxacin Increased in Non-Empirically Treated *gyr*A Wild-Type *N. Gonorrhoea* cases



Klausner J et. al; Implementation of a Rapid Genotypic Assay to Promote Targeted Ciprofloxacin Therapy of *Neisseria gonorrhoeae* in a Large Health System, *Clinical Infectious Diseases*, Volume 64, Issue 9, 1 May 2017, Pages 1268–1270, https://doi.org/10.1093/cid/ciw864

World Health Organization

GLOBAL PRIORITY LIST OF ANTIBIOTIC-RESISTANT BACTERIA TO GUIDE RESEARCH, DISCOVERY, AND DEVELOPMENT OF NEW ANTIBIOTICS

NTY OF LOS ANGELES
blic Health

Priority 1: CRITICAL#

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae**, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

- *Enterococcus faecium*, vancomycin-resistant
- *Staphylococcus aureus*, methicillin-resistant, vancomycin intermediate and resistant
- *Helicobacter pylori*, clarithromycin-resistant
- *Campylobacter*, fluoroquinolone-resistant
- *Salmonella spp.*, fluoroquinolone-resistant
- *Neisseria gonorrhoeae*, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

- *Streptococcus pneumoniae*, penicillin-non-susceptible
- *Haemophilus influenzae*, ampicillin-resistant
- *Shigella spp.*, fluoroquinolone-resistant

Publication date:
February 27, 2017

Antibiotics in the Pipeline

- Solithromycin: novel oral fluoroketolide
- Phase 2 trial (1200 mg and 1000 mg) GC treatment
  - 100% cured (neg culture) with either dose
  - GI side effects common and dose-related
- Two phase 3 trials demonstrate non-inferiority to moxifloxacin for CAP
- Submitted for fast-track FDA approval for CAP

- **Drugs in Development**
  - Zoliflodacin (ETX0914/AZD0914)
    - Topoisomerase II inhibitor (spiropyrimidinetrione)
    - Activity against NG isolates with ciprofloxacin resistance and reduced susceptibility to extended-spectrum cephalosporins

Hook EW et al, CID 2015; Fernandez P et al, Bioorg Med Chem 2016; Alm RA, Antimicrob Agents Chem. 2015

Emerging infections: *Neisseria meningitides* as an STD

- Japanese patient, 2013: Urethritis in MSM with HIV
- Ohio and Michigan, 2015: urethritis in MSW, no capsule, serogroup C
- Associated with urethritis, cervicitis, proctitis, and PID
- Treat as for GC:

Ceftriaxone 250mg IM once

AND

Azithromycin 1g PO once

Hayakawa, K et al EID 2014.
Bazan, JA et al MMWR 2015.

Effectiveness of a group B outer membrane vesicle meningococcal vaccine against gonorrhea in New Zealand: a retrospective case-control study

- Exposure to MeNZB was associated with reduced rates of gonorrhea diagnosis, the first time a vaccine has shown any protection against gonorrhea. These results provide a proof of principle that can inform prospective vaccine development not only for gonorrhea but also for meningococcal vaccines.

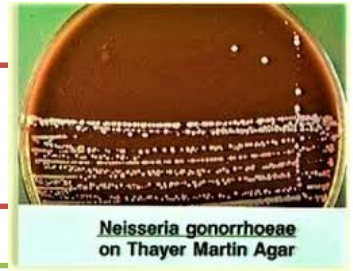
Petousis-Harris H et. al. Lancet. 2017;390 :1603-1610

Suspected GC Treatment Failure

County of Los Angeles Public Health

TEST WITH CULTURE AND NAAT:

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



Neisseria gonorrhoeae on Thayer Martin Agar

REPEAT TREATMENT:

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

REPORT:

- To your local health department within 24 hours

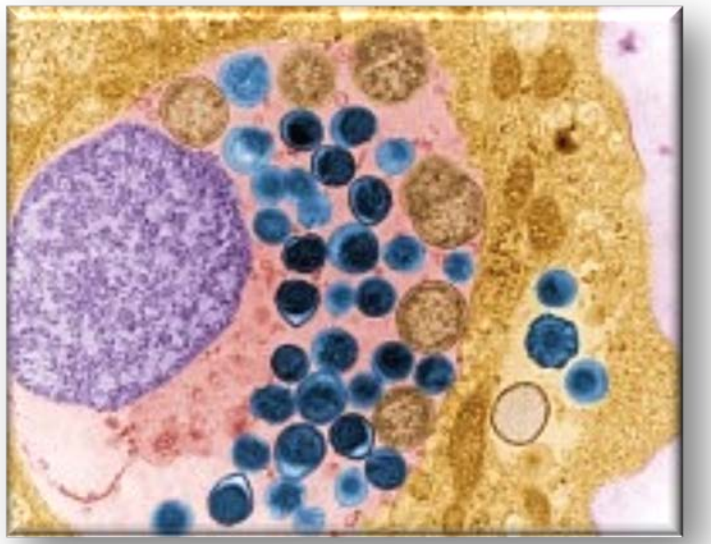
TEST AND TREAT PARTNERS:

