Syphilis in Ontario: Impact of changes in diagnostic testing

Public Health Ontario Rounds

Michael Whelan
& Vanessa G. Allen
October 23, 2012
Purpose: To describe laboratory testing changes in syphilis serology in Ontario

1. Review of epidemiology and clinical presentation of syphilis

2. Syphilis laboratory testing
   • Basic principles of syphilis serology tests
   • Syphilis serology algorithms
   • Impact of different syphilis testing algorithms
     • Classic algorithm to “reverse sequence” algorithm

3. Changes to syphilis serology in Ontario, October 2012
   • Review of syphilis algorithms
   • Preliminary data of changing syphilis serological screening assay
CHICAGO WILL CONTROL SYPHILIS

YOU MAY HAVE YOUR BLOOD TEST FREE AND CONFIDENTIALLY AT ONE OF THE FOLLOWING STATIONS

CHICAGO BOARD OF HEALTH

Herman N. Bundesen, Pres.
SYPHILIS EPIDEMIOLOGY
Syphilis - a brief description

• Caused by the spirochete *Treponema pallidum*

• Infection may result in:
  • Primary lesions
  • Secondary symptoms that may include rash
  • A period of latency following initial symptoms
  • Involvement of the central nervous system resulting in neurosyphilis

• Most commonly transmitted via sexual contact
Reporting of syphilis in Ontario

- Syphilis is reportable under O. Reg. 559/91 of the *Health Protection and Promotion Act* and has been reportable in Ontario since 1991

- The provincial case definition for syphilis was updated effective April 30, 2009
  - Infectious neurosyphilis was added
  - Time frame for early latent syphilis was shortened from ‘infection for less than two years’ to ‘infection for less than one year’
  - These changes may have resulted in a change in the number of infectious syphilis cases reported
Reporting of syphilis in Ontario

• Syphilis stages captured under ‘infectious syphilis’:
  • Primary syphilis
  • Secondary syphilis
  • Early latent syphilis
  • Infectious neurosyphilis

• Other stages of syphilis include:
  • Late latent syphilis
  • Tertiary syphilis
  • Non-infectious neurosyphilis
Infectious syphilis in Ontario

• Prior to 2002, low rates of infectious syphilis were reported in Ontario

• Two substantial increases were observed between 2002 and 2011
  • From 2002 to 2004
  • From 2008 to 2009

• Since 2009 the number of new cases has plateaued

• The majority of cases from 2001 to 2011 have been among males (4852/5127, 94.6%)

• Of male cases reporting risk factors from 2008 to 2011, 84.2% (2021/2400) reported ‘sex with same sex’
Infectious syphilis by year and sex, Ontario, 2001-2011

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario April 9, 2012

Note: Does not include 1 case with sex reported as ‘other’ in 2008
Infectious syphilis by year and sex, Ontario, 2001-2011

• The trend of infectious syphilis in Ontario has largely been driven by cases among men
  • Rates among males have increased by more than 1600% over the 11 year time period (or by 82% since 2007)

• Rates among females have been fairly low and mostly stable across the same time period

• From 2001 to 2011, there were only 1 or 2 cases of congenital syphilis per year
Infectious syphilis by age and sex, Ontario, 2008-2011

• Males
  • Large increases in number of cases among all age groups 15 years and up
  • Highest case counts and reported incidence rates among 40-44 year-olds
  • Number of cases in 15-24 year olds declined in 2010 compared to 2009 and remained lower in 2011

• Females
  • Cases predominantly seen in 15 to 39 year olds
  • Highest case counts and reported incidence rates among 20-24 year-olds
Incidence of infectious syphilis by Public Health Unit, Ontario, 2011

Infectious Syphilis in Ontario, by Health Unit, 2011

Legend
Incidence rate per 100,000
- 0.00 (10 HUs)
- 0.01 - 1.00 (7)
- 1.01 - 2.00 (11)
- 2.01 - 5.00 (5)
- 5.01 - 19.52 (3)

