2020 Ryan White HIV/AIDS Program
CLINICAL CONFERENCE

Syphilis: Reemergence of the Great Pretender? (It never really left!)

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Financial Relationships With Commercial Entities

Dr Augenbraun has no relevant financial affiliations to disclose. (Updated 08/05/20)

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Learning Objectives

After attending this presentation, learners will be able to:

- Describe the natural history of syphilis
- Initiate diagnostic work up for syphilis
- Manage syphilis

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- spirochete *Treponema pallidum spp. pallidum*

- Other treponemal pathogens:

T. pallidum spp. pertenue (yaws)
T. pallidum spp. endemicum (bejel)
T. carateum (pinta)
Cannot be cultivated in vitro

Darkfield Microscopy

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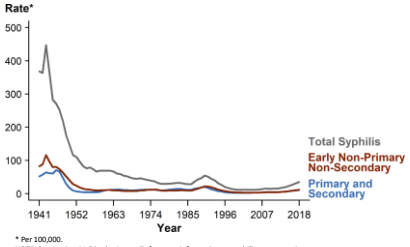
Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2018



* Per 100,000.
NOTE: See section A1.3 in the Appendix for more information on syphilis case reporting.

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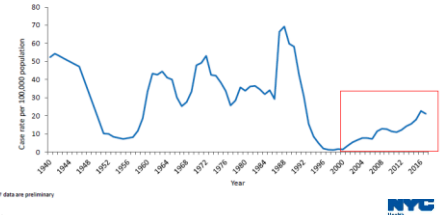
Primary and secondary syphilis case rates (per 100,000), New York City, 1940-2017*



* 2017 data are preliminary

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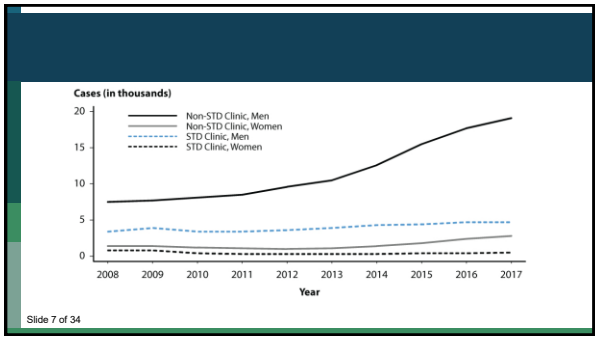
Cases (in thousands)
20
15
10
5
0
Non-STD Clinic, Men
Non-STD Clinic, Women
STD Clinic, Men
STD Clinic, Women
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Year
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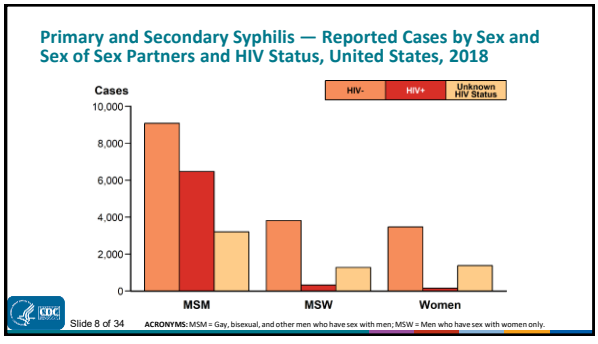
Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners and HIV Status, United States, 2018
Cases
HIV-
HIV+
Unknown HIV Status
10,000
8,000
6,000
4,000
2,000
0
MSM
MSW
Women
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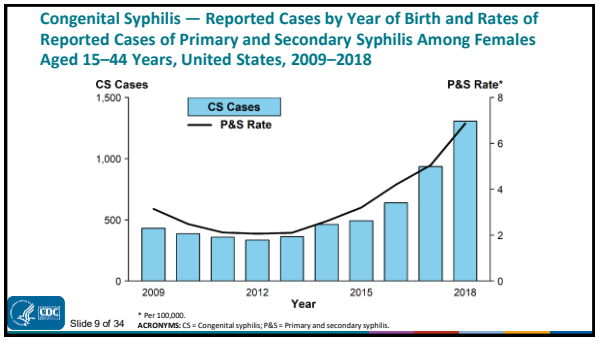
ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only.


Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Females Aged 15–44 Years, United States, 2009–2018
CS Cases
P&S Rate*
1,500
1,000
500
0
CS Cases
P&S Rate
8
6
4
2
0
2009
2012
2015
2018
Year
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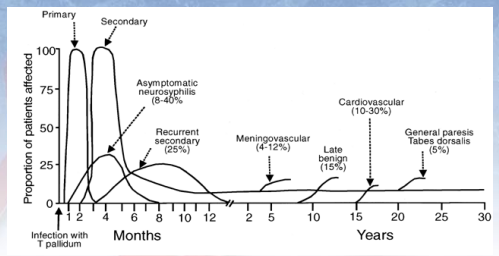
* Per 100,000.
ACRONYMS: CS = Congenital syphilis; P&S = Primary and secondary syphilis.

Natural History of Syphilis



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Neurosyphilis

- Early CNS invasion-clinical implications?
- Acute Symptomatic Meningitis
- Asymptomatic Meningitis
- Meningovascular events
- General Paresis
- Tabes dorsalis
- Gumma
- Ocular and otic

- Neurosyphilis should be considered for anyone with serologic evidence of syphilis and neuropsychiatric and/or ocular or otic disease.

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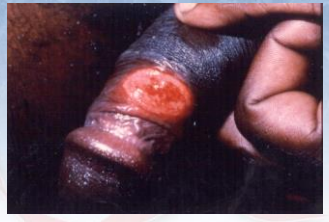
Chancre of Primary Syphilis



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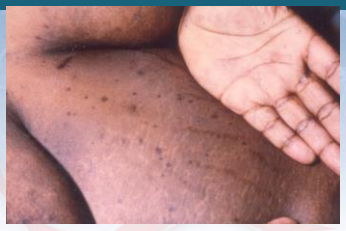
Secondary Syphilis



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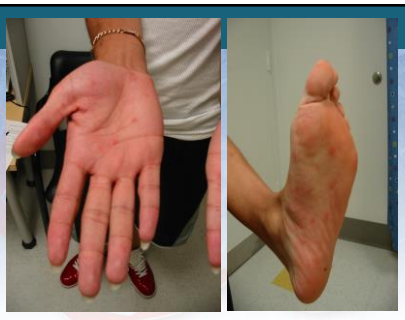

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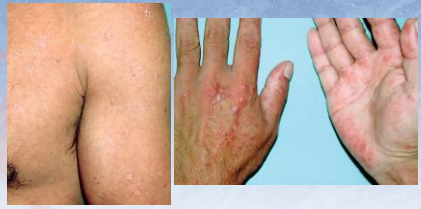

Kingston, A. A. et al. Arch Dermatol 2005;141:431-433.

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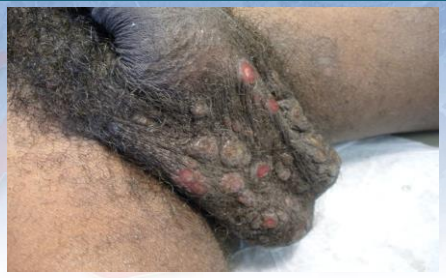
Condylomata lata/Condyloma latum



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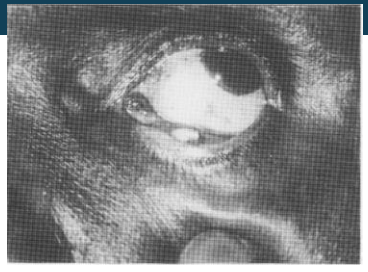

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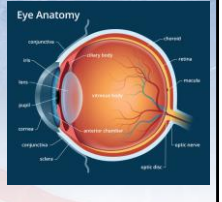
Ocular Syphilis

- **Eye involvement occurs most frequently in secondary syphilis and late syphilis**
- **Almost every part of the eye can be involved.**
- **The vast majority of eye problems associated with syphilis are also associated with many other infectious and non-infectious diseases.**
- **Therefore- there are almost no eye findings that are absolutely specific for syphilis.**