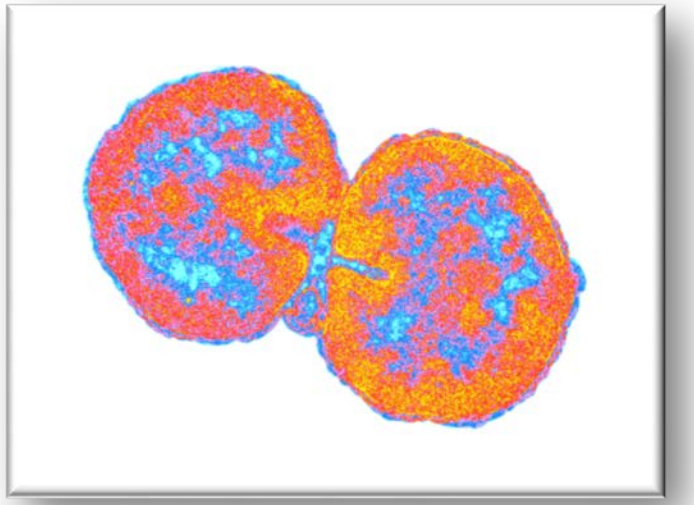
- Treat all partners in last 60 days with same regimen

TEST OF CURE (TOC):

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

Expert consultation available at www.stdccn.org





Partner Treatment

CT/GC Partner Management Options:

All sexual contacts in past 60 days need treatment

Health department referral

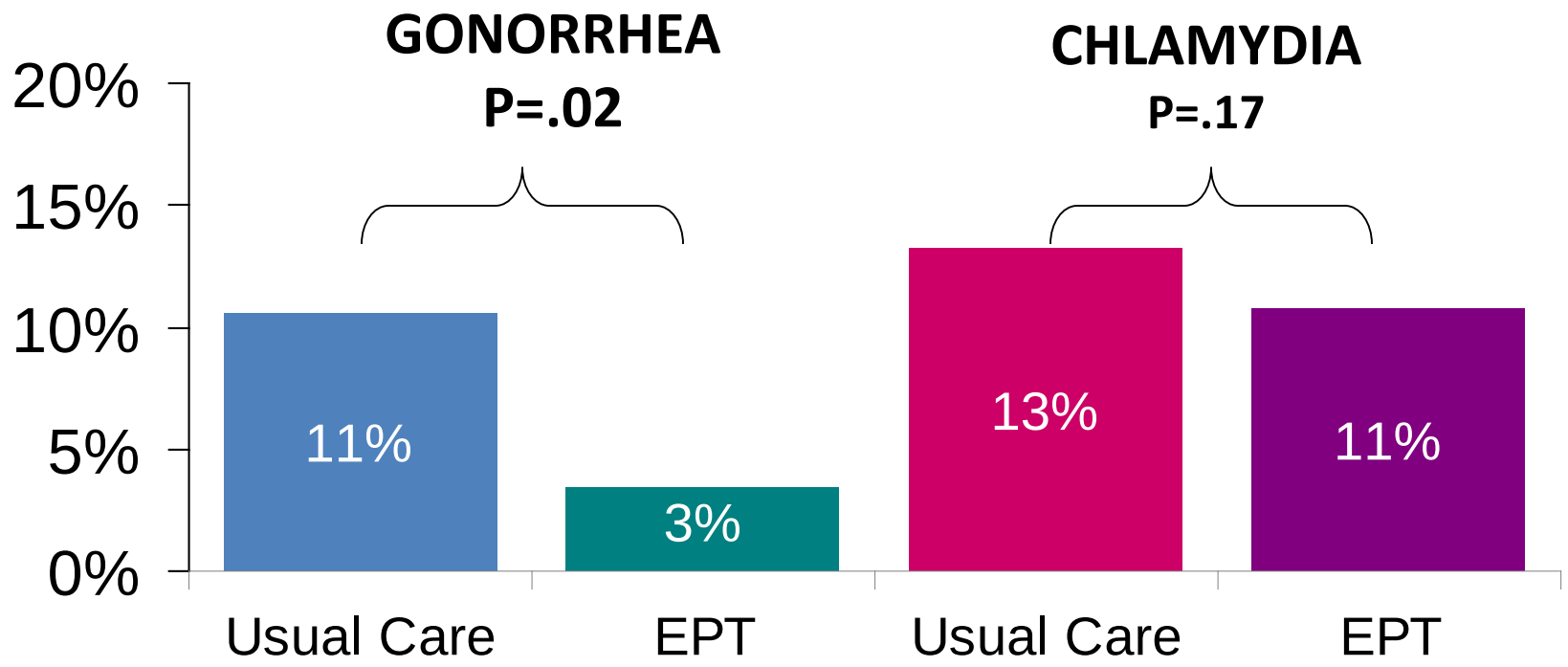
Provider or clinic-based referral

Expedited partner treatment (EPT)

Patient referral

- Suggest patient bring partner to clinic for concurrent treatment (“BYOP” or “CTOP”)
- Ask patient to notify partner and ensure treatment
- Suggest anonymous notification via Internet

