

EVALUATION OF FIVE RAPID POINT-OF-CARE TESTS FOR SYPHILIS: TWO TREPONEMAL ONLY, AND THREE DUAL TREPONEMAL/ HIV ASSAYS

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Syphilis Quick Facts

- ✓ Caused by - *Treponema pallidum* subspecies *pallidum* (spirochete bacterium)
- ✓ Transmission: Mostly by Sexual, or maternal – fetal route, rarely by blood transfusion
- ✓ Various stages of disease – Primary, Secondary, Latent (early or Late), and Tertiary syphilis.
- ✓ Syphilis - in pregnancy – miscarriage, stillbirth, prematurity and organ damage, low birth weight, congenital syphilis.
- ✓ Syphilis increases risk of acquiring HIV in high risk population.
- ✓ Syphilis can be easily treated and adverse outcomes can be prevented (Benzathine penicillin G)

Background

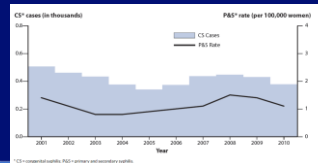
- ✓ WHO, PAHO, UNICEF - Global initiative to prevent MTCT of HIV/ Syphilis
- ✓ Traditional syphilis and HIV screening strategies require laboratory capacity.
- ✓ Affordable, rapid point-of-care tests (RPOCT), high sensitivity and specificity.
- ✓ Same-day testing and referral for treatment of syphilis and HIV in pregnant women.



Global incidence of Syphilis

- **WHO** - Global problem with an estimated 12 million people infected each year.
- Estimated two million pregnancies are affected annually.
 - ~ 25% of these pregnancies end in stillbirth or spontaneous abortion
 - ~ 25% the newborn has a low birth weight or serious infection, both of which are associated with an increased risk of perinatal death.

Congenital Syphilis—Reported Cases Among Infants by Year of Birth and Rates of Primary and Secondary Syphilis Among Women United States, 2001–2010



<http://www.cdc.gov/std/stats10/figures/47.htm>

Objectives

- ✓ Primary - To compare the sensitivity and specificity of two point-of-care (POC) treponemal tests and three treponemal/HIV tests for detection of treponemal antibodies in sera.
- ✓ Secondary - To determine the sensitivity and specificity of three POC treponemal/HIV tests for detection of HIV antibodies in sera.



Methods – Test Population

Test Population

- **1186** – Previously characterized sera for syphilis from
 - A. Kaiser Permanente Northern California (KPNC)**
 - CIA+, RPR-, TP-PA+
 - CIA+, RPR-, TP-PA-
 - CIA+, RPR+
 - CIA-
 - B. Kaiser Permanente Southern California (KPSC)**
 - EIA+, RPR-, TP-PA+
 - EIA+, RPR-, TP-PA-
 - EIA+, RPR+
 - EIA-
 - C. San Francisco Department of Public Health** - Sera from patients with diagnoses of primary and secondary syphilis.
- **437** known HIV-positive samples - CDC Atlanta/ HIV
- **Total – 1623**

Methods – Rapid tests

	TEST	vol	Syphilis	HIV	Manufacturer
A) Dual HIV/ syphilis assays					
1	Multiplo TP/HIV	~30ul	IgG/IgM - Recombinant Treponemal (R TP) antigen 15 kDa, 17 kDa, 47 kDa	HIV-1 and/or HIV-2 synthetic HIV peptides to gp36, gp41, gp120 and HIV-1 group O	MedMira
2	DPP HIV/ syphilis	10ul	IgG/IgM R TP antigen	HIV 1/2 immobilized antigens	Chembio
3	SD Bioline HIV Syphilis Duo	20ul	R TP (17kDa) antigen	HIV 1/2	Standard Diagnostics
B) Single syphilis assays					
4	SD Bioline syphilis 3.0	10ul	R TP (17,19kDa) antigen	NA	Standard Diagnostics
5	Determine Syphilis TP	50ul	R TP 47kDa	NA	Standard Diagnostics

All 1623 sera - tested by all rapid tests by CDC technicians blindly.

