Education and debate

Ethics of screening for asymptomatic herpes virus type 2 infection

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Commercial tests for herpes simplex virus are now widely available, and some experts have advocated screening. But can screening be ethical when false positive results occur, many infected people are asymptomatic, and no cure is available?

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Infection with herpes simplex virus type 2 (HSV-2) is a common sexually transmitted disease. It is mostly asymptomatic, and currently no cure exists.¹ The prevalence by age differs between populations and geographical areas.² Serology tests are commercially available with acceptable sensitivity and specificity and are a valuable aid to diagnosis. However, many questions remain over their use for screening. We use an ethical model to consider the potential biotechnical, medical, epidemiological, and psychosocial advantages and disadvantages of screening at the individual and public health levels.

Transmission

Most people seem to be infected with HSV-2 through a partner who is unaware of having the infection. Virus is shed intermittently from the genital tract of infected asymptomatic people and also between attacks in people with typical mucocutaneous symptoms.³ Patients with unrecognised infections could thus be an important source of sexual transmission.

A serious consequence of genital HSV infection is neonatal herpes, which results from transmission from mother to infant. The risk of perinatal transmission is less than 1% in women with longstanding infection but substantially higher if the maternal infection is acquired during late pregnancy.⁴ Untreated herpes infection has among the highest mortality of any infection in the neonatal period, and neurological sequelae are common among the survivors.

Identification of infected people

The only practical way to identify people with asymptomatic HSV-2 infection is by serological tests. Discussion is ongoing about how far to extend testing for HSV and for which groups, mostly with arguments from a biomedical perspective.^{2,9,12} Routine screening of pregnant women has been advocated, especially in the United States,¹⁰ but its cost effectiveness has been questioned.⁵ Screening of asymptomatic people presenting for treatment of a suspected sexually transmitted disease has also been suggested, although no evidence exists to guide practice.⁶

Immunofluorescent photomicrograph of herpes simplex virus type 2

DR CRAIG LIVERLACDC

Proponents for HSV-2 serology testing argue that patients seeking care for a suspected sexually transmitted disease have a right to be tested. One of the strongest arguments against such opportunistic screening is the possible psychosocial and psychosexual effects on asymptomatic people of discovering they have a disease that is sexually transmissible, incurable, and life long.

Effectiveness of tests for screening

Commercial tests for HSV generally have sensitivities and specificities of about 95%. Sensitivity of the commercial tests is usually more variable than specificity.⁷ The more commonly used tests could be verified by an assay with maximal specificity—for example, western blot. The western blot assay is expensive, labour intensive, and unlikely to become widely available.

References w1-w17 and definitions of ethical principles are on
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Predictive values depend on the sensitivity and specificity of a test and, most importantly, on the occurrence of the disease in the groups being tested. The positive predictive value of a test may be very low if the prevalence is low, even with a high sensitivity and a high specificity (table 1). The wide variation in seroprevalence of HSV-2 makes prevalence important in assessing the value of a test. In low prevalence populations, 30-40% of the tested individuals will wrongly be diagnosed as being infected, and even in high prevalence groups, such as those attending a sexually transmitted disease (STD) clinic, around 10% are at risk of a false diagnosis. Likewise, a proportion will wrongly be labelled as non-infected.

An alternative way of applying the tests is to select candidates using information on well known risk factors. High risk groups could then be tested with an initial test with high sensitivity followed by other tests with higher specificity.

Ethical considerations

Respect for individual autonomy often makes discussions about interventions that are justified by concerns for public health difficult and non-productive. But the issue in this case is not simply an individual one. HSV infection may have consequences for partners and offspring—some of them serious and even lethal.

A comprehensive ethical model is needed which considers the concerns of both individuals and public health. We have devised a framework for identifying and analysing the ethical conflicts inherent in screening for HSV-2 in asymptomatic individuals.^{10 11} The model identifies the people involved, formulates the relevant ethical principles, and assesses and weighs the ethical benefits and costs. The ethical deliberations below are made within a Swedish context, where the estimated seroprevalence is 15-20% and most cases of sexually transmitted infections are treated at STD clinics.¹² No screening is done for HSV-2. Medical staff cannot coerce patients attending clinics to take the test because it is not on the list of diseases requiring statutory notification. In principle, but not always in practice, patients have a free choice about whether to take the test and inform partners of the results after being given neutral information.

Affected groups and three relevant ethical principles

The first task is to identify those affected or considered to be so in the public debate. The most important groups are people suspected to have an STD, their partners, and their unborn children. We also have to consider the staff at the STD clinics, as they would have to explain to patients why testing is important and then counsel those who test positive. This requires considerable knowledge of the natural course of the disease and the possibilities, benefits, and costs of treatment. Also relevant are policy makers, who are responsible for national surveillance of STDs, the public health, and the general public (table 2). The principles of autonomy (or respect for a person), beneficence (including non-maleficence), and justice (both solidarity and non-discrimination) seem relevant here.^{13 14} A

Table 1 Predictive values when screening for HSV-2 among populations with varying prevalence of genital herpes infection assuming 96% sensitivity and 97% specificity of test method

