The Rise in Syphilis and the Role of the Emergency Department

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Disclosures/Conflicts of Interest

- None

Case Presentation

- 75 year old woman who presents to ED with progressive left vision loss.
- Symptoms started about 1 month prior, was seen at an outside facility where she was found to have left sided choroidal infarcts on exam – at the time she also endorsed headaches and was found to have elevated inflammatory markers – so the diagnosis of giant cell arteritis (GCA) was made
- Patient was treated with 1 gram IV methylprednisolone, followed by 75 mg daily of prednisone x 1 month (to present)

Case Presentation

- At some point did undergo a temporal artery biopsy, which was negative for findings suggestive of GCA
- Reported that initially visual symptoms improved with steroids, but over the last several days she noticed significant decrease in vision in the left eye
- Ophthalmologic exam was notable for active choroiditis with new uveitis/vitritis in the left eye. Admitted to the hospital for further evaluation

Case Presentation

- Further history reveals that the patient currently lives at home by herself in Ohio. She has 2 cats at home and no other animal exposures
- Currently retired (worked in retail in the past)
- No recent travel, no history of any international travel
- Has 2 adult children who live out of state
- No tobacco, alcohol or other drug use
- Not currently sexually active

Case Presentation

- Physical exam was unremarkable other evidence of a very faint, healing rash on the trunk and upper arms
- On further questioning, the patient reports that several weeks ago she developed a severe rash over her entire body – went to an urgent care and was diagnosed with a bad allergic reaction. States the rash has been improving slowly over time.

Case Presentation

- Patient reported she had a male new sexual partner about 6 months prior, although they are no longer in contact
- Barrier protection used but not every time
- She reports that the prior partner had several other sexual partners (both men and women); she was screened for HIV a few months ago after her partner notified her that he may have had unprotected sexual contact with a person with HIV
- No prior history of gonorrhea, chlamydia, syphilis or HSV

Case Presentation

- HIV 1/2 Ab/p24 Ag: Non-reactive
- Urine/oral chlamydia/gonorrhea NAAT: Negative
- **Syphilis IgM/IgG: REACTIVE**
- **RPR: 1:512**
- Lumbar puncture: WBC 15, RBC <3, Protein 62, glucose 75
- CSF VDRL: Reactive 1:2

Taking a sexual history

BOX 1. The Five P's approach for health care providers obtaining sexual histories: partners, practices, protection from sexually transmitted infections, past history of sexually transmitted infections, and pregnancy intention

1. Partners
- "Are you currently having sex of any kind?"
- "What is the gender(s) of your partner(s)?"

2. Practices
- "To understand any risks for sexually transmitted infections (STIs), I need to ask more specific questions about the kind of sex you have had recently."
- "What kind of sexual contact do you have or have you had?"
  - "Do you have vaginal sex, meaning 'penis in vagina' sex?"
  - "Do you have anal sex, meaning 'penis in rectum/anus' sex?"
  - "Do you have oral sex, meaning 'mouth on penis/vagina'?"

3. Protection from STIs
- "Do you and your partner(s) discuss prevention of STIs and human immunodeficiency virus (HIV)?"
- "Do you and your partner(s) discuss getting tested?"
- For condoms:
  - "What protection methods do you use? In what situations do you use condoms?"

4. Past history of STIs
- "Have you ever been tested for STIs and HIV?"
- "Have you ever been diagnosed with an STI in the past?"
- "Have any of your partners had an STI?"

Additional questions for identifying HIV and viral hepatitis risk:
- "Have you or any of your partner(s) ever injected drugs?"
- "Is there anything about your sexual health that you have questions about?"

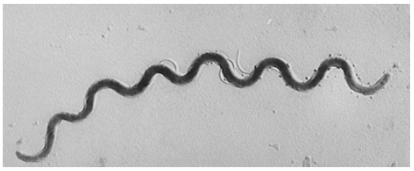
5. Pregnancy intention
- "Do you think you would like to have (more) children in the future?"
- "How important is it to you to prevent pregnancy (until then)?"
- "Are you or your partner using contraception or practicing any form of birth control?"
- "Would you like to talk about ways to prevent pregnancy?"

Source: CDC Sexually Transmitted Infections Treatment Guidelines, 2021

Taking a sexual history

- Establish rapport and make your patient feel comfortable before asking sensitive questions
- Use neutral and inclusive terms (e.g. partner) and pose your questions in a non-judgmental manner
- Avoid making assumptions about your patients' sexual orientation, gender identity or sexual behaviors based on age, appearance, marital status, or other factors

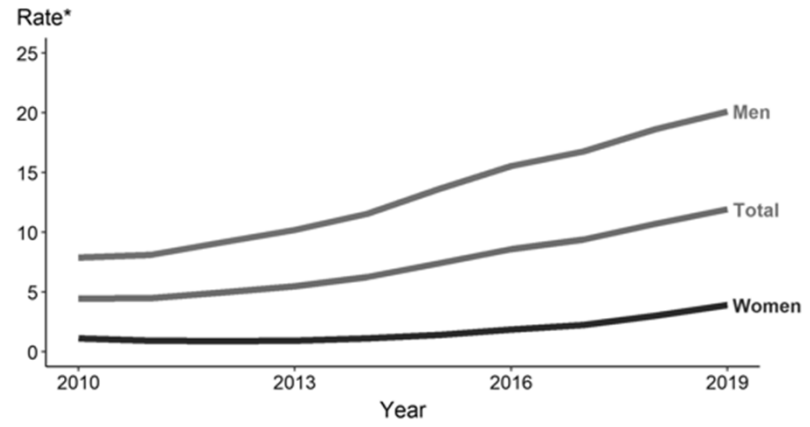
Syphilis: a review



- Syphilis is caused by the spirochete *Treponema pallidum*
- Major mode of transmission is via sexual contact
- Vertical transmission can occur (congenital syphilis)
- Can cause a wide variety of clinical manifestations, including periods of clinical latency (asymptomatic) if left untreated

Syphilis: a review

Primary and Secondary Syphilis — Rates of Reported Cases by Sex, United States, 2010–2019