The Effectiveness of Expedited Partner Treatment on Re-Infection Rates

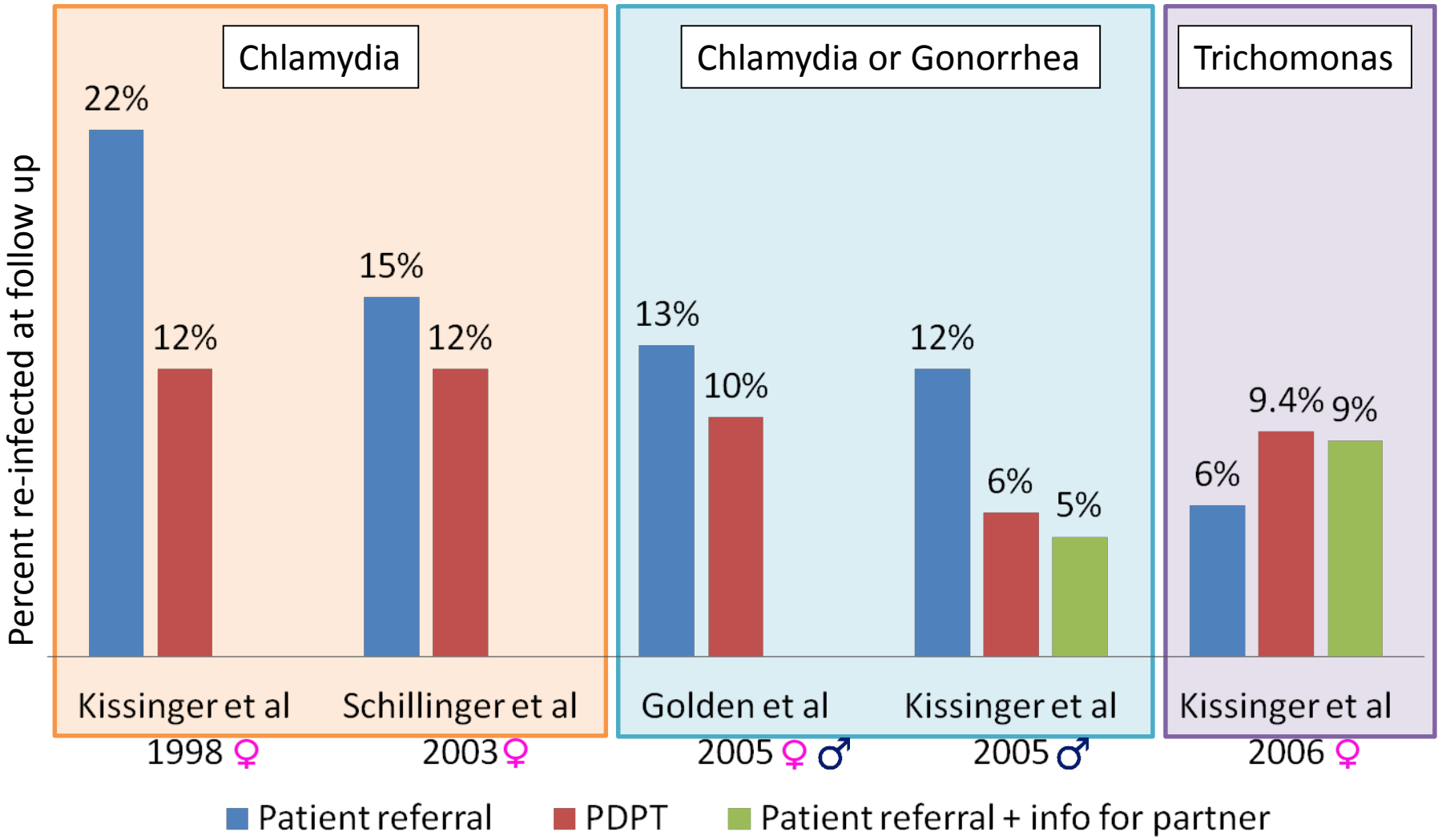


Golden M, et al. N Engl J Med 2005 Feb 17;352(7):676-85.

