HIV and Syphilis: A syndemic with no end in sight?

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Outline

• Brief epidemiology
• Interventions
• Chemoprophylaxis/PrEP
• Treatment
• Subtyping
• Neurosyphilis
• Cytokines and markers of disease status

Epidemiology of HIV and syphilis

Syphilis notifications in HIV positive gay and bisexual men continue to increase

Canada
300x rate in general pop
Burchell et al. BMC Infectious Diseases 2015

USA
50% increase in HIV pop
Su et al. STD prevention 2014

NSW, Australia
49% in HIV pop
87% of reinfections
Botham et al. Sex Health 2013

Syphilis notifications in high income countries

Male to female ratio increasing in 17/28 OECD countries
Proportion of cases in MSM >50%
No country succeeded in significantly reducing trend between 2000-2013
None report HIV status systematically

Not just high income countries....

Syphilis control: sexual behaviour


Gray RT et al. Sex Transm Dis 2011
McCarn PD et al. Sex Transm Dis 2011

Rates of syphilis 10% in Brazil, 7% in South Africa, 6% Thailand
Solomon et al. CIID 2014

Would MSM do it for 3m?

Personal benefit

Community benefit
Syphilis control: increase MSM

Syphilis control: Chemoprophylaxis

Doxycline prophylaxis pilot: Bolan et al STD 2015

30 HIV positive GBM randomised
- 15 received 100mg od doxycycline
- 15 received financial incentive based contingency management

Followed for 48 weeks
- 77% retention rate; drug levels reasonable
- 1 gastro reflux

STIs and HIV PrEP - “a good problem to have?”

- PROUD: high baseline prevalence (>50% incidence any STI, 10% syphilis)
- IPERGAY: 10% syphilis incidence
- Kaiser Cohort: San Francisco
  - 50% STI at 12 months
  - 5.5% syphilis (95% CI: 3.5-9.1%)
- Critical component of PrEP care

How much benzathine is enough?

478 patients – US Military HIV cohort
All had syphilis of <1yr duration

578 HIV patients across Taiwan
Compared RPR at 6, 12 months
N= 295 1x BPG vs n= 273 3xBPG

Can we use other treatment for syphilis in HIV+ve?

Japan: 3g Amoxycillin + probenecid
286 HIV pos men: Observational
1/3 late/unknown duration with RPR ≥1:8
Excluded neurosyphilis
150 on ART, median CD4 390

Overall 95% cure rate at 24 months
- 1/monthly: 95%
Treatment guidelines for early syphilis and HIV

US CDC 2015:
1 x 2.4 MU BPG for early syphilis
If no treatment response, give 3 x BPG unless CSF shows neurosyphilis
No need for enhanced regimens
No need for LP unless neuro signs

Despite this: Australian data shows 40% of HIV pos are treated with enhanced regimens - no difference in cure
Read et al Sex Health 2015

What can syphilis subtyping tell us about syphilis and HIV?

1998 CDC classification - ARP/TPR
Enhanced in 2010 - CDC +

Distribution of strain types over time in Sydney - no relation to HIV status

Graph courtesy Christina Marra

Strain Type and Neurosyphilis

<table>
<thead>
<tr>
<th></th>
<th>Adj OR</th>
<th>P-value</th>
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<tbody>
<tr>
<td>RPR</td>
<td>1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type f</td>
<td>3.5</td>
<td>0.02</td>
</tr>
<tr>
<td>&gt; 2005</td>
<td>0.7</td>
<td>0.4</td>
</tr>
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Graph courtesy Christina Marra

Neurosyphilis and host immunity

Impairment of innate immunity
Natural polymorphisms of TLR
Reduced opsonisation?
Higher levels of serum TNF in HIV pos who developed NS vs those who didn’t - more immune activation/dysregulation
May explain OR for NS with cART of 0.2

Graph courtesy Christina Marra

What’s new in neurosyphilis and HIV?

Tuddenham- STD 2015
Confirmed finding that negative serum RPR predicts absence of NS

Graph courtesy Christina Marra
Relation between Neurosyphilis and HIV neurocognitive impairment?

CHARTER study:
Case control study
Prior syphilis OR of 2.6 for learning impairment (controlled for methamphetamine use), and greater number of domains with reduced function

No relation to current CSF findings

Marra et al. 2013 Int J STD AIDS

Need for better markers of disease activity

TP-PCR in blood-pooled sensitivity meta-analysis-
Gayet-Ageron STI 2013

<table>
<thead>
<tr>
<th>Domain</th>
<th>Sensitivity (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>APN</td>
<td>0.762</td>
<td>0.847</td>
</tr>
<tr>
<td>CD40</td>
<td>0.763</td>
<td>0.848</td>
</tr>
<tr>
<td>CD43</td>
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<tr>
<td>EDA</td>
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<tr>
<td>PCA3</td>
<td>0.763</td>
<td>0.848</td>
</tr>
<tr>
<td>Plasma HIV RNA load, log 10</td>
<td>0.763</td>
<td>0.848</td>
</tr>
</tbody>
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No association with HIV and spirochaetaemia

Vera et al. HIV Med 2012

Significant for reinfection

Vera et al HIV Med 2012

Quantitative TP-PCR changes post treatment

Half life 5.7 hours, clearance 56 hours


Inflammatory markers and infection

Bristow et al. ISSTDR 2015

HIV-positive patient on ART (CD4+=380, VL=15,000) with recent syphilis infection, PET Scan

First visit (RPR = 1:64) pre-treatment with probable syphilitic aortitis

Follow up visit (RPR 1:16) post-treatment without aortitis

PICASSO Study NIH/NIAID R01 AI099727

Slide courtesy Jeff Klausner

Summary-
Maybe there is light at the end of the tunnel?

• Overlapping epidemiology of HIV and syphilis continues
• Greater understanding of range of prevention options
• Evidence that current treatments do work in HIV
• Role of prophylaxis and molecular epidemiology
• Evolving data on biological basis for possible risk of neurosyphilis
• Development of better tools to establish disease activity

• Significant social and structural challenges- but never give up.
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