British Co-operative Clinical Group national survey on diagnostic issues surrounding genital herpes

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Objectives: To investigate the current use of diagnostic methods for genital herpes simplex virus (HSV) infection, to determine how information from these tests influences clinical practice, and to identify areas for future guideline development within genitourinary medicine (GUM) clinics in the United Kingdom.


Results: Completed questionnaires were returned by 146 (84%) consultants. Cell culture was the first line diagnostic method for 133 (91%) respondents, the remaining 13 (9%) used antigen detection tests. Typing of isolates (HSV-1 or HSV-2) was available in their local laboratory to 109 (75%) clinicians; however, less than two thirds routinely pass this information on to their patients. Although 74 (51%) respondents had access to serological diagnosis, the majority of methods described were non-specific; only three (2%) had access to type specific tests. Only 81 (56%) respondents frequently (>90% of the time) recommend notification of recent sexual partners of genital herpes patients.

Conclusions: While access to culture based diagnosis is widespread, type specific serology has limited availability. Information on typing of isolates as HSV-1 or 2, although available in three quarters of centres, is underutilised in counselling patients. As HSV type influences both clinical and subclinical reactivation rates and may also affect probability of transmission, this is an important omission. Future guidelines need to address the optimal use of viral typing and new diagnostic tests to optimise health gain; there is also a need for evidence based recommendations about partner notification in genital herpes.

Keywords: genital herpes; herpes simplex virus; partner notification; type specific serology

Introduction

There have been many recent advances in diagnostic techniques for herpes virus infections, including new methods of viral detection and highly specific serological tests. These are crucially important in the context of genital herpes, because clinical diagnosis is frequently inaccurate and only a minority (estimated at 20%) of those patients presenting to physicians with symptomatic genital herpes receive a correct diagnosis. These new tests for herpes simplex virus (HSV) include rapid culture techniques, nucleic acid detection (such as polymerase chain reaction), and type specific antibody tests for glycoprotein G1 or G2 using either western blot or enzyme linked immunosorbent assays (ELISA). At least five ELISAs are in commercial development, although only western blot has been extensively validated in large, epidemiological studies. Most of the currently available commercial serological assays are not type specific.

The wider availability of new type specific tests will present major challenges to all professionals working in the field of sexual health. The diagnosis of a chronic, sexually transmissible infection in an otherwise asymptomatic individual carries the potential for substantial harm as well as good. Previous studies have suggested that the prevalence of subclinical HSV-2 infection in patients attending UK genitourinary medicine (GUM) clinics is high. HSV diagnostic tests will require careful application if their use is to result in overall health gain.

This survey was designed to investigate current use of diagnostic tests for HSV in GUM clinics throughout the United Kingdom and to determine how information derived from tests influences clinical practice. This will inform the development of guidelines for the use of HSV test methodologies.

Methods

In September 1997, a questionnaire was distributed on a single occasion, via British Co-operative Clinical Group regional representatives, to 173 consultants responsible for GUM clinics in the United Kingdom. Questions addressed the following aspects of genital herpes—diagnostic methods for first clinical presentations, typing of isolates, use of serology in diagnosis, and departmental policy for partner notification.

Where opinions were sought about the frequency of actions, responses were classified as follows: almost always/routinely (>90% occasions); usually (50–90% occasions); sometimes (10–50% occasions); rarely (0–10% occasions).
Results
Completed questionnaires were returned by 146/173 (84%) consultants.

DIAGNOSIS OF FIRST CLINICAL EPISODES OF GENITAL HERPES
HSV culture was available to 139 (95%) respondents and was the favoured detection method for 133 (91%), while antigen detection methods were favoured by the remaining 13 (9%). A clinical specimen for HSV detection was almost always (>90% occasions) taken by 141 (97%) respondents.

TYPING OF ISOLATES
The provision of isolate typing (as HSV-1 or HSV-2) by their local laboratory was indicated by 109 (75%) respondents. Five consultants commented that it was not routinely performed on all isolates and engendered additional costs.

Figure 1 shows the proportion of respondents, with access to typing information from their laboratory, who pass typing information on to their patients.

SEROLOGICAL DIAGNOSIS OF GENITAL HERPES
Although 74 (51%) respondents had access to serological tests for HSV diagnosis, only three (2%) clearly stated that they had access to type specific tests. The majority of other methods described were non-specific, including terms such as “HSV antibody test” by 14 respondents, complement fixation tests by 37, and ELISA by five. The methodology used was unknown to eight respondents.