PDPT Effectiveness in Randomized Controlled Trials

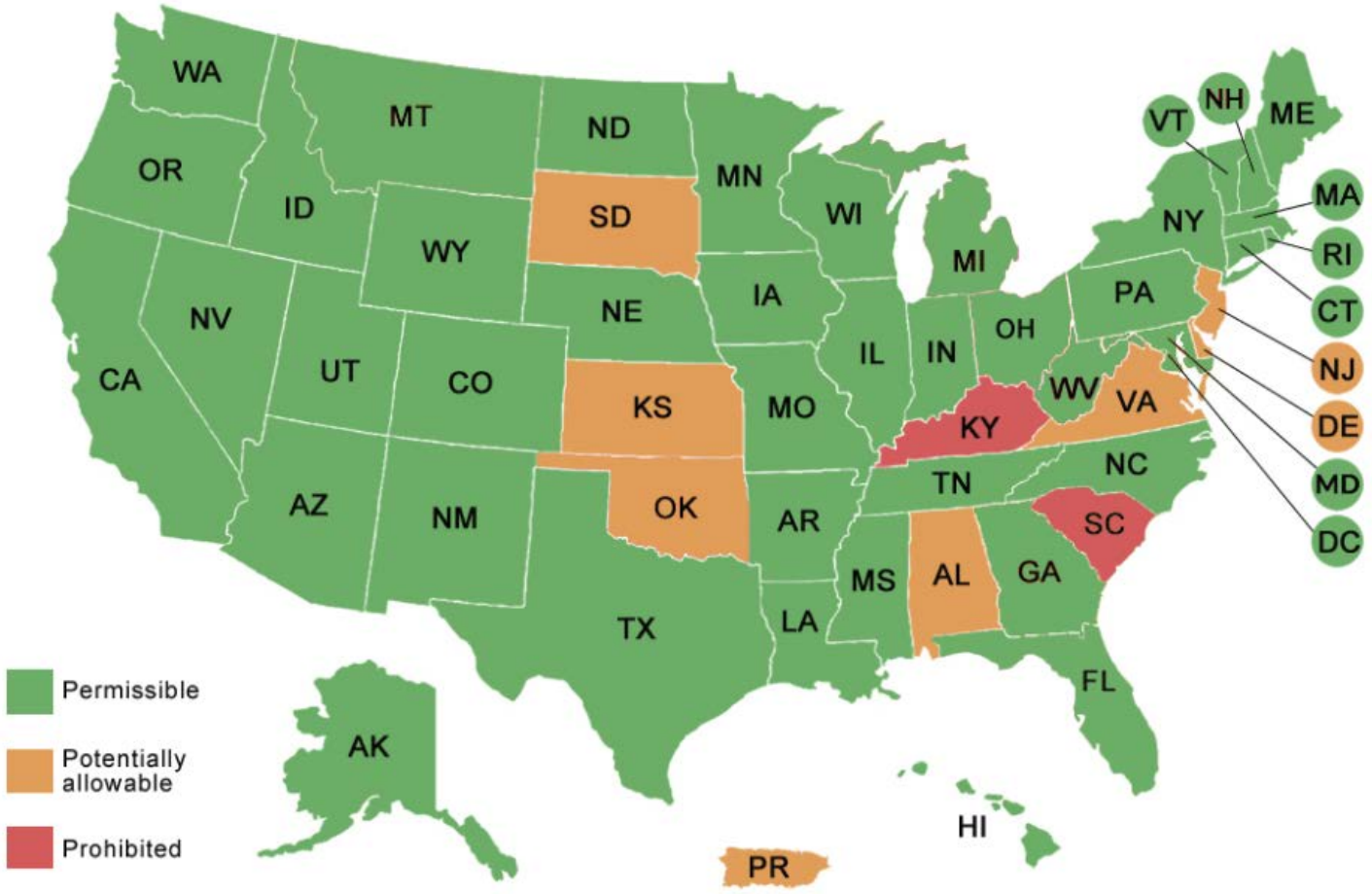
County of Los Angeles Public Health

Reduces reinfection with chlamydia & gonorrhea, but not trichomonas



Source: Trelle S, et al. Improved effectiveness of partner notification for patients with sexually transmitted infections: systematic review. BMJ. 2007;334:354.

Legal Status in U.S.



Centers for Disease Control and Prevention. Legal Status of Expedited Partner Therapy. July 2017. http://www.cdc.gov/std/ept/legal/default.htm

