Syphilis – A Review

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Association Between Genital Ulcers and HIV

- Any genital ulceration is associated with an increased risk of HIV acquisition and transmission
- HIV can be cultured from lesion exudate
- Therefore, HIV serology for all patients with genital ulcers and vice versa
Reported Infectious Syphilis Rates in Alberta and Canada, 1994 to 2007

<table>
<thead>
<tr>
<th>Year</th>
<th>Canada</th>
<th>Alberta</th>
</tr>
</thead>
<tbody>
<tr>
<td>94</td>
<td>0.7</td>
<td>0.3</td>
</tr>
<tr>
<td>95</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>96</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>97</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>98</td>
<td>0.5</td>
<td>0.2</td>
</tr>
<tr>
<td>99</td>
<td>0.6</td>
<td>0.1</td>
</tr>
<tr>
<td>00</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>01</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>02</td>
<td>1.5</td>
<td>0.6</td>
</tr>
<tr>
<td>03</td>
<td>2.9</td>
<td>1.2</td>
</tr>
<tr>
<td>04</td>
<td>3.5</td>
<td>2.3</td>
</tr>
<tr>
<td>05</td>
<td>3</td>
<td>4.5</td>
</tr>
<tr>
<td>06</td>
<td>4</td>
<td>6.6</td>
</tr>
<tr>
<td>07</td>
<td>3.5</td>
<td>7.3</td>
</tr>
</tbody>
</table>

Note: National rates for 2006 and 2007 are preliminary.
Infectious and Congenital Syphilis Cases in Alberta 2007 (n=255)

* 4 of the 7 symptomatic CNS cases were ocular

Source: Alberta Health and Wellness Communicable Disease Reporting System: Notifiable Diseases and Sexually Transmitted Infections Databases as of June 11, 2008
Gender-Specific Age Distribution of Infectious Syphilis Cases in Alberta, 2007

Source: Alberta Health and Wellness Communicable Disease Reporting System: Notifiable Diseases and Sexually Transmitted Infections Databases as of June 11, 2008

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Infectious Syphilis – HIV Status in Regions 3 and 6, Alberta, 2007

Calgary Health (Region 3)

- Negative, 66, 66%
- Positive, 24, 24%
- Unknown, 10, 10%

n=100 cases

Capital Health (Region 6)

- Negative, 81, 77%
- Positive, 9, 8%
- Unknown, 16, 15%

n=106 cases

Note: In 2007, there was one HIV positive infectious syphilis case outside of Capital and Calgary Health Region.

Source: Alberta Health and Wellness Communicable Disease Reporting System: Notifiable Diseases and Sexually Transmitted Infections Databases as of June 11, 2008
Sexual Contact
3-4 weeks
Primary Syphilis
chancre
6-8 weeks
Secondary Syphilis
rash
lymphadenopathy
Latent Syphilis
Early <2 years
Late > 2 years
Spontaneous Cure
Static positive serology
Tertiary
Primary Syphilis

Incubation 9-90 days (average 21 days)

- Chancre
- Regional lymphadenopathy
Secondary Syphilis

- Mucocutaneous eruption
- Generalized lymphadenopathy
- Constitutional symptoms
Latent Syphilis

- asymptomatic
- positive serology
  - $< 2$ years – early latent infectious
  - $25\%$ relapse to secondary
  - $> 2$ years – late latent non-infectious
Tertiary Syphilis

- 3-30 years after primary infection
- Non-infectious
- Types
  - Late benign – skin, bone, viscera
  - Cardiovascular – aorta, heart
  - Neurosyphilis – meninges, brain
## Outcome of Pregnancy in Relation to Stage of Untreated Maternal Syphilis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Primary or Secondary</th>
<th>Early Latent</th>
<th>Late Latent</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prematurity</td>
<td>50%</td>
<td>20%</td>
<td>9%</td>
<td>8%</td>
</tr>
<tr>
<td>Perinatal death</td>
<td>20%</td>
<td>11%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>50%</td>
<td>40%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Healthy child</td>
<td>20%</td>
<td>70%</td>
<td>90%</td>
<td></td>
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</table>
Congenital Syphilis

Early < 2 years of age
- mucocutaneous & bony lesions
- hepatosplenomegaly
- meningitis