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario April 9, 2012
Syphilis-HIV co-infection in Ontario

• Syphilis-HIV co-infections are common among syphilis cases in Ontario
  • Co-infection defined as HIV diagnosis prior to or concurrently (within 1 year) with syphilis diagnosis

• Since 2002, the percentage of syphilis-HIV co-infected cases ranged between 35-47%
  • Prior to 2002, this percentage was below 15% each year

• From 2008 to 2011, this percentage was stable with 42-45% of syphilis cases co-infected each year
Syphilis re-infections

- Of 759 infectious syphilis cases reported in 2011, 184 (24%) had reports of previous infectious syphilis, some in 2011

<table>
<thead>
<tr>
<th>Number of previous infections</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>101</td>
<td>54.9%</td>
</tr>
<tr>
<td>2</td>
<td>55</td>
<td>29.9%</td>
</tr>
<tr>
<td>3</td>
<td>16</td>
<td>8.7%</td>
</tr>
<tr>
<td>4 or more</td>
<td>12</td>
<td>6.5%</td>
</tr>
<tr>
<td>Total</td>
<td>184</td>
<td>100%</td>
</tr>
</tbody>
</table>

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario April 9, 2012

- The epidemiology of infectious syphilis in 2012 is similar to previous years
  - 390 cases reported
  - Most cases seen in Toronto and Ottawa (298/390, ~76%)
  - Most cases are male (380/390, ~97%)
  - Age breakdown among male and female cases is similar

- We will undertake an analysis of repeat infections, HIV co-infection and risk factors once all of the data in 2012 have been collected

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario September 26, 2012
OVERVIEW OF DIAGNOSTIC METHODS FOR SYPHILIS
Clinical stages of syphilis infection

Primary syphilis

- Chancre
  - 0.3 to 3 cm in diameter
- Incubation period: 3 weeks (3-90 days)
- Initially a painless papule
  - Painless ulcer
  - Clean base
  - Rolled border
  - Associated lymphadenopathy
- Heals spontaneously in 1-12 weeks
- 60% of those with secondary syphilis do not recall primary lesion
Secondary syphilis

- Disseminated disease
- Usually 2-8 weeks after primary lesion
  - Can occur concurrently
- Symptoms include
  - Rash often involving palms and soles
  - Fever and other systemic symptoms
  - Neurological involvement (8-40%)
  - Condyloma latum
  - Patchy alopecia
  - Lymphadenopathy
  - Rare
    - Ocular and auditory symptoms
    - Renal and hepatic involvement

Goh B T Sex Transm Infect 2005;81:448-452
Tertiary syphilis

- Late complications
  - Late Neurosyphilis
    - Tabes dorsalis, Argyll-Robertson pupil
  - Cardiovascular syphilis
    - Aortitis of ascending aorta most common
      - Symptomatic aortic involvement in 10% of untreated
      - 55-86% on autopsy of those with untreated syphilis
  - Gumma
    - Commonly occur in skin, bone and liver
    - 15 years after secondary syphilis
Current methods for syphilis testing

- *Treponema pallidum* cannot be cultured routinely
- Main diagnostic tools for the detection of syphilis
  - Direct detection (only when available lesions)
  - Serology (serum and plasma)
  - CSF testing (also via serology)
Distinct reasons for diagnosing and treating syphilis infection

- For public health protection
  - To reduce transmission to others via
    - Sexual (limited to primary, secondary, and early syphilis)
    - Vertical transmission (can occur at early and later stages of disease)

- For individual clinical decisions
  - Prevention of symptoms and sequelae related to disease
  - Decrease risk of HIV transmission and acquisition
  - Decrease risk of late (tertiary) complications
Reasons for testing and clinical stage of syphilis infection

