CURRENT ALGORITHM FOR DIAGNOSIS OF SYPHILIS IN MMP HASA

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INTRODUCTION

- Syphilis is a sexually transmitted disease with varied and often subtle clinical manifestations.
- Primary syphilis typically presents as a solitary, painless chancre, whereas secondary syphilis can have a wide variety of symptoms, especially fever, lymphadenopathy, rash, and genital or perineal condyloma latum.
- In latent syphilis, all clinical manifestations subside, and infection is apparent only on serologic testing.
- Late or tertiary syphilis can manifest years after infection as gummatous disease, cardiovascular disease, or central nervous system involvement.
- Neurosyphilis can develop in any stage of syphilis.
- Vertical transmission can cause congenital syphilis, which might result in spontaneous abortions, miscarriages, or stillbirths; infants with congenital syphilis can have clinical signs of infection at birth or months to years after birth.

Laboratory diagnosis of syphilis

- Causative organism: *Treponema pallidum* subspecies *pallidum* (spirochaete bacteria)
- Darkfield examination
- Molecular tests

Detecting organism directly from lesion

- Serology: A presumptive diagnosis of syphilis requires use of two laboratory serologic tests: a nontreponemal test (i.e., Venereal Disease Research Laboratory [VDRL] or rapid plasma reagin [RPR] test) and a treponemal test (i.e., the *T. pallidum* passive particle agglutination [TP-PA] assay, various EIAs, chemiluminescence immunoassays [CIAs], or rapid treponemal assays)

LIMITATION OF TESTS

- Non treponemal test (RPR, VDRL)
  - Biological false positive- (e.g. autoimmune disease, acute viral infection, recent immunization, HIV infection, elderly, IDU, pregnancy and malignancy.
  - False negative- Early phase of primary syphilis, late latent syphilis, prozone phenomenon (due to high concentration of non-treponemal antibodies).

- Treponemal test (Treponema EIA, ECLIA, TPPA and rapid treponema assays)
  - Unable to distinguish syphilis from endemic treponemes:
    - yaws: *Treponema pallidum* subsp*. pertenue*
    - bejel: *Treponema pallidum* subsp*. endemicum*
    - pinta: *Treponema pallidum* subsp*. Carateum*
  - Persists for life (85% of patients)[2], hence not an indicator for treatment response.
  - Unable to distinguish between current or past infection as the antibodies remain reactive for life.

LIMITATION OF TESTS

- Molecular
  - The specificity ranges from 97% to 100%, but the sensitivity varies depending on specimen type and stages of infection.[3]
  - They are, however, insensitive for detection from whole blood or blood fractions and are therefore not recommended.[4]
  - Used for diagnosis of early and congenital syphilis.

DIAGNOSTIC ALGORITHM

Traditional algorithm

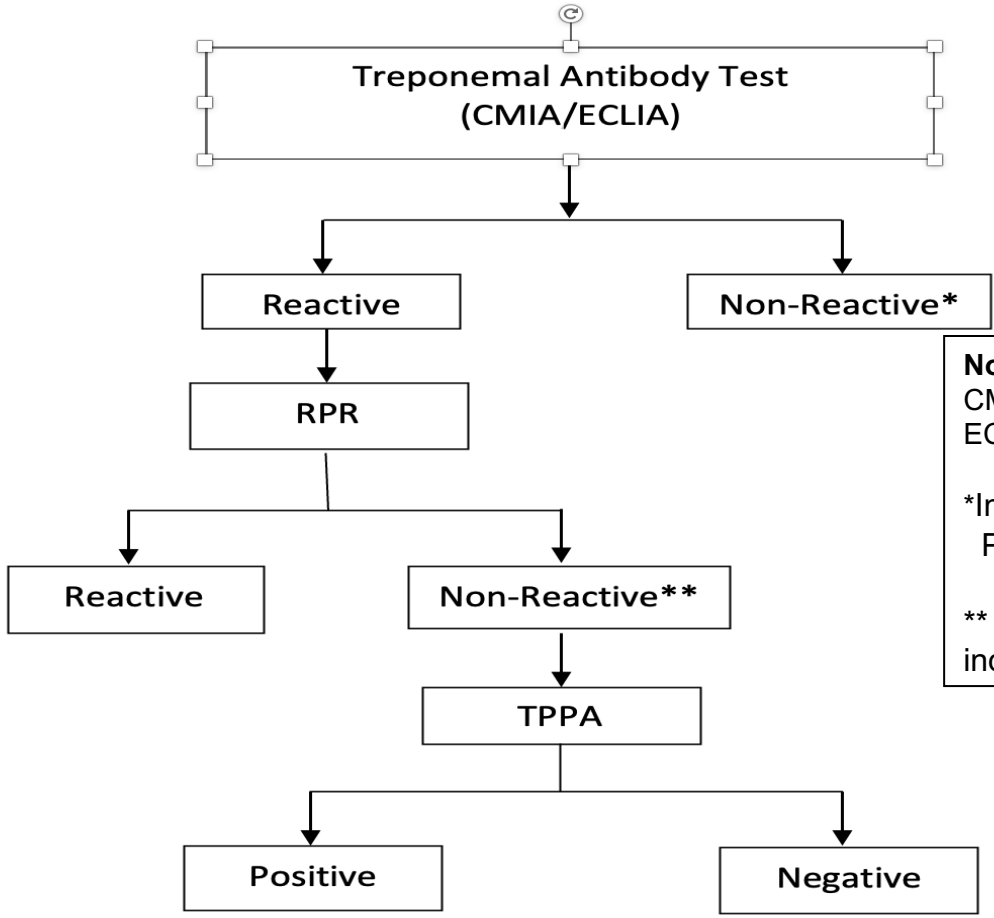
- Uses non-treponemal tests for screening followed by a confirmatory treponemal tests for reactive samples only.
- Less sensitive in early and late/latent disease (15% of patient with primary syphilis will be seronegative at initial presentation).[1]
- Lack of specificity, manually operated, subjective interpretation but cost effective.

