Sexually Transmitted Infections: Cases from the Clinic(ians)

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IAS–USA

Learning Objectives

After attending this presentation, learners will be able to:

- Describe current epidemiology of important sexually transmitted diseases in HIV-infected patients, especially syphilis, gonorrhea and chlamydia
- Know recommended indications for and approach to screening for asymptomatic sexually transmitted infections in HIV-infected patients
- Recognize common clinical syndromes associated with sexually transmitted pathogens in HIV-infected patients

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ARS 1: Among men who have sex with men, what percent of gonorrhea or chlamydia infections are missed if only urine is screened?

1. 0%
2. 10%
3. 40%
4. 70%

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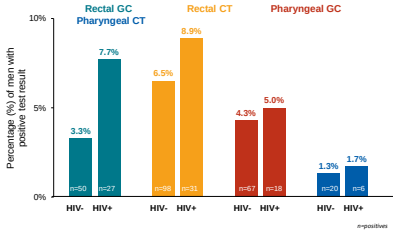
Prevalence of extragenital gonorrhea (GC) and chlamydia (CT) among venue-attending MSM by HIV status, NHBS, 2017



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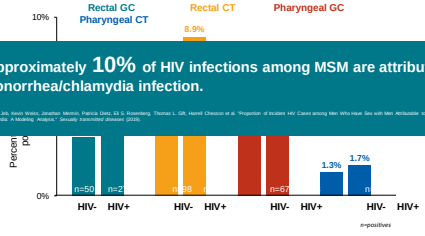
Prevalence of extragenital gonorrhea (GC) and chlamydia (CT) among venue-attending MSM by HIV status, NHBS, 2017



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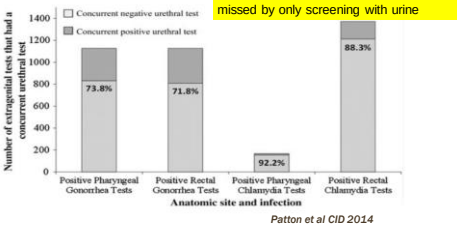
High Proportion of Extragenital CT/GC associated with negative urine test, STD Surveillance Network (n=21994)

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



Patton et al CID 2014

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2015 CDC STD Screening Recommendations for MSM with HIV

- **Gonorrhea, chlamydia, syphilis**
  - During first HIV evaluation
  - At least annually and every 3-6 months if at increased risk
- **Gonorrhea and chlamydia at sites of contact regardless of condom use**
  - Gonorrhea: urethra, rectum, and pharynx
  - Chlamydia: urethra, rectum
- **Hepatitis C**
  - During first HIV evaluation
  - Annually

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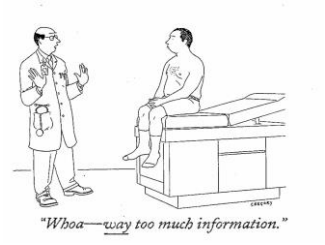
Workowski H, Bolan G. 2015, MMWR Recomm Rep 64(No.3)

Targeted Prevention: Requires Asking!



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STD Testing in Past 12 Months by Ryan White Program Facility Funding Status

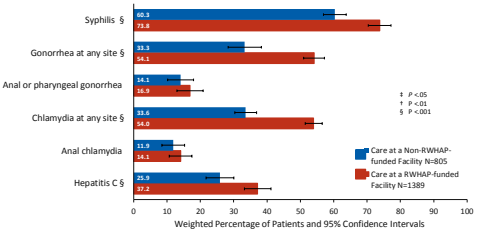

Figure 3. STD testing during the past year among HIV-positive men who have sex with men, stratified by Ryan White Program facility funding status, 2015-2016, N=2194

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STI Self-Testing Program
Seattle STD Prevention Training Center
http://www.uwptc.org

http://www.uwptc.org

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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
- May save the provider time

Van der helm, 2009, STDDodge, 2012 Sex Health
Freeman 2011, STD; Alexander 2008, STI; Moncada 2009, STD

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20 yo man referred by a partner "who had syphilis"

- Considers himself healthy, no symptoms
- Two episodes of rectal gonorrhea last year
- Sometimes uses meth on weekends
- 6 partners in last 3 months; receptive/insertive anal & oral sex. Last unprotected sex 12 h ago.
- No information on recent partners' health
- Otherwise healthy, taking no medications
- Rapid HIV Ab test negative today

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20 yo man referred by a partner "who had syphilis"

- His physical examination is normal.
- You order syphilis serology (EIA with reflexive quantitative RPR if positive) and screen for gonorrhea in pharynx, urine and rectum; chlamydia in urine and rectum.
- Which of the following do you do now?

