

STDCCN Potpourri

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STDCCN: Syphilis

Question

- 45M with positive syphilis serology, no known history chancre/rash. possible childhood exposure to YAWS. no prior treatment. has previously declined treatment. 7/2022 neg RPR, +CIA, equivocal TPPA 2/2020 neg RPR, +CIA, equivocal TPPA 2019 neg RPR, +CIA, neg TPPA Any treatment indicated? Other recommendations? thank you!

Answer

- Dear X,I see that your patient has a history of possible childhood yaws and no known prior history of syphilis, rash, chancre, or syphilis treatment. I assume your patient is also currently asymptomatic with regard to syphilis. On testing in 2019, 2020, and 2022, your patient has had a non-reactive RPR, positive treponemal antibody CIA, and negative or equivocal TPPA. Serologic testing can unfortunately not distinguish between syphilis and yaws. In scenarios like these, I would usually send an additional treponemal antibody (e.g., FTA antibody). If this is positive, I would treat for latent syphilis. If it is negative, I think it would reasonable to forgo treatment, as the patient would lack a confirmed positive treponemal test. Please let me know if you have any additional questions or concerns.Kind regards,Y

CDC Recommendations

- **All reactive EIA/CIAs should be reflexed to a quantitative non-treponemal test (e.g. RPR, VDRL)**
 - Confirm reactive EIA/CIA
 - Detect active infection
- **Discordant specimens (e.g. EIA+/RPR-) should be confirmed with a 2nd treponemal test**
- **Confirmatory treponemal test should ideally be similarly sensitive and more specific than EIA/CIA**
 - TP-PA recommended
 - FTA-ABS test not recommended (lower specificity than other treponemal tests and probably lower sensitivity; also requires trained personnel and a dedicated fluorescence microscope)
- **Results of all 3 tests (EIA, RPR, TP-PA) should be reported simultaneously to provider**

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Clinical Infectious Diseases

MAJOR ARTICLE



Performance of Treponemal Tests for the Diagnosis of Syphilis

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Background. Treponemal immunoassays are increasingly used for syphilis screening with the reverse sequence algorithm. There are few data describing performance of treponemal immunoassays compared to traditional treponemal tests in patients with and without syphilis.

Methods. We calculated sensitivity and specificity of 7 treponemal assays: (1) ADVIA Centaur (chemiluminescence immunoassay [CIA]); (2) Bioplex 2200 (microbead immunoassay); (3) fluorescent treponemal antibody absorption test (FTA-ABS); (4) INNO-LIA (line immunoassay); (5) LIAISON CIA; (6) *Treponema pallidum* particle agglutination assay (TPPA); and (7) Treponema enzyme immunoassay [EIA], using a reference standard combining clinical diagnosis and serology results. Sera were collected between May 2012–January 2013. Cases were characterized as: (1) current clinical diagnosis of syphilis: primary, secondary, latent, late latent; (2) prior treated syphilis only; (3) no evidence of current syphilis, no prior history of syphilis, and at least 1 treponemal tests negative.

Results. Among 959 participants, 262 had current syphilis, 294 had prior syphilis, and 403 did not have syphilis. FTA-ABS was less sensitive for primary syphilis (78.2%) than the immunoassays or TPPA (94.5%–96.4%) (all $P \leq .01$). All immunoassays were 100% sensitive for secondary syphilis, 95.2%–100% sensitive for early latent disease, and 86.8%–98.5% sensitive in late latent disease. TPPA had 100% specificity.

Conclusions. Treponemal immunoassays demonstrated excellent sensitivity for secondary, early latent, and seropositive primary syphilis. Sensitivity of FTA-ABS in primary syphilis was poor. Given its high specificity and superior sensitivity, TPPA preferred to adjudicate discordant results with the reverse sequence algorithm over the FTA-ABS.

Keywords. syphilis; immunoassay; treponemal; diagnostic performance.

