26th Annual Conference of the British HIV Association 2020

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Neurosyphilis

Patrick French

The Mortimer Market Centre

Central and North West London NHS Trust

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Declaration of Interests relating to this presentation

- No conflicts of interest.

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Neurosyphilis

- Natural history
- Epidemiology
- Diagnosis
- Treatment

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Neurosyphilis – clinical presentations

Classical Definitions

- Asymptomatic

or

- Symptomatic

- Early – meningovascular

or

- Late – general paresis, tabes dorsalis, late meningovascular

But

- Early invasion (15-40% syphilis)

- Importance of asymptomatic neurosyphilis uncertain

- Most neurosyphilis is part of early meningovascular syphilis - uveitis, sensineural deafness, stroke.

- General paresis and tabes dorsalis are rare.

Tertiary syphilis

- 20 – 40% patients with untreated latent syphilis develop tertiary syphilis after 3-40 years
  - 15% gummata
  - 10% cardiovascular
  - 7% neurosyphilis

Clark *JCD* 1955 311

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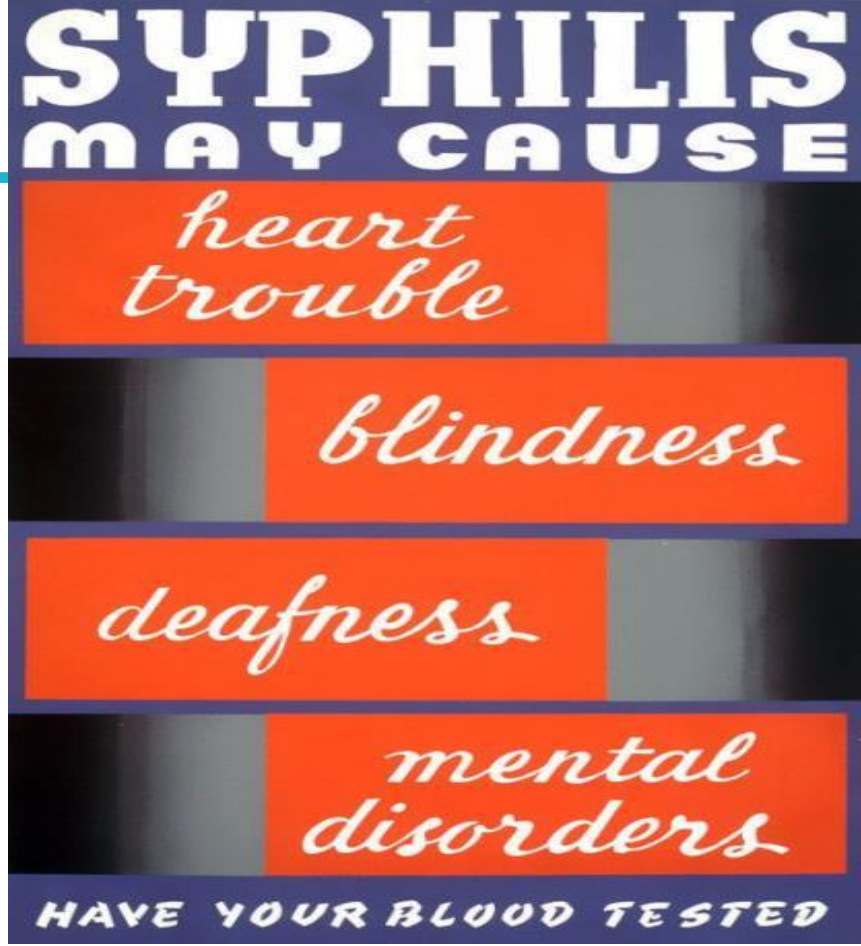

Neurosyphilis – incidence (among people with syphilis)

- Depends on definitions:
- 1.8% - 3% of early syphilis

de Vaux *CDSC* 2018; 4539

- 7% of untreated syphilis

Clark *JCD* 1955 311

- 7.9% of all syphilis diagnoses (Seattle U.S.)

Dowbrowski *STD* 2015, 702

- 1.9% of all syphilis in England 2018)

PHE

HIV and Neurosyphilis

Important epidemiological association between HIV and syphilis.

Impact of HIV in progression to neurosyphilis is less certain.

- Early case reports - progression to neurosyphilis might be quicker.

  Johns *NEJM* 1987: 316.

- Studies of early syphilis showed impact of HIV – larger, painful, multiple ulcers etc.