SEROLOGICAL TESTING FOR SYPHILIS
## Syphilis serology

<table>
<thead>
<tr>
<th>Non-treponemal serology</th>
<th>Treponemal serology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid Plasma Reagin (RPR)</td>
<td>Treponema Particle Agglutination (TPPA)</td>
</tr>
<tr>
<td>Venereal Disease Research Laboratory (VDRL)</td>
<td>Fluorescent Treponemal Antibody Absorbed (FTA-Abs)</td>
</tr>
<tr>
<td>Toluidine Red Unheated Serum Test (TRUST)</td>
<td>Microhemagglutination assay to antibodies of Treponema pallidum (MHA-TP)</td>
</tr>
<tr>
<td>Unheated Serum Reagin (USR)</td>
<td></td>
</tr>
</tbody>
</table>
Key differences between treponemal and non-treponemal syphilis serology tests

<table>
<thead>
<tr>
<th>Non-treponemal serology</th>
<th>Treponemal serology</th>
</tr>
</thead>
<tbody>
<tr>
<td>May miss early infection</td>
<td>May be more sensitive early in infection</td>
</tr>
<tr>
<td>False positives (known)</td>
<td>False positives (less well defined but also occur)</td>
</tr>
<tr>
<td>Will convert to non-reactive over time</td>
<td>Usually reactive “for life”</td>
</tr>
<tr>
<td>Quantitative (Can be used to monitor therapy)</td>
<td>Qualitative (Cannot be used to monitor therapy)</td>
</tr>
<tr>
<td>Manual test</td>
<td>Can be automated</td>
</tr>
</tbody>
</table>
Fig. 1. Common patterns of serological reactivity in syphilis patients

- EIA / CMIA/ CLIA
- FTA-Abs
- TPHA
- IgM^*
- untreated
- VDRL / RPR
- treated

<table>
<thead>
<tr>
<th>Clinical stages of syphilis</th>
<th>primary lesion</th>
<th>secondary lesion</th>
<th>latent (asymptomatic)</th>
<th>tertiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>primary</td>
<td>primary</td>
<td>secondary</td>
<td>latent (asymptomatic)</td>
<td>tertiary</td>
</tr>
</tbody>
</table>

ALGORITHMS FOR SYPHILIS SEROLOGY
Comparison of syphilis testing algorithms

Standard Algorithm

- RPR
- TPPA
- FTA-Abs

Reverse Algorithm

- EIA
- RPR
- TPPA

Screen test
If +
Confirmatory testing
Comparisons between the two syphilis serology algorithms

<table>
<thead>
<tr>
<th></th>
<th>Classic</th>
<th>Reverse sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficiency</td>
<td>Screen is currently manual</td>
<td>Screen can be automated</td>
</tr>
<tr>
<td>Clinical correlates</td>
<td>Historical data of clinical correlates</td>
<td>Less historical data on clinical correlates</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>May miss 1/3 of those with primary disease</td>
<td>May pick up more in early disease</td>
</tr>
<tr>
<td>Specificity</td>
<td>False positives screens</td>
<td>False positive screens</td>
</tr>
</tbody>
</table>
Efficiency of reverse sequence syphilis serology algorithms

- Automated assays enable increased throughput
  - Currently only treponemal assays are automated
  - 20 tests per hour when performed manually vs ~200/ hour for automated assays
  - Which can lead to quicker turn around times

- Objective results
  - Manual assay has some degree of subjectivity
  - Automated assays can be more standardly compared

- Decreased injury secondary to ergonomic concerns
  - Repetitive strain injury with manual RPR
INCREASED SENSITIVITY OF REVERSE SEQUENCE SYPHILIS SEROLOGY ALGORITHMS (AKA THE ABILITY TO DETECT TRUE POSITIVES)
Sensitivity of syphilis screening algorithms

• Sensitivity dependent on
  • Sensitivity of syphilis screen test
  • Stage of disease tested
  • Reference used
    • standardly TPPA or FTA
    • Classic algorithm with RPR screen
    • Clinical status
Increased detection of primary syphilis using reverse sequence algorithm