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ARS 2: Which of the following do you do?

1. Base future treatment on results of screening tests
2. Treat him now with a single injection of BZN PCN 2.4 x 10-6 mu IM
3. Treat him now with the first of three weekly injections of BZN PCN 2.4 x 10-6 mu IM
4. Give him doxycycline to give to his most recent sex partner

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Syphilis Treatment Primary, Secondary, Early Latent

- **Penicillin treatment of choice**
  - Benzathine penicillin 2.4 mu IM x 1
- **No benefit of additional therapy**
  - Enhanced (IM + oral)
  - Single vs. 3 weekly injections under study (NCT03637660)
- **Penicillin alternatives**
  - Doxycycline (100 mg BID x 14 days), ceftriaxone (1-2 g daily x 10-14 days)
  - Azithromycin 2 gm (A2058G mutation/treatment failure)
    - Most common in MSM
    - Not recommended

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Partner Management in Syphilis

- Sex partners of a person with primary, secondary, or early latent syphilis
  - **Within 90 days before the diagnosis** treat presumptively for early syphilis, even if serologic test results are negative.
  - **>90 days before the diagnosis:** treat presumptively for early syphilis if serologic test results are not immediately available and opportunity for follow-up uncertain. If serology is negative, no treatment is needed. If serology is positive, base treatment on clinical and serologic evaluation and stage of syphilis.
- Sexual transmission likely occurs only when mucocutaneous syphilitic lesions are present (uncommon after first year of infection).
- Long-term sex partners of persons who have late latent syphilis: evaluate clinically and serologically and treat on basis of findings

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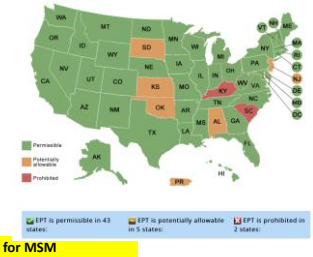
Expedited Partner Management?

- Expedited partner management is an option for chlamydia & gonorrhea, but not for syphilis
  - Safe and effective at reducing reinfection for GC
  - Dual therapy (cefixime 400 mg + azithromycin 1 g)
  - Consider for trichomonas
  - Review laws in your state: www.cdc.gov/std/ept



Some do not NOT recommend for MSM
>5% of MSM with bacterial STI will be diagnosed with HIV

ARS 3: Would you offer him doxycycline post-exposure prophylaxis for STI?

1. Yes
2. No
3. I have no idea, that sounds crazy for more reasons than I have time to discuss

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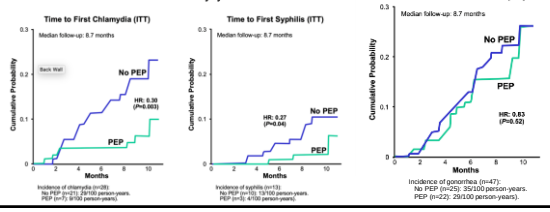
Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

On Demand PEP Doxycycline 200 mg (~24 hours after sex, up to 72 hours)

No PEP

Visits: baseline and every 2 months
Serologic assays for HIV and syphilis
PCR assays for chlamydia and gonorrhea
Urine, anal, and throat samples collected

Time to First Chlamydia and Syphilis With On-Demand PEP With Doxycycline for MSM



Doxy-PrEP/PEP for Syphilis & Chlamydia?

Pros

- Effective in early work
- Relatively safe drug
  - Chronic use in acne vulgaris
- Easy to administer
- Few other options for prevention
- Considerable interest among some MSM surveyed, with use already reported (Spinelli 2018)

Cons

- Limited data; duration?
- Costs
- Side effects of doxycycline
  - Esophagitis/ulceration
  - Photosensitivity
- Risk compensation?
- Reproductive concerns (women)?
- Antibiotic resistance*
- Microbiome effects*

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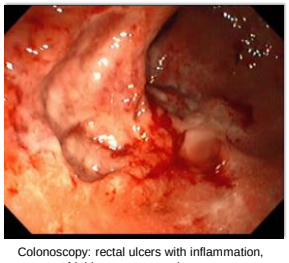
- 34 y.o. HIV+ (CD4 200) man w/ rectal discharge, bleeding, pain that first occurred 2 mos prior, off ART
- Given routine GC, chlamydia, & syphilis treatment
- Symptoms recur with severe pelvic pain radiating to back
- Monogamous with male partner; family history of Crohn's disease and colon cancer