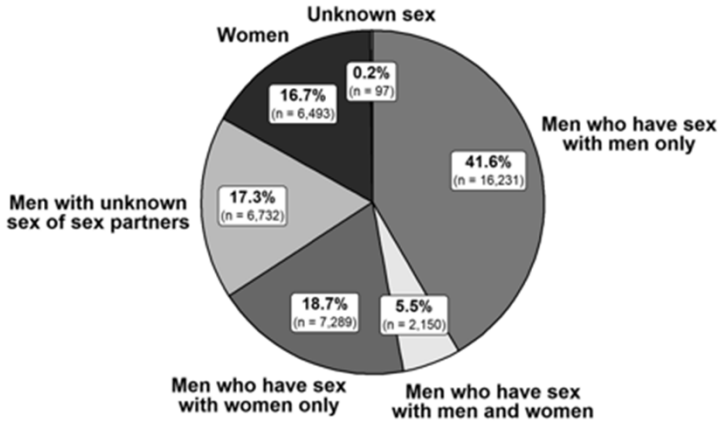


* Per 100,000

Source: U.S. Centers for Disease Control and Prevention

Syphilis: a review

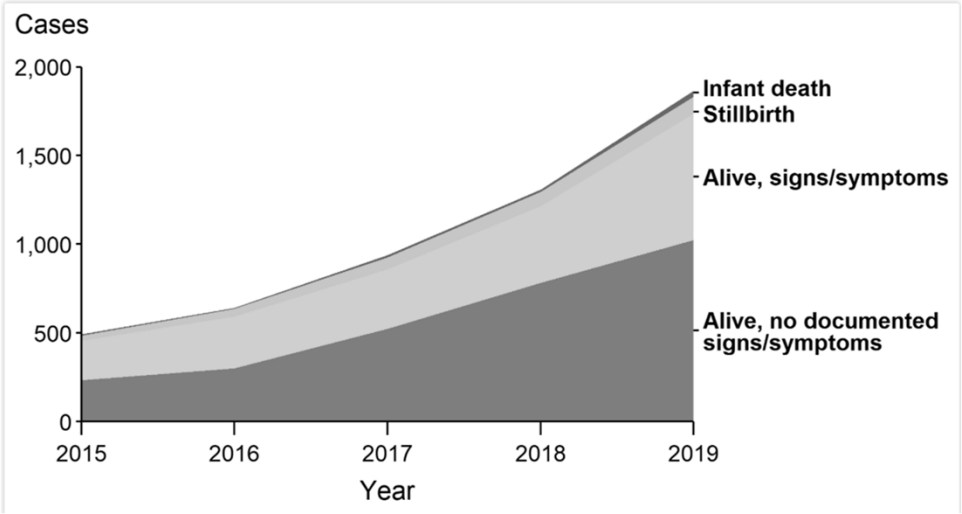
Primary and Secondary Syphilis — Distribution of Cases by Sex and Sex of Sex Partners, United States, 2019



Source: U.S. Centers for Disease Control and Prevention

Congenital Syphilis

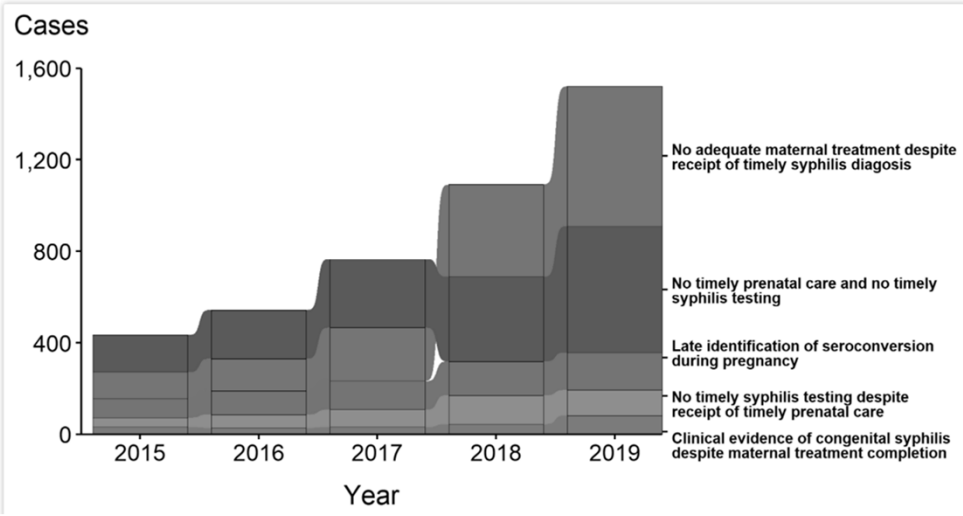
Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms* of Infection, United States, 2015–2019



Source: U.S. Centers for Disease Control and Prevention

Congenital Syphilis

Congenital Syphilis — Missed Prevention Opportunities Among Mothers Delivering Infants with Congenital Syphilis, United States, 2015–2019

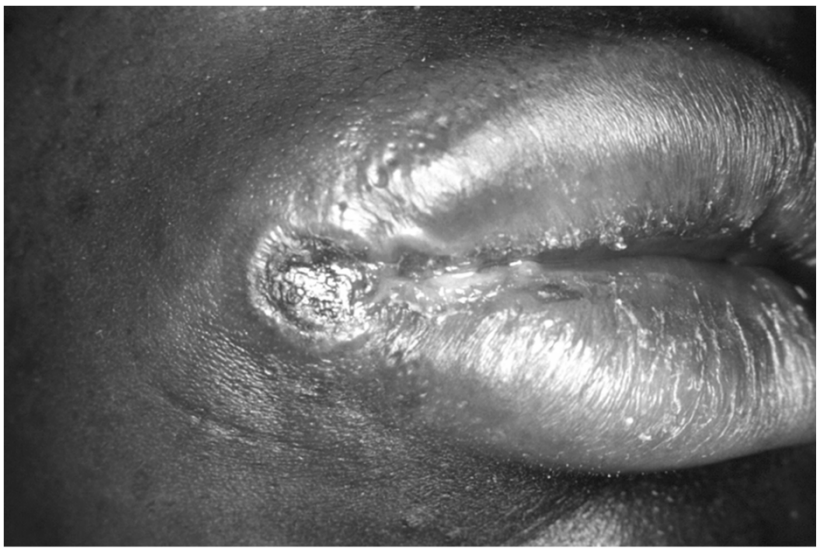


Source: U.S. Centers for Disease Control and Prevention

Primary syphilis

- Painless ulcer (chancre) appears at site of inoculation – can go unnoticed depending on the location.
- Regional lymphadenopathy can occur (inguinal, cervical)
- Chancres are highly infections and may resolve without treatment within 1-6 weeks