Methods – RPOCT devices

✓ **Treponemal/HIV POC tests**

✓ SD BIOLINE HIV Syphilis Duo (Standard Diagnostics)



✓ Multiplo TP/HIV (MedMira)*



✓ DPP HIV-syphilis Assay (Chembio)



✓ **Treponemal RPOCT:**

✓ SD Syphilis 3.0 (Standard Diagnostics),



✓ Determine SyphilisTP (Alere)



Results

Treponemal results

- 1623 samples tested.
- 1606 with all results.
- Only 27 samples known to be cases of P&S syphilis so far
- An overall agreement on reactivities of 84.1% (1350/1606) among the 5 tests on TP results.
- Traditional treponemal results (EIA, CIA or TPPA)
 - Reactive - 30.3% (487/1606)
 - Nonreactive - 69.7% (1119/ 1606)

HIV results

- 1623 samples - agreement of 96.6% among the 3 tests of 1569/1623.
- Only 437 samples had a known HIV status- there was 100% agreement among all 3 devices and known status.
- Need all patient data to come in before sensitivity and specificity can be calculated

Results

Sensitivity and specificity of treponemal results from rapid tests compared to previous treponemal results

Rapid Test	Sensitivity%	Specificity%
SD Duo TP	77.2%	98.05%
Chembio TP	83.68%	97.07%
Multiplo TP	79.92%	91.58%
SD 3.0	75.31%	98.05%
Determine TP	89.96%	97.78%

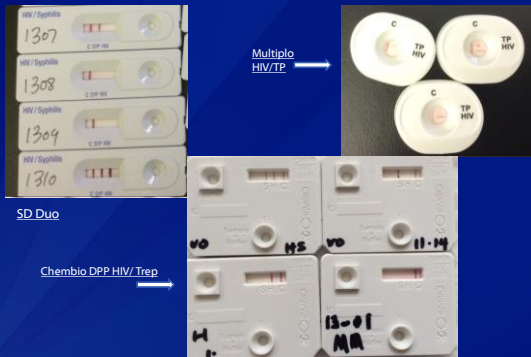
Sensitivity of treponemal results vs known P&S cases

Test	Sensitivity%
SD Duo TP	92.69%
Chembio TP	96.3%
Multiplo TP	100%
SD 3.0	92.69%
Determine TP	96.3%

n=27

N=1606

Results – RPOCT



Results

SD 3.0



Determine TP



Multiplo, SD duo and Chembio HIV/ TP
Reaction to same sample



Mini-Report

Evaluation of the use of Rapid Treponemal tests in the WHO/ CDC Syphilis Proficiency Testing Program

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Carter Acet
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Background: For approximately 30 years, the WHO/ CDC Syphilis Proficiency Testing (PT) Program has served to provide external quality assurance programs to laboratories worldwide performing serological tests for syphilis. These laboratories, usually reference labs are expected to be proficient in testing for syphilis using acceptable non-treponemal tests (RPR, VDRL) and treponemal tests (TPPA, FTA-Abs, EIA, CVA). These assays have the ability to detect non-specific and specific antibodies to *Treponema pallidum*, the causative agent of syphilis. The participating laboratories are provided with panels of 5 serologically distinct panels of reactivity as measured by multiple treponemal and non-treponemal tests. The laboratories return their results and are

Sensitivity and Specificity of 5 Rapid-point-of-Care tests compared to consensus traditional treponemal result when testing syphilis PT samples

	SD 3.0	Determine	SD Duo	Chembio	Multiplo
Sensitivity	94.74%	100.00%	94.74%	94.74%	98.25%
Specificity	94.44%	100.00%	100.00%	100.00%	100.00%

50 PT serum samples repeated once a week for 3 weeks.
Known reactivities previously confirmed with TPPA, FTA-Abs and EIA.


Fakile Y, Acet C, Hopkins A. Unpublished Mini report Jan. 2015

Challenges and Limitations

- ❖ Flow issues with some devices.
- ❖ Control lines not properly formed.
- ❖ Extremely faint lines – difficult to read.
- ❖ Complexity – Multiplo most challenging and Determine easiest to use.
- ❖ Serum samples of unknown freeze thaw cycles.

Summary

- ❖ Positive agreement was greater for HIV antibodies than for treponemal antibodies
- ❖ Using banked sera could have affected performance of treponemal assays.
- ❖ Further prospective studies need to be performed in field to better characterize performance of RPOCT treponemal tests.
- ❖ Need more studies to generate independent data to provide to countries' in the selection of RPOCTs for syphilis and HIV.



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Many thanks

- Standard diagnostics – Alere
- Medmira
- Chembio

Thank you!

Any questions?




For more information please contact Centers for Disease Control and Prevention

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Telephone: 1-800-CDC-INFO (232-4636) / TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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2016 STD Prevention Conference

Atlanta, GA | September 2016

www.cdc.gov/stdconference/