Reference	Population and time	Place	Prevalence of HSV-2 (%)	Predictive value (%)	
				Positive	Negative
Vyse et al ¹³	3337 citizens, 1994-5	United Kingdom	4.2	58.4	99.8
Copas et al ¹⁴	1359 blood donors, 1992	London	7.7	72.7	99.7
Mindel et al ¹⁵	2616 antenatal clinic attendants, 1995-8	Sydney, Australia	12.5	82.1	99.4
Malkin et al ¹⁶	4412 citizens, 1996	France	17.2	90.0	98.9
Fleming et al ⁸	13 094 citizens, 1988-94	United States	21.9	89.9	98.9
Roest et al ⁹	654 STD clinic attendants, 1998	Rotterdam, Netherlands	22.0	90.0	98.9
Cowan et al ¹⁷	833 GUM clinic attendants*, 1990-1	London	22.7	90.4	98.8

*Clinics specialised in genitourinary medicine and thus treating not only sexually transmitted diseases.

combination of the six groups of people considered with the three ethical principles above will result in a matrix table, a checklist with 18 points noted by the letters A to R (table 2).

Autonomy

The patient—that is, the person suspected to have an STD—has a right to decide whether to be tested. The prerequisite for exercising this right is adequate information. The decision is relatively easy for patients with suspected herpetic lesions, when the test is used to confirm the diagnosis. The situation is much more complicated for asymptomatic people, for whom the implications of a positive or negative result are not straightforward.

The partners' situation is also complicated. Again, testing can help confirm a diagnosis suspected on clinical grounds. An asymptomatic partner, however, will have the same problem as the index patient in understanding all the implications of the outcome of serotesting.

Current tests will have an ethical benefit when they are used to corroborate a clinical diagnosis and for asymptomatic people who are aware of the intricacies and implications of the testing procedure. On the other hand, the ethical costs will be very high if asymptomatic people who are not informed adequately are screened when attending an STD clinic. A positive result could raise questions of infidelity without due cause.

Screening of asymptomatic pregnant women and their partners is fraught with the same interpretation problems as for patients and complicated by deliberations on probabilities of transmission and occurrence of neonatal herpes. Since the risk of neonatal herpes is low in communities with low seroprevalence of HSV-2

Table 2 Matrix showing points for discussion regarding ethical benefits and costs to those involved in screening for herpes simplex virus

Groups involved	Ethical principles		
	Autonomy	Beneficence	Justice/solidarity
People suspected to have an STD	A	G	M
Partners	B	H	N
Unborn children	C	I	O
Staff	D	J	P
Policy administrators	E	K	Q
Public	F	L	R

and the serological status of the mother is not a reliable indicator of whether neonatal herpes is going to occur, the ethical costs of antenatal screening are high and the benefits doubtful.

Doctors often claim that it is better to know if you are infected than not to know. The evidence base for HSV-2 is patchy, and knowledge among non-specialists is sometimes lacking.¹⁵ The prerequisite of adequate information for exercising the right of autonomy will mostly not be met, implying ethical costs of screening in asymptomatic people even without persuasion taking place.

Staff also have a right to autonomy.¹⁶ This implies a delicate balance between the individual's personal morality and professional ethical guidelines. In our opinion, staff have an obligation to answer any questions related to health care. But do they have a professional obligation to inform all patients? If the patient refuses information this does not imply any autonomy costs for the staff.

We do not know the preferences of policy makers or the opinion of the general public. We assume that if genital herpes was experienced as an emerging epidemic, policy bodies would exercise their autonomous rights to intervene—for example, by making it a notifiable disease, introducing partner notification, and compulsory screening. Such action would imply ethical costs for the individual but benefits for the general public.

Beneficence

What are the best consequences for someone attending an STD clinic or general practice? The answer depends on whether the disease screened for is treatable by cure or relief of non-recognised symptoms. Symptomatic genital herpes can be relieved by antiviral drugs. Thus, a correct diagnosis provides ethical benefits for patients with symptoms. For asymptomatic people the costs would predominate, especially if they experience stigma and anxiety without having a true infection.

Such costs and benefits would also affect the partners. The patients' decisions regarding their partners might be based on self interest rather than what is best for a partner. A positive test result and counselling could have the desirable effect of preventing transmission. If testing is limited to patients with HIV, the risk of stigmatisation is substantial, although such patients could benefit for therapeutic reasons.¹⁷

Testing would benefit babies if it could correctly predict a serious outcome. Unfortunately, this is not the case.

Staff at STD clinics are unaffected by issues of beneficence, and the ethical benefits of a low prevalence of genital herpes for policy makers and the general public is obvious. However, it is not clear whether the same benefits apply to a low seroprevalence of HSV-2. A primary infection during late pregnancy is associated with a higher risk of transmission during delivery, which means high risk of viral exposure of the infant and a possible caesarean section. Here society would benefit more if the primary infections were experienced in age groups before pregnancy usually takes place.

