

SYPHILIS TREATMENT 2,3				
		NON-PREGNANT		PREGNANT
		HIV-	HIV+ ▼	
Primary Stage, Secondary Stage, or Early Latent Stage	Recommended: Bicillin® L-A x1 IM	Recommended: Bicillin® L-A x1 IM	Recommended: Bicillin® L-A x1 IM	Recommended: Bicillin® L-A x1 IM
	Alternatives: Doxycycline 100 mg po bid x 14 d Tetracycline 500 mg po qid x 14 d Ceftriaxone 1g IM / IV x 8-10 d	Alternatives: Doxycycline 100 mg po bid x 14 d Tetracycline 500 mg po qid x 14 d Ceftriaxone 1g IM / IV x 8-10 d	Alternatives: Doxycycline 100 mg po bid x 14 d Tetracycline 500 mg po qid x 14 d Ceftriaxone 1g IM / IV x 8-10 d	Alternatives: None.
Late Latent Stage or Unknown Duration Stage	Recommended: Bicillin® L-A x3 IM (1 dose/wk x3 wks)	Recommended: Bicillin® L-A x3 IM (1 dose/wk x3 wks)	Recommended: Bicillin® L-A x3 IM (1 dose/wk x3 wks)	Recommended: Bicillin® L-A x3 IM (1 dose/wk x3 wks)
	Alternatives: Doxycycline 100 mg po bid x 28 d Tetracycline 500 mg po qid x 28 d	Alternatives: Doxycycline 100 mg po bid x 28 d Tetracycline 500 mg po qid x 28 d	Alternatives: Doxycycline 100 mg po bid x 28 d Tetracycline 500 mg po qid x 28 d	Alternatives: None.
Neurosyphilis (can occur at any stage)	Recommended: AqPCN IV x 10-14 d	Recommended: AqPCN IV x 10-14 d	Recommended: AqPCN IV x 10-14 d	Recommended: AqPCN IV x 10-14 d
	Alternative: ProPCN IM + Prob po x 10-14 d	Alternative: ProPCN IM + Prob po x 10-14 d	Alternative: ProPCN IM + Prob po x 10-14 d	Alternative: ProPCN IM + Prob po x 10-14 d

KEY: AqPCN = Aqueous crystalline penicillin G, 18-24 million units daily, administered as 3-4 million units IV q 4 hours x 10-14 d.
Bicillin® L-A = Bicillin® Long-Acting (trade) / Benzathine penicillin G (generic) 2.4 million units IM per dose. (Do **NOT** use Bicillin® C-R.)
ProPCN + Prob = Procaine penicillin G 2.4 million units IM qd x 10-14 d plus Probenecid 500 mg po qid x 10-14 d.

Jarisch-Herxheimer Reaction (JHR): Advise patients of this possible acute febrile reaction with chills, headache, myalgias, nausea, etc. that can occur within hours of treatment initiation and usually resolves within 24 hrs. It is thought to be an endotoxin reaction to spirochete destruction, and is more common in early stages. Antipyretics may be used, but are not considered preventative. *In the 2nd half of pregnancy, the JHR might induce early labor or cause fetal distress, but this should not prevent or delay therapy.*

▼ CDC's 2006 Guidelines recommend a Cerebral Spinal Fluid (CSF) exam for HIV+ patients before treatment for either Late Latent or Latent-Unknown Duration, even in the absence of clinical findings of neurosyphilis. However, CDC's 2010 Guidelines (update in progress) will likely downgrade this to "CSF exam may be considered" in these patients.

