

# IMPROVED SYPHILIS REVERSE SCREENING CASCADE

July 14, 2023

## Introduction:

Syphilis is a complex systemic illness. It is a sexually transmitted disease (STD) caused by the bacterium *Treponema pallidum*. Without treatment, syphilis causes serious health problems. It can permanently damage heart, brain, muscles, bones, and eyes.

Syphilis can progress through four different stages. The infection causes different symptoms in each stage. Infected individuals are most infectious early in the disease (primary and secondary stages). Below is a general overview of the stages. Additional detail is available on the CDC website:

<https://www.cdc.gov/std/syphilis/stdfact-syphilis-detailed.htm>

### National surveillance data shows:

- ➔ Syphilis cases continue to increase
- ➔ Most were congenital
- ➔ High risk factors: MSM, Sex workers, and poverty
- ➔ Diagnosis requires thorough clinical evaluation

STAGE	TIMELINE	TYPICAL SYMPTOMS	IF LEFT UNTREATED
Incubation period after exposure	Can be from 9-90 days after exposure.	No symptoms.	Progresses to primary syphilis.
Primary	Starts 9-90 days after exposure and can last up to 6 months.	Hard sore (chancre) that lasts 3-6 weeks.	Chancre heals regardless of treatment. However, the infection will progress to the secondary stage if no treatment is received.
Secondary	Starts 1-6 months after syphilis sore (chancre) goes away and can last up to 2 years.	Skin rashes and/or mucous membrane lesions mark the second stage. Symptoms may also include: fever, fatigue, muscle aches, headaches, swollen lymph nodes.	The symptoms of secondary syphilis will go away with or without treatment. However, without treatment, the infection will progress to the latent and possibly tertiary stage of disease.
Latent	Up to 20 years.	No outwards symptoms but can damage heart, bones, nerves, organs.	Without treatment, syphilis will remain in the body even though there are no signs or symptoms.
Late (Tertiary)	Tertiary syphilis is rare and develops in a subset of untreated syphilis infections. It can appear 10-30 years after a person gets the infection.	Affect multiple organ systems which can cause brain damage, heart disease, movement disorders, nerve damage, seizures, vision problems.	Serious health problems that will vary depending on the organs impacted. It can be fatal.

## Laboratory Diagnosis of Syphilis:

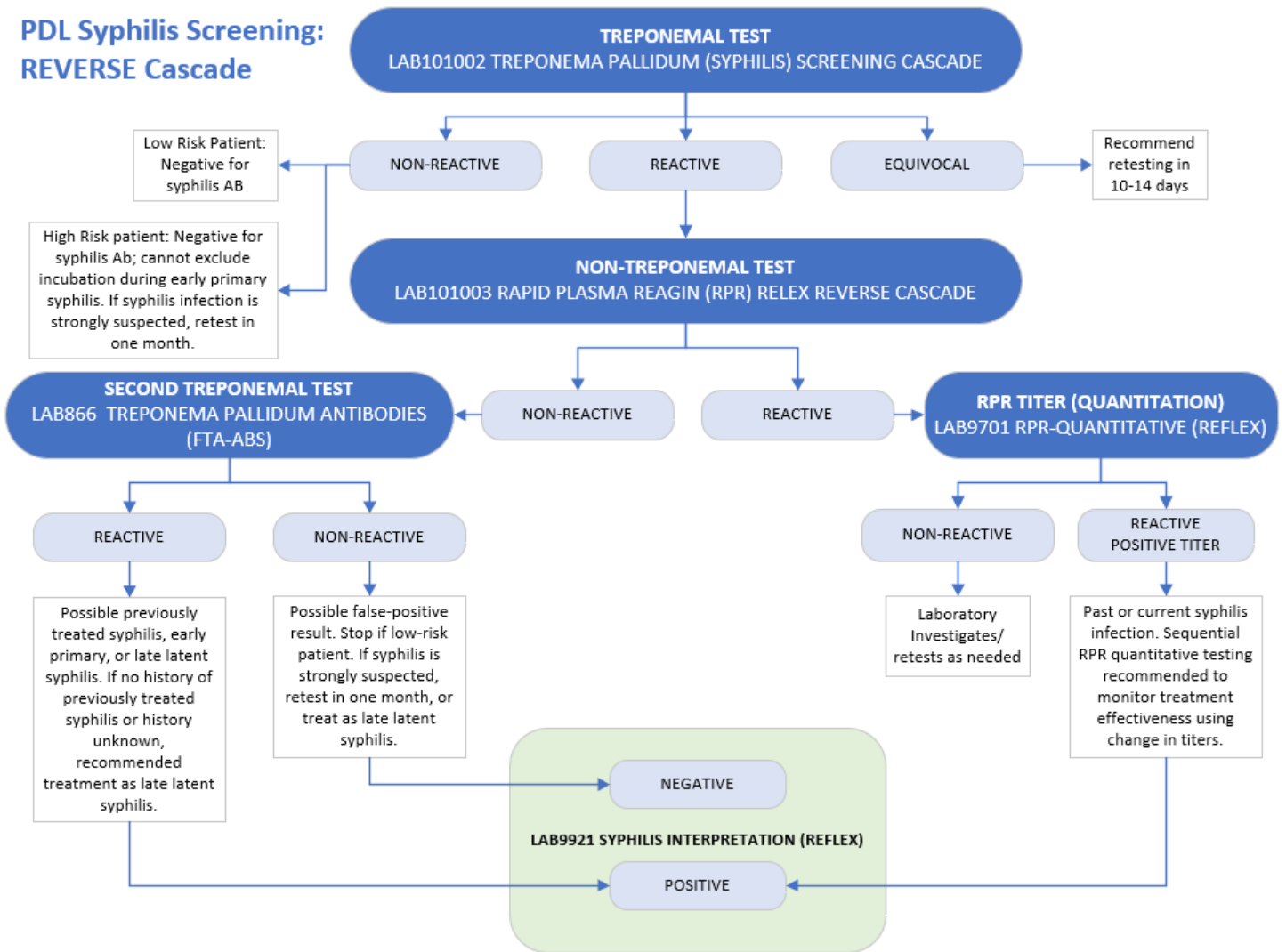
- A serological testing algorithm is utilized that includes both treponemal and non-treponemal serology tests; there are two approaches 1) the reverse algorithm and 2) the traditional algorithm (Note: neurosyphilis cannot be diagnosed using the serological approach; several CSF tests are recommended)
- The reverse algorithm:
  - Uses a treponemal test first (syphilis IgG/IgM antibodies) followed by a non-treponemal test (RPR) to confirm; if the initial test and second test do not confirm then a third test will be performed (a second treponema test by a different method) to adjudicate the results
  - Shows a reduction of false positive results over the traditional algorithm (nontreponemal tests can be positive due to other medical conditions not related to syphilis)
  - Can provide earlier detection
  - Can identify persons with untreated or incompletely treated syphilis and persons previously treated for syphilis
- NOTE: Pretest probability and thorough historical and clinical evaluation are critical when ordering and interpreting syphilis serology.