Colonoscopy: rectal ulcers with inflammation, friable mucosa; no abscess

Courtesy of Catherine McLean, CDC

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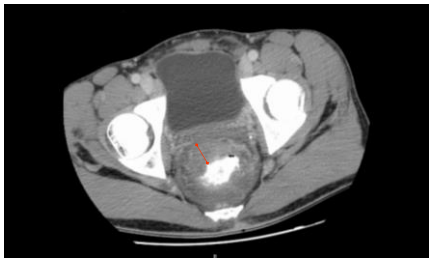

CT scan: Perirectal wall thickening and surrounding inflammatory changes. Limited local lymphadenopathy

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ARS 4: What Would You Do Now?

1. Start immunomodulatory therapy to treat for inflammatory bowel disease
2. Retreat for gonorrhea assuming infection with fluoroquinolone-resistant strain
3. Obtain diagnostic tests for *Chlamydia trachomatis* from rectal mucosa and start doxycycline therapy
4. Treat empirically for genital herpes and do nothing else

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Results

- Colon Bx: fibropurulent debris, granulation tissue; special stains-AFB, PAS, Steiner negative
- Rectal swab of ulcer: *Chlamydia trachomatis* (NAAT); negative for HSV, GC, chancroid, enteric pathogens
- Urine negative for *C. trachomatis*, GC
- Sent for genotyping to CDC

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Lymphogranuloma venereum

- Caused by L1-L3 serovars of *C. trachomatis*
- MSM presenting with protocolitis should be tested with rectal NAATs (chlamydia)
  - Additional molecular testing (PCR based genotyping) can be used to differentiate LGV vs. non LGV strains
  - LGV proctocolitis can resemble *C. difficile,* and be mistaken for inflammatory bowel disease
  - Clinical syndrome of severe protocolitis should receive presumptive treatment (doxy 100 mg bid x 21 d)
    - In addition if painful perianal ulcers or mucosal ulcers (anoscopy) presumptive therapy for herpes
    - CROI 2019: azithromycin 1 g orally weekly x 3 weeks was effective (Blanco no. 1011)

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38 yo man with blurry vision

- Well-controlled HIV, CD4 488 (22%)
- Has had a week or so of increasingly blurry vision in R eye
- No other complaints
- 1 primary male partner, also HIV+, no condoms; occasional outside male partners
- Prior h/o of rectal GC; syphilis EIA negative 6 mo ago
- Normal neuro exam; ophthalmalogic exam unrevealing (undilated pupils)
- You are concerned about ocular syphilis, so you initiate presumptive treatment for neurosyphilis with IV Penicillin (PCN G) and refer him immediately for ophthalmology evaluation

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ARS 5: Assuming it is feasible, would you perform a lumbar puncture?

1. Yes
2. No

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Ocular Syphilis — Eight Jurisdictions, United States, 2014–2015

Sara E. Oliver, MD[1,2]; Mark Aubin[3]; Leah Atwell, MPH[4]; James Matthias, MPH[4,5]; Anna Cope, PhD[5,6]; Victoria Mobley, MD[6]; Alexandra Gossle, MSc[7]; Sydney Minnerly, MA[8]; Juliet Stoltey, MD[9]; Heidi M. Bauer, MD[3]; Robin R. Hennessy, MPH[3,10]; Dawne DiOrio, MPA[3,11]; Robyn Neblett Fanfair, MD[1,2]; Thomas A. Peterman, MD[3]; Lauri Markowitz, MD[3]

- 388 cases MMWR 11/4/16
- Most among MSM with HIV
  - A few among HIV-negative persons, including heterosexual men and women
- Several resulted in significant sequelae including blindness
- All should be reported within 24 h of diagnosis to Public Health

TABLE 1. Suspected ocular syphilis and total syphilis cases — eight jurisdictions, United States, 2014–2015

Jurisdiction	Suspected ocular syphilis		Total surveillance syphilis cases		% surveillance syphilis cases with suspected ocular syphilis	
	2014	2015	2014	2015	2014	2015
California*	48	60	6,238	7,824	0.77	0.77
Florida	10	32	6,030	7,154	0.17	0.45
Indiana†	—	8	—	714	—	1.10
Maryland	10	17	1,524	1,779	0.66	0.96
New York City	14	12	5,798	6,116	0.24	0.20
North Carolina	21	42	1,799	2,435	1.20	1.70
Texas	27	36	7,337	8,400	0.37	0.19
Washington	27	44	857	1,125	3.20	3.90
Total	**157**	**231**	**29,583**	**35,547**	**0.53**	**0.65**

* California does not include syphilis reports from San Francisco or Los Angeles.
† Indiana reviewed data from 2015 only.