Reverse algorithm

- Uses automated treponemal tests first followed by non-treponemal tests for reactive samples.
- A second treponemal tests (using different method e.g. TPPA) is performed for confirmation of discordant result.
- Allow detection for early syphilis.
- Detect past infections that were previously undetected by the traditional algorithm.
- Less labour intensive but costly.

REVERSE ALGORITHM

ALGORITHM 2 : SYPHILIS SCREENING USING 'REVERSE ALGORITHM'



Note:
CMIA = Chemiluminescence Immunoassay
ECLIA = Electrochemiluminescence Immunoassay

*In the absence of high risk behaviour/exposure, syphilis is unlikely. Please correlate with clinical findings.

** Check for previous TPPA result. If TPPA is positive, there is no indication to perform/repeat the test.

Laboratory interpretations

Treponemal Antibody Test (ECLIA)	RPR	TPPA	INTERPRETATION
Non-Reactive	N/A	N/A	In the absence of high risk behaviour/exposure, syphilis is unlikely. Please correlate with clinical findings. Suggest to repeat testing after 2-4 weeks if clinically indicated.
Reactive	Reactive	N/A	Consistent with syphilis
Reactive	Non-Reactive	Positive	Suggestive of syphilis infection (previously treated or untreated syphilis).
Reactive	Non-Reactive	Negative	Syphilis unlikely. If at risk for syphilis, repeat test in 2-4 weeks.

Syphilis monitoring

Clinical and serologic response should be performed at 6 and 12 months after treatment.

Quantitative non-treponemal test titres (RPR or VDRL) can be used to monitor response to treatment. Titres are expected to decrease following effective treatment and increase in untreated active infection.

A four-fold reduction in titre (e.g. from 1: 16 to 1: 4 indicate effective response to treatment. Sequential serologic tests for a patient should be performed using the same testing method (VDRL or RPR), preferably by the same laboratory.

Syphilis monitoring

RPR usually decrease after treatment and might become nonreactive with time. However, for certain persons, nontreponemal antibodies might decrease less than fourfold after treatment (i.e., inadequate serologic response)

For majority persons with HIV infection, serologic tests are accurate and reliable for diagnosing syphilis and evaluating response to treatment.

Summary

Use of only one type of serologic test (nontreponemal or treponemal) is insufficient for diagnosis and can result in false-negative results among persons tested during primary syphilis and false-positive results among persons without syphilis or previously treated syphilis.

The majority of patients who have reactive treponemal tests will have reactive tests for the remainder of their lives, regardless of adequate treatment or disease activity.

