

SHORT REPORT

Seroprevalence of HSV-1 and HSV-2 infection in the general French population

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Sex Transm Infect 2002;**78**:201–203

Background: In spite of the large prevalence and growing incidence of herpes simplex infection (HSV-1 and HSV-2), relatively few large serological surveys are available worldwide and it is still difficult compare frequencies of HSV contaminations in various countries. We present the results of HERPIMAX, the first epidemiological inquiry on HSV prevalence in the general French population.

Methods: Of a cohort of 12 735 presumed healthy adult volunteers included in the prospective study SU.VI.MAX, designed to assess the relation between nutritional supplementations and degenerative diseases, HERPIMAX randomly selected 4412 subjects (females 66.5%, males 33.5%). All serum samples were assessed for HSV-1 and HSV-2 IgG antibodies with a HSV type specific, enzyme immunosorbent assay (EIA). Equivocal result were retested with another HSV type specific immunoblot assay combined with a type common HSV IgG EIA in order to give a definitive interpretation.

Results: The mean seroprevalence was 67% for HSV-1 and 17.2% for HSV-2. For HSV-2 the seroprevalence was higher in females (17.9%) compared with males (13.7%) ($p < 0.001$). For both HSV types, there was no significant difference in prevalence as regards age distribution in males and females, whereas prevalence increased significantly with age in females for HSV-1. Univariate analysis showed a significant association between HSV-1 prevalence and education level in males and females ($p < 0.001$) and between HSV-2 prevalence and marital status in both sexes ($p < 0.001$). There were geographical disparities, with a higher HSV-2 prevalence in the south of France as well as in Paris.

Conclusion: These results confirm a high prevalence of HSV infection in France. They are also in agreement with previous results of other survey carried out in other developed countries as regards higher prevalence of HSV-2 infection in women, the stability of seroprevalence for both HSV types after 35 years of age in females and 45 years of age in males.

Herpes simplex virus (HSV) infections are quite common throughout the world.¹ Apart from the morbidity due to symptomatic episodes, HSV infections may have severe consequences in immunosuppressed hosts or neonates.² Furthermore, genital ulcer disease due to HSV is a risk factor for sexual acquisition and transmission of HIV infection.³ Assessing the extent of HSV infections is notoriously difficult for a variety of reasons: in most countries, they are not notified diseases, the majority of infected subjects are asymptomatic⁴ or unaware of their infection. However, since the 1980s, serological methods have made it possible to study the epidemiol-

ogy of HSV infection and recent improvements in available tests allow discrimination between HSV-1 and HSV-2.

Here, we report the results of the HERPIMAX survey, which was the first epidemiological assessment of HSV prevalence carried out in France in the general population.

METHODS**Study population**

The survey population was a random sample of the SU.VI.MAX programme, which was primarily a French prospective, randomised, double blind study designed to assess the impact of a daily supplementation in minerals and vitamins to reduce the frequency of degenerative diseases such as cancers or cardiovascular diseases.⁵ SU.VI.MAX included 12 735 presumed healthy volunteers of each sex, aged between 35 and 60 years (females) or 45 and 60 years (males), representative of the geographical and socioeconomic status of the French population.

Of the SU.VI.MAX population, 4412 people were randomly selected and included into the HERPIMAX survey; 33.5% of them were male and 66.5% were women, this imbalance being ascribable to the difference in age groups included according to sex. The serum samples used in this survey were collected during the year 1996 and stored at -20°C until use at inclusion in SU.VI.MAX. Informed consent was obtained from all individuals.

Serological testing

Serum testing was performed in two different laboratories according to the same procedures (Institut A Fournier, Paris; Laboratoire de virologie, CHU, Grenoble, France) and the samples were randomly distributed between both of them. Serum samples were first screened with a commercial HSV type specific enzyme immunosorbent assay (EIA) (Gull HSV gG-EIA, Gull Laboratories Salt Lake City, UT, USA). Equivocal serum samples (with absorbance values between 0.91 and 0.99 times the value for the reference) were then tested with the type common HSV IgG EIA Enzygnost (Dade Behring). A negative result to this latter test was interpreted as reflecting lack of HSV infection. A positive or equivocal result led to a confirmatory test using an HSV type specific immunoblot (RIBA HSV type 1/2 Strip Immunoblot Assay, Chiron Corporation, Emeryville, CA, USA). Those samples remaining untyped by this test were definitely considered as negative.

The sensibility and sensitivity of the two HSV type specific tests have been demonstrated in previous studies.^{6,7}

Statistical analysis

The χ^2 test was used to compare the distribution of infected subjects according to their demographic characteristics. Single linear regression was used to identify predictors of HSV infection related to socioeconomic status or geographical location in France. Statistical analyses were performed with sas software (SAS Institute, Cary, NC, USA). All reported values are two sided.