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TABLE 2. Demographic characteristics of patients with suspected ocular syphilis — eight jurisdictions, United States, 2014–2015

Characteristic	No.	(%)
Total	**388**	**(100.0)**
Male	362	(93.3)
Known MSM (among 362 males)	249	(68.8)
Race		
White	217	(55.9)
Black	81	(20.9)
Hispanic	48	(12.4)
Asian	13	(3.4)
Native Hawaiian/Pacific Islander	1	(0.3)
Other/Unknown	28	(7.2)
HIV-positive	198	(51.0)

Abbreviations: HIV = human immunodeficiency virus; MSM = men who have sex with men.

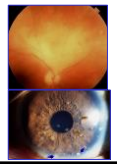

TABLE 3. Clinical characteristics, laboratory results and diagnoses for syphilis and suspected ocular syphilis — eight jurisdictions, United States, 2014–2015

Characteristic	No.	(%)
Total	**388**	**(100.0)**
Stage of syphilis		
Primary	8	(2.1)
Secondary	101	(26.0)
Early latent	79	(20.4)
Late or latent of unknown duration	193	(49.7)
Unknown	7	(1.8)
Additional symptoms of neurosyphilis	87	(22.4)
Reported ocular symptoms (among 326 with symptoms)		
Blurry vision	210	(64.4)
Vision loss	107	(32.8)
Eye pain or red eye	46	(14.1)
Eye exam	158	(40.7)
Diagnosis (among 158 with documented eye exam)*		
Uveitis	72	(45.6)
Retinitis	20	(12.7)
Optic neuritis	18	(11.4)
Retinal detachment	6	(3.8)
CSF analysis performed	188	(48.5)
CSF VDRL (among 174 with a documented result)		
Reactive	122	(70.1)
Nonreactive	52	(29.9)
Treatment		
Aqueous penicillin G IV	230	(59.3)
Other treatment	146	(37.6)
Not/Unknown treatment	12	(3.1)

Abbreviations: CSF = cerebrospinal fluid; IV = intravenous; VDRL = Venereal Disease Research Laboratory test.
* Can be included in multiple categories.

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Ocular Syphilis and Human Immunodeficiency Virus Coinfection Among Syphilis Patients in North Carolina, 2014–2016

Anna B. Cope, PhD,† Victoria L. Mobley, MD,‡ Sara E. Oliver, MD,* Mara Larson, MPH,‡ Nicole Ditzkovy, MSc,‡ Jason Maxwell, BS,§ Jessica L. Rineky, PhD,*† Thomas A. Peterman, MD,* Aaron Fleischauer, PhD,¶† and Erika Samoff, PhD‖*

Methods: We reviewed all syphilis cases (early and late) reported to the North Carolina Division of Public Health during 2014 to 2016 and categorized HIV status (positive, negative, unknown) and OS status based on report of ocular symptoms with no other defined etiology. We estimated prevalence ratios (PR) and 95% confidence intervals (CI) for OS by HIV status. Among syphilis patients with HIV, we compared viral loads and CD4 cell counts by OS status. We compared symptom resolution by HIV status for a subset of OS patients.

Results: Among 7123 confirmed syphilis cases, 2846 (39.9%) were living with HIV, 109 (1.5%) had OS, and 59 (0.8%) had both. Ocular syphilis was more prevalent in syphilis patients with HIV compared to HIV-negative/unknown-status patients (PR, 1.8; 95% CI, 1.2–2.6). Compared with other patients with HIV, the prevalence of OS was higher in patients with viral loads greater than 200 copies/mL (1.7; 1.0–2.8) and in patients with a CD4 count of 200 cells/mL or less (PR, 2.3; 95% CI, 1.3–4.2). Among 11 patients with severe OS, 9 (81.8%) were HIV-positive. Among 39 interviewed OS patients, OS symptom resolution was similar for HIV-positive (70.0%) and HIV-negative/unknown-status (68.4%) patients.