- Mishra et al. Sexually transmitted diseases 2011
    - Early detection of primary disease
      - Of 9137 with EIA reactive and RPR non reactive
      - 54 seroconverted
    - Increase in confirmed positives
      - 2.24% vs 0.59%
      - 69.6% of confirmed positives during the EIA screening period were RPR non-reactive
Use of treponemal syphilis screening to detect early disease

The Architect Syphilis assay for antibodies to *Treponema pallidum*: an automated screening assay with high sensitivity in primary syphilis

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Reactivity of the Architect Syphilis assay with stored sera from 129 cases of untreated syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage</td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>79</td>
</tr>
<tr>
<td>Secondary</td>
<td>29</td>
</tr>
<tr>
<td>Early latent</td>
<td>9</td>
</tr>
<tr>
<td>Latent—unknown duration</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>129</td>
</tr>
</tbody>
</table>

ICE, immune capture enzyme immunoassay; TPPA, *Treponema pallidum* particle agglutination test; VDRL, Venereal Disease Research Laboratory test.
Impact of the change to reverse sequence syphilis screening in the Greater Toronto Area

- ~3 fold increase in positives (mostly EIA+/RPR-)
- 0.59% of 9137 of these later converted (RPR+)

Change of syphilis serology algorithm and Impact on testing rates

Increase of 1.26 per 100,000 (p< 0.001)

Comparing two different syphilis testing algorithms in low prevalence populations

### TABLE 1 Clinical data and results of traditional and reverse syphilis screening algorithms for patients with a positive screening result (\( n = 15 \))

<table>
<thead>
<tr>
<th>Patient</th>
<th>Traditional algorithm(^a)</th>
<th>Reverse algorithm(^a)</th>
<th>Interpretation(^b)</th>
<th>Reason for testing(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RPR (titer)</td>
<td>TP-PA</td>
<td>BioPlex</td>
<td>RPR (titer)</td>
</tr>
<tr>
<td>1</td>
<td>+ (128)</td>
<td>+</td>
<td>+</td>
<td>+ (128)</td>
</tr>
<tr>
<td>2</td>
<td>+ (1)</td>
<td>+</td>
<td>+</td>
<td>+ (1)</td>
</tr>
<tr>
<td>3</td>
<td>+ (1)</td>
<td>+</td>
<td>+</td>
<td>+ (1)</td>
</tr>
<tr>
<td>4</td>
<td>+ (1)</td>
<td>+</td>
<td>+</td>
<td>+ (1)</td>
</tr>
<tr>
<td>5</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>9</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>12</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>13</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>14</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>15</td>
<td>–</td>
<td>N/A</td>
<td>+</td>
<td>–</td>
</tr>
</tbody>
</table>

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DEPARTMENT OF CORRECTION-CITY OF NEW YORK

DON'T WAIT

70% ARE DOOMED

IF TREATMENT OF SYPHILIS IS DELAYED FOR 3 YEARS AFTER THE DISEASE IS CONTRACTED

CONSULT A REPUTABLE PHYSICIAN
SPECIFICITY OF REVERSE SEQUENCE SYPHILIS SEROLOGY ALGORITHMS (AKA THE RISK OF FALSE POSITIVES)
Specificity of syphilis serology algorithm