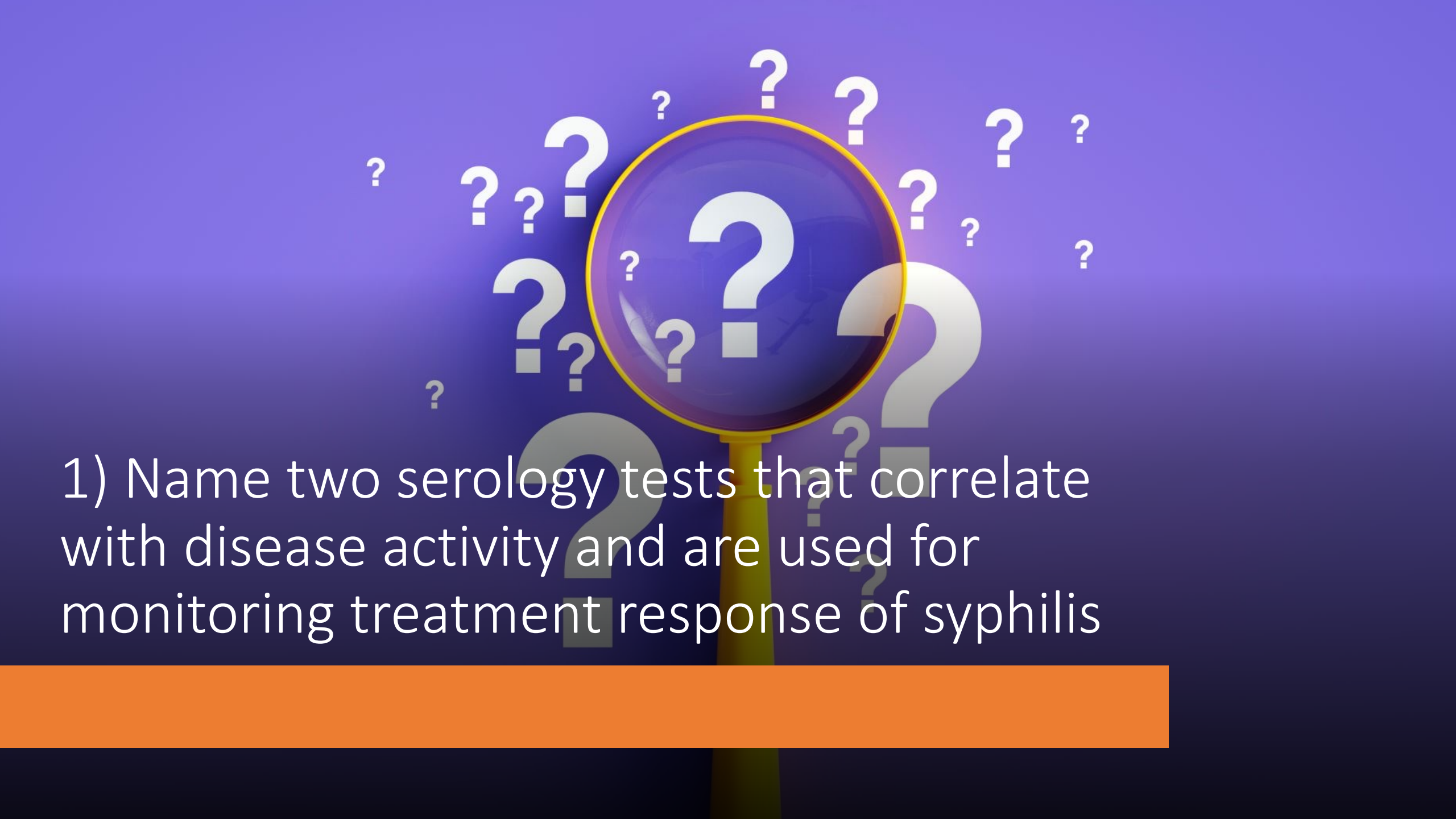
Treponemal antibody titers do not predict treatment response and therefore should not be used for this purpose.

Nontreponemal test (RPR or VDRL) antibody titers correlate with disease activity and are used for monitoring treatment response.