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CDC, MMWR November 4, 2016
Ocular Syphilis – Eight Jurisdictions, U.S., 2014-2015

- Following April 2015 report, eight jurisdictions (CA, FL, IN, MD, NYC, NC, TX, WA) reviewed syphilis surveillance and case data
- 388 suspected ocular syphilis were identified: 157 in 2014 and 231 in 2015 (0.53% and 0.65%)
- 93% men (high proportion MSM), 51% HIV co-infected
- 84% had symptoms: 54% blurry vision; 28% vision loss
- 158 (41%) had a specific dx: Uveitis (n=72); retinitis (N=20), optic neuritis (N=18) and retinal detachment (N=6)
- Of 136 patients with available data, 64 (47%) had one eye involved and 72 (53%) had both eyes involved
- 174 had CSF results, 122 (70%) had +CSF VDRL

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Diagnostics: Traditional Serologic Testing

Two-step testing:

NTST: Non-Treponemal Serologic Test (e.g RPR, VDRL)
- can be quantified
- rises with active disease or failed therapy
- declines with successful therapy or latency

If reactive then followed by

TST: Treponemal Serologic Test (e.g. FTA, TPPA, Treponemal IgG)
- not quantifiable
- life long reactivity

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Screening for Syphilis: Updated Evidence Report and Systemic Review for the US Preventive Service Task Force
JAMA 2016(315): 2328

Table 1. Sensitivity and Specificity of Commonly Used Syphilis Tests[a,10a]

Syphilis Screening Test	Sensitivity by Stage of Untreated Syphilis, % (Range)[b]					Specificity, % (Range)[b]
	Mixed	Primary	Secondary	Latent	Tertiary	
Nontreponemal						
VDRL[c]		78 (74-87)	100	96 (88-100)	71 (37-94)	98 (96-99)
RPR[c]		86 (77-99)	100	98 (95-100)	73	98 (93-99)
TRUST[c]		85 (77-86)	100	98 (95-100)		99 (98-99)
USR[c]		80 (72-88)	100	95 (88-100)		99
Treponemal						
FTA-ABS[d]		84 (70-100)	100	100	96	97 (84-100)
TPPA[e]		88 (86-100)	100	97 (97-100)	94	96 (95-100)
Enzyme immunoassay		(77-100)	(85-100)	(64-100)	NA	(99-100)
Trep-Check	95.9[e]					98.5[e]
Trep-Sure	96.9[e]					95.4[e]
Chemiluminescence immunoassay		98	100	100	100	99
LIAISON[e]	99.2					99.9
Multiplex flow immunoassay						
BioPlex 2200, Syphilis IgG	96.9[e]					98.0[e]
Syphilis Health Check	95.6,[e] 98.5[e]					90.5,[e] 97.4[e]

Abbreviations: FTA-ABS, fluorescent treponemal antibody absorption; NA, not applicable; RPR, rapid plasma reagin; TPPA, *Treponema pallidum* particle agglutination; TRUST, toluidine red unheated serum test; USR, unheated serum reagin; VDRL, Venereal Disease Research Laboratory.

[a] This is not a comprehensive list of tests available in the United States.

[b] Sensitivity and specificity of tests are also dependent on the disease prevalence in the population tested and may vary considerably by manufacturer or the standard used as a comparison.

[c] Unknown reference standard.

[d] When compared with FTA-ABS test results.

[e] When compared with results from Western blotting.

[f] When compared with nontreponemal test results.

[g] When compared with treponemal test results.