• Challenge is lack of direct comparison
  • Specificity of syphilis confirmatory test
  • Stage of disease tested
  • Reference used
    • standardly TPPA or FTA
    • Classic algorithm with RPR screen
    • Clinical status
<table>
<thead>
<tr>
<th>Population/laboratory</th>
<th>Screen test</th>
<th># Screened</th>
<th>Reactive EIA/CIA (%)</th>
<th>Non reactive RPR (%)</th>
<th>Non reactive TPPA or FTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td>140,176</td>
<td>4834 (3.4%)</td>
<td>2,743 (56.7%)</td>
<td>866 (31.6%)</td>
</tr>
<tr>
<td>Southern California</td>
<td>Trep-Chek</td>
<td>47,952</td>
<td>1,278 (2.7%)</td>
<td>765 (59.9%)</td>
<td>459 (60.0%)</td>
</tr>
<tr>
<td>Northern California</td>
<td>Liaison</td>
<td>21,623</td>
<td>438 (2.0%)</td>
<td>287 (65.5%)</td>
<td>88 (30.7%)</td>
</tr>
<tr>
<td>Southern California</td>
<td>Trep-Sure</td>
<td>57,827</td>
<td>1,268 (2.2%)</td>
<td>755 (59.5%)</td>
<td>190 (25.2%)</td>
</tr>
<tr>
<td>New York City</td>
<td>Trep-Chek</td>
<td>7,607</td>
<td>1,165 (15.3%)</td>
<td>639 (54.8%)</td>
<td>129 (14.1%)</td>
</tr>
<tr>
<td>Chicago</td>
<td>Trep-Sure</td>
<td>5,167</td>
<td>685 (13.3%)</td>
<td>297 (43.4%)</td>
<td>51 (18.6%)</td>
</tr>
</tbody>
</table>
Discordant and false positive syphilis testing

<table>
<thead>
<tr>
<th>5 Laboratories (N=140, 176)</th>
<th>High Prevalence</th>
<th>Low Prevalence</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>14.5%</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Discordant Results</td>
<td>50.6%</td>
<td>60.6%</td>
<td>1.2</td>
</tr>
<tr>
<td>(EIA/CIA +, RPR non-reactive)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>False positive</td>
<td>14.1%</td>
<td>40.8%</td>
<td>2.9</td>
</tr>
<tr>
<td>(EIA/CIA +, TPPA/ FTA-)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MMWR. February 11, 2011; Vol. 60, No. 5
FIGURE. CDC-recommended algorithm for reverse sequence syphilis screening (treponemal test screening followed by nontreponemal test confirmation)*

- EIA or CIA
  - EIA/CIA +
  - EIA/CIA –
  - Quantitative RPR or other nontreponemal test
    - RPR + (Syphilis [past or present])
    - RPR –
    - TP-PA
      - TP-PA + (Syphilis [past or present])
      - TP-PA – (Syphilis unlikely)
Direct comparison of classic vs reverse sequence syphilis serology algorithms

**TABLE 1** Results of syphilis screening by a treponemal CMIA test and a nontreponemal RPR test followed by a confirmatory treponemal TP-PA test

<table>
<thead>
<tr>
<th>Result of CMIA test/ result of RPR test</th>
<th>No. of specimens (%) of total no. of specimens</th>
<th>No. of specimens reactive in TP-PA test</th>
<th>% agreement with TP-PA test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactive/reactive</td>
<td>157 (1.3)</td>
<td>155</td>
<td>98.7</td>
</tr>
<tr>
<td>Reactive/nonreactive</td>
<td>334 (2.7)</td>
<td>197</td>
<td>58.9</td>
</tr>
<tr>
<td>Nonreactive/reactive</td>
<td>65 (0.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nonreactive/nonreactive</td>
<td>11,679 (95.5)</td>
<td>ND&lt;sup&gt;b&lt;/sup&gt;</td>
<td>ND</td>
</tr>
</tbody>
</table>

<sup>a</sup> The total number of specimens was 12,235.

<sup>b</sup> ND, not done.
IUSTI: 2008 European Guidelines on the Management of Syphilis

P French (Chair) FRCP, M Gomberg MD, M Janier MD PhD, B Schmidt MD, P van Voorst Vader MD and H Young MD

The Mortimer Market Centre, Camden Primary Care Trust and University College London, Mortimer Market, London WC1E 6JB, UK


Primary screening test: $^{30–32,35}$

- A treponemal antigen test EIA or TPPA (preferred to TPHA) is recommended as a single screening test;

- The RPR/VDRL is not recommended as a primary screening test; $^{4,36–38}$ It may be used for the rapid detection of symptom-
Reverse sequence screening in Ontario

