Reverse Syphilis Screening: ADPH Clinical Update

Satellite Conference and Live Webcast
Thursday, June 9, 2011
8:00 - 9:30 a.m. Central Time

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Faculty

Mary G. McIntyre, MD, MPH
Medical Officer
Bureau of Communicable Disease
Alabama Department of Public Health

Objectives

- Discuss the reason for changes from the traditional to reverse sequence testing
- Review algorithm for the new reverse sequence syphilis screening

Objectives

- Describe the evaluation, management and treatment of persons based on the new reverse syphilis screening algorithm using scenarios developed
- Identify three reasons for discordant test results and the management of a person with a discordant test result
  - Refer to scenarios

Paradigm Shift!

- 1980s
  - FDA approves EIA for use as confirmatory test and in blood bank screening
- 2000
  - UK Public Laboratory Guidelines: EIA “appropriate alternative” to VDRL/RPR + TPPA

Paradigm Shift!

- 2001
  - EIA cleared by FDA for clinical diagnostic use
- 2008
  - EU Guidelines: EIA/TPPA recommended for screening, VDRL and RPR no longer recommended

Paradigm Shift!

- 2009
  - CDC-APHL Report: Presents algorithm for screening with Trep EIA

Which Algorithm?

Traditional	Reverse Sequence
Detects active infection	Detects early primary and treated infection that may be missed by traditional screening
High rate of biologic false positives - Confirmation with treponemal test - Use of both tests results in a high positive predictive value	Nontreponemal test needed to detect active infection
Can miss early primary and treated infection	Ideally, EIAs and CIAs should have perfect specificity - EIAs and CIAs are nonspecific - Varies by risk of population

Why Switch to EIA/CIA?

- Automated
  - High throughput
- Low cost in high volume settings
- Less lab occupational hazard
  - Pipetting
- No false negatives due to prozone reaction

Why Switch to EIA/CIA?

- Objective results
- Some EIA/CIAs detect antibodies
  - Potentially useful for diagnosis of early syphilis

Diagnosis of Syphilis

- *Treponema pallidum* cannot be cultured
- Ideally, early syphilis would be diagnosed using direct detection methods
- Direct detection methods are not widely available

Diagnosis of Syphilis

- Direct detection methods can miss cases
- Most persons present without symptoms or signs
- Syphilis is usually diagnosed via serologic tests

Serologic Tests

- Nontreponemal
  - Venereal Disease Research Laboratory (VDRL) test
  - Rapid Plasma Reagin (RPR) test
  - Toluidine Red Unheated Serum Test (TRUST)

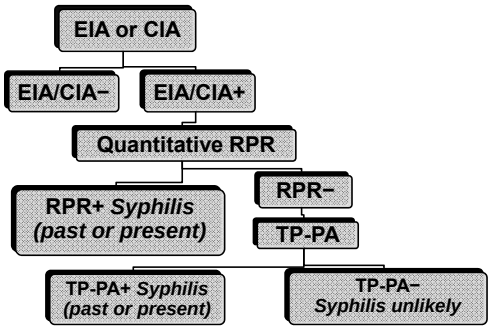
Serologic Tests

- Treponemal
  - Enzyme Immunoassays (EIAs)
    - Trep-Chek
    - Trep-Sure
  - Treponema pallidum article agglutination (TP-PA)

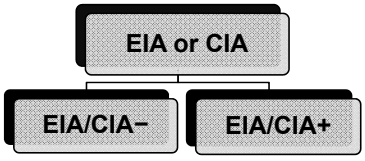
Serologic Tests

- Fluorescent treponemal antibody absorbed (FTA-ABS)
- Chemiluminescence Immunoassays (CIAs)
  - LIAISON
  - Architect

Reverse Sequence Algorithm

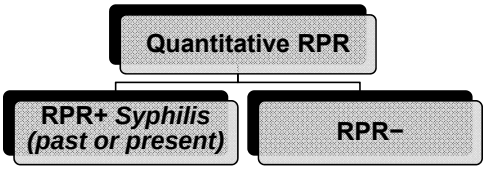


Reverse Sequence Algorithm



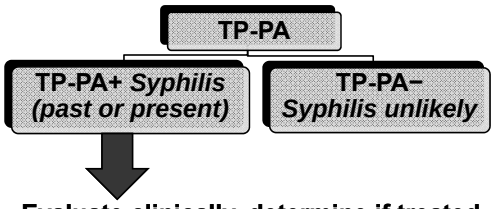
If incubating or primary syphilis is suspected, treat

