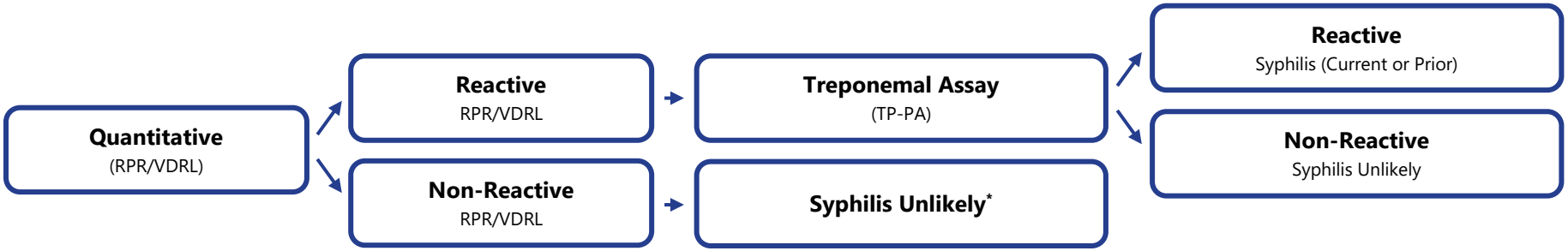
Interpretation of Syphilis Serology

Indiana Department of Health

Traditional Algorithm[1]

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



*Primary syphilis and late, untreated syphilis are possible if RPR/VDRL are non-reactive—see below for recommended actions.

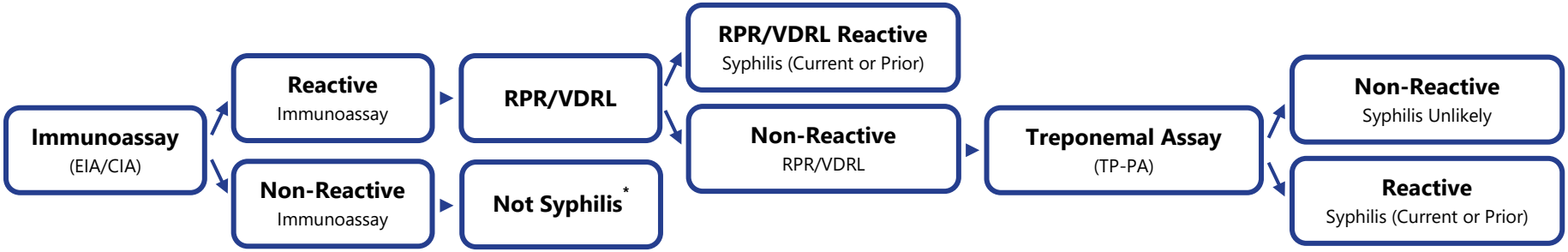
Non-Treponemal	Treponemal	Interpretations	Recommended Actions
Non-Reactive	Non-Reactive or Not Done	1. No syphilis 2. Early/incubating syphilis (too early to be detected by serology)	• If syphilis is unlikely, no further action is needed. • If early syphilis is suspected, run treponemal test (if not done initially) and repeat RPR/VDRL in 1-2 weeks; if either test is reactive, stage and 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 non-reactive, again in 2-4 weeks to assess for seroconversion.
Non-Reactive	Reactive	1. Prior treated syphilis 2. Untreated syphilis	• Treponemal tests (e.g., TP-PA) often stay reactive for life; if patient has history of adequate treatment for syphilis and no new exposures/symptoms, no further action is needed. • If early syphilis is suspected (e.g., chancre present or known exposure), treat presumptively according to staging. If treating presumptively, repeat RPR/VDRL on day of treatment and, if non-reactive, again in 2-4 weeks to assess for seroconversion.

Non-Treponemal	Treponemal	Interpretations	Recommended Actions
Reactive	Non-Reactive	1. False-Positive RPR or VDRL	• Likely a false-positive (not syphilis).[2] • In pregnancy or patients at high-risk for syphilis, consider repeating serologic testing in 2-4 weeks, If unchanged, no action needed.[3]
	Reactive	1. Current syphilis 2. Treated syphilis with residual RPR/VDRL titer	• If RPR/VDRL is newly reactive, stage and treat. • If previously treated and sustained (≥2 weeks) four-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[4] • RPR/VDRL can remain reactive after treatment. If there is a four-fold decline within 12-24 months, treatment is considered adequate despite RPR/VDRL reactivity. • Some treated patients may have a persistent, low-level RPR/VDRL titer. Re-treatment is not necessary in the absence of new exposure(s) and/or symptom(s).