STDCCN: Congenital Syphilis

Question

- 2 month old baby new to us (born in AZ) tx'd for "probable congenital syphilis" postpartum-mom reports being tx'd for syphilis post-partum (no prenatal care; 33 y o Angolan female-we have incomplete records as of this email), the records we've rec'd show RPR 1:128 in placenta/cord blood. Baby's labs-neg w/u (LP wnl, normal long bones, CBC/CMP wnl-lab error and VRDL not done) (incomplete records). Mom had NEG TREP and NEG RPR on baseline labs here. Any thoughts about the 1:128 RPR in placenta and neg syphilis tests here? thank you!
- Hi X, Would it be okay for me to give you a quick call at the number you listed? I'd like to clarify mother syphilis results around the time of birth (if you have that) and infant testing results now (if you are following the infant). I will try you at the number you listed.- Y

Key Points:

- Obtain more info if needed
- Cite references where helpful
- Public health – clinician collaboration to optimize outcomes

Answer

- Hi X,
- Very nice to speak with you today. I will await the results of the Arizona Dept of Health details on maternal and infant testing at birth. I wanted to make sure that I suggested doing an RPR on the infant at this time - hopefully the pediatrician can order that, but would recommend this.
- My pediatric ID colleagues reminded me of the section of the STI guidelines that addresses cord blood testing: "All neonates born to mothers who have reactive nontreponemal and treponemal test results should be evaluated with a quantitative nontreponemal serologic test (RPR or VDRL) performed on the neonate's serum because umbilical cord blood can become contaminated with maternal blood and yield a false-positive result, and Wharton's jelly within the umbilical cord can yield a false-negative result." (<https://www.cdc.gov/std/treatment-guidelines/congenital-syphilis.htm>) (this is also reinforced in the AAP Red Book)
- So good that the infant received serum testing. In your patient's case I would not expect a false positive unless the maternal birth RPR (which we do not have) was elevated (this is possible if mother was treated, now nonreactive RPR, and could be one of the small percent where the treponemal test reverts to nonreactive after treatment, which isn't as common, but possible in the setting of early treatment).
- Talk soon, Y

STDCCN: Gonorrhea

Question

- We have a 24 yo Male who has sex with men, reports 3 partners past year. We are concerned with resistant oral Gonorrhea with Gentamicin 240mg/Azithromycin 2grams treatment. Pt has allergy to cephalosporins, Ceftin, Ceclor. with full body rash.
- Background is as follows: 7/14/21 - Oral GCCT - Negative; Urogenital GCCT - Negative 5/24/22 - Oral GCCT - Pos GC, Neg CT; Urogenital GCCT - Negative; Rectal GCCT - Pos GC, Pos CT; HIV - Negative, Syphilis Negative Treated with Gentamicin 240mg/Azithromycin 2grams same DOS 6/8/22 Oral GCCT - Pos GC, Neg CT (Patient states did abstain from sex for at least 7 days post treatment, was sexually active with a new partner after the 7 days). 6/17/22 - Treated with Gent 240mg/Azithromycin 2grams 7/8/22 - Oral GCCT - Pos GC, Neg CT (21 days after treatment, no intercourse since treatment). Should PPSNE refer him to a Infectious Disease doctor? Please advise. Thank you!

Key Points:

- Aminoglycosides (gentamicin, spectinomycin) do not eradicate oropharyngeal GC
- Cephalosporins don't necessarily x-react
- No rush – patient is likely asx (OP GC)
 - Allergy testing, and/or
 - Culture+Susceptibility to guide

Answer

- Dear X, Thank you for your question. I see from the history you provided that your patient is a 24-year-old man who has sex with men who tested positive for oral GC on 5/24/2022. He was then treated with gentamicin and azithromycin. He subsequently tested positive for pharyngeal gonorrhea on 6/8/2022 and was again treated with the same regimen. He again tested positive on 7/8/2022. I think this scenario is less concerning for resistance per se than for treatment failure due to the known difficulties eradicating gonorrhea at the pharyngeal site, particularly when ceftriaxone is not used. There is thought to be no reliable alternative to ceftriaxone for treatment of pharyngeal gonorrhea. One question would be whether the patient could receive ceftriaxone. Cross-reactivity for allergies among cephalosporins are generally driven by the drug's side chains. It is not apparent to me that there is a high risk of cross-reactivity among ceftriaxone and cefaclor or cefuroxime. I recommend an allergy consultation to determine if this patient could safely receive ceftriaxone. If he can, I would administer that as the preferred therapy. A less preferred option would be to culture the throat for gonorrhea, perform antimicrobial susceptibility testing, and choose an agent for treatment to which the organism tests susceptible (that is not gentamicin/azithromycin - that approach has already failed). Please let me know if you have any additional questions. Kind regards, Y