  Rompalo *STD* 2001: 158.

- But more recent (post HAART) studies of early syphilis show no impact of HIV status.

  Towns *STI* 2016: 110

Are there similar post-HAART studies for neurosyphilis?

- Neurosyphilis (CSF criteria) more likely if HIV positive and associated with lower CD4

  Marra *JID* 2004 369.

- Neurosyphilis commoner in HIV (denominator not defined)

  de Vaux CDSC 2018; 4539 - 41

Neurosyphilis in England 2010-2019 (Q3) PHE

Diagnoses in GUMCAD (SHHAPT A5)

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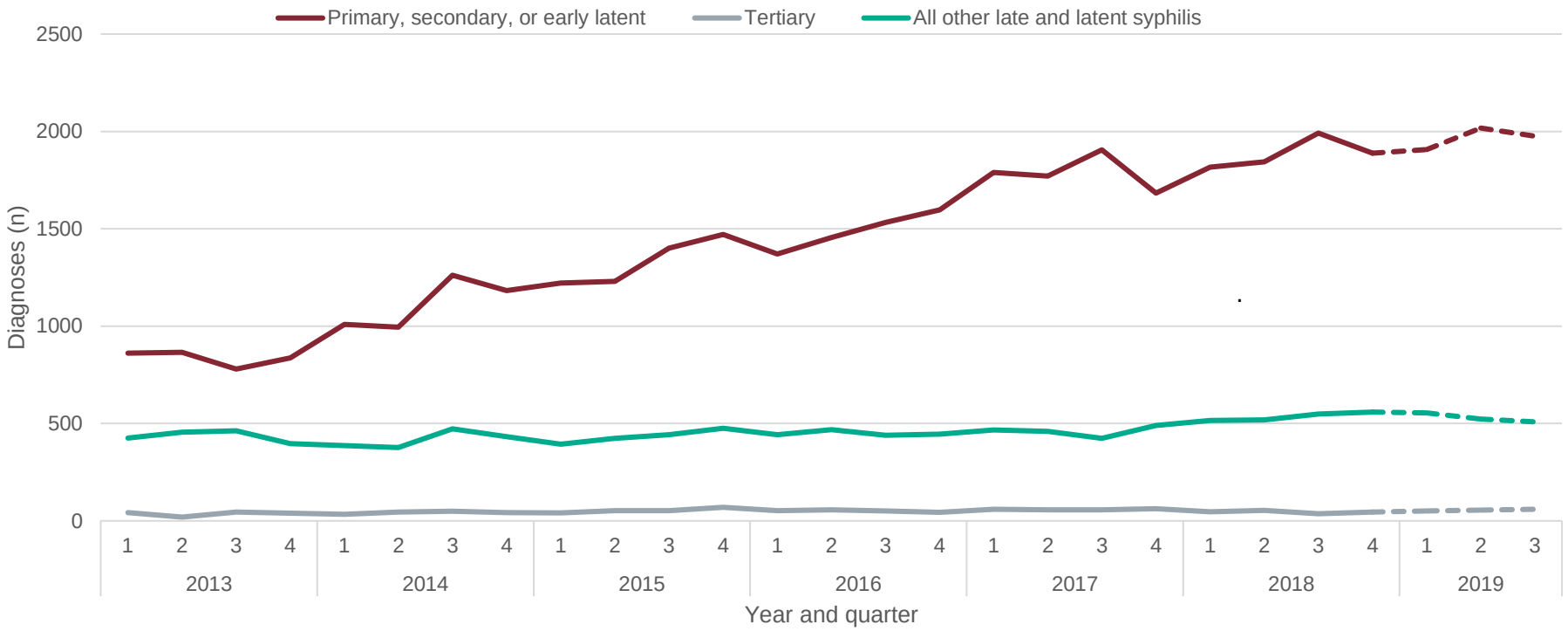
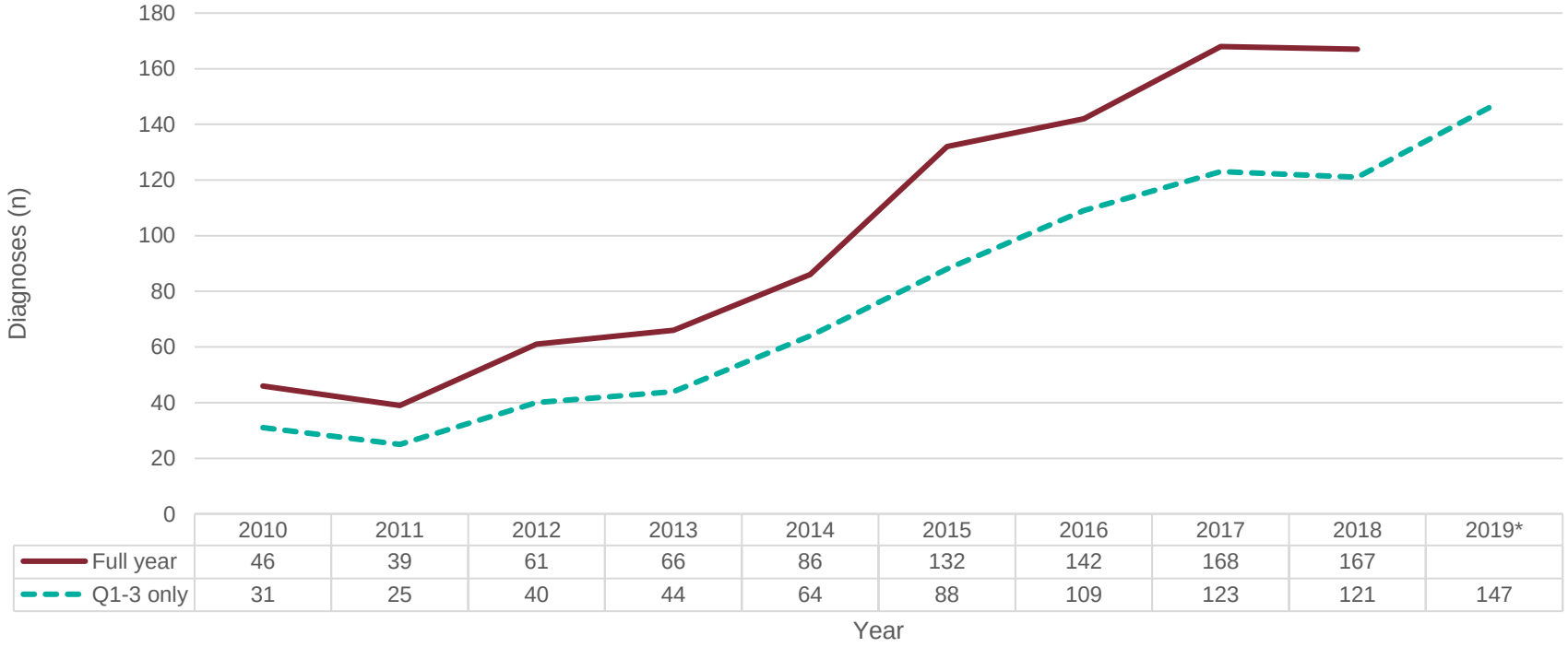
Early syphilis in England