1. The traditional algorithm starts with a non-treponemal test. If reactive, it is followed by a treponemal test.
2. False-positive results are often observed in pregnancy and in patients with autoimmune disorders, Lyme disease, certain viral infections, injection drug use and other conditions.
3. It is recommended that all pregnant women be screened for syphilis three times during pregnancy — at confirmation of pregnancy or at first prenatal encounter, again between 28-32-weeks' gestation, and again at the time of delivery.
4. For patients determined to have new syphilis or treatment failure, guidelines published by the Centers for Disease Control and Prevention should be used to determine treatment and follow-up recommendations.

Reverse-Sequence Algorithm[1]

1. Screen with immunoassay treponemal assay.
2. Confirm reactive immunoassay with non-treponemal assay.
3. Clarify discordant EIA/CIA and RPR/VDRL results with second treponemal assay.



*Primary syphilis and late, untreated syphilis are possible if RPR/VDRL are non-reactive, see below for recommended actions.

Immunoassay	RPR/VDRL	TP-PA	Interpretations	Recommended Actions
Non-Reactive	Non-Reactive or Not Done	Non-Reactive or Not Done	1. Syphilis unlikely 2. Early/incubating syphilis (too early to be detected by serology)	• If syphilis is unlikely—no further action is needed. • If immunoassay is non-reactive but there is high clinical suspicion (such as chancre or known exposure), treat presumptively for early syphilis. If treating presumptively, obtain RPR/VDRL on day of treatment and, if non-reactive, again in 2-4 weeks to assess for seroconversion.
Reactive	Non-Reactive	Non-Reactive or Not Done	1. False-positive immunoassay 2. Early/incubating syphilis 3. Latent or prior syphilis (treated or untreated)	• If no signs/symptoms and low risk for syphilis, most likely a false-positive immunoassay.[2] No further action needed. • If concerned for early infection or in pregnant patients, re-screen in 2-4 weeks.[3] • If signs/symptoms or contact to early syphilis, treat presumptively. Repeat RPR/VDRL on day of treatment and, if non-reactive, again in 2-4 weeks to assess for seroconversion.

Immunoassay	RPR/VDRL	TP-PA	Interpretations	Recommended Actions
Reactive	Non-Reactive	Reactive	1. Latent or prior syphilis (treated or untreated) 2. Early syphilis (prior to RPR/VDRL seroconversion)	• No further action needed if patient treated appropriately for syphilis in the past—assuming no new exposure/symptoms and a negative physical exam. • If no symptoms and no known prior adequate treatment, treat presumptively for latent syphilis. • If early syphilis is suspected (symptoms or known exposure), treat presumptively. Obtain RPR/VDRL on day of treatment and, if non-reactive, again in 2-4 weeks to assess for seroconversion.
	Reactive	Not Done or Reactive	1. Current syphilis 2. Prior syphilis (treated or untreated)	• If RPR/VDRL is newly reactive, stage and treat. • If previously treated and sustained (>2 weeks) four-fold rise in RPR/VDRL titer, manage as treatment failure versus re-infection.[4] • If known prior adequate treatment for stage of infection and RPR/VDRL is declining appropriately (i.e., a four-fold decline within 12-24 months), no further action is needed. • Some treated patients may have a persistent, low-level RPR/VDRL titer—re-treatment is not necessary in the absence of new exposure(s) and/or symptom(s).

1. The reverse-sequence 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 non-reactive), a treponemal test (TP-PA) serves as the tiebreaker.
2. False-positive immunoassays can occur with Lyme disease or non-syphilitic treponemal infections.
3. It is recommended that all pregnant women be screened for syphilis three times during pregnancy— at confirmation of pregnancy or at first prenatal encounter and again between 28-32-weeks' gestation, and again at the time of delivery.
4. For patients determined to have new syphilis or treatment failure, guidelines published by the Centers for Disease Control and Prevention should be used to determine treatment and follow-up recommendations.