Primary syphilis

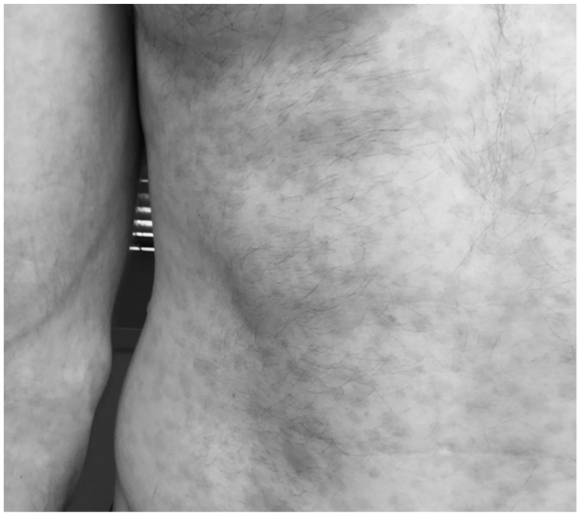


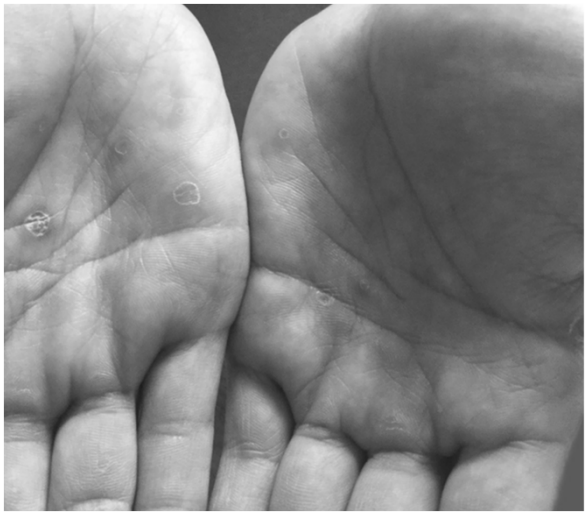
Source: Centers for Disease Control and Prevention Public Health Image Library

Secondary syphilis

- Typically occurs about 4-8 weeks after onset of primary chancre, more likely to prompt medical evaluation
- The classic symptom is a diffuse maculopapular rash, which commonly involves the palms, soles, chest and back
- Lymphadenopathy, malaise, fever, mucous patches (genitals, mouth), patchy alopecia, and condyloma lata can occur as well

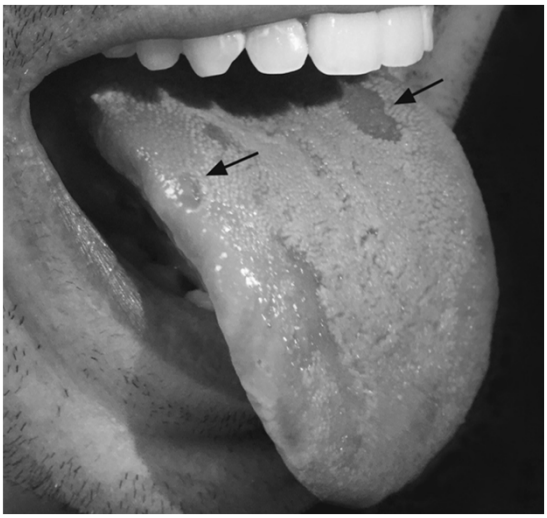
Secondary syphilis

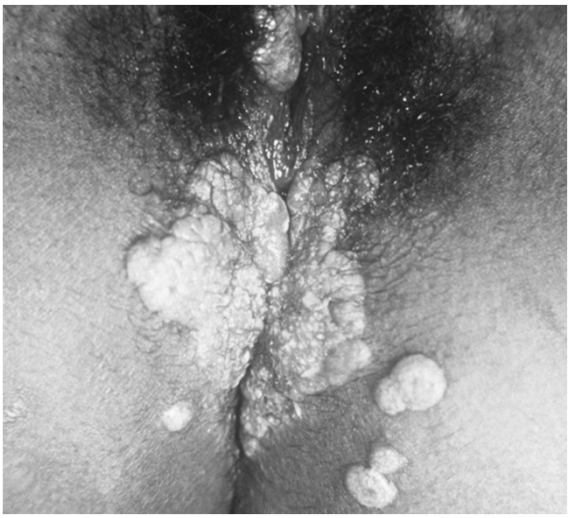




Source: Negusse Ocbamichael, PA; Public Health—Seattle & King County STD Clinic

Secondary syphilis



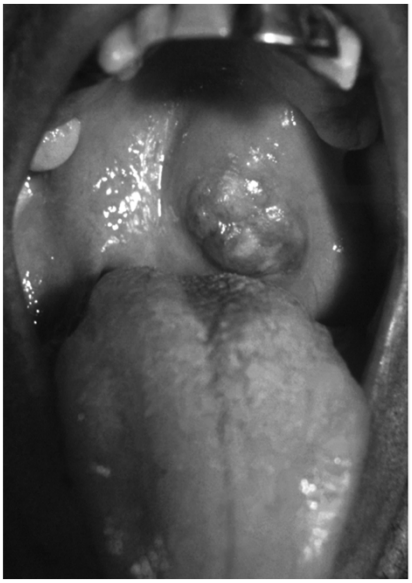


Source: Negusse Ocbamichael, PA; Public Health—Seattle & King County STD Clinic
Source: Centers for Disease Control and Prevention Public Health Image Library