CDC Centers for Disease Control and Prevention

CDPH California Department of PublicHealth

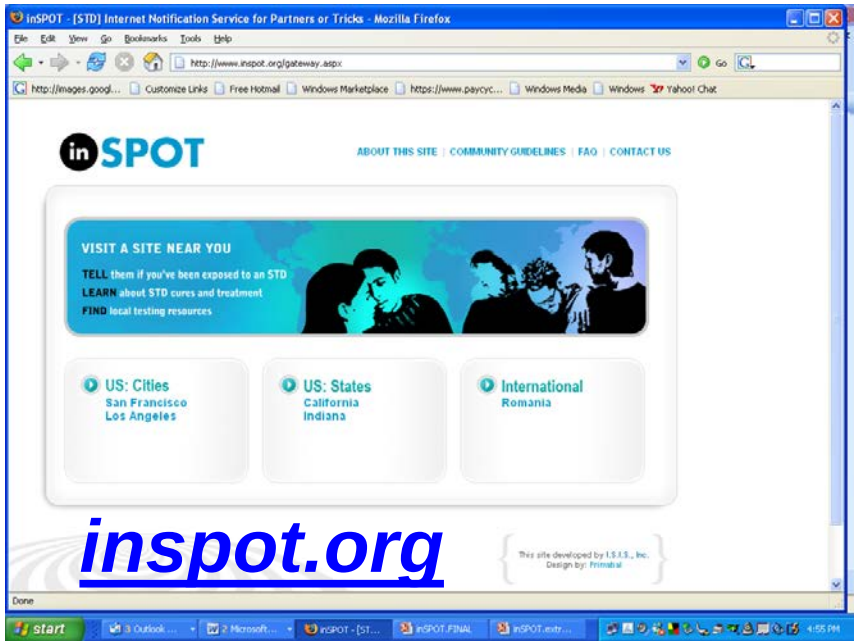
STD Controllers association

CAPTC

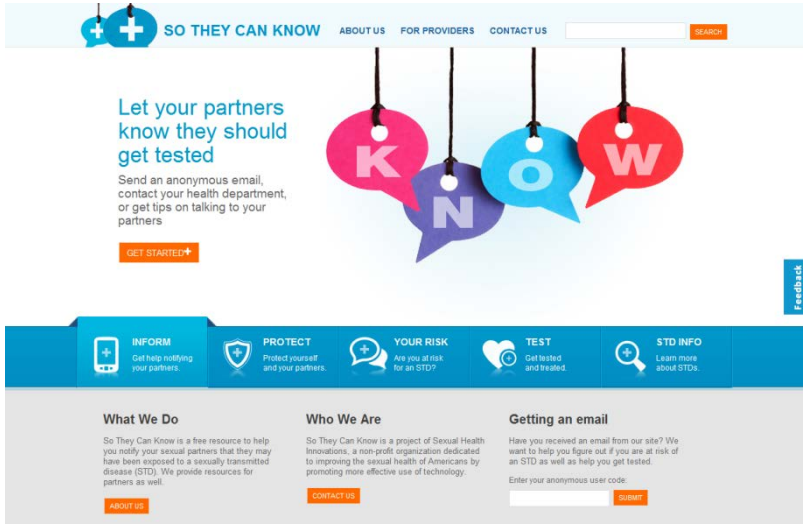
Patient-Delivered Partner Therapy (PDPT) for Chlamydia, Gonorrhea, and Trichomoniasis: Guidance for Medical Providers in California

www.std.ca.gov: https://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/Clinical-Guidelines-CA-STD-PDPT.pdf

Online Anonymous Partner Referral

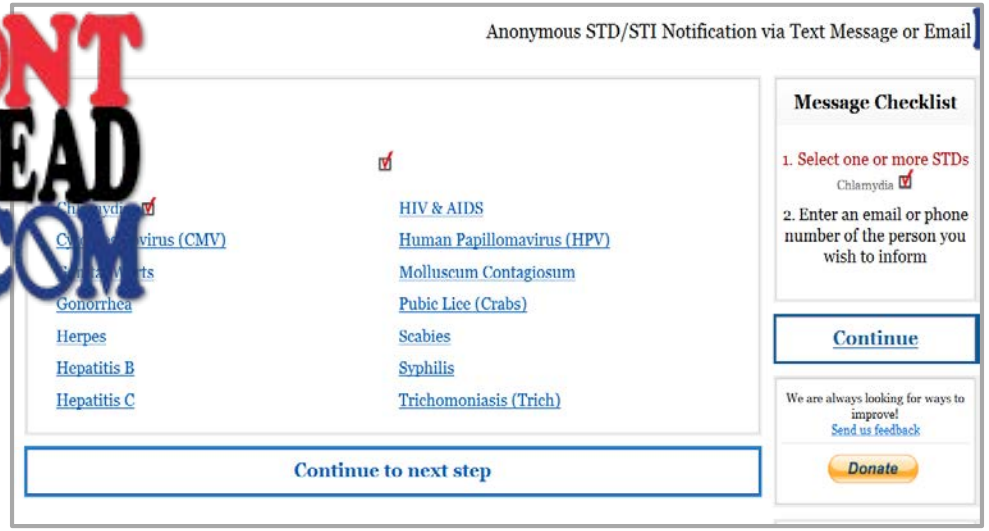


inspot.org

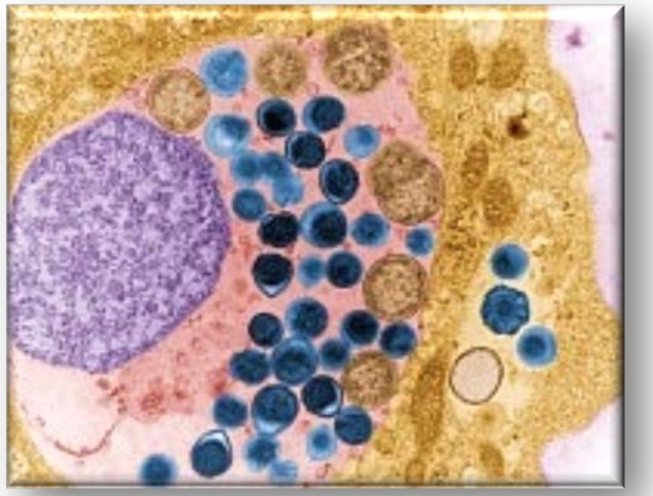


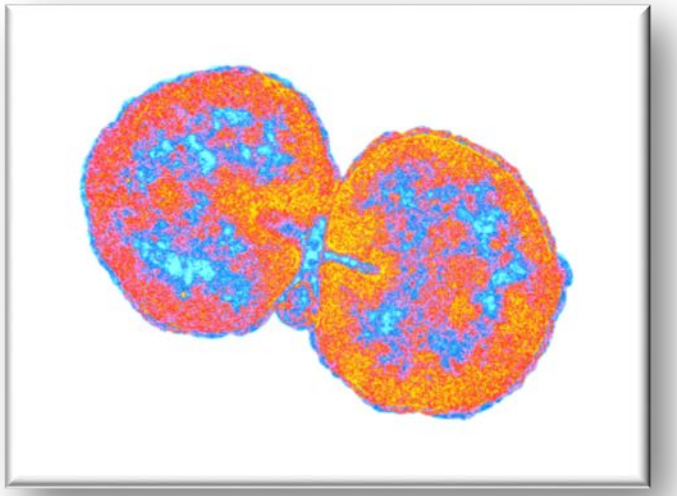
sotheycanknow.org

DONT SPREAD IT.COM



dontspreadit.com

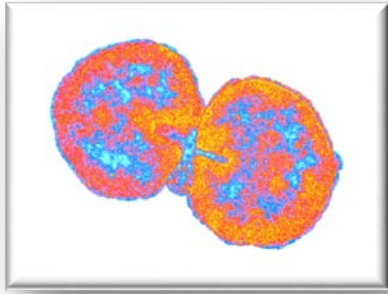


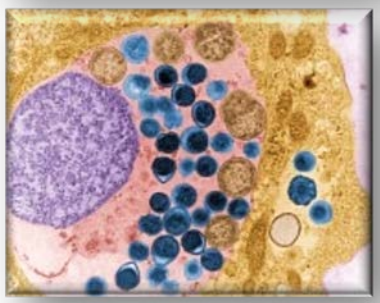


CT/GC Retesting for Repeat Infection

CT/GC Retesting for Repeat Infection

County of Los Angeles Public Health





How soon can I retest for CT/GC?