Sex Transm Dis. 2019 Feb;46(2):80-85

Syphilitic hepatitis and neurosyphilis: an observational study of Danish HIV-infected individuals during a 13-year period

Kirsten Salado-Rasmussen,[1,] Maria Wessman,[2,3] Susan A Cowan,[1] Jan Gerstoft,[4] Terese Lea Katzenstein[4]

Methods This retrospective study included all HIV-infected individuals ≥18 years diagnosed with syphilis between 1 May 2004 and 31 December 2016 in Copenhagen, Denmark. We used the unique 10-digit personal identification number assigned to all individuals in Denmark to link data from two nationwide registers to identify the patients. Patient files were revised to obtain clinical and laboratory data.

Results A total of 509 episodes of syphilis were diagnosed in 427 HIV-infected individuals attending three hospitals in Copenhagen, Denmark. The majority of the patients were men (99.5%), and the majority of men were men who have sex with men (96%). Twenty-seven patients (6%) met the criteria for neurosyphilis, and the neurological symptoms included ocular and auditory abnormalities, headache, paraesthesia, vertigo, facial paresis, motor weakness and unexplained pain in the legs. The patients with neurosyphilis were diagnosed in the secondary stage (84%) and in the early latent (8%) or late latent (8%) stage. Among the patients tested for liver affection, 41% met the criteria for syphilitic hepatitis. The patients with syphilitic hepatitis were diagnosed in the secondary stage (82%), primary stage (10%), and in the early latent (5%) or late latent (3%) stage.

Sex Transm Infect epub ahead of print: April 2019 doi:10.1136/ sextrans-2018-053921

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LP in Syphilis / HIV

In Favor	Against
• CNS involvement in early syphilis is common (40%) & predicted clinical neurosyphilis in the pre-antibiotic era • BZN PCN does not penetrate CNS • Syphilis contained by cell-mediated immunity, and may be more severe in HIV • NS associated with CD4 <350, serum RPR >1:32 (Marra 2004; Libois 2007)	• Frequency of serious neurosyphilis low in both untreated syphilis & early syphilis treated with BZN PCN • PCN in CNS may not be needed to suppress early CNS invasion • Cost & inconvenience of LP

Recommendation: careful evaluation for signs & symptoms, treatment failure

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- 16 yr old previously healthy female presented to the dermatologist with facial rash for past 2 months, which started on her arm and spread to her axilla, chest and face
  - Pt was seen by primary care provider for this rash about a month ago, prescribed topical steroids with no improvement
  - Rash was not itchy, no redness, no pain
- Denied fever, URI, headache, malaise, anorexia, sore throat, myalgias, weight loss and lymphadenopathy
- Social history: recently at summer camp, denied being sexually active (ever)

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Exam: 1 cm hypopigmented macules with central sparing, on face, extending to trunk, few spots scattered on arms, no palm/sole involvement

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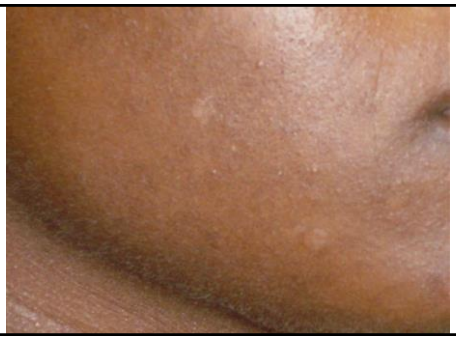

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ARS 6: What is the rash from?

1. Pityriasis rosea
2. *Treponema pallidum*
3. Tinea corporis
4. Discoid lupus
5. Eczema

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Discharge/Follow-up

- Dermatology: Biopsy of the axillary lesion performed
- Patient was sent home with diagnosis of possible discoid lupus
- A week later, path results prompted patient to be recalled to care

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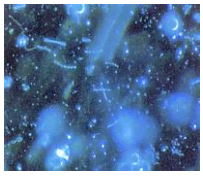
Labs

- Biopsy revealed *Treponema pallidum* on Warthin Starry silver stain
- RPR 1:64, TPPA positive
- HIV Ag-Ab test positive



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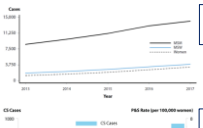
The U.S. Syphilis Epidemic: 2017

Primary / Secondary Syphilis in Men



- 88% of cases
  - 80% in MSM
- 46% in MSM HIV+

Primary/ Secondary & Congenital Syphilis in Women

- Primary / Secondary: 156% increase compared with 2013
- Congenital syphilis: 154% increase

- 918 congenital cases
- In California, >50% of cases without prenatal care
- Strong links to meth, heroin

CDC

#0047 Dionne-Odom

Source:

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A 45 year old woman is diagnosed with HIV (CD4 = 26, VL = 265,000). She is started on dolutegravir & TAF/FTC. She returns 4 weeks after initiating ART with painful genital lesions, myalgias and fevers. She has never had these symptoms before and denies a history of genital herpes. She has one long-term sexual partner. Last sex was 2 months ago. Her examination shows:

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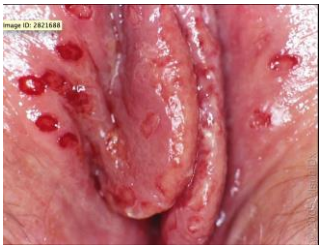
Exam



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ARS 7: Which of the following is the most likely cause of her symptoms?

