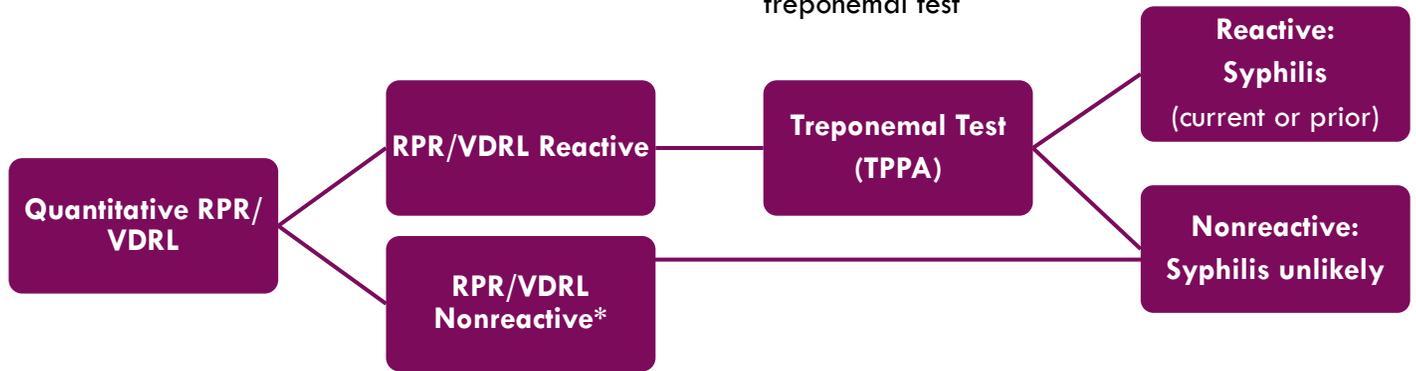


Clinical Interpretation of Syphilis Screening Algorithms A Resource for Local Health Jurisdictions

Testing: Traditional Algorithm^a

1. Screen with non-treponemal test (RPR/VDRL)

2. Confirm reactive non-treponemal test with treponemal test



*Early primary syphilis and late untreated syphilis possible if RPR/VDRL are nonreactive; see below for recommended actions

Table 1: Interpretation of Syphilis Serologies, Traditional Algorithm

Non-Treponemal (RPR/VDRL)	Treponemal (TPPA)	Possible Interpretations	Recommended Actions
Nonreactive	Nonreactive or not done	<ol style="list-style-type: none"> No syphilis Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> If syphilis unlikely, no further action needed. If early syphilis suspected, consider ordering a treponemal test (if not done initially) and repeating an RPR/VDRL in 1-2 weeks; if either test is reactive, treat for syphilis. If concerned for early syphilis (e.g., chancre present or known exposure) treat presumptively. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
	Reactive	<ol style="list-style-type: none"> Prior treated syphilis Untreated syphilis 	<ul style="list-style-type: none"> Treponemal tests (e.g., TPPA) often stay reactive for life; if patient has a history of adequate treatment for syphilis & no new exposures/symptoms, no further action needed. If early syphilis suspected (e.g., chancre present or known exposure), treat presumptively according to stage. If treating presumptively, repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion. If no signs or symptoms, order a second treponemal test (e.g., EIA or CIA); see table 2 for recommendations based on results.
Reactive	Nonreactive	<ol style="list-style-type: none"> False positive RPR or VDRL 	<ul style="list-style-type: none"> Likely false positive (not syphilis).^b In pregnancy or in patients at high risk for syphilis, consider rescreening with serologic testing in 2-4 weeks – if unchanged, no action needed.^c
	Reactive	<ol style="list-style-type: none"> Current syphilis Treated syphilis with residual/persistent RPR/VDRL titer 	<ul style="list-style-type: none"> If RPR/VDRL is newly reactive, stage and treat. If previously treated and sustained (≥ 2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.^d Note that RPR/VDRL may still be reactive after treatment; if there is a fourfold decline within 12-24 months, treatment is considered to have been adequate even if RPR/VDRL remains reactive. Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

^a The traditional algorithm starts with a non-treponemal test (RPR or VDRL) which, if reactive, is followed by a confirmatory treponemal test (TPPA). In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

^b False positives can be seen in pregnancy and/ in patients with autoimmune diseases, Lyme disease, certain viral infections (including HIV), injection drug use, and other conditions.

^c In the state of California, all pregnant people should be screened for syphilis at least twice during pregnancy: once at either confirmation of pregnancy or at the first pre-natal encounter, and again during the third trimester (ideally between 28-32 weeks). Patients should also be screened at delivery, except those at low risk who have a documented negative screen in the third trimester. See

https://files.medical.ca.gov/pubsdoco/publications/misc/Dear_Colleague_Letter_Expanded_Syphilis_Screening_Recommendations_12-8-20.pdf.

^d For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at

<https://www.cdc.gov/std/treatment-guidelines/syphilis.htm> for treatment and follow up recommendations.