STDCCN: HSV

Question

- 27 yo female who has a long term male partner known to be HSV-1 + (gets cold sores no genital lesions). Partner performed oral sex on patient. Later that night male partner developed cold sore. Patient then had blood work done by another provider showing she is HSV antibody +. She has never had an outbreak. Her question is does that positivity protect her from the possibility of a primary genital outbreak. Thanks!

Answer

- Maybe? But as you know, commercially available antibody testing for HSV is notoriously unreliable, and can be both falsely positive and falsely negative. Only time will tell, and of course, if she ever develops genital lesions, HSV PCR should be done on the lesions, early in the course of the lesions, to make the diagnosis, and help with management and counseling.
<https://www.cdc.gov/std/treatment-guidelines/herpes.htm>

STDCCN: *Mycoplasma genitalium*

Question

- 20 year old asymptomatic female with positive mycoplasma genitalium rRNA, TMA testing on 9/20/22. She was tested because she had a partner who tested positive. Patient herself has no dysuria, abnormal vaginal discharge, pelvic pain, or symptoms of PID. Treatment guidelines are confusing for asymptomatic partners. Resistance testing is not available. Do I need to treat her with the full course of the Doxy and then moxifloxacin? Thank you!

Answer

- Treatment guidelines are varied because, as you know, there is not a lot of evidence upon which to decide how to manage partners.
- When you look across U.S., Canadian, U.K, Australian, and European guidelines, one generally agreed-upon approach is to test and treat positive-but-asymptomatic-current-sex-partners of the index case who was originally positive, with the same regimen as what the index case received, in order to reduce the chance of reinfection of the index case.
- There is an alternative approach, IF your patient, the positive-but-asymptomatic-partner, has NOT had any azithromycin treatment recently (if she has had azithromycin recently, most would assume she has developed macrolide-resistant *M. genitalium*, and therefore most would not use any azithromycin-containing regimen). Assuming no contraindications, I would consider treating your patient with the high-dose azithromycin regimen (1 g on day 1 followed by 500 mg on days 2 through 4). Whether you start with doxycycline (i.e. use the Doxycycline 100 mg orally 2 times/day for 7 days, followed by azithromycin 1 g orally initial dose, followed by 500 mg orally once daily for 3 additional days), or whether you just do the azithromycin, is uncertain - current U.S., U.K., and Australian guidelines espouse two-stage therapy (doxy followed by azithro); Canadian and European guidelines espouse simply doing the azithro.
- I myself hesitate in treating the positive-but-asymptomatic-partner with the two-stage therapy of Doxycycline 100 mg orally 2 times/day for 7 days followed by moxifloxacin 400 mg orally once daily for 7 days. This is because you're right, in the U.S. we don't have resistance testing yet (in countries where resistance testing is available, moxifloxacin is used when the organism is known to be macrolide-resistant), and quinolones like moxifloxacin have the potential for serious adverse reactions, so I find it more difficult to justify treating an asymptomatic partner with approaches using moxifloxacin, right-off-the-bat.
- Regardless of what antibiotic choices are made, it's important to share with the patient how controversial this area of medicine is, and have her collaborate in the decision-making. (What if she is no longer with the index patient who was positive? The guidelines only advise testing and treating CURRENT sex partners of *M. genitalium* positive cases.) And if the choice is made to treat, please do usual counseling that all of these antibiotics are generally better tolerated after meals (i.e. not taken on an empty stomach), and to let you know if she has too much GI intolerance (some patients need some ondansetron (Zofran) to get them through the course of treatment).