2019 data are provisional.

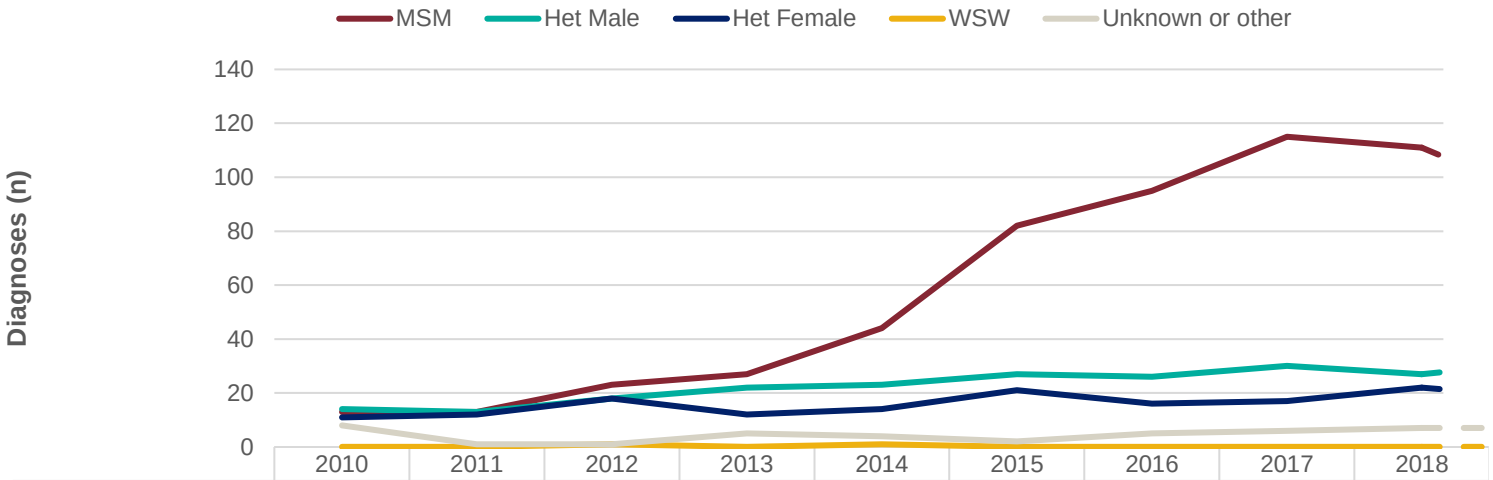
Neurosyphilis diagnoses in GUMCAD 2010-2019*