FOLLOW-UP OF TREATED SYPHILIS CASES 3,5				
		F/U RPR Titers		Inadequate Response to Treatment (Tx)
		HIV-	HIV+	
Primary Stage or Secondary Stage	6 mos	HIV-	3 mos	> Signs/Sx persist or recur. > Titers shows a sustained 4-fold rise since initiation of Tx, compared with 'baseline' titer drawn Tx day #1 (or titer obtained closest and prior to start of Tx). Examples of 4-fold rise: 1:8→1:32, 1:16→1:64, 1:32→128, etc. > Titers that don't decline 4-fold (ie 1:64→1:16) within 6-12 mos of Tx for 1°/2° <u>may</u> indicate Tx failure.‡
		HIV+	6 mos	
	12 mos	HIV-	9 mos	
		HIV+	12 mos	
Latent Stages (Early Latent, Late Latent, or Unknown Duration)	6 mos	HIV-	6 mos	> Signs/Sx attributable to syphilis develop. > Titers show a sustained 4-fold rise since initiation of Tx, compared with 'baseline' drawn on Tx day #1 (or titer obtained closest and prior to start of Tx). > An initially high titer (≥1:32) that doesn't decline 4-fold (ie 1:32→1:8) within 12-24 mos of Tx for a Latent Stage.‡
		HIV+	6 mos	
	12 mos	HIV-	12 mos	
		HIV+	18 mos	
Pregnancy, Any Stage	At 28 (-32) wks EGA	HIV-	24 mos	> Inadequate maternal Tx is likely if: > Delivery occurs within 4 weeks of Tx, > Mother has clinical signs/Sx that are present at delivery, or > Maternal titer rises 4-fold compare to the pre-Tx titer. <i>Most women will deliver before the treatment response can be assessed definitively.</i> > Syphilis diagnosed during the 2 nd half of pregnancy: ultrasound findings that indicate greater risk for fetal treatment failure include placental thickening, hepatosplenomegaly, polyhydramnios, ascites, etc. Specialty consultation needed. ‡ Decline in titers may be slower in some, ie those who are HIV+ and those who were treated previously for syphilis.
		HIV+	24 mos	
	At delivery (Consider checking titers <u>monthly</u> in women at high-risk for re-infection, per CDC 2006 MMWR, p. 30.)	HIV-		
		HIV+		
Clinical Considerations Regarding Inadequate Tx Response				
> Re-infection: Does sexual history shows risk of re-exposure? If so, re-treat Using appropriate regimen. > Tx failure: If po meds given, was pt compliant?; if not, recommend Bicillin® L-A (desensitize if allergic). HIV seroconversion?; re-screen pts whose previous HIV was -. Unrecognized CNS infection, especially if HIV+? Consider CSF exam.				

INTERPRETING CHANGES IN RPR TITERS 5	
Negative / Non-reactive	One increase or decrease in dilution represents a 2-fold change in titer, so 2 dilutions would yield a '4-fold' change (ie rise of 1:4→1:16). A 2 dilution or 4-fold change is regarded as clinically significant between 2 sequential test results. With adequately treated syphilis, a 1 dilution increase (ie 1:4→1:8) can result from testing variation without clinical significance and can be followed expectantly; a 2 dilution or 4-fold rise should be evaluated for possible re-infection or treatment failure.
1:1	
1:2	
1:4	
1:8	
1:16	
1:32	
1:64	
1:128	
1:256	
1:512	

CONGENITAL SYPHILIS: See next page.

References, pp. 2-4:

1. AAP. Syphilis. In: Pickering LK et al eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: AAP; 2009:638-651.
2. Calif. Dept. of Public Health (CDPH) STD Branch. STD Treatment Guidelines Table for California, Nov 2007 http://www.sicphs.org/healthcare_providers/providers.htm
3. CDC. STD treatment guidelines, 2006. *MMWR* 2006;55 (No. RR-11) See latest guidance at <http://www.cdc.gov/std/treatment/>
4. CDC. Syphilis Testing Algorithms Using Treponemal Tests for Initial Screening — 4 Labs. *MMWR* 2008;57:872-875 <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5732a2.htm>
5. Cherneskie, T. An Update & Review of the Dx & Mgt of Syphilis. Region II STD/HIV PTC; NYC DHMH: 2006. <http://www.nyc.gov/html/doh/downloads/pdf/std/syphilis-report.pdf>
6. Katz, K. Newer lab testing algorithms for syphilis begin with EIA. *Medical Laboratory Observer*. Jan 2010 http://www.mlo-online.com/features/2010_january/0110_clinical_issues.pdf
7. T. Narula, T. et al. HIV and Syphilis: The Great Imitator. *HIV Clinician*. Spring 2010. <http://www.deltatetac.org/hcissues/hcspring2010.pdf>

Other Resources:

- California STD/HIV Prevention Training Center. *In-person and online training* <http://www.stdhivtraining.org/> | *Syphilis Clinical Algorithms – Primary Syphilis Algorithm:* http://www.stdhivtraining.org/resource.php?id=38&ret=clinical_resources | *Secondary Syphilis Algorithm:* http://www.stdhivtraining.org/resource.php?id=42&ret=clinical_resources
- CDC. Self-Study STD Module for Clinicians - Syphilis <http://www2a.cdc.gov/stdtraining/self-study/syphilis.asp>
- Hardin Library, U. of Iowa. Link to CDC's syphilis pictures <http://www.lib.uiowa.edu/hardin/md/cdc/syphilis.htm>

SJC PHS Website:

This *Summary Guidance* and the *Syphilis Alert* are posted at http://www.sicphs.org/healthcare_providers/providers.htm

CONGENITAL SYPHILIS (CS): Maternal-fetal transmission can occur via the transplacental route during any stage, but is much more likely with recent infection (1°/2°>Early Latent>Late Latent). **Untreated 1°/2° maternal syphilis can result in ~40% fetal loss.** Congenital Syphilis can be prevented by early detection of maternal infection & treatment with PCN more than 4 wks before delivery. *No infant or mother should leave the hospital unless maternal serostatus has been documented at least once during pregnancy (& at delivery for women at higher risk for STDs[§]).* Any woman delivering a stillborn >20 weeks EGA should also be tested for syphilis.

Only severe cases of Congenital Syphilis are clinically apparent at birth. Infected infants may return in weeks to months with “snuffles” (syphilitic rhinitis), rash (some have peeling of palms/soles), anemia, jaundice, etc.

All infants of mothers with reactive serology should have a serum RPR (& titer if reactive); **do not use** cord blood, which can be contaminated with maternal blood. Treponemal testing of infants is **not** necessary. Interpretation of a reactive RPR in infants is complicated by passive transfer of maternal non-treponemal antibodies (treponemal also transfer). In newborns with RPR titers $\geq 4x$ the maternal titer, diagnosis is straightforward. In practice, diagnosis is often based on maternal serology & whether or not the mother had adequate Tx during pregnancy.

Infants should be treated for presumed CS if they have any evidence of active disease, RPR titer $\geq 4x$ maternal titer, or were born to mothers who at delivery: 1) had untreated syphilis, 2) were treated with a *non-PCN* regimen during pregnancy, 3) were treated ≤ 4 weeks before delivery, or 4) had evidence of relapse or re-infection after treatment.

Infants with a reactive RPR should be re-tested q 2-3 mos until it becomes non-reactive or titer decreases 4-fold (titers should decrease by 3 mos & become non-reactive by 6 mos if infant was adequately treated, or was uninfected & initially reactive due to passive maternal transfer).