Tertiary Syphilis

- Form of late syphilis – can occur decades after initial infection if treatment is not administered
- Gummatous disease (granulomatous disease of skin, subcutaneous tissues, bones or viscera)
- Cardiovascular syphilis (involvement of vasa vasorum – aortic aneurysm, aortic insufficiency)

Tertiary Syphilis



Source: Centers for Disease Control and Prevention Public Health Image Library

Latent syphilis

- Early latent syphilis (infection of less than 1 year duration)
- Late latent syphilis (infection greater than 1 year duration)
- Latent syphilis of unknown duration

Neurosyphilis, ocular syphilis, otosyphilis

- CNS involvement can occur during any stage of infection
- Early neurosyphilis - cranial nerve dysfunction, meningitis, meningovascular syphilis, stroke and/or acute altered mental status
- Late neurosyphilis – general paresis/tabes dorsalis (less common)
- Ocular syphilis (anterior, posterior or pan-uveitis), can occur with or without other associated neurologic manifestations
- Otosyphilis: usually presents with tinnitus, vertigo, sensorineural hearing loss

Screening for syphilis

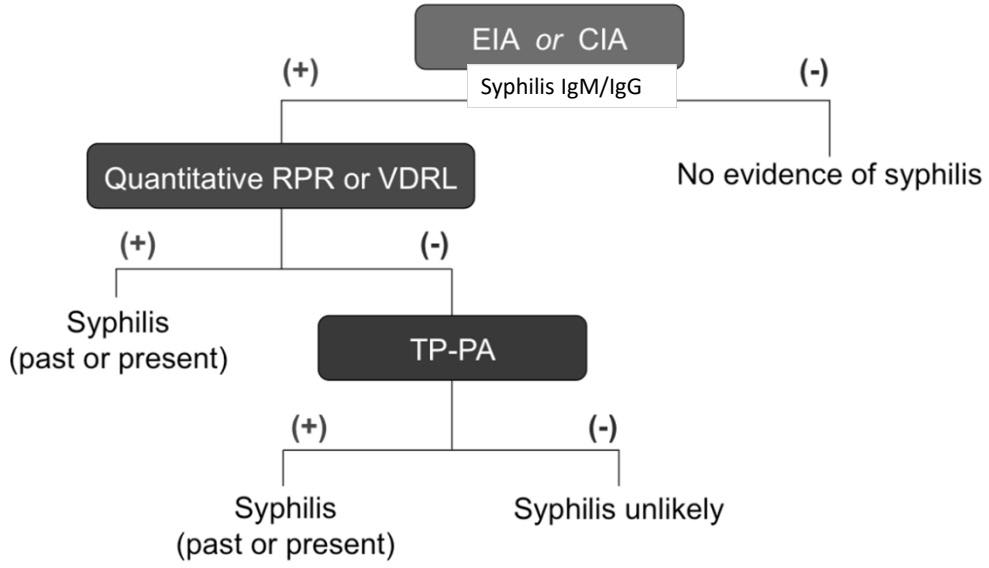
Syphilis	
Women and Men	• Screen asymptomatic adults at increased risk (history of incarceration or commercial sex work, geography, race/ethnicity, and being a male younger than 29 year) for syphilis infection[2,7]
Pregnant Women	• All pregnant women at the first prenatal visit[8] • Retest at 28 weeks gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy (using drugs, STIs during pregnancy, multiple partners, a new partner, partner with STIs)[2]
Men Who Have Sex With Men (MSM)	• At least annually for sexually active MSM[2] • Every 3 to 6 months if at increased risk[2]
Transgender and Gender Diverse People	• Consider screening at least annually based on reported sexual behaviors and exposure[2]
Persons with HIV	• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter[9,10] • More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology[2]

Source: CDC Sexually Transmitted Infections Treatment Guidelines, 2021

Screening for syphilis

- Laboratory testing - Reverse sequence algorithm
- Treponemal specific tests: Syphilis IgM/IgG, T.pallidum particle agglutination assay (TP-PA)
- Non-treponemal specific tests: rapid plasma reagin (RPR)

Diagnosis



Treatment

- Early syphilis (primary, secondary, early latent): 2.4 million units Benzathine penicillin G IM in a single dose
  - Alternative for penicillin allergic, non-pregnant adults: doxycycline 100 mg twice daily x 14 days

Treatment

- Late syphilis (late latent syphilis, latent syphilis of unknown duration, tertiary syphilis if CNS disease excluded): 2.4 million units Benzathine penicillin G IM weekly x 3 doses
  - Alternative for penicillin allergic, non-pregnant adults: doxycycline 100 mg twice daily x 28 days

Treatment

- Neurosyphilis: Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 MU IV every 4 hours or continuous infusion given for 10-14 days
  - Alternative procaine penicillin G 2.4 million units IM once daily plus probenecid 500 mg orally 4 times/day for 10-14 days

Other treatment considerations

- All people with syphilis should be screened for HIV
- Syphilis exposure has been associated with an increased risk of future HIV acquisition, particularly in men– counseling on safer sex practices and HIV Pre-Exposure Prophylaxis (PrEP)
- Sexual partners should be treated

Peterman TA, Newman DR, Maddox L, Schmitt K, Shiver S. High risk for HIV following syphilis diagnosis among men in Florida, 2000-2011. *Public Health Rep*. 2014;129(2):164-169.

References

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- Peterman TA, Newman DR, Maddox L, Schmitt K, Shiver S. High risk for HIV following syphilis diagnosis among men in Florida, 2000-2011. *Public Health Rep*. 2014;129(2):164-169.

Syphilis and co-existent sexually transmitted diseases

Syphilis re-infection?