	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*
Full year	46	39	61	66	86	132	142	168	167	
Q1-3 only	31	25	40	44	64	88	109	123	121	147

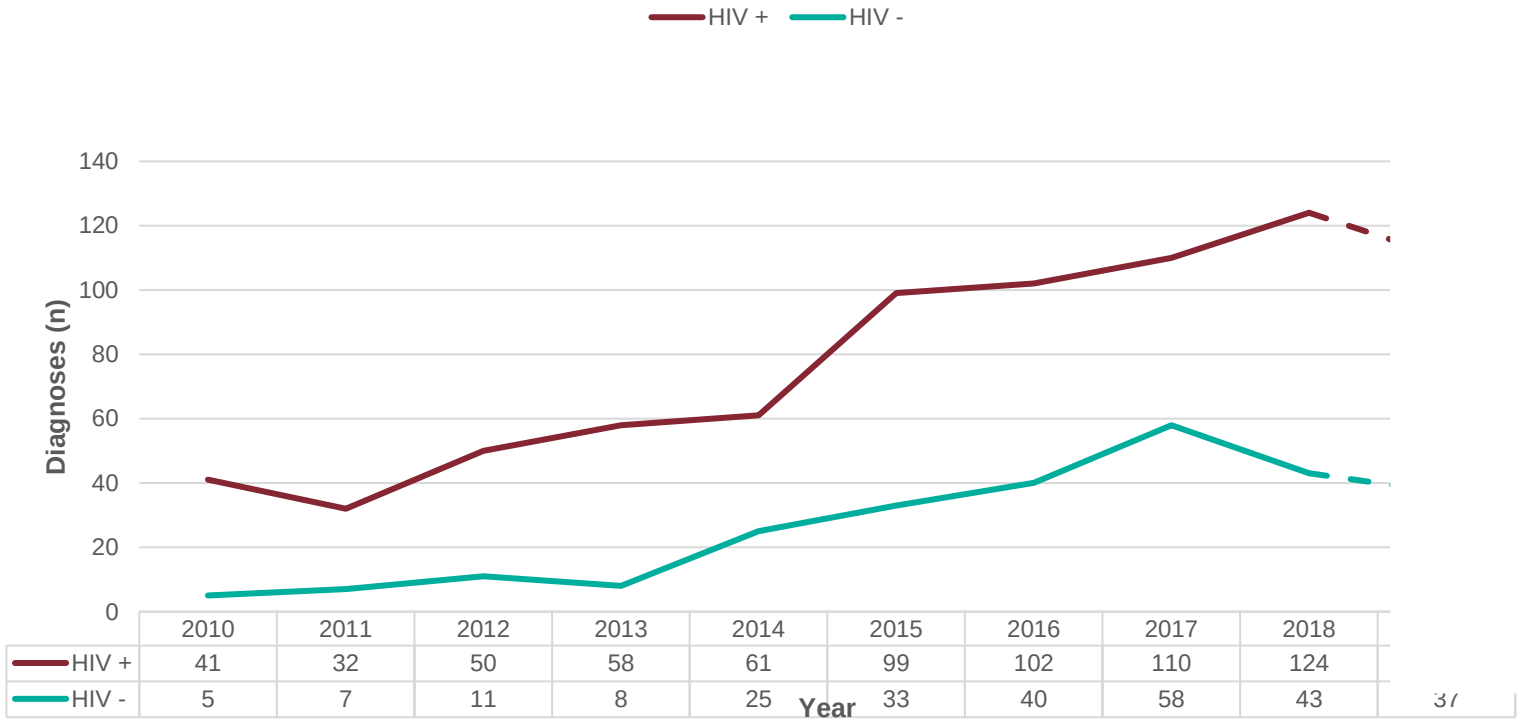
*2019 data are provisional

Neurosyphilis diagnoses in GUMCAD 2010-2018 by gender and sexual orientation



	2010	2011	2012	2013	2014	2015	2016	2017	2018
MSM	13	13	23	27	44	82	95	115	111
Het Male	14	13	18	22	23	27	26	30	27
Het Female	11	12	18	12	14	21	16	17	22
WSW	0	0	1	0	1	0	0	0	0
Unknown or other	8	1	1	5	4	2	5	6	7

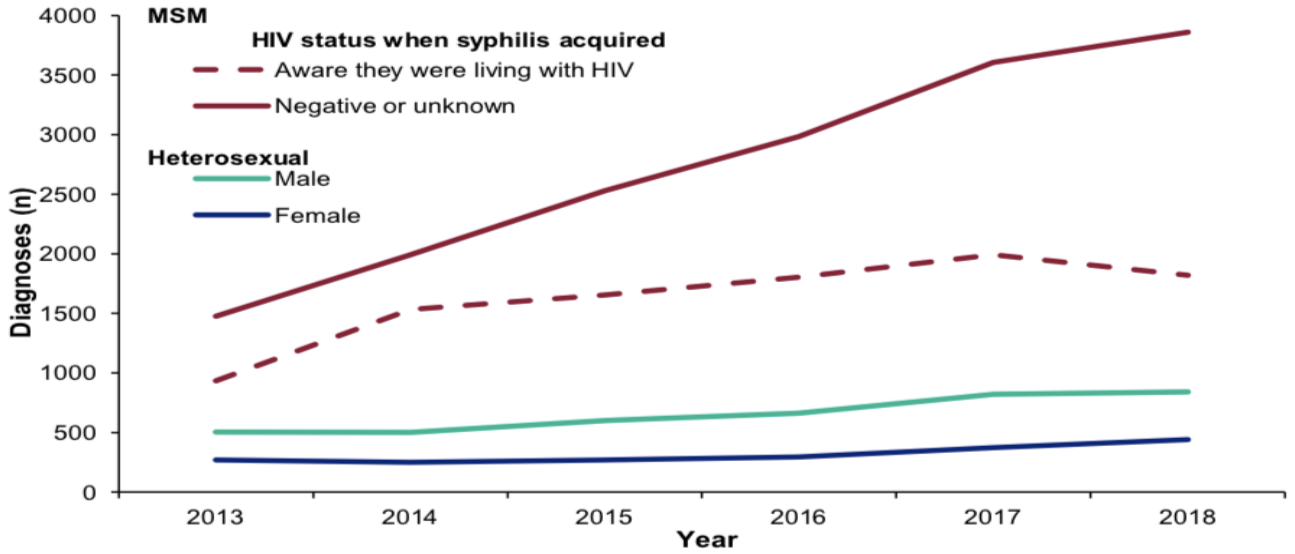
Neurosyphilis diagnoses in GUMCAD 2010-2018 by HIV status



	2010	2011	2012	2013	2014	2015	2016	2017	2018
HIV +	41	32	50	58	61	99	102	110	124
HIV -	5	7	11	8	25	33	40	58	43

HIV status and early syphilis – England

Figure 2. Diagnoses of syphilis (primary, secondary & early latent), by sex, risk group and awareness of HIV status when syphilis acquired, England: 2013 to 2018



MSM & Syphilis HIV Positive – 41% in 2013. 31% in 2019.

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Epidemiology of syphilis in England

- 2019

- Launch of two new syphilis diagnosis codes

- A10 – ocular syphilis
- A11 - oto-syphilis

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Case

- Man, 40s, HIV positive, HIV viral load < 50. CD4 640
- Acute onset left hemiplegia
- MRI - Right MCA thrombosis – MRI suggests vasculitis
- Previous syphilis but negative RPR eight months before this presentation.

- Normotensive. No diabetes. Normal echocardiogram, carotids, autoantibodies negative.