Reverse Sequence Algorithm



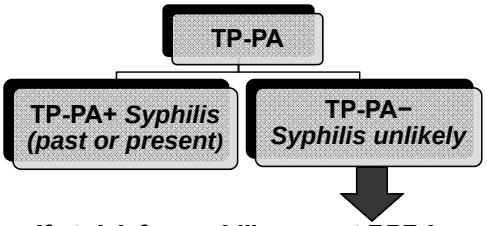
Evaluate clinically, determine if treated in past, assess risk of infection, and treat per CDCs STD Treatment Guidelines if not previously treated

Reverse Sequence Algorithm



Evaluate clinically, determine if treated in past, assess risk for infection, and treat per CDC STD Guidelines if not previously treated

Reverse Sequence Algorithm



If at risk for syphilis, repeat RPR in several weeks

Scenarios Review

Syphilis EIA-POS VDRL-POS: Scenario 1

Exam/History	Impression	Management/ Treatment
Exam findings not consistent with syphilis AND History of past treatment with adequate treatment response AND No recent exposure to an infectious case	Old treated syphilis	•No treatment •No further follow-up needed

Syphilis EIA-POS VDRL-POS: Scenario 2

Exam/History	Impression	Management/ Treatment
Exam findings consistent with syphilis OR History of recent exposure to an infectious case AND No history of treatment in the past	New syphilis infection	•Treat based upon stage of the disease •Examine and treat contacts •Monitor serologic response to treatment •Follow-up per protocol

Syphilis EIA-POS VDRL-POS: Scenario 3

Exam/History	Impression	Management/ Treatment
History of past treatment AND Exam findings/recent symptoms consistent with syphilis OR Inadequate serologic response to past treatment or no test results available OR Recent exposure history OR ≥4-fold increase in VDRL titer compared with previous titer	Inadequate response to syphilis treatment Possible syphilis re-infection	•Treat based upon stage of the disease •Examine and treat contacts •Follow-up per protocol •Monitor serologic response to treatment

Syphilis EIA-POS VDRL-POS: Scenario 4

Exam/History	Impression	Management/ Treatment
No positive exam findings for syphilis AND No history of recent symptoms/exposure to primary or secondary syphilis AND No history of treatment in the past	Possible syphilis re-infection	•Treat based upon stage of the disease •Examine contacts and treat based on results •Follow-up per protocol •Monitor serologic response to treatment

Syphilis EIA-POS VDRL-NEG T-PA-POS: Scenario 1

Exam/History	Impression	Management/ Treatment
History of past treatment AND No history of recent exposure or re-infection	Old treated syphilis	•No treatment •No further follow-up needed

Syphilis EIA-POS VDRL-NEG T-PA-POS: Scenario 2

Exam/History	Impression	Management/ Treatment
Exam findings consistent OR History of recent exposure to an infectious case OR History of serologic conversion	Syphilis infection present	•Treat based upon stage of the disease •Examine and treat contacts •Follow-up per protocol •No further follow-up if repeat VDRL is negative

Syphilis EIA-POS VDRL-NEG T-PA-POS: Scenario 3

Exam/History	Impression	Management/ Treatment
No history of past treatment AND No history of recent symptoms/ exposure or re-infection	Syphilis infection present	•Treat as Late Latent Syphilis •No further follow-up after treatment

Syphilis EIA-POS VDRL-NEG T-PA-NEG: Scenario 1

Exam/History	Impression	Management / Treatment
No exam findings consistent with syphilis AND No history of recent exposure to an infectious case	Old treated syphilis Possible false positive	•No treatment •No further follow-up needed

Syphilis EIA-POS VDRL-NEG T-PA-NEG: Scenario 2

Exam/History	Impression	Management/ Treatment
Exam findings consistent with syphilis OR History of recent exposure to an infectious case	Syphilis infection present	•Treat based upon stage of the disease •Examine and treat contacts •Follow-up per protocol •No further action if repeat VDRL and TP-PA is negative

What Are the Reasons for Discordant Test Results?

- False-positive EIA/CIA
- Treated syphilis
- Early primary syphilis

Challenges/Limitations of EIA/CIA

- Cannot distinguish between active and old disease
- Studies to compare test performance with other serologic tests are lacking
- Studies evaluating performance of EIA/CIA to detect IgM antibodies in early syphilis are lacking

Challenges/Limitations of EIA/CIA

- Confusion about management of patients with discordant serology ***

Conclusions

- EIA/CIA have high sensitivity but lower specificity
- All reactive EIA/CIAs must be reflexly tested with a quantitative RPR
  - Confirm reactive EIA/CIA
  - Detect active infection

Conclusions

- Test performance varies by prevalence in the population and all discordant results must be confirmed with a treponemal test
- Confirmatory test recommended by CDC is TP-PA not FTA-ABS

Contact Information

Mary G. McIntyre, MD, MPH

Email:
mary.mcintyre@adph.state.al.us

Phone:
334 - 206 - 5100
334 - 206 - 5325