Only 74 (51%) respondents commented on use of serological diagnosis; 17 stated that they never used serology, and 10 stated that they rarely used it. Only 47 specified any clinical indication for their use, listed as follows: establishing a diagnosis when culture is negative (18 respondents), in pregnancy (8), investigation of partners of index patients with a confirmed HSV diagnosis (6), differentiation of true primary from first symptomatic recurrence (4), medical/legal reasons (4), and all new patients with genital herpes (3). Overall, these findings suggest that currently available serological tests play a minimal part in routine diagnosis in the United Kingdom.

Discussion
This report provides a broad based survey of the availability and clinician utilisation of diagnostic tests for genital herpes in the United Kingdom. The survey demonstrates that access to culture facilities is widespread. Information on typing of isolates as HSV-1 or HSV-2, although available in three quarters of centres, is reliably communicated to patients in only 65% of centres. There is limited availability of type specific serological tests at present. The use of existing non-specific serological tests is both infrequent and inconsistent. Finally, partner notification, even in index patients with first episodes of genital herpes, is generally infrequent.

Although information on typing of isolates is available to most clinicians, it is surprising to find that only two thirds regularly pass this information on to their patients. There is a clear relation between HSV type and both clinical recurrence risk and subclinical shedding,4 so information about the causative viral type may influence the approach to counselling affected individuals about the source of infection and future transmission risks. Hence, we believe that appropriate management of first episode genital herpes must include viral typing as an essential component of initial assessment. There appears to be a need for consensus development among physicians in this area.

There was no consensus within the survey population about the indications for use of currently available (non-type specific) serological tests. The potential for confusion (and psychological harm to patients) may increase when commercial type specific tests become more widely available.5 The need for evidence based guidelines on their use is imperative. At present, in the absence of a therapeutic intervention which is proved to alter the natural history or transmission characteristics of asymptomatic HSV infection, there is no evidence to support routine screening for HSV-2 carriers. However, it is likely that type specific HSV-2 tests (once we have available tests which perform adequately in low prevalence populations) will contribute to the clinical management of individual patients with recurrent genital ulceration of unknown cause. They also have potential value in assessing asymptomatic partners of index patients with known HSV-2 infection, particularly in...
pregnancy, where a seronegative woman may be at risk of acquiring primary infection from a seropositive partner, posing a risk of neonatal HSV infection. However, randomised controlled trials assessing the performance of serological tests have not been performed and their overall cost-benefit ratio, even in the clinical situations mentioned above, is undetermined. It is important that commercial assays are not introduced into clinical practice before they have been fully validated.

Only about half of the respondents regularly initiate partner notification when patients present for the first time with genital herpes. Previous work suggests that partner notification may be an effective way of detecting individuals with unrecognised clinical disease. Asymptomatic shedding plays a major part in HSV transmission. Mertz et al found that 65% of source contacts either reported a history consistent with previous HSV infection or were experiencing a first episode of HSV when initially examined, of whom 60% were unaware that they had transmissible HSV infection. Although, at a population level, there is no definitive evidence that either antiviral treatment or patient education/counselling alters transmission rates, it seems logical to increase awareness of HSV among partners, with the aim of inhibiting further onward transmission. A study by Langenberg et al demonstrated that 50% of HSV-2 seropositive women who did not initially report a history of genital herpes could, after counselling, distinguish symptomatic genital herpes from other genital infections. A recent patient survey in a UK GUM clinic suggested that the overwhelming majority of patients would want to know if they were infected with HSV-2.

This survey has highlighted several important diagnostic issues surrounding genital herpes in the United Kingdom. The wider availability of new antigen detection and type specific serological tests will present additional challenges to all professionals working in the field of sexual health. Consensus development and evidence based guidelines are required if use of these tests is to result in overall health gain.

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Contributors: Anne Scoular analysed data which were compiled by the BCCG and wrote the first draft of the manuscript; George Kinghorn reviewed the first draft of the manuscript and contributed to writing the paper in its final form.

5 Ashley RL, Corey L. HSV type specific antibody tests: patients are ready, are clinicians? Genitourin Med 1997;73:235–7.