The acceptability of the introduction of a type specific herpes antibody screening test into a genitourinary medicine clinic in the United Kingdom

H M Mullan, P E Munday

Objective: To determine the uptake of a type specific herpes simplex antibody test if it were offered as part of routine screening in a genitourinary medicine clinic in a district general hospital in the United Kingdom.

Methods: Stage 1. A series of 207 consecutive new attenders and 205 patients who had attended the clinic previously were given written information about the test and asked whether they would want to have the test if it were available. They were asked whether they would wish to discuss it further with a counsellor before making a decision. Stage 2. Another series of 434 consecutive patients were offered the test after reading an information leaflet detailing the advantages and disadvantages of being tested. They were also offered the opportunity to see a counsellor for further information.

Results: In stage 1 of the study, 51% of men and 54% of women said they would want the test if it were available. 32% of men and 40% of women requested counselling. In stage 2, when the HSV-1 was offered, 41% of men and 37% of women chose to have it, and 23% of men and 7% of women requested further information from the counsellor. 20 patients were herpes simplex virus type 2 (HSV-2) positive—four of whom would have been diagnosed on clinical grounds at the time of presentation. A further 12 men and 20 women excluded themselves from the study because they were known to have genital herpes. Therefore, type specific serology contributed 30% to total diagnoses in this population—16 out of a population of 52 would have remained undiagnosed without having had the test.

Conclusion: In this population, the uptake of the type specific herpes simplex antibody test was much less than expected and screening was of limited benefit in identifying large numbers of previously unrecognised HSV-2 positive patients.

The incidence of genital herpes is increasing in many developed countries. The annual number of new cases presenting to genitourinary medicine (GUM) clinics in England and Wales increased by 40% between 1988 and 1999.1 The proportion due to herpes simplex virus types 1 and 2 (HSV-1) and HSV-2 varies geographically but infection with HSV-1 appears to be becoming commoner, especially in women.2 In the general population, higher HSV-2 seropositivity rates are seen with increasing duration of sexual activity, increasing numbers of lifetime sexual partners and increasing number of past infections with other sexually transmitted diseases. The prevalence of antibody to HSV-2 is significantly greater in genitourinary medicine clinic attenders compared with blood donors, women, and homosexual men. Among clinic attenders, antibodies to HSV-2 are associated with increasing age.3 Results of recent epidemiological studies of genital herpes indicate that most infected individuals are unaware of their infection4 and that asymptomatic shedding is common5 and appears to be the source of most transmission to new partners.6 Thus, strategies aimed at those presenting with clinical lesions will only reach a small proportion of those capable of transmitting the infection.

Up until recently, the diagnosis of genital herpes infection relied on viral culture from clinically visible lesions. Serological tests to distinguish HSV-1 from HSV-2 were available in only a few centres on a research basis. Type specific herpes antibody assays are now being marketed but their role in the clinic setting has been a controversial subject.

It has been suggested that type specific serology might be used to provide diagnostic information for individual patient management and limit the spread of herpes infection. Studies indicate that many infected individuals can be taught to recognise mild symptoms.7 Some have advocated its use as part of routine screening in GUM clinics.8 Opponents of its use argue that because of the low predictive value of positive results in low prevalence populations, the lack of treatment options, the likelihood of a positive result leading to anxiety and relationship difficulties, and the fact that HSV-1 is becoming of more clinical significance, its use should be limited to specific clinical situations.9

In 1997, investigators in Leeds assessing patient attitudes to the use of type specific serology as a screening test showed a strong desire among patients for routine serological testing with 92.4% wanting to know if they, and 90.8% wanting to know if their partners, had been infected with herpes simplex virus; 65% expected the test as part of routine screening.9 The purpose of our study was to assess the attitudes of our clinic population to such a proposal, to evaluate the uptake of the test, and the effect of its use as a screening test on workload within the clinic.

METHODS

Approval of the local research ethics committee was obtained before the study was started. Informed written consent was obtained from the patients for the second stage of the study.

