Syphilis: An update of diagnostics and treatment

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Outline

• Epidemiology
• Clinical Syphilis
• Testing and Treatment Strategies
Happy 111th Birthday

Hoffman
Schaudinn
T. pallidum
The last 111 years

Sir Alexander Fleming
1881-1955
Discovered Penicillin
In the second storey
Room above this plaque
The last 111 years

OLD

NEW

There’s nothing sexy about a rash.
A rash on your body, especially hands or feet, could be syphilis. The rash will go but the infection won’t.
So get it checked.
ECDC 2013

Only 14% of cases in young people (15-24)

8.4/100,000 men
1.6/100,000 women

Ratio 5.3 : 1
(increased from 2.1 : 1 in 2004)

Transmission: 58% MSM,
36% Heterosexual, 7% unknown

32%* of cases among HIV-1 infected individuals

* HIV status known in 12% of cases
Figure 3.12: Relative increase or decrease in the number of reported syphilis cases, EU/EEA, 2008–2013

- Decrease > 30%
- Decrease 10–30%
- Change 9–10%
- Increase 11–50%
- Increase > 50%
- No data available or not reporting
- Not included
England, 2014

33% rise from 3236 to 4317
86% MSM (46% rise)
Seroadaptive behaviour

- Sero-sorting
- Sero-positioning
# Chemsex

<table>
<thead>
<tr>
<th>Drug</th>
<th>% London MSM used in the last month(^1) (n=4900)</th>
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<tbody>
<tr>
<td>Mephedrone (Meph, M)</td>
<td>6.3%</td>
</tr>
<tr>
<td>Crystal Methamphetamine (Meth, Crystal, Tina)</td>
<td>3.4%</td>
</tr>
<tr>
<td>GHB/GBL (‘G’)</td>
<td>8.2%</td>
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Associated with risky sexual behaviour and STI transmission

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Number of STI diagnoses among MSM by HIV status: England, 2013

- Data from routine GUM service returns
- * First episode; ** Includes diagnoses of primary, secondary & early latent syphilis
- HIV diagnosed includes those who were diagnosed with HIV more than 6 weeks prior to their STI infection
- Data type: service data
Women

• 263 cases in women in 2014\(^1\)
• Rates of congenital syphilis are correspondingly low (0.0025/1000 live births in 2011\(^2\))
  – Chaotic women
  – socio-economically deprived
  – Presentation in the third trimester

\(^1\)Health Protection Report 2014;9:22-29
\(^2\)Infection Reports 2013;7(44)
The Disease

Contact with *Treponema pallidum* (ID$_{50} = 57$ organisms)

9-90 days

Primary Disease
(genital, perianal or extra-genital chancre)

4-10 weeks

Secondary Disease
(rash, neurological/eye, condylomata, alopecia, hepatitis)

3-12 weeks

Latent Disease
(Early within 2 years and late thereafter)

Tertiary Disease
Neurological, cardiovascular and gummatous disease

25%
Who to test?

• SRH/GU clinics:
  – Everyone, but particularly MSM
• Universal antenatal screening and blood donor screening

• Psychiatrists/General physicians:
  – New onset of dementia
  – Suspected organic component during MSE
  – Atypical illness not responding to treatment
  – Risk-taking behaviour (sexual) whilst manic/psychotic/using drugs
How to test?

Who do we test?
– Symptomatic patients (early or late disease)
– Asymptomatic screening

• How do we test?
– Depends on stage of disease and samples available...
– Serologic Tests – treponemal and non-treponemal
– Rapid serological tests (POCT)
– Direct visualisation
– PCR
Serology

Treponemal screening test (EIA)
Total IgG/IgM

Confirmatory treponemal test (TPPA/TPHA)

Quantitative RPR testing to help identify stage

N.B. Repeat screening at 12 (+/- 6) weeks after exposure if initially negative

1 Hart G. Ann Intern Med. 1986;104(3):368
Diagnosing Early Syphilis: Ulcer PCR

• A positive result has clinical significance

• Sensitivity of 80-100% and a characteristically high specificity (92.1-99.8%)\(^1\)

• Described in a multiplex format for the diagnosis of genital ulcer disease\(^2\)
  – *T. pallidum*, *H. ducreyi*, HSV
  – 91% sensitivity compared with DGM

• Better than DGM?

\(^1\)Gayet-Ageron *et al* (online first) *Sex Transm Infect* doi:10.1136 sextrans-2012-050622
CSF testing

• No gold standard definition. No absolute criteria.
• VDRL/RPR testing and EIA/TPPA can be performed on CSF
• Negative CSF TPPA rules out neurosyphilis
  – Less than 2% of NS cases will have negative CSF TPPA$^{1,2}$
• CSF VDRL is specific
  – Low sensitivity overall (15-30%)$^3$
  – Much higher in GP (90%)$^4$
  – VDRL and modified VDRL more sensitive than RPR$^5$

Selecting patients for LP - guidelines

Which patients should have a lumbar puncture?