- Syphilis serology
  - Total antibody EIA +ve
  - TPPA +ve >1:1280
  - RPR 1:32

Criteria for brain scan & CSF examination

BASHH 2015

- Symptoms / signs of possible neurosyphilis
- Untreated syphilis

- Does this apply in uveitis and otosyphilis?

- Previously thought that patients with low / negative RPR could have neurosyphilis.

Hooshmand *JAMA* 1972 726

- If RPR low: neurosyphilis unlikely.

Neurosyphilis rare if VDRL < 1:4

Wöhrl *Act Derm Venereol* 2006; 335

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Case – CSF results

- WBC 350/μL
- RBC 0
- Protein – 1.5g/L
- Glucose normal

- Syphilis EIA positive
- TPPA + ve 1:1280
- RPR – 1:4

CSF criteria for neurosyphilis diagnosis
(BASHH 2015)

- Protein >0.45 g/l
- RPR/VDRL positive
- TPPA >1:320

- WBC > 5 cells (> 20 if HIV positive)

Case - Treatment

- Prednisolone 60mg for three days (-1,0,1)

- 1st line I.V. benzylpenicillin 2.4 gms 4 hrly followed by I.M. procaine penicillin 2.4 MIU penicillin unit & probenecid 500mg PO QDS - for a 14 day treatment in total.
- Full recovery
- Normal CSF (WBC < 5, RPR negative at 6 months)

Treatment – second line – penicillin allergy

- No role for macrolides
- Allergy testing and desensitisation is an option
- Doxycycline 200mg BD for 28 days – used widely with little evidence.
- Ceftriaxone 2gm IV or IM – 14 days – case reports / case series / pilot studies. Looks promising.
- Marra *CID* 2000: 30 (3): 540. Smith *Int J STD AIDS*: 2004: 328.
- Very little cross sensitivity between penicillin and third generation cephalosporins.

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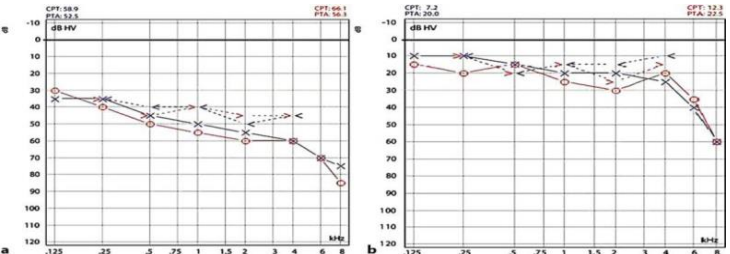
Syphilis of the ear and eye

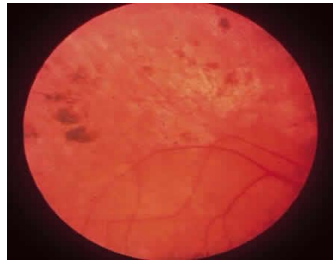
Otosyphilis

- Sensineural (high frequency) hearing loss. Sudden. Sometimes fluctuating.
- Usually bilateral (but often apparent symptoms unilateral)
- Can be associated with labyrinthitis.
- Response to treatment usually good.



Uveitis

- Usually bilateral (33% unilateral)
- Anterior / Posterior / Pan-uveitis.
- Can be associated with retinitis / papilitis / optic neuritis
- Response to treatment usually good.



Uveitis and Otosyphilis - CSF examination or not?

- In favour of CSF
- Extra piece of information potentially useful in uncertain diagnoses – if CSF suggestive on neurosyphilis
- Potentially useful of poor / inadequate response to treatment (CSF should normalise at 6 months)

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Uveitis & Otosyphilis – reasons to not do CSF – what does it add?