The study has the power to detect a 50% uptake of screening to within 5%. In order to detect an uptake of 50% to within plus or minus 5%, it would be necessary to enrol 400 patients. Response rates of greater than 50% would be detected with greater precision with this number of patients.
Statistical analysis was performed using the SPSS for Windows software package, Release 10.0. Statistical significance was considered when a p value was 0.05 or less. Continuous variables were compared using Mann-Whitney test. Relative risk was used to examine the association between expecting to test versus accepting test for both male and female.

The study was undertaken in two stages.

Stage 1
A series of 207 consecutive new attenders (103 male and 104 female) and 205 consecutive patients (102 male and 103 female) who had attended the clinic on a previous occasion (re-attenders) were asked to read a leaflet about type specific herpes serology testing. They were then asked to indicate whether or not they would wish to have the test performed if it were available and whether they would wish to discuss the test further with a counsellor before testing.

Stage 2
A further series of 434 consecutive patients (173 male and 261 female) were offered the type specific herpes serology test along with their standard screening tests, after reading an information leaflet detailing the advantages and disadvantages of having the test (see fig 1) and some information about herpes itself. The information leaflet was given to the patient at reception and read by them while they were waiting to be seen by a doctor. They were then asked during their consultation whether they wished to have the test and were offered the opportunity to see the counsellor. This group comprised both new patients and reattendees.

Three options were provided. Patients deciding to have the test were asked to sign a consent form and were given an appointment to return in 2 weeks for their results. Those requesting further discussion were referred to one of two designated counsellors who had been trained to ensure they provided similar information and the time taken for discussion noted.

The tests were performed using the Gull HSV type 2 specific IgG ELISA test and the PHLS Central Public Health Laboratory in-house blocking HSV-2 IgG assay on sera that were negative for HSV-2 in the Gull assay.

Patients under 16 years of age or who were unable to give informed consent and those who had had genital herpes in the past or were presenting with genital herpes that day were excluded from the study.

RESULTS
Stage 1
In the first phase of the study, 51.2% of males and 53.6% of females said they would wish to have the type specific herpes serology test if such a test were available. There was no significant difference in response between the new and the reattending patients. A total of 31.6% of men and 35.8% of women said they would wish to discuss the test further with a counsellor (table 1).

Stage 2
When the test was offered, 41% of males and 37% of females decided to be tested (table 2). This number differed significantly from the number expected to request testing, based on the results from stage 1 and the difference was more

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**Table 1** Patient responses when asked whether they would have the test if available and whether they would wish to discuss it with counsellor

<table>
<thead>
<tr>
<th></th>
<th>Yes (%)</th>
<th>No (%)</th>
<th>Did not respond (%)</th>
</tr>
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<tbody>
<tr>
<td>New patients (n=207)</td>
<td>103</td>
<td>67</td>
<td>32</td>
</tr>
<tr>
<td>Returning patients (n=205)</td>
<td>113</td>
<td>54</td>
<td>26.3</td>
</tr>
<tr>
<td>All males (n=205)</td>
<td>105</td>
<td>64</td>
<td>31.2</td>
</tr>
<tr>
<td>All females (n=207)</td>
<td>111</td>
<td>57</td>
<td>27.5</td>
</tr>
<tr>
<td>Males requesting counsellor (n=205)</td>
<td>30</td>
<td>14.6</td>
<td>14.8</td>
</tr>
<tr>
<td>Females requesting counsellor (n=207)</td>
<td>46</td>
<td>22.2</td>
<td>7.3</td>
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marked among females (p<0.05 for males and p<0.01 for females). There was a positive association between expected to test and accepting the test at the 5% significance level for the male group since the relative risk was >1 and the corresponding 95% confidence interval did not include 1 (table 3). On the other hand, the relative risk between expected to test and accepting the test for females was <1 and the 95% confidence interval did include 1. This indicated that the association of expected to test and accepting the test for this group was not proved by the study at the 5% significance level. HSV-2 antibodies were detected in 20 of the 167 (11.9%) tested (table 4). Those deciding not to test provided a number of reasons for their decision—some offering more than one reason (table 5).

Forty male patients (23% of total) and 18 females (6.8% of total) requested further discussion with the counsellor. The males behaved as might have been predicted from the first stage of the study but fewer women requested further information and this difference reached statistical significance (p<0.001).