Sexually Transmitted Diseases

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Background

National Data

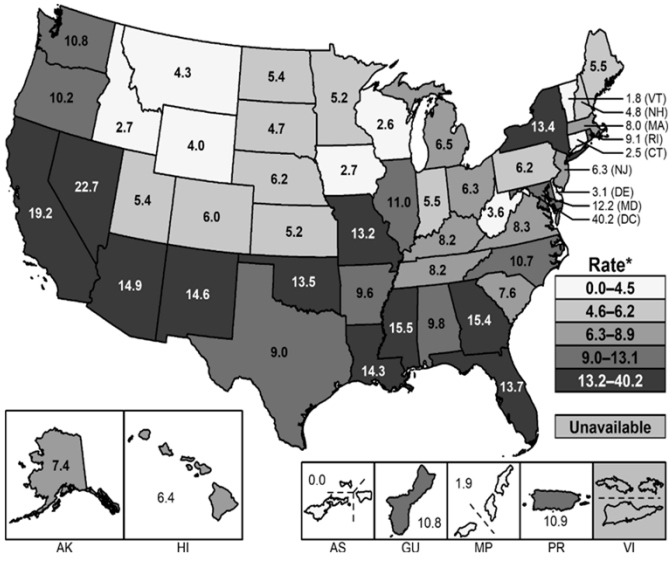
- Sexually transmitted infections are on the rise
- **Syphilis**
  - 35,063 new cases since 2014, 71% increase
    - Several demographics have shown increased case numbers
    - Gonorrhea and syphilis increase the likelihood of transmission of HIV

STI testing in Urban Emergency Departments

Ideal Population

- Indigent population
- Uninsured
- No Primary Care
- ED is point of healthcare access
- High risk populations:
  - Minorities
  - Transient/homeless
  - IVDU
  - prostitution
  - multiple partners with diverse sexual orientation
- Perfect opportunity to screen for syphilis in a population that is under tested and under treated

Primary and Secondary Syphilis — Rates of Reported Cases by State and Territory, United States, 2018



Source: CDC

* Per 100,000.
NOTE: Section A1.11 in the Appendix for more information on interpreting reported rates in US territories.

Franklin County

- Ranks 21st amongst counties in nation in number of new cases of syphilis
- Half of all new cases of syphilis in just 28 counties nationally
  - Less than 1% counties nationwide
- One of 48 counties identified nationally as HIV hot spot

Source: CDC

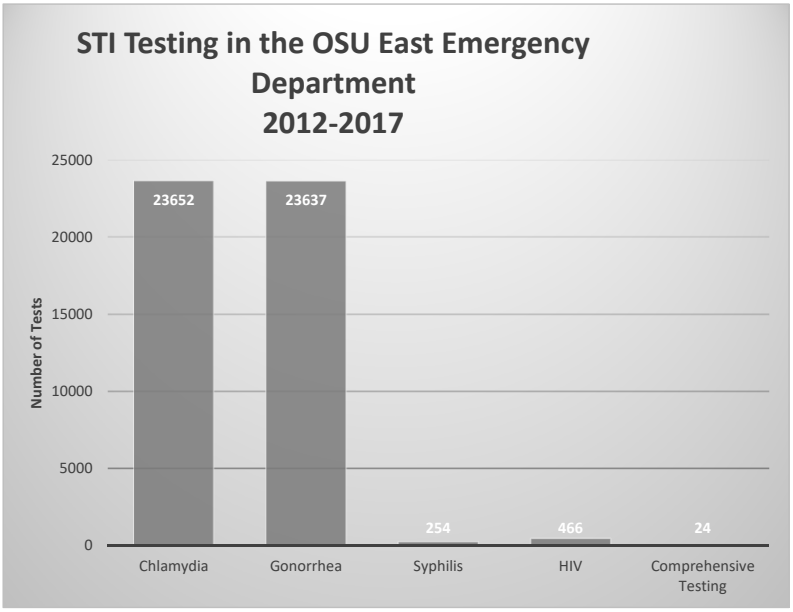
Emergency department visits: trends

YEAR	NHAMCS ESTIMATED ED VISITS (MILLIONS)
2001	107.5
2002	110.2
2003	113.9
2004	110.2
2005	115.3
2006	119.2
2007	116.8
2008	123.8
2009	136.1
2010	129.8
2011	136.3
2012	130.9
2013	130.4
2014	141.4
2015	136.9
2016	**145.6**

Source: CDC

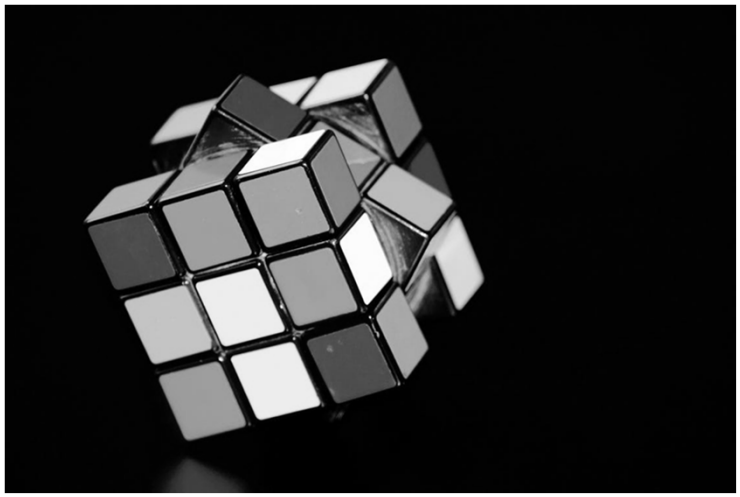
Pearson W, Peterman T, Gift T. An Increase in Sexually Transmitted Infections Seen in US Emergency Departments. Prev Med. 2017 July; 100:143-144.
Emerg Med Clin N Am 36 (2018) 767–776 https://doi.org/10.1016/j.emc.2018.06.007

Order practice prior to initiation of study



Why didn't we do this sooner?

- It's Complicated



https://www.kff.org/hivaids/fact-sheet/hiv-testing-in-the-united-states/
JAMA Network Open. 2019;2(6):e195042. doi:10.1001/jamanetworkopen.2019.5042 (Reprinted) June 11, 2019 2/4

Source: CDC

Why didn't we do this sooner?