Justice

Patients experience no justice costs if they are offered the test independently of social or economic status and are informed in a way that respects the individual variation in understanding and preparedness to internalise and act on the information. Within a high risk population, appeals to solidarity, as a requirement for diminishing the transmission and thereby the suffering, would be a possible strategy. However, because of the difficulties of understanding the problems and implications of the tests, equity might be jeopardised if all patients do not have access to specialists in venereology.¹⁵

The partners have to carry an unjust burden of the disease if infected but also if they are falsely labelled as having the disease. Nevertheless, we believe that tracing and contacting the partners for testing implies some justice benefits.

The risk of neonatal herpes is extremely small, especially in low prevalence populations. Thus, screening pregnant women for the benefit of unborn children seems to imply neither costs nor benefits with reference to justice.

Staffs and policy makers have a professional obligation to prevent transmission and promote safe sexual behaviour. A non-coercive, non-judgmental policy reflects a moral commitment to the interests of the individual patient. Lifestyle would not justify routine screening of so called "risk groups" without individual consent after adequate information. The definition of adequate information will vary with people and circumstances.

Is screening justified?

Considerable concern has been expressed that the world is in the grip of an HSV-2 epidemic.¹⁸ Data from the United States, although claimed to be based on two samples representative of the general population, might have selection problems.^{8 19} The absolute rise in prevalence from 16.8% to 21.7% is often expressed as a rise of 30%, which sounds alarming. Data from low income countries are usually from selected high risk populations. In Europe, however, seroprevalence seems to be falling (table 1).^{9 12}

Our model for ethical analysis is complex, especially for an issue where the bioepidemiology is as intricate as for genital herpes. However, it suggests that universal serological screening would be inappropriate, at least in northern European countries. European countries should not be rushed into screening on the basis of evidence accrued in the United States. The fundamental promise we make when we solicit people for preventive interventions must be that, on average, they will be the better for it.

The wish to be tested is of course initially steered by a person's suspicion of having been infected; this perception is anchored in that person's knowledge and context. We assume that agreement to be tested for something you don't think you have or have a nagging suspicion you might have, relies on the way the information is given. Used considerately, the test could help people deal more responsibly with

Summary points

Infection with herpes simplex virus type 2 is mostly asymptomatic and cannot be cured

Prevalence by age differs between populations and geographical areas

Serology tests are commercially available with acceptable sensitivity and specificity

Use of the tests to screen low prevalence groups would give high rates of false positive results

Potential biotechnical, medical, epidemiological, psychosocial and ethical advantages and disadvantages must be balanced at both the individual and public health level

Screening cannot currently be ethically justified

their sexual relationships and also prevent transmission. Concern about infecting a partner is common among those diagnosed, although relationship issues and not infection control seem to be the main cause for this.^{w1}

The chosen ethical principles for guidance should be intellectually and emotionally acceptable in the affected society, in our case primarily patients at an STD clinic, their partners, the clinic staff, and policy officials. We do not know whether this is the case, and more information is needed from social science research.

In our opinion, justice as solidarity (see bmj.com) should be paired with autonomy in ethical deliberations of preventive health interventions. If the goal is solidarity rather than conformity, patients must be free to decide what they think is right, because that is what moral responsibility is all about. Without professional truthfulness—the basic tenet of patient involvement in clinical decisions—solidarity could never be accepted as an argument by itself. Patients must understand and feel comfortable with the messages from health institutions. They must also be convinced that reasonable societal support will be available and affordable for those infected with HSV-2 as well as for their partners.

We thank the seminar group in medical ethics, Lund, for helpful comments.

Contributors and sources: IK is a specialist in infectious diseases and professor in epidemiology and public health with an interest in the ethics of public health. G-BL, IK, and BMA are part of a herpes research network in western Sweden. TN is professor in medical ethics. IK and TN had the idea for this paper, and IK wrote the first draft. All authors contributed to the final version from their special fields of competence. The article is based on sources from the Pub Med and medical ethics research literature. They are all guarantors.

Competing interests: None declared.

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(Accepted 28 June 2004)

Corrections and clarifications

Scandals have eroded US public's confidence in drug industry

In this news article by Jeanne Lenzer (31 July, p 247) we wrongly said that one of the authors of a study on the sources of lead in children living near a smelter failed to acknowledge that her husband owned the smelter in question. In fact, her husband didn't own the smelter; he owned the consulting firm that advised the owner of the smelter.

How protective is the working time directive?

We appeared to slash the salaries of new doctors in this editorial by Rhona MacDonald (7 August, pp 301-2). In the fifth paragraph we dropped a zero by mistake: 12 550 additional UK doctors would cost up to £780m [not £78m] (\$1420m; €1150).

Assessing the quality of research

One of the authors of this Education and Debate article by Paul Glasziou and colleagues has advised us that his published name was missing his middle initial (*BMJ* 2004;328:39-41). Jan Vandenbroucke is in fact Jan P Vandenbroucke.

UK health minister under pressure to ban smoking in public

In this news article by Claire Laurent (14 August, p 368), we said that a *BMJ* paper reinforced the findings of earlier studies linking passive smoking to coronary heart disease. Unfortunately, we inadvertently cited the wrong paper. The correct citation is: *BMJ* 2004;329:200-5. The web version and link have been amended.