The time taken for pretest and post-test counselling was recorded (table 6). There was no difference between the average time spent by males and females in either pretest or post-test counselling though patients testing positive consumed significantly more time than those testing negative (p<0.05).

A total of 20 patients tested positive for HSV-2 antibodies. Of the 20 patients apparently diagnosed serologically, review of their notes revealed that three had been diagnosed with acute genital herpes on the day of their test, although culture for herpes simplex virus was negative in two of the three, and one other was known to have genital herpes but had not excluded himself. Thus there were 16 new diagnoses as a result of type specific serology screening though it did add weight to the clinical diagnosis in the case of two others.

Five of these 16 patients were HIV positive but had no symptoms of genital herpes. A further three patients did not return for the results of their type specific serology. Written reminders were sent to two of the patients but they failed to respond. One had refused permission for us to contact her.

In summary, of the 434 patients offered testing, 38% accepted. The number of patients who tested positive was 20 (4.6% of the total). One of these had already had a positive viral culture in 1996; one had a positive culture from a specimen taken on the day of the study. Two others were diagnosed clinically as having having herpes infection on the day of the study though cultures proved negative, and their serology results supported the clinical diagnosis.

**DISCUSSION**

Just over half the men and women who completed the questionnaires in the first stage of this study stated that they would wish to be tested for type specific herpes antibodies if such a test were available. This was in marked contrast to the 92% quoted in the Leeds study.

It is interesting to consider why this population was apparently reluctant to consider testing when the study from Leeds suggested considerable interest. It may reflect differences in the content of the information leaflet or it may reflect the population studied. In our study many of the patients, especially women, were at low risk for sexually transmitted
infections and attended the clinic for other genitourinary conditions. Such patients may consider HSV testing to be irrelevant for them. Further weight to this interpretation is given by the poor uptake of HIV testing demonstrated in an earlier study. It might have been possible to increase uptake by presenting the test in a strongly positive light. However, the benefits of identifying asymptomatic HSV carriers, either for individuals or for the public health remain unclear. Furthermore, concerns about the sensitivity and specificity of the test need to be included in a discussion and may deter some people.

There was no significant difference in response between new and returning patients. The two groups were analysed separately as it was felt that patients making their first visit to the clinic might be overwhelmed by the amount of new information being given them and that this might make them less receptive to the offer of type specific serology. Alternatively, new patients might be more likely to accept screening for as many infections as possible, whereas a person previously diagnosed with a chronic infection might be more wary and so more likely to decline testing. We also wondered whether returning patients might have a better knowledge about sexually transmitted infections generally as they had visited the clinic previously and that this might influence them one way or the other. In the event, the groups responded in a similar way.

More than one third of the patients indicated that they would wish to discuss the test further with a counsellor. Provision was made for this presumed extra workload for the counsellors when the second stage of the study was planned. However, the actual uptake of type specific herpes serology testing when it was made available was significantly less; 41% of men and 37% of women chose to be tested. The demand for further information was also significantly less—only 23% of men and 6.8% of women.

Over half the patients (55% of both men and women) gave reasons for declining the test—many giving more than one reason. Of those who declined testing (96 men and 145 women) 12.5% of men and 14% of women already knew they had herpes so self excluded on this basis. One fifth of each group claimed a fear of blood tests, which seemed a very large proportion in comparison with the refusal rate for syphilis serology that is normally seen at first visit. A lack of time, either to see the counsellor that day or to return for results, was stated as a reason for declining testing by 47% of men and 30.4% of women. Interestingly, 21.8% of men and 14.5% of women said they would not wish to know the result.

The time spent by the group as a whole with counsellors for pretest discussion was 4 hours 19 minutes spread over a 2 week period. The average consultation was 6.2 minutes. The time spent for post-test counselling was almost 10 hours. This was a considerable burden on clinic resources but is essential if knowledge of HSV-2 status is to make any impact on spread of herpes simplex virus infection.