- Practitioners unaware of syphilis surge
- Who is responsible for follow-up on these results?
- Interpretation of results
- Tracking patients down
- Collaboration with outpatient clinics
- Linkage to care and initiation of PrEP
- Insurance coverage: US Preventative Services Task Force
  - Medicaid mostly cover routine screening or "medically necessary" testing

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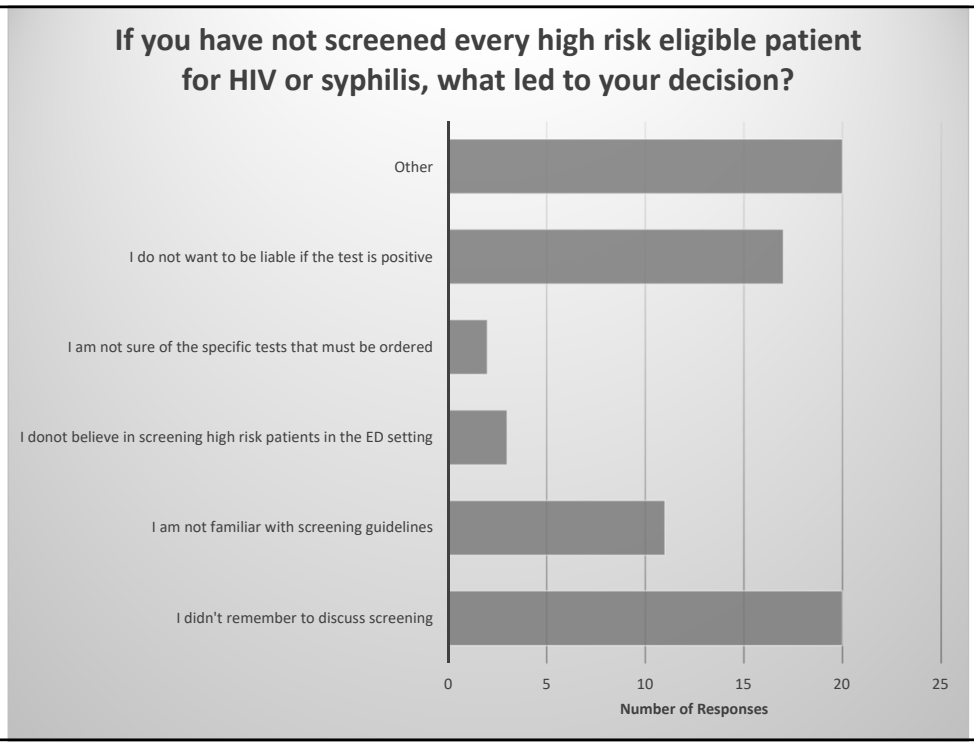
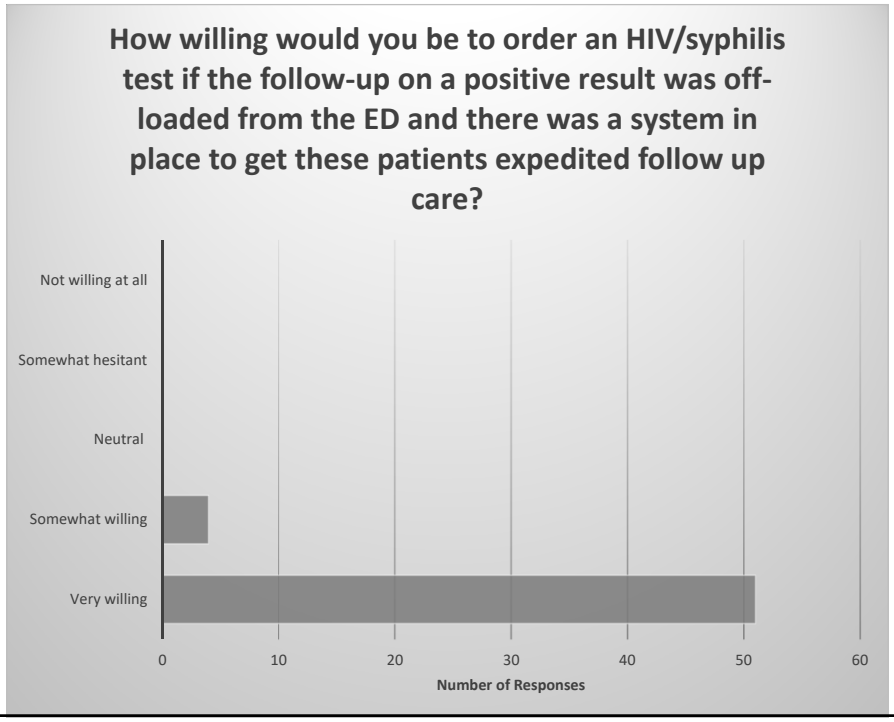
Source: CDC

The test has been there. Why aren't you ordering it?

- Survey of all EM faculty, residents, NPs at OSU Main and East
- Questions address hesitation to ordering HIV/syphilis testing from ED

Source: CDC


If you have not screened every high risk eligible patient for HIV or syphilis, what led to your decision?
Other
I do not want to be liable if the test is positive
I am not sure of the specific tests that must be ordered
I donot believe in screening high risk patients in the ED setting
I am not familiar with screening guidelines
I didn't remember to discuss screening
0
5
10
15
20
25
Number of Responses


How willing would you be to order an HIV/syphilis test if the follow-up on a positive result was off-loaded from the ED and there was a system in place to get these patients expedited follow up care?
Not willing at all
Somewhat hesitant
Neutral
Somewhat willing
Very willing
0
10
20
30
40
50
60
Number of Responses

Solution: Guarantee follow-up outside the ED

- ID generated list daily
  - All patients tested for HIV/syphilis and their results
- Interpretation of results
- Contacting patient
  - CPH and ODH help
- Arranging for treatment or continued surveillance
- PrEP
- STI ID Attending on call pager on WebExchange