- Need to wait at least **3 weeks** for CT to clear
- GC can clear by 1-2 weeks (2 weeks for pharyngeal infection)
- 3 months is the target, but retest opportunistically whenever patient returns in the next 1-12 months
- Pregnant patients, 14 days after tx, using NAAT
- Obtain test of cure 14 days after tx, using either culture or NAAT
  - Patients with pharyngeal GC treated with an alternative tx
  - Cases of suspected tx failure (culture AND simultaneous NAAT)
  - Consider if using non-recommended or monotherapy

CDC 2015 STD Tx Guidelines, www.cdc.gov/std/treatment

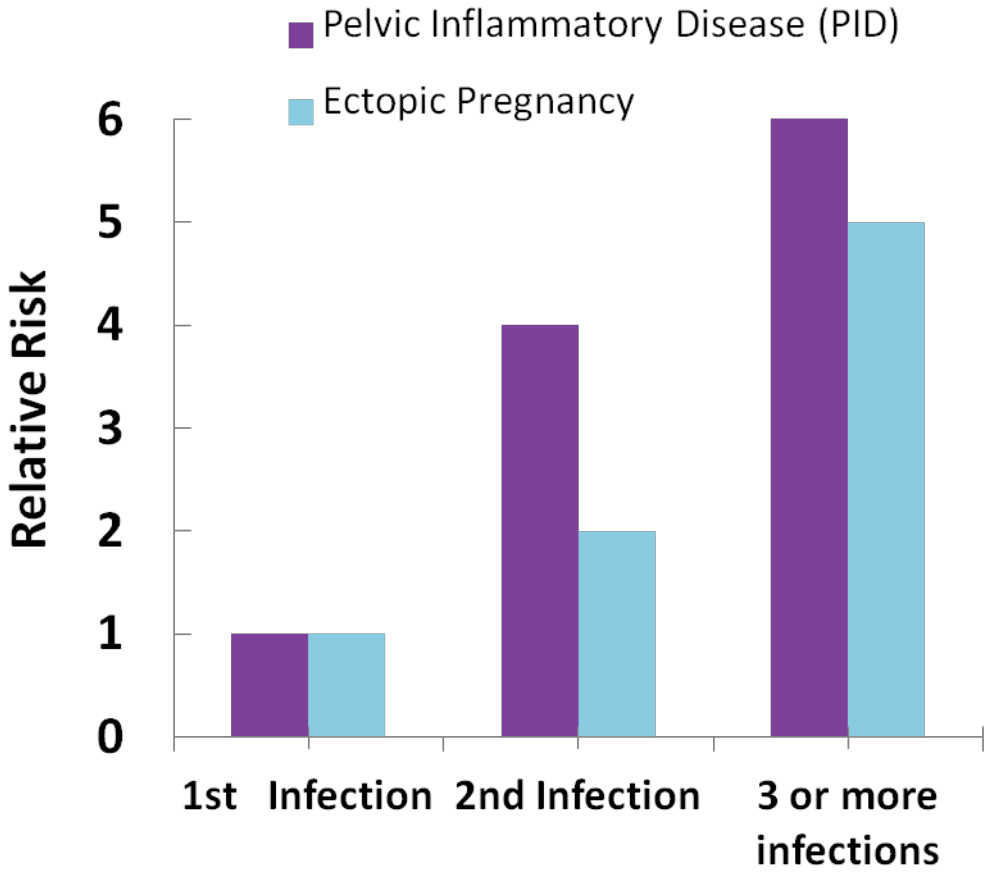
Reinfection is Dangerous

2nd infection:

- 4x risk of PID
- 2x risk of ectopic pregnancy

3+ infections:

- 6x risk of PID
- 5x risk of ectopic pregnancy



Prepared by: CDPH STD Control Branch

Hillis SD, et al. (1997). Am J Obstet Gynecol 176: 103-7

Testing After an STD Infection

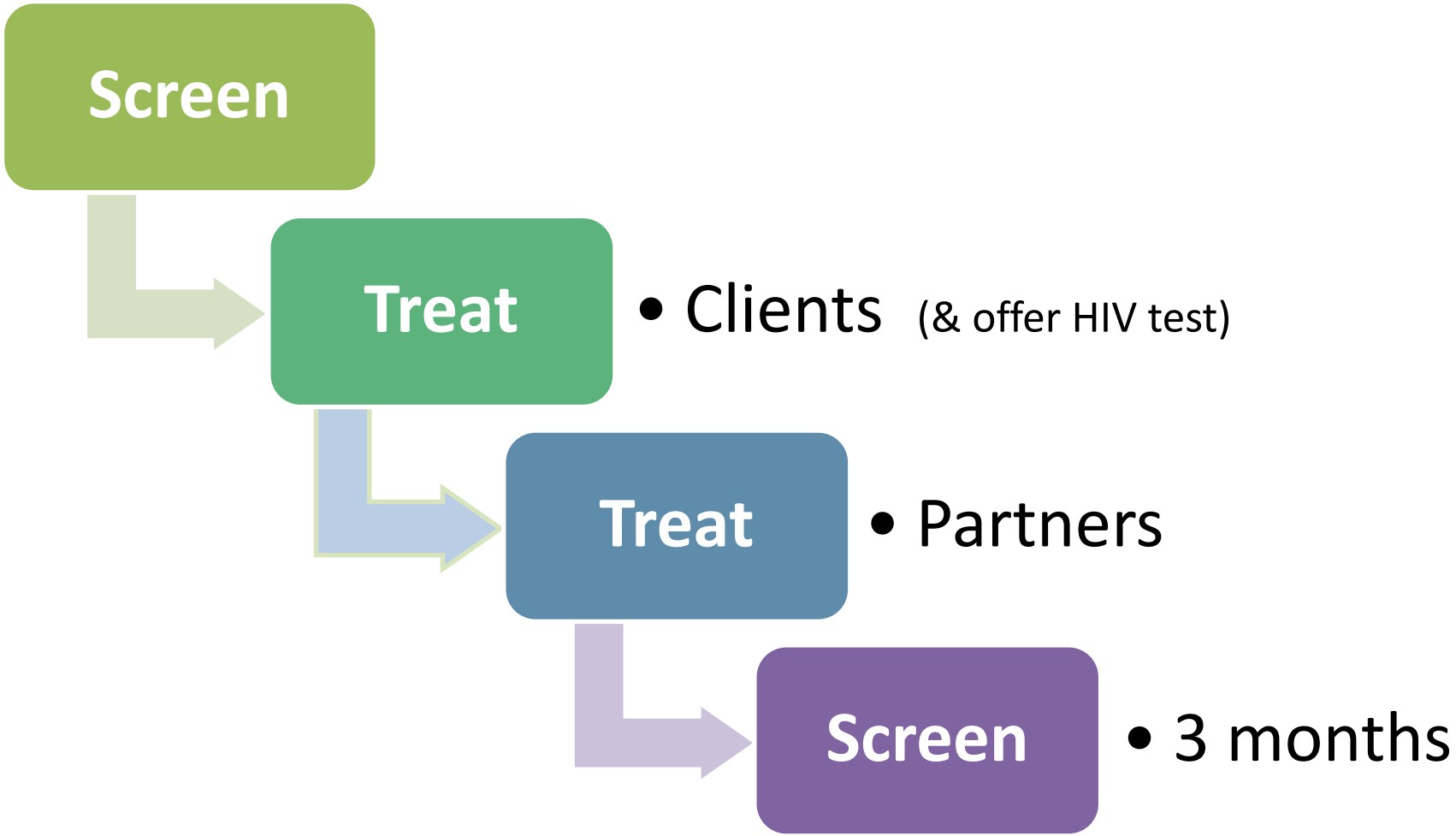
- Women who test positive for CT/GC, or trichomonas should be rescreened three months following treatment

- Men who test positive for chlamydia or gonorrhea should be rescreened at three months after adequate therapy

- All patients with a bacterial STDs or trichomonas should be tested for other STDs including CT/GC, syphilis, and HIV

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

CT/GC Management in a Nutshell…



Screening Guidelines

Gonorrhea	
Women	• Sexually active women under 25 years of age[1] • Sexually active women age 25 years and older if at increased risk[9] • Retest 3 months after treatment[10]
Pregnant Women	• All pregnant women under 25 years of age and older women if at increased risk[11] • Retest 3 months after treatment[10]
Men Who have Sex With Men (MSM)	• At least annually for sexually active MSM at sites of contact (urethra, rectum, pharynx) regardless of condom use[10] • Every 3 to 6 months if at increased risk[7]
Persons with HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter[10] • More frequent screening for might be appropriate depending on individual risk behaviors and the local epidemiology[10]

SOURCE: CDC.GOV

Chlamydia	
Women	• Sexually active women under 25 years of age[1] • Sexually active women aged 25 years and older if at increased risk[2] • Retest approximately 3 months after treatment[3]
Pregnant Women	• All pregnant women under 25 years of age[1] • Pregnant women, aged 25 and older if at increased risk[2] • Retest during the 3rd trimester for women under 25 years of age or at risk[3,4] • Pregnant women with chlamydial infection should have a test-of-cure 3-4 weeks after treatment and be retested within 3 months[1]
Men	• *Consider screening young men in high prevalence clinical settings[5] or in populations with high burden of infection (e.g. MSM)[6]
Men Who have Sex With Men (MSM)	• At least annually for sexually active MSM at sites of contact (urethra, rectum) regardless of condom use[6] • Every 3 to 6 months if at increased risk[7]
Persons with HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter[8] • More frequent screening for might be appropriate depending on individual risk behaviors and the local epidemiology[8]