FOR MORE INFORMATION PLEASE CONTACT PDL CLIENT SERVICES AT 805-879-8100

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PDL Syphilis Screening: REVERSE Cascade



The use of the reverse cascade is outlined in the Center for Disease Control (CDC) and Prevention Morbidity and Mortality Weekly Report (MMWR) Recommendations and Reports /Vol. 70/No. 4 July 23, 2021 Sexually Transmitted Infections Treatment Guidelines, 2021. This report demonstrated that some syphilis infections could be missed using serological testing, and a number of false positive results could occur, especially in low-incidence settings. Pretest probability and thorough historical and clinical evaluation are critical when ordering and interpreting syphilis serology.

STI Treatment Guidelines available on the CDC website:  
<https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf>

REVERSE CASCADE TEST INFORMATION

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Test Name	Order/Interface Code	Test Code	Order LOINC	Insurance Price	
<b>Treponema pallidum (Syphilis) Screening Cascade (Diagnostic)</b>	LAB101002	1230119126	24110-9	\$60.65	
<i>Result name</i>		<i>Result Code</i>	<i>Result LOINC</i>	<i>CPT</i>	<i>CDM</i>
Syphilis Antibody IgG/IgM		1230011079	24110-9	86780	30200246
Test Name	Order/Interface Code	Test Code	Order LOINC	Insurance Price	
<b>RPR – QUANTITATIVE (REFLEX)</b>	LAB9701	1230111077		\$20.15	
<i>Result name</i>		<i>Result Code</i>	<i>Result LOINC</i>	<i>CPT</i>	<i>CDM</i>
RPR		1810249	20507-0	N/A	N/A
RPR Titer		1230014901	31147-2	86593	30200385
Test Name	Order/Interface Code	Test Code	Order LOINC	Referral Lab Price	
<b>TREPONEMA PALLIDUM ANTIBODIES (FTA-ABS)</b>	LAB866/SFTA	1230116436	5393-4	\$10.77	
<i>Result name</i>		<i>Result Code</i>	<i>Result LOINC</i>	<i>CPT</i>	<i>CDM</i>
T pallidum AB (FTA-AB)		1230016451	5393-4	86780	30200217
Test Name	Order/Interface Code	Test Code	Order LOINC	Insurance Price	
<b>SYPHILIS INTERPRETATION (REFLEX)</b>	LAB9921/SYPHIT	189543	56850-1	\$0	
<i>Result name</i>		<i>Result Code</i>	<i>Result LOINC</i>	<i>CPT</i>	<i>CDM</i>
Syphilis Interpretation		1230601917	56850-1	N/A	N/A
Test Name	Order/Interface Code	Test Code	Order LOINC	Insurance Price	
<b>REFLEX RPR (REFLEX REVERSE CASCADE)</b>	LAB101003	1230119127	20507-0	\$19.60	
<i>Result name</i>		<i>Result Code</i>	<i>Result LOINC</i>	<i>CPT</i>	<i>CDM</i>
RPR		1810249	20507-0	86592	30200206