Carter MW, Wu H, Cohen S, et al. Linkage and referral to HIV and other medical and social services: a focused literature review for sexually transmitted disease prevention and control programs. Sex Transm Dis. 2016;43(2 Suppl 1):S76-S82. **(Systematic review; 33 studies)**

ED STI Protocol

Management of STIs

Patient examination:
Previous STIs including HIV status, barrier protection, sex of partners, number of partners, rectal, oral, vaginal intercourse

STI orders:
Female: gonorrhea and chlamydia (cervix)
Affirm (wet prep-BV, yeast, trich)
Syphilis (STAT not next day lab)
Rapid HIV (blood)
Male: gonorrhea and chlamydia (urine/urethra)
Urine micro (trich)
Syphilis (STAT not next day lab)
Rapid HIV (blood)

ED STI Protocol — Management of STIs

May provide presumptive treatment for gonorrhea and chlamydia based upon history, exam, and/or high-risk status while in the ED.

If HIV or syphilis +, notification will be sent to Infectious Disease and the health department for follow up (by lab, not the ED provider). ID will then contact the patient regarding treatment options/locations, follow-up, and PrEP initiation for high risk patients.

ED STI Protocol — Management of STIs

Current CDC treatment Recommendations:
Chlamydia: Zithromax 1000 mg PO x1 OR Doxycycline 100mg BID x7 days
Gonorrhea: Rocephin 250mg IM x1 PLUS Zithromax 1000 mg PO x1
Trichomoniasis: Flagyl 2000 mg PO x1 OR Flagyl 500mg BID x7 days
Syphilis: Benzathine (PCN G) 2.4 million units IM x1

Update: Gonorrhea 500mg IM x 1 for 300 lbs or less, 1 gram IM x 1 for greater than 300 lbs

ED protocol

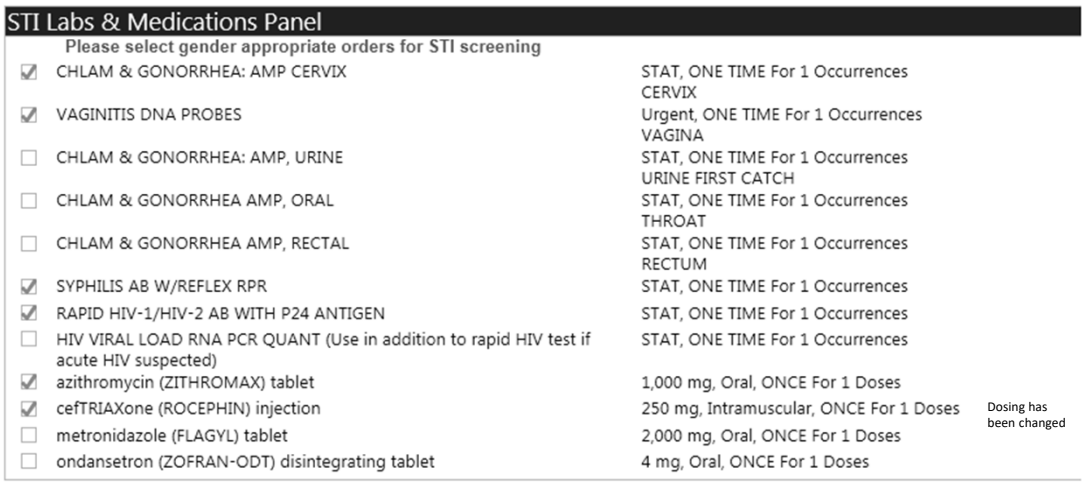
- STI-related complaint/Concern for STI based on clinical presentation
- History
  - Number sexual partners
  - Known HIV or syphilis diagnosis?
  - Barrier methods used
  - Sexual contact
    - Need for oral, rectal, and/or vaginal swabs
- Test for GC/Chlamydia (oral, urine, rectal, urethral, vaginal swabs), HIV (serum), syphilis (serum)
- Rapid HIV, with p24 antigen and syphilis AB with reflex RPR

Source: CDC

ED Order Set

UPDATE: Rapid Gonorrhea and Chlamydia testing now available. ALSO added pregnancy test and UA to streamline ordering

- Order set
  - Type "STI" in order set box on IHIS



STI Labs & Medications Panel

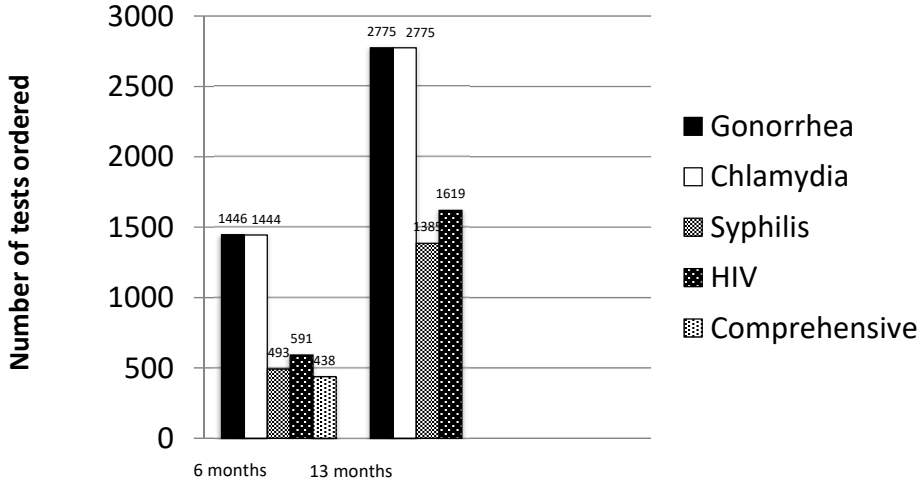
Please select gender appropriate orders for STI screening