– General consensus with current UK, IUSTI and CDC guidelines

1, 2, 3

– Relevant symptoms and signs:
  • Neurological/Psychiatric
  • Eye involvement
  • Auditory symptoms
  • Tertiary Disease

– Asymptomatic patients when:
  • Serological treatment failure
  • HIV +ve and CD4 count <350 and/or RPR >1:32

3. CDC STD Treatment Guidelines 2010):729-40
1. Know which serological tests your lab uses and how to interpret them
2. Repeat negative serology if high index of suspicion (6 and 12 weeks)
3. Measure RPR on the first day of treatment, then 3 & 6 months after.
4. DGM still valuable. PCR can be sent on suspicious lesions which are DGM negative.
Key management

• All patients with syphilis should have screening for other STIs, especially HIV

• Patients should be given a clear explanation of their diagnosis and written information
  – New BASHH leaflet soon available

• Testing and treatment for HIV positive patients is no different to HIV negative patients

• Patients with early disease should be warned about the Jarisch-Herxheimer reaction
Treatment

• Penicillin remains effective treatment
• IM Benzathine for those without neurologic involvement
  – 1 or 3 doses
• IV Benzylpenicillin or IM procaine (+ probenecid) for those with neurological involvement (suspected or proven)
• Doxycycline (or ceftriaxone) in case of penicillin allergy
  – Dose and duration vary according to neurologic involvement and stage of disease
Treatment changes 2015

- Procaine penicillin now an alternative treatment
  - Pain, cost and inconvenience of multiple injections.
- Macrolide antibiotics
  - No suitable alternative
  - Follow-up assured
- The duration for the recommended treatment of neurosyphilis is changed from 17 to 14 days.
Management changes 2015

• In asymptomatic disease, no need for full routine examination or CXR.
• 2 weeks sexual abstinence following treatment of early infectious syphilis.
• Follow-up serology at 3, 6 (and possibly 12) months following treatment.
  – Perhaps 1/12 phone call if given oral treatment
Macrolide resistance

• 1977: Patient fails erythromycin treatment
  – Street 14 strain shows *in vitro* macrolide resistance (1988)¹

• 2000: Link made between genotypic and phenotypic resistance
  – A→G point mutation in 23srRNA gene at position 2058²

• 2002: Clinical failures reported³

• 2004: Proof of resistance in rabbit study⁴

• 2009: Second mutation discovered: A2059G⁵

Worldwide

- Western Canada
  - 2007-2008 4/14 (28.6%)
- Dublin
  - 2004 88%
- London
  - 2006-8 12/18 (66.7%)
  - 2011-12 20/25 (80%)
- Czech Republic
  - 2004-10 17/75 (22.6%) A2058G,
  - 11/75 (18.7%) A2059G
  - 2011-13 56.5% A2058G, 10.1% A2059G
- Shanghai 2007-2008
  - 37/37 (100%)
- Seattle
  - 2002 3/13 (23.1%)
  - 2007 10/11 (90%)
  - 2009 14/15 (90%)
- San Francisco
  - 2000 0%
  - 2004 56%
  - 2004-2007 68%
- Baltimore
  - 1999-2001 11%
- South Africa
  - 2005-2010 0/63 (0%)
- Lesotho
  - 2007 1/37 (3%)
- Madagascar
  - 2000-2007 0/141 (0%)
- China 2008-2011
  - 194/211 (91.9%)
- North 95.2%
- East 93.8%
- South 88.6%
- Taiwan
  - 2009-2011 0%
- Sydney
  - 2004-2011 84%
Macrolide resistance

St Mary’s, London

<table>
<thead>
<tr>
<th>Year</th>
<th>Wild-type (%)</th>
<th>Resistant (%)</th>
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<tbody>
<tr>
<td>2006-7</td>
<td>33.3</td>
<td>66.7</td>
</tr>
<tr>
<td>2011-12</td>
<td>22</td>
<td>78</td>
</tr>
</tbody>
</table>

Tipple C et al. Sex Transm Infect. 2011;87(6):486-8
Chisholm et al, ECCMID conference abstract, May 2013
Summary

• Rising syphilis incidence in the UK, predominantly among MSM.
• Serology still the cornerstone of diagnosis, but PCR useful and DGM not yet to be retired.
• Recent changes to management and new UK guideline soon to be published in IJSTDA.
• Penicillin remains effective treatment.
• Macrolides to be used with upmost caution.
Thank you

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