Table 1 HSV-1 and HSV-2 seroprevalence in HERPIMAX by age group and sex (%)

	35–40 years	40–45 years	45–50 years	50–55 years	>55 years
HSV-1					
Male	–	–	64.5	64.6	70.9
Female	58.8*	59.2*	66.4*	68.5*	74.7*
HSV-2					
Male	–	–	12.5	14.2	15.0
Female	15.7	18.8	18.1	17.0	19.5

*p<0.01.

Table 2 HSV-1 and HSV-2 seroprevalence in HERPIMAX according to education level and to marital status (%)

	HSV-1		HSV-2	
	Male	Female	Male	Female
No diploma or undergraduate	72.2	73.5	14.0	16.7
Graduate or postgraduate	62.5	61.1	13.5	19.0
p Value	<0.001	<0.001	ns	ns
Married	66.0	66.8	12.7	15.8
Single	64.8	54.0	20.4	24.9
Widowed/separated/divorced	68.4	62.9	23.7	25.6
p Value	ns	ns	0.001	0.001

RESULTS

Among the 4412 selected subjects the mean seroprevalence was 67% for HSV-1 and 17.2% for HSV-2. According to sex the seroprevalence was comparable in males (66.4%) and in females (65.0%) for HSV-1 but it was significantly higher in females (17.9%) than in males (13.7%) for HSV-2 ($p < 0.001$).

Although there was a slight increase with age in prevalence of both HSV-1 and HSV-2 infections, the differences between age groups did not reach statistical significance for males; for females, there was a significant increase for HSV-1 but not for HSV-2. Within each age group, no significant sex effect was observed for HSV-1, whereas HSV-2 seroprevalence remained consistently higher in females compared to males (table 1).

Univariate analysis suggested inverse correlation between HSV-1 seroprevalence and education level, the relation reaching statistical significance ($p < 0.001$) for both males and females. Likewise, there was a marked association in both genders between marital status and HSV-2 prevalence (table 2), with a significantly higher prevalence in people living alone (single, widowed, separated, or divorced) (>20% in both sexes) compared to people living in couples (<15%; $p < 0.001$).

DISCUSSION

The primary result of this survey is a demonstration of a high prevalence of HSV infections in French adults, with more than two thirds of the population infected with HSV-1 and almost one fifth with HSV-2. Nevertheless our study shows a prevalence of HSV-2 infection lower in France (17.2%) than in United States (21.9%) where a population based survey (NHANES III) was performed during a period from 1988 to 1994.⁸

HSV-2 prevalence appears significantly higher in women than in men. This finding could be explained in part by a transmission of HSV-2 much more efficient from men to women compared with from women to men and possibly by differences between women and men in sexual behaviour.⁹ The stability of this prevalence after 35–45 years was also an expected result which suggests that the first contamination mainly occurs within the first two decades of sexual life.¹⁰ Comparing with previous studies^{8–11} our results confirm a higher HSV-2 seroprevalence in widowed, separated, and divorced people than in married people, but are inconsistent

with the finding of the same studies showing a lower seroprevalence in single individuals than in married people. This discrepancy could be explained by the fact that the HERPIMAX population does not include young age groups and therefore single individuals included in our study should have a greater lifetime sexual activity than single people included in other studies. Likewise, the higher prevalence of HSV-1 infection founded in people of low education level was not an unexpected result either.¹² Whereas the NHANES III survey showed that a less formal education was a predictor of HSV-2 infection,⁸ our study did not found the same correlation in France.

Finally, HERPIMAX suggests significant geographical disparities in HSV prevalence, with highest rates of HSV-2 infections being found in the south of France as well as in the city of Paris.

These geographical differences could be due to variations in sexual behaviour: a previous study has shown that the presence of antibody to HSV-2 is a marker of sexual lifestyle.¹¹ These variations in sexual behaviour could be related to cultural diversity and/or to the level of urbanisation (Paris area and south of France are two of the most inhabited regions in France).

Further analysis of these data will focus on correlations between serological status and the clinical expression of the disease. Epidemiological research should also focus on the identification of additional predictors and the design of preventive measures.

ACKNOWLEDGEMENT

Gull and Chiron Laboratories provided kits for serological testing.

This work was supported by a grant from GlaxoWellcome France.

CONTRIBUTORS

CdL and AEH were responsible for raising the design of the study; PM, BC, and TDL did the serological analysis; DM and SHg conducted the study and were responsible for statistical analysis; JEM coordinated the study and wrote the paper.

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Accepted for publication 7 March 2002

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