1. Primary HSV-2
2. Fixed drug eruption
3. HSV-2 IRIS
4. Erosive lichen planus
5. Secondary syphilis

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Key Points: HSV-2 & IRIS

- Can occur in 6 months after ART initiation
- More severe than recurrences with local and systemic symptoms
- Most people with HSV-2 are not aware of their infection (like this patient); consider HSV-2 serologic screening in HIV care
- For patients with known HSV-2 and low CD4 counts initiating ART, consider suppressive therapy

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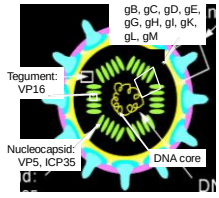
Accurate HSV Serology: Type Specific



Glycoprotein gG tests

- Western blot
- gG ELISA
- gG-membrane tests
- gG immunoblot

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Genital Herpes: HIV OI Guidelines Preventing Recurrence

- Suppressive therapy for HSV may be continued indefinitely, without regard for improved CD4 cell count, although need for continuation should be addressed on an annual basis, particularly if immune reconstitution has occurred (BIII).
- In persons starting ART with CD4 cell counts <250 cells/mm3, there is in increased risk of HSV-2 shedding and genital ulcer disease in the first 6 months; suppressive ACV decreases the risk of GUD nearly 60% compared to placebo, and may be recommended for persons with CD4 cell counts <250 cells/mm3 starting ART (BI).
- The use of daily suppressive therapy (when compared to episodic therapy) has been associated with a lower risk of development of acyclovir-resistant HSV in hematopoietic stem cell recipients; there are no specific data for persons with HIV infection.

U.S. O.I. Guidelines, September 2015 (no revisions on this in recent updates)

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- 47-y.o. man complaining of painful lesion penis for 2 weeks
- Sexual history: 1 male partner in past 3 months; oral sex (both insertive and receptive) and insertive anal sex only
- No history of STIs
- No history of (injection) drug use
- Last HIV test >2 years ago (negative)

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2.5 cm round, superficial ulceration on shaft

No lymphadenopathy

HIV (rapid test): reactive

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- 24 y.o. male complaining of initially non-painful penile lesions for 1 month; they have gradually become more uncomfortable
- Pt denies new female partners, sex with men, or injection drug use
- No history of STI
- Last HIV test: 4 months ago – negative by self-report

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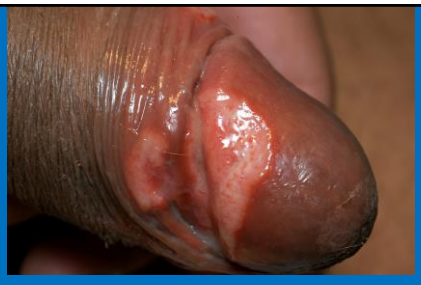

Large, partly confluent, superficial erosions inside foreskin, corona and extending onto glans penis, painful to the touch
Tender, bilateral inguinal lymphadenopathy

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ARS 8: What do you do now?

1. Treat for primary syphilis
2. Treat for genital herpes
3. Treat for syphilis and herpes
4. Provide NSAIDs and await test results (syphilis serology; HSV2 PCR)

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Both Cases

- Initially treated for syphilis and herpes
- Herpes cultures positive for HSV-2
- CD4 counts 23 and 12, respectively
- Syphilis serologies negative

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A Vexing Problem

- 33 yo man with well-controlled HIV diagnosed with rash of secondary syphilis, confirmed by serology; no indication for LP
- Treated with appropriate BZN PCN therapy
- Serum RPR 1:1024 (day of treatment)
- Two recent sex partners; both treated in same clinic

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A Vexing Problem

- Returned in 3 months
- Serum RPR 1:512

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A Vexing Problem

- Returned in 6 months
- Serum RPR 1:64

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A Vexing Problem

- Returned in 9 months
- Serum RPR 1:32

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A Vexing Problem

- Returned in 1 year
- Serum RPR 1:8
- No new partners or known exposures to syphilis
- No intercurrent STD
- What now?