<table>
<thead>
<tr>
<th></th>
<th>RPR screen</th>
<th>EIA screen</th>
<th>CMIA screen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Screen</strong></td>
<td>Sept 04-Feb 05</td>
<td>Aug 07-Oct 07</td>
<td>Aug 08-Oct 08</td>
</tr>
<tr>
<td><strong>Tests</strong></td>
<td>163,897</td>
<td>136,656</td>
<td>127,316</td>
</tr>
<tr>
<td><strong>Screen Positive</strong></td>
<td>1,945 (1.2%)</td>
<td>2,232 (1.6%)</td>
<td>2,326 (1.8%)</td>
</tr>
<tr>
<td><strong>“False Positive”</strong></td>
<td>296 (0.2%)</td>
<td>225 (0.2%)</td>
<td>310 (0.2%)</td>
</tr>
<tr>
<td><strong>True Positive</strong></td>
<td>1,438 (0.9%)</td>
<td>1,872 (1.3%)</td>
<td>1,725 (1.4%)</td>
</tr>
<tr>
<td><strong>Inconclusive Result</strong></td>
<td>211 (0.1%)</td>
<td>146 (0.1%)</td>
<td>287 (0.2%)</td>
</tr>
</tbody>
</table>

1. False positive: screening test not confirmed by a second treponemal test
2. True positive: screening test confirmed by a second treponemal test
3. Inconclusive result: positive screening serology with an inconclusive treponemal confirmatory test
False positives and discordant syphilis testing in Ontario

<table>
<thead>
<tr>
<th></th>
<th>CMIA screen (2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Screen Tests</td>
<td>548,742</td>
</tr>
<tr>
<td>Screen Positive</td>
<td>12,122 (2.2%)</td>
</tr>
<tr>
<td>“False Positive”</td>
<td>2,896 (23.9%)</td>
</tr>
<tr>
<td>Acute positive (+ RPR)</td>
<td>1,479 (12.2%)</td>
</tr>
<tr>
<td>Discordant result</td>
<td>7,748 (63.9%)</td>
</tr>
</tbody>
</table>

1. False positive: screening test not confirmed by a second treponemal test
2. Acute positive: screening test confirmed by a second treponemal test and a reactive RPR
3. Discordant result defined as two reactive treponemal tests, with a non reactive non-treponemal test
ECONOMIC ANALYSIS OF SYPHILIS SEROLOGY ALGORITHMS
Economic analysis of reverse sequence syphilis screening

- Standard:
  - RPR Screen
  - TPPA/FTA confirmatory

- Alternate:
  - EIA screen
  - INNOLIA confirmatory

- $461 saved per positive case using alternate algorithm
Economic analysis of the two algorithms

- Owusu-Edusei, Kwame Jr. et al STD May 2011
- Economic modelling of 4 algorithms including classic and reverse sequence

<table>
<thead>
<tr>
<th>TABLE 3. Summary Results Expected Effects (Actual Cases Treated), Overtreatment Rate, No. Confirmatory Tests, and Total Net Costs*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect (Cases Treated)</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Low prevalence setting (0.5%)</td>
</tr>
<tr>
<td>Nontrep-First</td>
</tr>
<tr>
<td>Trep-First</td>
</tr>
<tr>
<td>Trep-Only</td>
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<tr>
<td>Nontrep-Only</td>
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<tr>
<td>High prevalence setting (10%)</td>
</tr>
<tr>
<td>Trep-First</td>
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<tr>
<td>Nontrep-First</td>
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<td>Nontrep-Only</td>
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<td>Trep-Only</td>
</tr>
</tbody>
</table>
CHANGES IN SYPHILIS SCREENING SEROLOGY
IN ONTARIO
OCTOBER 2012
New syphilis serological screen introduced in Ontario, Oct 22, 2012

• The result of a competitive procurement process
  • Contract awarded to Siemens® chemoluminescent assay (CLIA)

• Still using the reverse sequence syphilis serology algorithm
  • Screen with CLIA
  • If reactive or indeterminate
    • RPR, TPPA +/- FTA performed