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Treponemal Serologic Tests (TSTs) as Screening Tests- 'Reverse Algorithm'

- EIA (*T.pallidum* sonicate or recombinant antigen)
- Low cost, automation, standardization etc.
- More sensitive and more specific than traditional NTSTs
- Doesn't distinguish new, old, treated or untreated
- Recent CAP survey- 63% used traditional algorithm (Rhoads et al Arch Pathol Lab Med 2017)

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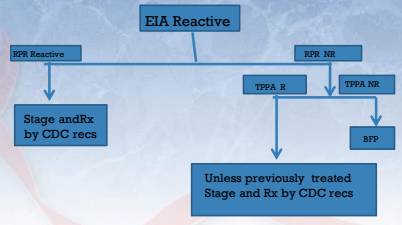
Testing and Treatment Approach



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CDC Syphilis Screening Recommendations

- All pregnant women at 1st prenatal (early)
- Retest at 28 weeks and at delivery if high risk
- MSM at least annually
- MSM every 3-6 months if high risk
- HIV if sexually active at first visit and annually
- HIV more frequently if high risk

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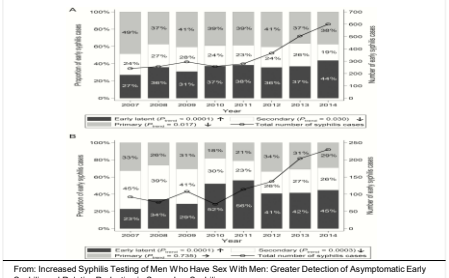

From: Increased Syphilis Testing of Men Who Have Sex With Men: Greater Detection of Asymptomatic Early Syphilis and Relative Reduction in Secondary Syphilis
Clin Infect Dis. 2017;65(3):389-395. doi:10.1093/cid/cix326
Clin Infect Dis | © The Author 2017. Published by Oxford University Press for the Infectious Diseases Society of America. All rights reserved. For permissions, e-mail: journals.permissions@oup.com.

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To Treat is First to Stage

- **Primary, Secondary and Early Latent**
  - **Benzathine penicillin 2.4million units IM once (Jarisch-Herxheimer Rxn)**
- **Late Latent and Latent of Unknown Duration***
  - **Benzathine penicillin 2.4million units IM once weekly for three weeks**
- **Late Tertiary Syphilis Except Neurosyphilis - R/O Neurosyphilis then same as latent syphilis**

***Intervals between weekly doses optimally no more than 7-9 days.**
In pregnancy definitely no missed doses!

***Pregnant women and HIV+ pts get standard therapies.**

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Alternatives to Penicillin

- **Tetracyclines (Doxycycline)**
  - **Two weeks for early or four weeks for latent**
- **Ceftriaxone**
  - **-Dose and duration unclear**

- **There are no alternatives to penicillin in pregnancy**

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Who needs an LP to Rule Out Neurosyphilis?

- 'If you think about doing an LP then do an LP'
- Diagnosis requires CSF evaluation
- CDC STD Rx Guideline:
  - neurologic or ophthalmic signs or symptoms,
  - evidence of active tertiary syphilis (e.g., aortitis and gumma),
  - treatment failure-definition?
  - HIV: RPR>1:32 and/or CD4 <350???

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CSF Abnormalities

- CSF VDRL-highly specific, variably sensitive
- CSF WBC-lymphocytic pleocytosis/ not specific in HIV+
- CSF protein elevations
- CSF FTA-ABS-sensitive, not approved for this use
- PCR?
- Cytokines?

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Neurosyphilis Treatment

Aqueous PCN G 18-24mu qd in divided doses for 10-14 days (follow with Rx for latent)

Alternative: Procaine PCN G 2.4mu IM daily + probenecid 500mg po qid 10-14days

Ceftriaxone- dose? Duration?

- Doxycycline?
- Ocular Syphilis- treat as NS with or without +CSF findings but LP should be done to follow if abnormal

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Syphilis Post Rx follow-up for all stages

- **Partner notification**
- **HIV testing**
- **Two fold declines in non treponemal serologic test like the RPR over 3-6m early and 12-24m in latent**
- **Some titers never go away**
- **Some titers don't decline properly**
- **CSF WBC should resolve 3-6 months, VDRL over a much longer period**
- **CSF usually normal if the RPR becomes non reactive.**

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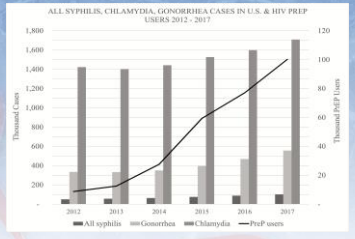

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Question-and-Answer Session