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BMC Infectious Diseases

RESEARCH ARTICLE Open Access

A systematic review of syphilis serological treatment outcomes in HIV-infected and HIV-uninfected persons: rethinking the significance of serological non-responsiveness and the serofast state after therapy

Arlene C. Seña[1*], Xiao-Hui Zhang[2†], Trudy Li[3], He-Ping Zheng[2], Bin Yang[2], Li-Gang Yang[2], Juan C. Salazar[4], Myron S. Cohen[1], M. Anthony Moody[3,5], Justin D. Radolf[4,6] and Joseph D. Tucker[1]

- Identified 1693 reports in the literature, reviewed 20 studies that met selection criteria.
- Median proportion of patients withserological non-response was 12.1% overall (interquartile range, 4.9–25.6)
- Serofast proportion estimated from 2 studies, which ranged from 35.2–44.4 %. Serological cure was primarily associated with younger age, higher baseline nontreponemal titers, and earlier syphilis stage.
- Relationship between serological cure and HIV status inconsistent; among HIV-infected patients, CD4 count and HIV viral load was not associated with serological cure

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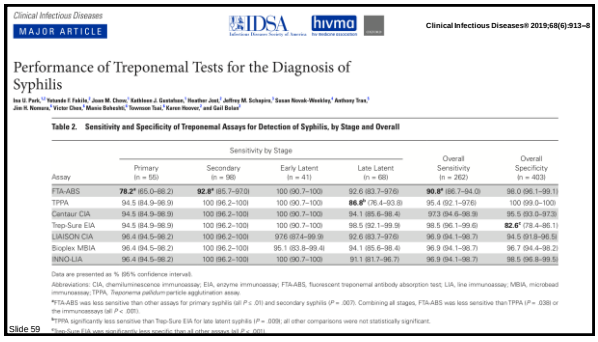

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA hivma

Clinical Infectious Diseases® 2019;68(6):913–8

Performance of Treponemal Tests for the Diagnosis of Syphilis

Ina U. Park,[1,a] Yolanda F. Fakile,[2] Joan M. Chow,[1] Kathleen J. Gustafson,[1] Heather Jost,[1] Jeffrey M. Schapiro,[1] Susan Novak-Weekley,[3] Anthony Tran,[3] Jin H. Nomura,[4] Victor Chen,[4] Mamie Bolanis,[4] Townson Tsai,[4] Karen Hoover,[4] and Gail Bolan[5]

Table 2. Sensitivity and Specificity of Treponemal Assays for Detection of Syphilis, by Stage and Overall

Assay	Sensitivity by Stage				Overall Sensitivity	Overall Specificity
	Primary (n = 55)	Secondary (n = 98)	Early Latent (n = 41)	Late Latent (n = 68)	(n = 262)	(n = 403)
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)

Data are presented as % (95% confidence interval).

Abbreviations: CIA, chemiluminescence immunoassay; EIA, enzyme immunoassay; FTA-ABS, fluorescent treponemal antibody absorption test; LIA, line immunoassay; MBIA, microbead immunoassay; TPPA, *Treponema pallidum* particle agglutination assay.

[a]FTA-ABS was less sensitive than other assays for primary syphilis (all $P < .01$) and secondary syphilis ($P = .007$). Combining all stages, FTA-ABS was less sensitive than TPPA ($P = .038$) or the immunoassays (all $P < .001$).

[b]TPPA significantly less sensitive than Trep-Sure EIA for late latent syphilis ($P = .009$); all other comparisons were not statistically significant.

[c]Trep-Sure EIA was significantly less specific than all other assays (all $P < .001$).

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- Healthy HIV+ 40 y.o. man sexually active with men, receptive/insertive anal/oral sex “usually” with condoms if receptive anal only
- Screening last week at all sites revealed +NAAT for *N. gonorrhoeae* at the pharynx.
- He reports hives on receipt of penicillin as a child, and has not received penicillin since.

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ARS 9: What do you do?

1. Treat with IM ceftriaxone, 250 mg, now
2. Document negative skin testing for PCN allergy prior to treatment with ceftriaxone
3. Treat with oral azithromycin, 2 gram, now
4. Treat with IM gentamicin (240 mg) and oral azithromycin (2 gram) now

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2015 CDC Gonorrhea Treatment Guidelines

PENICILLIN ALLERGY
RECOMMENDED THERAPY

Gentamicin 240 mg IM x 1
OR
Gemifloxacin 320 mg PO x 1

+

Azithromycin 2 g PO x 1

NOTES:
- Urogenital infections only
- Nausea is a common side effect of these regimens

Source: CDC and Prevention. MMWR. 2015.64(3).