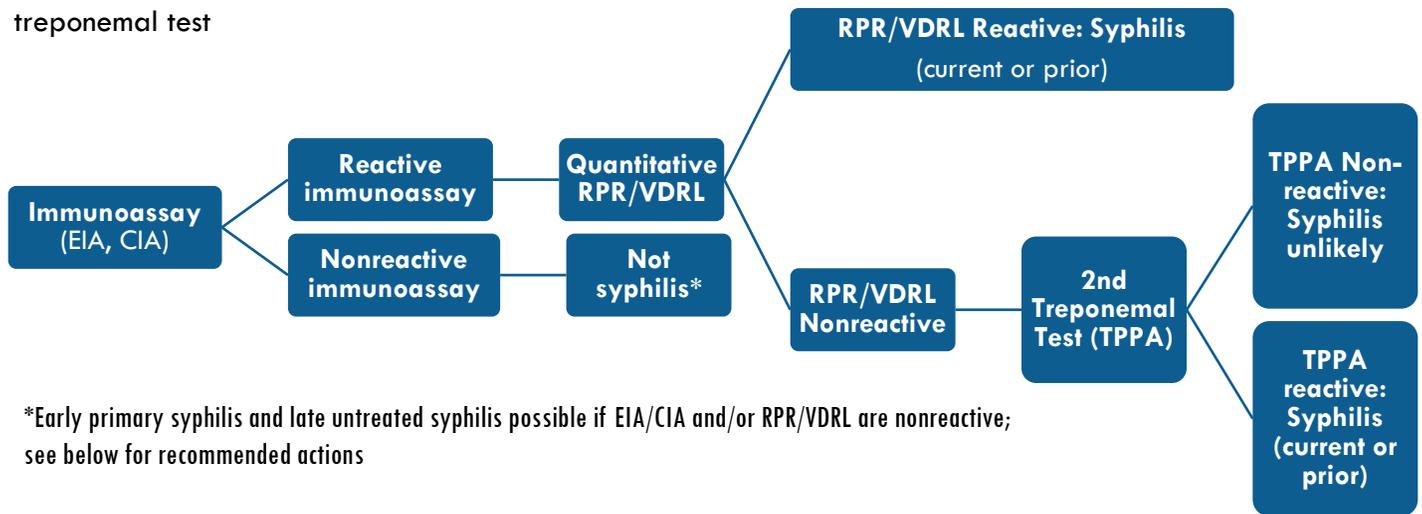
Clinical Interpretation of Syphilis Screening Algorithms A Resource for Local Health Jurisdictions

Testing: Reverse Algorithm^a

1. Screen with immunoassay treponemal test

2. Confirm reactive immunoassay test with non-treponemal test

3. Clarify discordant EIA/CIA and RPR/VDRL results with second treponemal test



*Early primary syphilis and late untreated syphilis possible if EIA/CIA and/or RPR/VDRL are nonreactive; see below for recommended actions

Table 2: Interpretation of Syphilis Serologies, Reverse Screening Algorithm

Immunoassay (CIA or EIA)	RPR/VDRL	TPPA	Possible Interpretations	Recommended Actions
Non-reactive	Non-reactive or not done	Non-reactive or not done	<ol style="list-style-type: none"> Syphilis unlikely Early/incubating syphilis (too early to be detected by serology) 	<ul style="list-style-type: none"> If syphilis unlikely, no further action needed. If immunoassay nonreactive but high clinical suspicion (such as a chancre or known exposure), treat presumptively for early syphilis. If treating presumptively, obtain RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
Reactive	Non-reactive	Non-reactive or not done	<ol style="list-style-type: none"> False positive immunoassay Early/incubating syphilis Latent or prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> If no signs/symptoms and low risk for syphilis, most likely a false positive immunoassay.^b No further action needed. If concerned for early infection or in pregnant patients, re-screen in 2-4 weeks.^c If signs/symptoms or contact to syphilis, treat presumptively. Repeat RPR/VDRL on day of treatment and, if nonreactive, again in 2-4 weeks to assess for seroconversion.
		Reactive	<ol style="list-style-type: none"> Latent or prior syphilis (treated or untreated) Early syphilis (prior to RPR/VDRL seroconversion) 	<ul style="list-style-type: none"> No further action needed if patient treated appropriately for syphilis in past, assuming no new exposures/symptoms and a negative clinical exam. If no symptoms and no known prior adequate treatment, treat presumptively for latent syphilis. If early syphilis suspected (symptoms or known exposure), treat presumptively. Obtain RPR/VDRL on day of treatment. If nonreactive, repeat in 2-4 weeks to assess for seroconversion.
	Reactive	Not done or Reactive	<ol style="list-style-type: none"> Current syphilis Prior syphilis (treated or untreated) 	<ul style="list-style-type: none"> If RPR/VDRL is newly reactive, stage and treat. If previously treated and sustained (≥ 2 weeks) 4-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.^d If known prior adequate treatment for stage of infection and RPR/VDRL declining appropriately (i.e., a fourfold decline within 12-24 months), no further action needed. Some treated patients may have a persistent low level RPR/VDRL titer for a prolonged period; re-treatment is not necessary in the absence of new exposures or symptoms.

^a The reverse algorithm starts with an immunoassay detecting syphilis antibodies which, if reactive, is followed by a quantitative RPR/VDRL. If there is a discrepancy between the immunoassay and RPR (one reactive, one nonreactive), a treponemal test (TPPA) serves as the tie-breaker. In interpreting serologies, it is helpful to know which testing algorithm (traditional vs reverse) is being used in your lab.

^b False positive immunoassays can occur with Lyme disease or non-syphilis treponemal infections.

^c In the state of California, all pregnant people should be screened for syphilis at least twice during pregnancy: once at either confirmation of pregnancy or at the first pre-natal encounter, and again during the third trimester (ideally between 28-32 weeks). Patients should also be screened at delivery, except those at low risk who have a documented negative screen in the third trimester. See https://files.medi-cal.ca.gov/pub/docs/publications/misc/Dear_Colleague_Letter_Expanded_Syphilis_Screening_Recommendations_12-8-20.pdf.

^d For patients determined to have new syphilis or treatment failure, refer to the Centers for Disease Control STD treatment guidelines at <https://www.cdc.gov/std/treatment-guidelines/syphilis.htm> for treatment and follow up recommendations.