Twenty patients were diagnosed positive for HSV-2 antibodies. Three of these would have been diagnosed clinically on that day anyway as they presented with symptoms. One of them had a previous diagnosis of herpes but had failed to self exclude. A further 12 men and 20 women excluded themselves from the study because they were known to have genital herpes. Thus, 36 patients (12 excluded men, 20 excluded women, and four discussed above) from this population were known to have herpes infection. Within our clinic population, approximately two thirds of the genital herpes diagnosed is due to HSV-2 and one third to HSV-1. So we would expect that two thirds of the above population of 36—that is, 24, would have HSV-2 infection. On the basis of Cowan et al’s work showing that only 23% of HSV-2 infected individuals have been formally diagnosed, we would have expected to identify a further 75% or 72 (24 × 3) asymptomatic patients. In the event we diagnosed an additional 16 patients.

CONCLUSIONS

In this clinic population, the use of type specific herpes serology testing as a routine screening tool would not appear acceptable to the majority of our clientele. The uptake of the test, at approximately 40%, was low. The demand for further counselling prior to testing, despite the provision of detailed written information, could have significant financial implications. Although screening detected 16 new HSV positive patients who would otherwise have remained undetected, this figure must be set against a background of a 40% uptake rate. It is unclear what impact interventions to limit transmission, if aimed at this group, would have on the herpes prevalence in the population as a whole.

In the past we have reviewed the role of type specific herpes serology testing in the diagnosis and management of genital herpes and found that it contributed to patient management in 79% of patients with recurrent genital ulceration of unknown cause. It was also found to be useful for counselling a number of patients with initial episodes of disease and the asymptomatic partners of some patients when the partners were shown to possess antibodies specific to HSV-2. A study of knowledge and attitudes of women at a central London antenatal clinic indicated a willingness of 80% of them to be screened with 76% stating that they would encourage their partner to have a blood test. However, its use as a screening tool in an attempt to limit the spread of herpes simplex infection in the general population is unlikely to contribute to any appreciable extent.

ACKNOWLEDGEMENTS

We wish to thank Dr Frances Cowan for her contribution in the design of the study.

The type specific herpes simplex serology tests were performed by Dr DWG Brown and Dr M Saville at the Enteric and Respiratory Viruses Laboratory, PHLS Central Public Health Laboratory, Colindale, London, using their in-house assay and we acknowledge their contribution to this paper.

We thank Josianne Vuddamalay, MLSO at Watford General Hospital, who coordinated all specimen transfer from one site to the other and Dr Azza Khalil and Dr Nazera Dakhil, both of Mount Vernon Hospital, who performed the statistical analysis of the study results.

We are very grateful to all the staff at the Department of Genitourinary Medicine at Watford for their support in doing this study.

CONTRIBUTORS

HMH, main author, collection and analysis of data, preparation of manuscript; PEM, study design, review of manuscript

Funding: None.

Conflict of interest: None.

Authors’ affiliations

H M Mullan, F E Munday, Department of Genitourinary Medicine, Watford General Hospital, Watford, Herts, UK
Type specific herpes antibody screening in a GUM clinic in the UK

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ECHO

Cases of TB with HIV co-infection have almost doubled in five years

The number of reported cases of tuberculosis with HIV co-infection has almost doubled in five years in England and Wales, the latest surveillance data show. Most of the increase has occurred in London.

Patients aged between 16 and 54 at diagnosis on the 1993 and 1998 National Tuberculosis Survey databases were matched with those on the HIV/AIDS patient database for the same period, to find out to what extent HIV infection has contributed to the recent national rise in TB prevalence.

In 1993, 2833 patients in this age group were included in the TB survey. By 1998 this had risen 21% to 3432. Database matching showed that 61 (2.2%) of patients with TB were co-infected with HIV in England and Wales in 1993. Five years later, this had risen to 112 (3.3%). Injecting drug use comprised only a small proportion of the likely route of co-infection.

HIV infection accounted for an estimated 8.5% of the increase in the numbers of new TB cases nationwide, and 11% in London. In both survey years the prevalence of co-infection was highest in the capital (64% and 77%), and among people of white and black African ethnicities.

These figures are unlikely to represent the true extent of co-infection, say the authors, who suggest that routine HIV testing of all patients with TB should now be considered, particularly those who are white or black African and under the age of 55.

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*Sex Transm Infect* 2003 79: 129-133
doi: 10.1136/sti.79.2.129

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