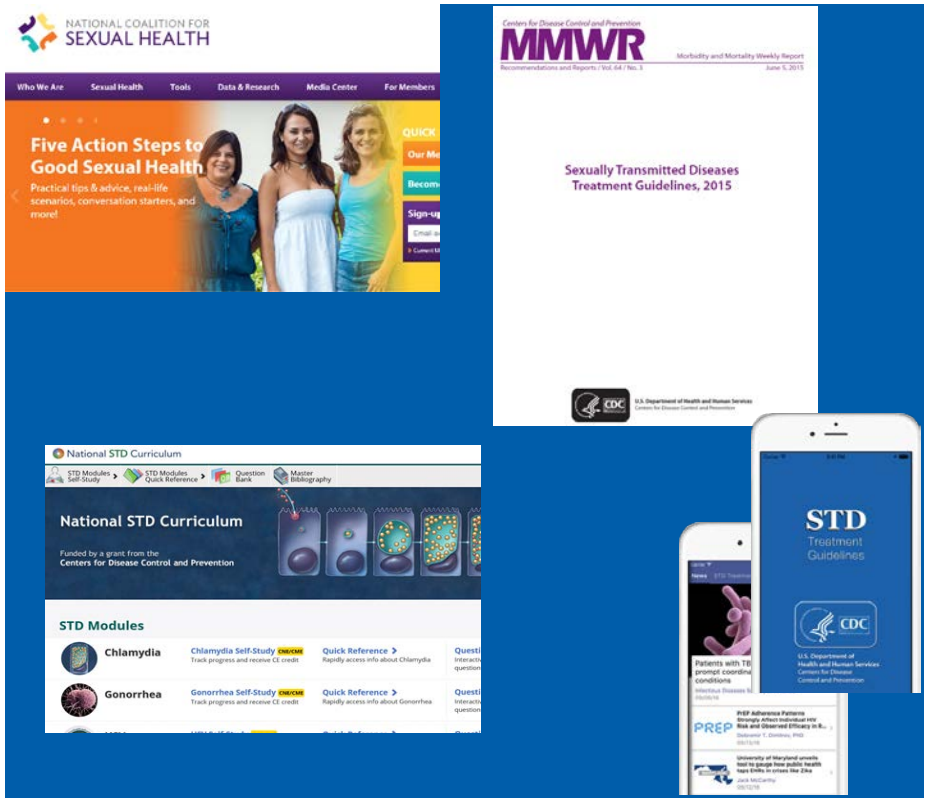
** USPSTF recommends screening in adults and adolescents ages 15-65

Take home points

- Upward trends:
  - CT: more than 1.7 million cases diagnosed in 2017, with 45 percent among 15- to 24-year-old females
  - GC: 333,004 cases reported in 2017: ~67% increase from 2013
- STI testing at extragenital sites is key—self collected swabs can help improve screening rates
- *N. gonorrheae* azithromycin resistance increasing-dual treatment indicated, a few new treatment options in the pipeline
- Expedited partner treatment helpful at reducing reinfections with CT/GC
- Remember to retest at 3 months after treatment (anytime after 3 weeks also ok)
- Cases of suspected resistance or treatment failure should be reported to public health and specimens sent for culture.
- *N. meningitidis* can cause urethritis that tests negative for GC on NAAT.
- Contact your local public health department for clinical consultation or go to stdccn.org

Emerging STI issues: *N. meningitides, M. genitalium; LGV, trichomonas, Zika*

STD Resources

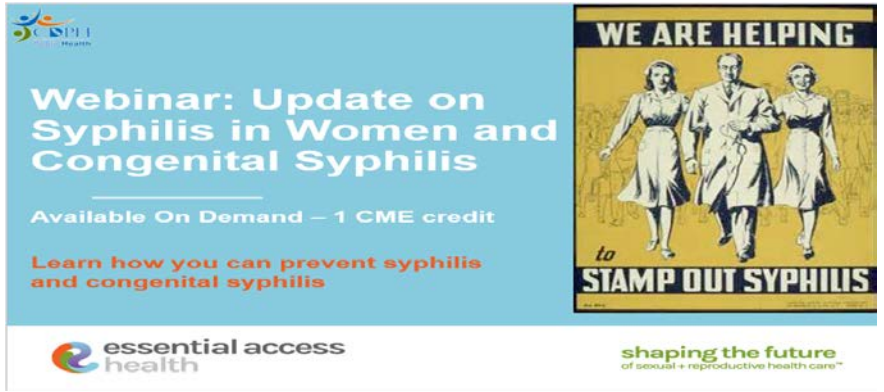


National Coalition for Sexual Health:
https://nationalcoalitionforsexualhealth.org/

CDC: cdc.gov/std/

STD Treatment Guidelines:
www.cdc.gov/std/tg2015 /default.htm
(*Free* app available for download)

Webinar presented by Dr. Julie Stoltey, STD Control Branch at the California Department of Public Health
Available at http://bit.ly/2hYhuME



Thank you!

Dr. Gail Bolan

Dr. Heidi Bauer

Dr. Sarah Guerry

Dr. Stephanie Cohen

Dr. Sarah Lewis

Dr. Sharon Adler

Dr. Ina Park

Dr. Leo Moore

Monica Munoz

Melissa Pap-Green

Our Amazing team at LA County DPH: DHSP

Questions ?

Downtown Los Angeles with San Gabriel Mountains in the background

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