Genital lesion producing pathogens diagnosed using *PlexPCR*

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Etiologic Agents of Genital Ulcers

- Herpes simplex virus 1 (HSV-1)
- Herpes simplex virus 2 (HSV-2)
- Treponema pallidum (causes syphilis)
- VZV
Syphilis Rates Increasing in Australia

Australia 2007–2016
Infectious syphilis notification rate

Gonorrhoea and syphilis on the rise in Melbourne
Clinical Stages of Syphilis

- PCR
  - direct detection method
  - definitive diagnosis
  - early detection for prompt partner notification

Swab PCR Window

- IgM
- VDRL/RPR
- TPHA
- FTA-Abs

Untreated

Treated

Serological windows and associated testing recommendations based on IUSTI and EU guidelines for management of syphilis.

* Appearance of primary lesion is typically 3 weeks after infection (early as 10- and as late as 90- days), lasting 3-6 weeks.

* Symptomology of secondary infections include mucous membrane lesions (appearing after primary lesions heal) in addition to skin rashes.
PCR Diagnosis of Primary Syphilis

Shields et al BMC Infectious Diseases 2012, 12:353
- 10% of PCR positives were serology negative
  - 4/5 showed delayed seroconversion

- 12% of PCR positives were negative by clinical diagnosis (dark-field and serology negative)
- 44% of cases suspected of primary syphilis were HSV1/2 positive

Positive PCR result from a lesion may precede development of any or all of the serological markers
Clinical presentation of primary syphilis

“Classic” chancre

<table>
<thead>
<tr>
<th>Single ulcer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painless, non-tender</td>
</tr>
<tr>
<td>Indurated base</td>
</tr>
</tbody>
</table>
### Clinical presentation of primary syphilis

<table>
<thead>
<tr>
<th>“Classic” chancre</th>
<th>“Atypical” presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single ulcer</td>
<td>Multiple: 33-47% 1,2,3,4</td>
</tr>
<tr>
<td>Painless, non-tender</td>
<td>Painful/tender: 25-49.2% 1,2,3,4</td>
</tr>
<tr>
<td>Indurated base</td>
<td>Non-indurated: 7.8% 2</td>
</tr>
</tbody>
</table>


Common “atypical” presentation of primary syphilis
Why Include VZV?

- 3% prevalence in adults presenting with genital herpes \(^1\)

- Case studies:
  - 3 children VZV genital infection \(^2\)
  - Perianal VZV presenting as suspected child abuse \(^3\)

- Implications for:
  - Therapy (increased dose); Likelihood of recurrence
  - Emotional and psychological well being

**PlexPCR VHS**

- **Delivers actionable clinical information**
  - Rapid qPCR format (<1.5 hours)
- **Specimen Types**
  - Cutaneous and mucocutaneous swabs

<table>
<thead>
<tr>
<th>Channel</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HSV-1</td>
</tr>
<tr>
<td>2</td>
<td>HSV-2</td>
</tr>
<tr>
<td>3</td>
<td>VZV</td>
</tr>
<tr>
<td>4</td>
<td><em>T. pallidum</em></td>
</tr>
<tr>
<td>5</td>
<td>Internal Control</td>
</tr>
</tbody>
</table>

**PlexPCR VHS combination provides cost-effective screening of genital ulcer disease**
Clinical Performance of PlexPCR VHS

- 427 lesion swab samples from genital and non-genital sites
- Public Health Laboratory (Bristol, UK)

<table>
<thead>
<tr>
<th>PlexPCR VHS</th>
<th>HSV-1</th>
<th>HSV-2</th>
<th>VZV</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>83</td>
<td>70</td>
<td>47</td>
<td>21</td>
</tr>
<tr>
<td>-</td>
<td>2</td>
<td>341</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>342</td>
<td>47</td>
<td>21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th></th>
<th>Specificity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>(95% CI</td>
<td></td>
<td>(95% CI</td>
</tr>
<tr>
<td>HSV-1</td>
<td>97.7%</td>
<td>91.8-99.7%</td>
<td>99.7%</td>
<td>98.4-100.0%</td>
</tr>
<tr>
<td>HSV-2</td>
<td>100.0%</td>
<td>94.9-100.0%</td>
<td>99.7%</td>
<td>98.5-100.0%</td>
</tr>
<tr>
<td>VZV</td>
<td>100.0%</td>
<td>92.5-100.0%</td>
<td>99.7%</td>
<td>98.5-100.0%</td>
</tr>
<tr>
<td>Syphilis</td>
<td>100.0%</td>
<td>83.9-100%</td>
<td>100.0%</td>
<td>99.1-100.0%</td>
</tr>
</tbody>
</table>

Excellent clinical sensitivity and specificity
Prevalence in genital lesions

- Prevalence study by Public Health Laboratory (Bristol, UK)
  - PlexPCR VHS tested on genital swabs from routine HSV testing (n=295)

<table>
<thead>
<tr>
<th>Target</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSV-1</td>
<td>24.1%</td>
</tr>
<tr>
<td>HSV-2</td>
<td>21.4%</td>
</tr>
<tr>
<td>HSV-1 &amp; HSV-2</td>
<td>0.68%</td>
</tr>
<tr>
<td>VZV</td>
<td>0.34%</td>
</tr>
<tr>
<td>T. pallidum</td>
<td>1.69%</td>
</tr>
</tbody>
</table>

VZV and Syphilis also detected in HSV requests from genital lesions
Summary

- PCR from lesions can aid diagnosis of syphilis
- VZV can also be found in genital lesions
- Clinical diagnosis alone can be unreliable
- PlexPCR VHS test can provide a cost-effective method to screen for the causes of genital ulcer disease
- Syphilis is increasing, including in ‘low risk’ populations
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