Late > 2 years of age
- interstitial keratitis
- mulberry molars
- Hutchinson’s teeth
- saddle nose
- perforation of hard palate
Summary of Congenital Syphilis Cases, Alberta, 2005 to 2007

- All 14 cases were born in Edmonton to 13 mothers (1 set of twins)
- 5 neonatal deaths
- Ethnicity: 8 First Nations, 4 Caucasian, 1 Asian
- Marital status: 6 married/common-law
- 5 sex trade workers
- 8 mothers did not access antenatal care and were not tested for syphilis until delivery; 1 mother was tested in the second trimester but could not be located and the remaining 4 tested negative for syphilis early in pregnancy

Source: Communicable Disease Reporting System: Notifiable Diseases and Sexually Transmitted Infections Databases as of June 11, 2008
Diagnosis of Syphilis

1. History

2. Physical Examination

3. Laboratory Investigations
   A) Darkfield examination / DFA
   B) Serology
Serologic Tests for Syphilis

- **Non-treponemal test**
  - RPR
  - VDRL
  - ART
  - EIA
  - RST

- **Treponemal test**
  - MHA-TP / TP-PA
  - FTA-Abs
Serologic Tests for Syphilis

- EIA – treponema specific test – detects IgG / IgM
- improved sensitivity / specificity
- has replaced RPR, TPPA, FTA-Abs
- cannot differentiate venereal from non-venereal treponemal infection i.e. yaws / pinta
INNO-LIA®

- measures antibodies to *T pallidum* antigens
- will remain positive for life
- will be only run initially to confirm EIA
Interpretation of Syphilis EIA

- **EIA -ve** - no syphilis or incubating. Consider repeating in 2 – 4 weeks

- **EIA +ve** - syphilis. RPR will be done to determine titres

- **EIA +ve / RPR –ve / LIA +ve** – syphilis
False Positive Reactions

NON-TREPONEMAL
- viral infections
- pregnancy
- malaria
- leprosy
- elderly
- injection drug abuse
- autoimmune disease

TREPONEMAL
- autoimmune disease
- genital herpes
- yaws
- pinta
- cirrhosis
Indications for CSF Examination

• any neurological abnormalities
• before re-treatment of patients who have had a relapse
• in all infants
• in the investigation of patients with late latent syphilis and an RPR $\geq 16$
Diagnosis of Congenital Syphilis

- physical examination
- serology
  - if maternal transfer – titre should gradually decrease & disappear by 6-12 months.
  - if congenital infection – titre will increase
- CSF examination
- long bone x-rays
Treatment of Syphilis

“A night on Venus, but a month on Mercury”

Primary, secondary, early latent

- Benzathine penicillin 2.4 mu IM STAT
- Doxycycline 100 mg bid x 14 days

Latent > 1 year duration

- Benzathine penicillin 2.4 mu IM weekly for 3 successive weeks
- Doxycycline 100 mg bid x 28 days
Treatment of Syphilis in Pregnancy

- All women not previously treated should receive penicillin appropriate to their stage of disease.

- Some experts suggest that pregnant women with early syphilis received 4.8 mu benzathine penicillin.

- Retreatment during pregnancy is unnecessary unless there is clinical or serologic evidence of new infection.

- When penicillin allergy is reported, desensitization should be attempted.
<table>
<thead>
<tr>
<th>Syphilis Screening during Pregnancy</th>
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<tbody>
<tr>
<td>• All pregnant women should have syphilis serology undertaken at their 1\textsuperscript{st} pre-natal visit</td>
</tr>
<tr>
<td>• Serology should be repeated at 28 – 32 weeks gestation</td>
</tr>
<tr>
<td>• For “high-risk’ women serology should again be repeated at term</td>
</tr>
</tbody>
</table>
Congenital Syphilis

Neonates should be treated at birth if:

• They demonstrate symptoms/signs of congenital syphilis
• Maternal treatment was inadequate
• Maternal treatment is unknown
• Maternal treatment was with drugs other than penicillin
RPR Titre Decrease After Treatment of Infectious Syphilis

**PRIMARY**
- 2 tube decrease at 6 months
- 3 and 4 tube decrease at 12 and 24 months

**SECONDARY**
- 3 and 4 tube decrease at 6 and 12 months

**EARLY LATENT**
- 2 tube decrease at 12 months

*Source: Romanowski B. Annals Int Med 1991;114:1005*