• Primary impact
  • New indeterminate category for screen results
  • Slight differences in test characteristics may lead to variability in testing results in a single individual, and at a population surveillance level
  • Preliminary data suggests possible increased specificity
Interpretation of syphilis serology performed in adults

**Syphilis Screen Test Result**

- **Non reactive**
  - **No evidence of syphilis infection**

- **Reactive or indeterminate**
  - **Does this individual have a history of treated syphilis or a previous reactive syphilis serology result?**
    - **No to both**
      - **What is the RPR result?**
        - **Non reactive**
          - **What is the TPPA result?**
            - **Non reactive**
              - **Likely false reactive syphilis screen**
            - **Reactive or indeterminate**
              - **Consistent with prior (treated or untreated) syphilis or acute infectious syphilis**
        - **Reactive**
          - **Consistent with acute infectious or prior (treated or untreated) syphilis**

    - **Yes to one or both**
      - **What is the RPR result?**
        - **Non reactive**
          - **Consistent with prior (treated or untreated) syphilis**
        - **Reactive**
          - **Is there a four fold rise in RPR in the last 12 months?**
            - **No**
              - **Consistent with acute infectious syphilis (re-infection or relapse)**
            - **Yes**
              - **Consistent with acute infectious syphilis (re-infection or relapse)**
Sensitivity of CLIA compared to previous screen test

<table>
<thead>
<tr>
<th></th>
<th>Immulite</th>
<th>Previous CMIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR (%)</td>
<td>397 (99.3%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>IND (%)</td>
<td>1 (0.3%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>R (%)</td>
<td>80 (20.0%)</td>
<td>319 (79.8%)</td>
</tr>
</tbody>
</table>

Sensitivity compared to previous CMIA = 79.9%
Specificity compared to previous CMIA = 99.5%
Sensitivity of CLIA compared to reference testing

Syphilis validation
Immulite vs TPPA (n=400)

<table>
<thead>
<tr>
<th></th>
<th>Immulite</th>
<th>TPPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR (%)</td>
<td>IND (%)</td>
<td>R (%)</td>
</tr>
<tr>
<td>NR</td>
<td>69 (90.8%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>IND</td>
<td>9 (16.1%)</td>
<td>47 (83.9%)</td>
</tr>
<tr>
<td>R</td>
<td>2 (0.7%)</td>
<td>266 (99.3%)</td>
</tr>
</tbody>
</table>

Sensitivity compared to TPPA = 96.6%
Labstract – October 2012

Syphilis (*Treponema pallidum*) Serology Testing and Interpretation – Update

To health care providers:

Effective October 22, 2012 the Public Health Ontario’s public health laboratories (PHL) will replace the serological assay used for syphilis screening from the previously used chemiluminescent microparticle immunoassay test (CMIA) to the chemiluminescent immunoassay (CLIA) test. The assay change is a result of a competitive procurement and technical evaluation of Health Canada approved Syphilis (*Treponema pallidum*) serological assays.
Conclusions

• Ongoing disease burden of syphilis in Ontario

• The diagnosis of syphilis relies on a combination of clinical and laboratory findings

• Serology is the primary laboratory test
  • Ontario uses the “reverse sequence” algorithm
  • Increased detection of latent syphilis and potentially early disease

• Change in screening test to the chemoluminescent assay
  • Generally similar to previous CMIA
  • Preliminary data suggests possible increase in specificity
Acknowledgements

• Public Health Units and their staff for their diligent collection and reporting of STI information in iPHIS

• Public Health Ontario Laboratory Staff including
  • Laura Burton
  • Patrice Simmons
  • Vandana Mohan
  • Sam Pizzolato
  • Laura Nangini
  • Tubani Ramoutar
  • Helen Meaney

• Dr. Tony Mazzulli, Dr. Ann Burchell, Dr. Darrell Tan
Questions?

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DEPARTMENT OF CORRECTION CITY OF NEW YORK

SYPHILIS STRIKES ONE OUT OF TEN ADULTS

Consult a reputable Physician
THANK YOU.