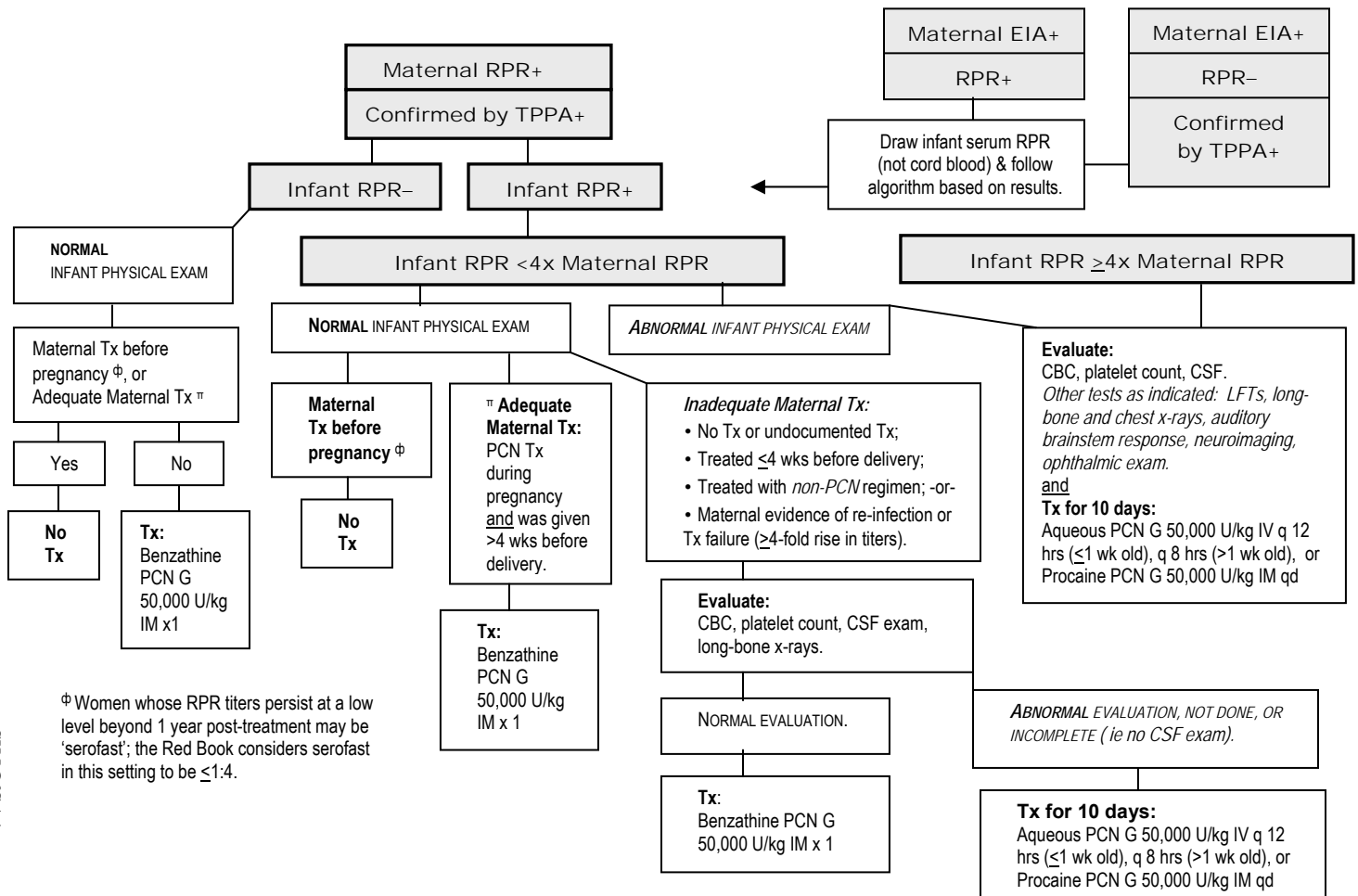
Mothers who screen EIA+: Some labs are now screening with the newer treponemal EIA test instead of the RPR. Reactive EIAs are reflexed to an RPR for confirmation; if the RPR is non-reactive, a 2nd treponemal test is used to confirm. The clinical significance of detecting asymptomatic patients who are EIA+/RPR-/TPPA+ is currently unknown. These test results may reflect old treated syphilis, old untreated syphilis, very early syphilis, or false positive treponemal tests (very rare). Asymptomatic pregnant women who test EIA+/RPR-/TPPA+ & have no documentation of previous Tx should be treated for Late Latent/Unknown Duration with Bicillin® L-A x3 (desensitize if allergic). Per the State STD Branch, these women should be re-evaluated in 1 wk to repeat the RPR & also to assess if they had a Jarisch-Herxheimer Reaction, which would be some evidence of early infection. If no change in results, testing should be repeated at 28 wks & at delivery.

Infants of mothers who are EIA+/RPR+ or EIA+/RPR-/TPPA+ need a serum RPR at birth; follow the algorithm below based on the results.

These cases can be complicated. If there are questions please call (209) 468-3845 / 3820. After hours, weekends, & holidays, medical providers may reach Public Health Services via the San Joaquin General Hospital operator at 468-6000.

[§]History of any STD, new partner or multiple sexual partners, illicit drug use, etc. Regarding geographic risk, the highest rates of female 1°/2° syphilis in the US are currently found in the south, including Alabama, Arkansas, Louisiana, Mississippi, Tennessee, & Texas

INFANTS BORN TO MOTHERS WITH REACTIVE SEROLOGY: EVALUATION & TREATMENT (Tx)^{1,3,4}



Φ Women whose RPR titers persist at a low level beyond 1 year post-treatment may be 'serofast'; the Red Book considers serofast in this setting to be $\leq 1:4$.