References

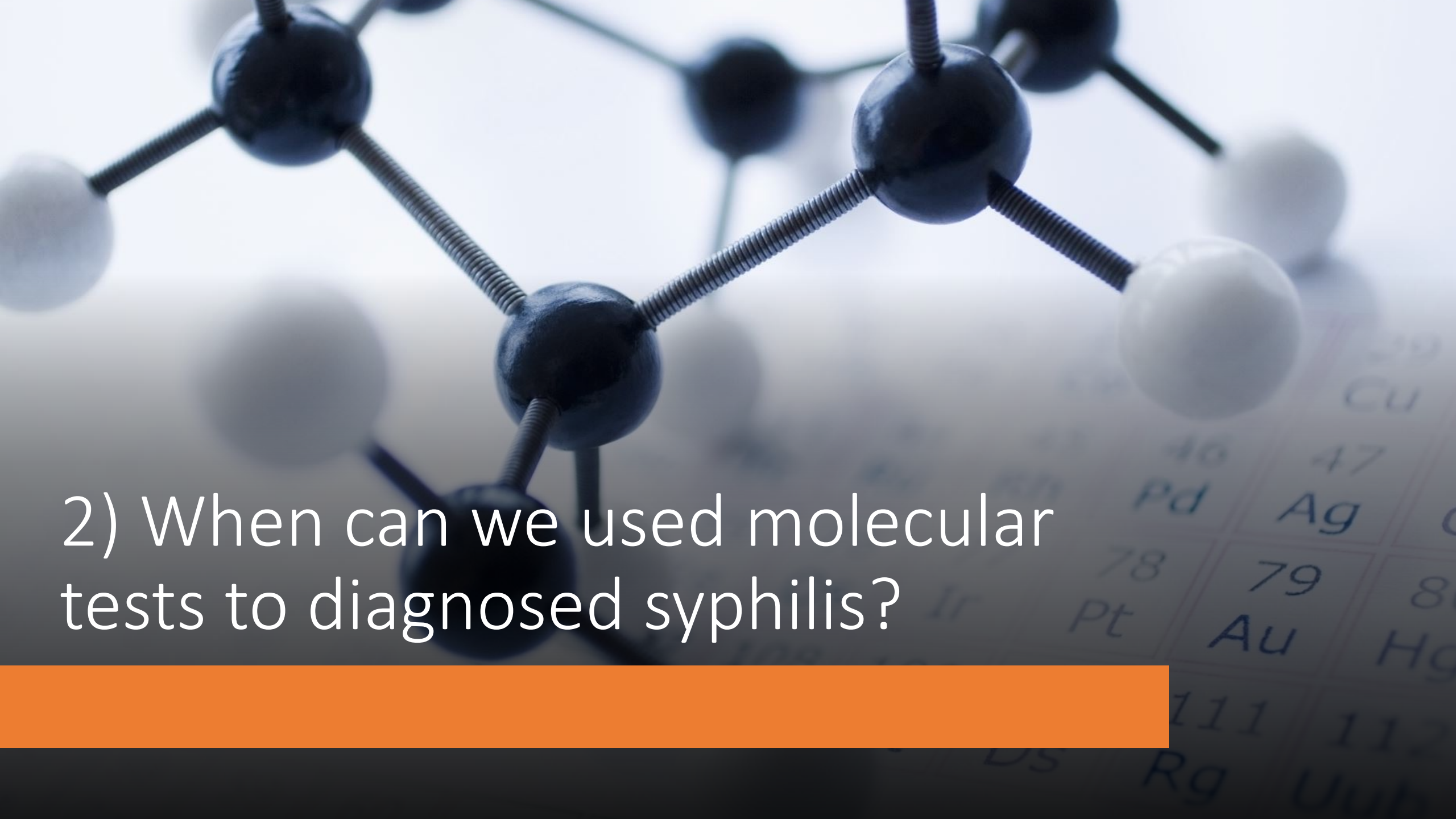
1. Anderson J, Mindel A, Tovey SJ, *et al.* Primary and secondary syphilis, 20 years' experience. 3: Diagnosis, treatment, and follow up. Genitourin Med 1989;**65**:239–43.
2. WHO. 2017. WHO Guideline on Syphilis screening and treatment for pregnant women. WHO, Geneva, Switzerland. www.who.int/publications/i/item/9789241550093
3. Australian Government Department of Health. 2020. Syphilis Laboratory Case Definition (LCD). https://www1.health.gov.au/internet/main/publishing .nsf/Content/cda-phln-syphilis.htm
4. Theel ES, Katz SS, Pillay A. 2020. Molecular and direct detection tests for Treponema pallidum subspecies pallidum: a review of the literature, 1964– 2017. Clin Infect Dis 71:S4–S12. https://doi.org/10.1093/cid/ciaa176.
5. CDC. 2021. Sexual Transmitted Infections Treatment Guideline 2021.


QUESTION



1) Name two serology tests that correlate with disease activity and are used for monitoring treatment response of syphilis

Rapid plasma reagin (RPR) or Venereal Disease Research Laboratory (VDRL)



2) When can we used molecular tests to diagnosed syphilis?

