

The 'Dark' Days Are Over

A move to routine syphilis PCR testing on all genital ulcer swabs

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Background

In the UK the burden of sexually transmitted genital ulcerative infection is limited to HSV (Herpes Simplex Virus) type 1 and 2 and to a lesser extent syphilis. Treatment and follow up is distinct, with little overlap. Accurate diagnosis at primary presentation has significant impact on patient management.

The clinical distinction between these aetiologies has traditionally been made by ascertaining whether the ulcers are painful (HSV type 1 and 2) or painless (syphilis). However, a study by Towns et al based in Melbourne and published in 2016 quantified that 'primary lesions in acute syphilis infection were painful in 49% of their studied population'.¹

PCR techniques have been at the forefront of HSV testing for some years however diagnosis of acute ulcerative syphilis infection has continued to rely heavily on serology; interpretation of which is not straightforward and is reliant on follow up testing. Dark field microscopy also plays a key role, however its utility is limited by site of lesion and local availability and technical experience of this diagnostic.



Figure 2

Figure 3

As real time multiplex PCR has become increasingly accessible the argument for routine syphilis PCR of all genital ulcerative lesions alongside HSV testing. This has the potential for more timely diagnosis and therefore, management of primary syphilis infection.

AIM

To ascertain what proportion of our patient cohort presenting with anogenital ulceration who were investigated with anogenital swabs for HSV had serologically confirmed syphilis infection in the three months preceding, or proceeding the swabs being taken. The implication being that a proportion of those presenting with genital ulceration although tested for HSV will actually be presenting with primary syphilis.

Methods

A retrospective audit looking at what proportion of symptomatic patients tested for HSV infection in the Bristol GUM (genitourinary medicine) setting between 01/05/2009 and 28/04/2017 using anogenital swabs had either concomitant, (in the case of positive HSV type 1 and 2 PCR) or isolated, (in the case of negative HSV type 1 and 2 PCR) active syphilis infection.

Active syphilis infection was defined as those with serological evidence of syphilis infection using a commercial platform; 'Newmarket'. Serology was considered positive if ;

1) The IgM was positive on the primary sample with seroconversion on subsequent serological testing

2) The RPR was positive at a titre of >1:8

- Unfortunately we did not have access to any clinical or dark field microscopy data .
- IgMs only became routinely performed on all syphilis serology from Jan 2012 onwards.

Results

5418 swabs (penile, vulvovaginal, rectal) were received for HSV PCR testing from the GUM clinic in Bristol between 01/05/2009 and 28/04/2017. All samples had accompanying treponemal serology performed 3 months either side of the swab being taken. 477 follow up serological samples were processed

• 36 samples equating to 33 patients had evidence of active syphilis infection as defined by an RPR of >1:8 on the first test.

• A further 4 acute syphilis infections were identified on early follow up serology between day 7 and day 20 following the primary sample as defined by the RPR became >1:8

• 61 patients were found to have a positive IgM, with 40 of these being RPR positive.

Tests	HSV +	HSV -	Total	χ^2/P
HSV 1 and 2 PCR	2331	3087	5418	
Treponemal serology performed	2331	3087	5418	
EIA positive/ equivocal	31	118	149	
RPR positive/ equivocal	15	74	89	
RPR positive \geq to 1:8	2	34	36	10.34/<0.002
TTPA positive/ equivocal	31	121	152	
IgM positive/ equivocal	6	55	61	27.71/0.00001
IgM positive with RPR positive at any level	3	37	40	20.74/0.00005
Follow up Treponemal Serology	177	300	477	

Discussion

This data demonstrates that a proportion of those being investigated for HSV type 1 and 2 infection, actually are presenting with primary syphilis. Routine use of multiplex PCR which incorporates HSV type 1 and 2 testing with syphilis would result in early, sensitive and specific identification of primary syphilis in those presenting to GUM services with ulceration. PCR is not limited by the constraints of observer skill and lesion site as dark field microscopy is, or by the complexities of interpreting treponemal serology particularly in early primary infection.

Moving to screening for syphilis via PCR of genital swabs presents the opportunity to manage infection in a timely fashion resulting in the following benefits:

• Prevent onward transmission of infection which has a wider impact on the population particularly in MSM communities.

• Simplification of treatment regimens which not only plays an important role in antimicrobial stewardship but allows rapid, one stop treatment. From a patients perspective this is convenient and from a public health perspective limits loss to follow up.

• Limits complications from secondary or tertiary disease

References

1) Towns et al: Painful and multiple anogenital lesions are common in men with Treponema pallidum PCR-positive primary syphilis without herpes simplex virus coinfection: a cross-sectional clinic-based study. Sex Transm Infect. 2016 Mar; 92(2):110-5

2) https://www.updatdate.com/contents/image?imageKey=ID%2F576378&topicKey=ID%2F7592&source=outline..._link&search=syphilis&selectedTitle=1-18 (accessed 09/11/2017)

3) <https://www.bing.com/images/search?view=detailv2&ccid=H1y86ne1&id=4909E3D5283D5641148CDDC0178745CFDD85939F&thid=OIP.H1y86ne1PQd5vMVFVBUaEsDE&q=dark+field+microscopy+syphilis&simid=608038951488260519&selectedIndex=23&mode=overlay&frst=1> (accessed 09/11/2017)