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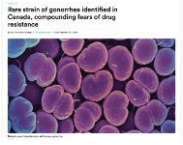
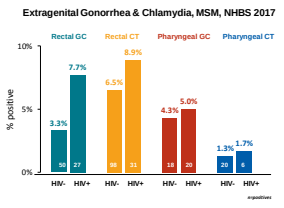
STD Surveillance Network, U.S.





International spread of gonococcal resistance to CTX
- Resistance to CTX plus high-level resistance to azithromycin in UK requiring treatment with ertapenem (2018)
- Contacts in South East Asia
- Two new cases of resistant gonorrhea in UK, January 2019

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www.cdc.gov/std; Stenger *STD* 2017

Countries with reported decreased susceptibility/resistance (DS/R) to ceftriaxone & azithromycin in *N. gonorrhoeae,* WHO GASP 2015-16

Ceftriaxone
15/63 (23.8%) countries
7 countries ≥ 5%

Azithromycin
50/62 (81%) countries
30 countries ≥ 5%

"Whether the global use of azithromycin in mono- or dual antimicrobial therapy of gonorrhoea is contributing to global increases in azithromycin resistance remains to be elucidated."

Cole, MJ *et al.* 2017. *BMC Infect Dis*; Barbee *Clin Infect Dis* 2018

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M. Unemo (submitted)

Additional Challenges…and Hope

Meager evidence base to address the role of pharyngeal infection:
- Contribution of commensal *Neisseria* spp to resistance
- PK / PD of antibiotics
- Natural history of infection
  - Resolution without antibiotics
  - Duration of infectivity
  - Bacterial shedding in oral secretions

NIH Workshop February 2019

BMC Infectious Diseases

STUDY PROTOCOL Open Access

A multicentre double-blind randomised controlled trial evaluating the efficacy of daily use of antibacterial mouthwash against oropharyngeal gonorrhoea among men who have sex with men: the OMEGA (Oral Mouthwash use to Eradicate GonorrhoeA) study protocol

Novel Antimicrobials Under Study for Gonorrhea

- **Zoliflodacin** (AZ D0914)
  - Spiropyrimidinetrione (topoisomerase inhibitor)
  - Activity at rectum; limited at pharynx
  - Activity vs. *C. trachomatis*, *M. genitalium*
  - Phase II trial completed (Taylor SA NEJM 2018)
- **Gepotidacin** (BTZ116576)
  - Triazaacenaphthylone (topoisomerase inhibitor)
  - High efficacy potential – 3 separate ribosomal targets
  - Phase II trial completed (Taylor SA CID 2018)
- **Solithromycin**
  - Fluoroketolide; inhibits protein synthesis
  - Initial Ph 3 trial did not show non-inferiority to standard-of-care; no resistance but given structural similarity to telithromycin, strains with high-level azithromycin resistance are concern (Hook EW CID 2015)
- **Delafloxacin**
  - Ineffective as single-dose therapy (Hook Sex Transm Dis 2019)

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

Gepotidacin for the Treatment of Uncomplicated Urogenital Gonorrhea: A Phase 2, Randomized, Dose-Ranging, Single-Oral Dose Evaluation

A Phase 2 Trial of Oral Solithromycin 1200 mg or 1000 mg as Single-Dose Oral Therapy for Uncomplicated Gonorrhea

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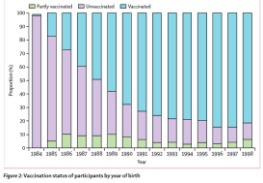
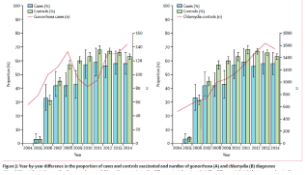
Retrospective case-control study of subjects immunized with NZ MenB OMV vaccine (2004-2014)

Petousis-Harris, *Lancet* July 2017





- 877 diagnoses of gonorrhea, 772 diagnoses of gonorrhea/chlamydia co-infection in participants
- Effectiveness of MenB vaccine against gonorrhea estimated to be 33%
- No reduced risk in individuals with gonorrhea/chlamydia coinfection

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THANK YOU!!

Slide courtesy of Ina Park, MD

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Download the CDC STD treatment guidelines app …

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Question-and-Answer

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