Early & congenital syphilis

Thank you for listening

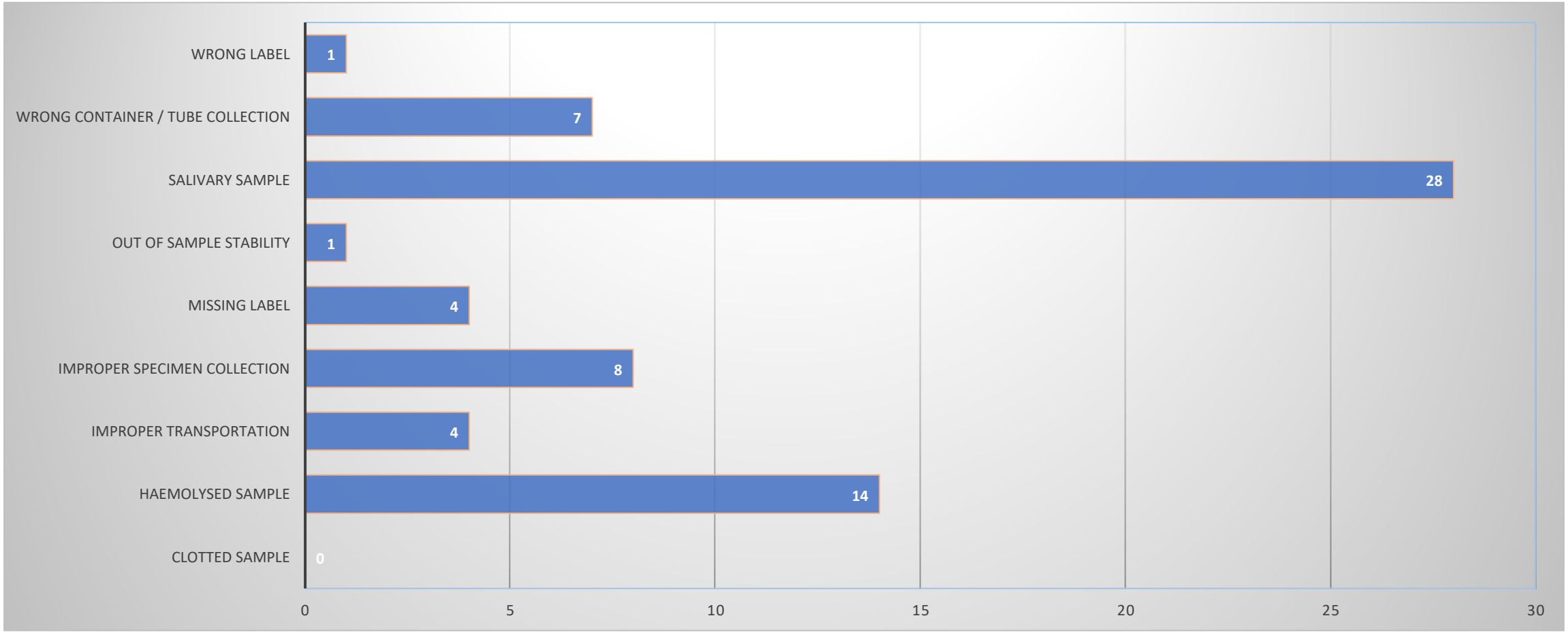
SPECIMEN REJECTION (MMP)

JUNE – DECEMBER 2023

SPECIMEN REJECTION 2023

NO	REJECTION CRITERIA	JUN	JUL	AUG	SEP	OCT	NOV	DEC
1	CLOTTED SAMPLE	0	0	0	0	0	0	0
2	HAEMOLYSED SAMPLE	1	5	0	2	3	3	0
3	IMPROPER TRANSPORTATION	4	0	0	0	0	0	0
4	IMPROPER SPECIMEN COLLECTION	2	1	1	1	0	3	0
4	MISSING LABEL	0	0	2	0	0	1	1
5	OUT OF SAMPLE STABILITY	0	1	0	0	0	0	0
6	SALIVARY SAMPLE	4	9	6	0	3	4	2
7	WRONG CONTAINER / TUBE COLLECTION	0	1	1	0	1	3	1
8	WRONG LABEL	0	0	0	0	1	0	0
	TOTAL REJECTION	11	17	10	3	8	14	4

TYPE OF SPECIMEN REJECTION



SUMMARY JUN TO DEC 2023

REJECTION CRITERIA	JUN	JUL	AUG	SEP	OCT	NOV	DEC
TOTAL REJECTION	11	17	10	3	8	14	4
TOTAL NO OF SPECIMEN RECEIVED	3016	3560	3941	3869	3942	3906	4173
REJECTION RATE (%)	0.365	0.478	0.254	0.078	0.203	0.358	0.096

SPECIMEN REJECTION RATE