☑	CHLAM & GONORRHEA: AMP CERVIX	STAT, ONE TIME For 1 Occurrences CERVIX
☑	VAGINITIS DNA PROBES	Urgent, ONE TIME For 1 Occurrences VAGINA
☐	CHLAM & GONORRHEA: AMP, URINE	STAT, ONE TIME For 1 Occurrences URINE FIRST CATCH
☐	CHLAM & GONORRHEA AMP, ORAL	STAT, ONE TIME For 1 Occurrences THROAT
☐	CHLAM & GONORRHEA AMP, RECTAL	STAT, ONE TIME For 1 Occurrences RECTUM
☑	SYPHILIS AB W/REFLEX RPR	STAT, ONE TIME For 1 Occurrences
☑	RAPID HIV-1/HIV-2 AB WITH P24 ANTIGEN	STAT, ONE TIME For 1 Occurrences
☐	HIV VIRAL LOAD RNA PCR QUANT (Use in addition to rapid HIV test if acute HIV suspected)	STAT, ONE TIME For 1 Occurrences
☑	azithromycin (ZITHROMAX) tablet	1,000 mg, Oral, ONCE For 1 Doses
☑	cefTRIAXone (ROCEPHIN) injection	250 mg, Intramuscular, ONCE For 1 Doses
☐	metronidazole (FLAGYL) tablet	2,000 mg, Oral, ONCE For 1 Doses
☐	ondansetron (ZOFRAN-ODT) disintegrating tablet	4 mg, Oral, ONCE For 1 Doses

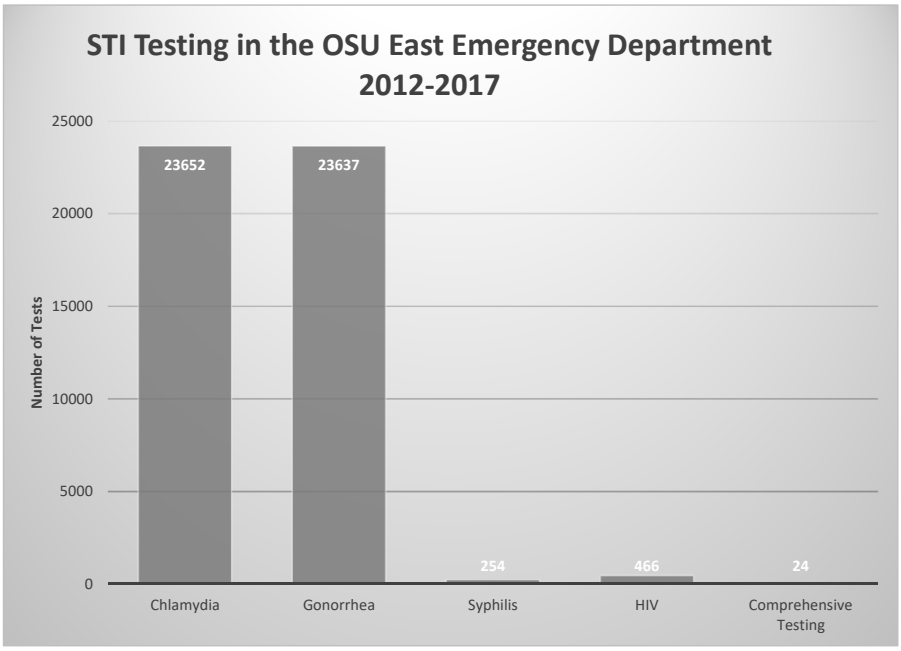
Dosing has been changed

Source: CDC

Data since initiation of project



Source: CDC



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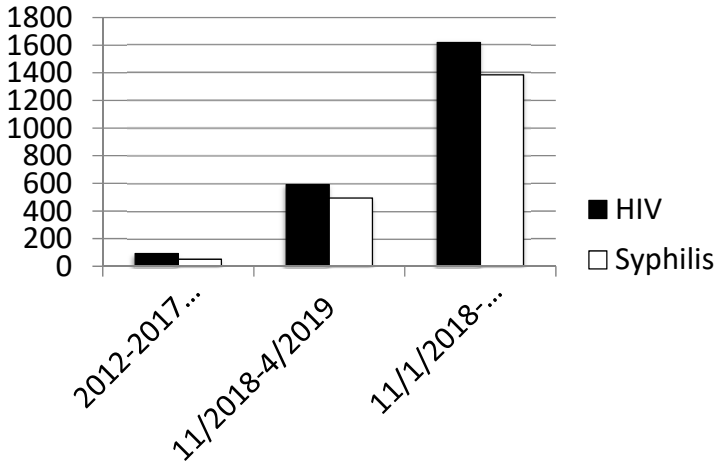
HIV and syphilis tests ordered from OSU EDs



SYPHILIS

- Between Nov 1 2018 and Nov 30 2019 there were

  57 positive syphilis antibody tests
  - 24 positive tests in women
  - 33 positive tests in men

- Totals:
  - 27/57 Previously treated infections
  - 19/57 Late latent infections (6 fully treated, 4 partially treated, 9 untreated)
  - 2/57 Secondary syphilis (2/2 fully treated)
  - 1/57 Primary syphilis (1/1 fully treated)
  - 8/57 false positives
  - 16 positive and/or inadequately treated cases found
    - 1 % of those tested had a positive result and inadequate/no treatment

Source: CDC

Moving Forward

- Protocol for STI testing in EDs nationally
- Exemplar of interdepartmental collaboration with OSU Infectious Disease and collaboration with Columbus Public Health
- Model for quick linkage to care and initiation of PrEP
  - PrEP can reduce risk of HIV acquisition through sex by 90%
  - Navigators in ED who will assist patients with LTC and PrEP
- Social Work resources
- Nurse case manager, establish primary care

Source: CDC

Goals

- PrEP referral in STI order set to specific sites
  - ID clinic, THW, FACES, Equitas, primary care, patient choice
- HPV vaccine in appropriate patients
- Introduce model to other area healthcare systems
- Retrospective analysis of how early detection/treatment of HIV reduces number of ED visits/year
- Study demographics of patient populations being tested
  - Visits to ED/year
  - Race
  - Age
  - Gender
  - Sexual Orientation
  - Insurance status

Source: CDC