CSF usually negative

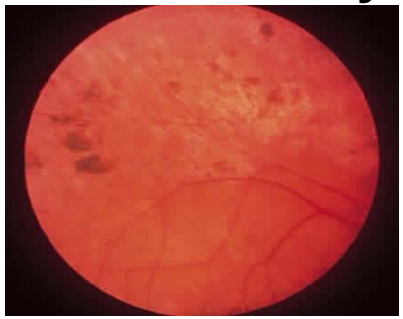
- Syphilitic uveitis: 35% CSF positive

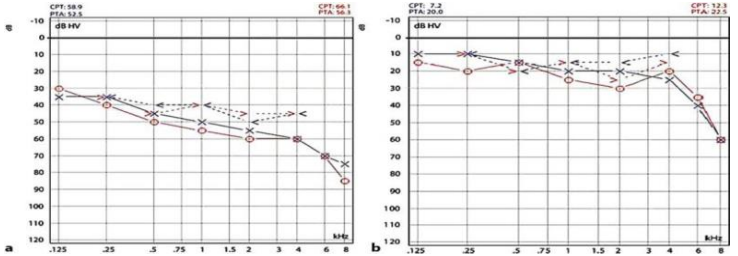
J Ophalmol 2017: 2, 2017 6594849

- Otosyphilis: 5-45% CSF positive

Laryng 1992 1255 & *Oto Head & Neck* 2007 67

Treatment response can be assessed clinically





Summary & Future Research

Summary

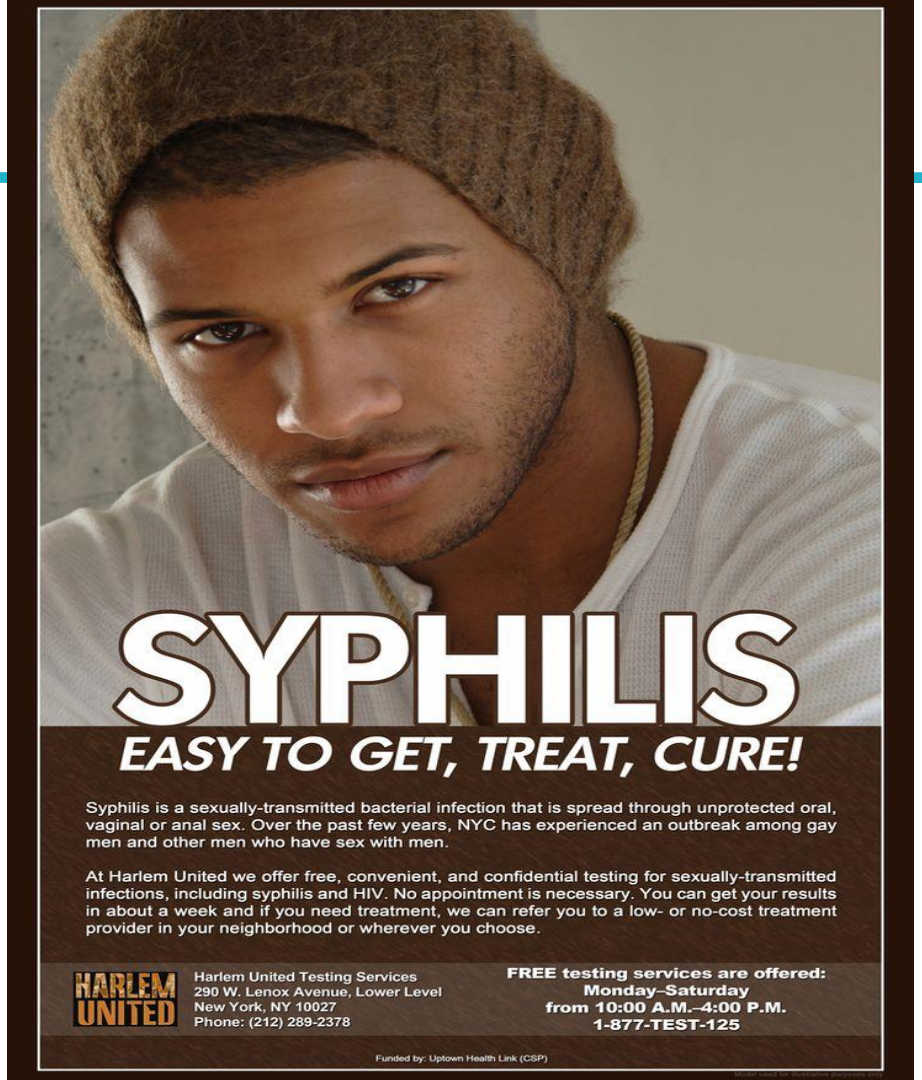
- Uveitis, otosyphilis and stroke are no longer rare complications of syphilis in the UK.
- Neurosyphilis diagnostics remain imperfect.
- IV benzyl penicillin and IM procaine penicillin remain the treatments of choice.

Future Research

- A better gold standard for diagnosis – is there any role for *T.pallidum* NAATs?
- A neurosyphilis RCT

Procaine / Benzylpenicilin vs. Ceftriaxone (+/- Doxycycline!)

Questions?



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