SHORT REPORT

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

J-E Malkin, P Morand, D Malvy, T D Ly, B Chanzy, C de Labareyre, A El Hasnaoui, S Hercberg

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 supplements 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. Apart from the morbidity due to symptomatic episodes, HSV infections may have severe consequences in immunosuppressed hosts or neonates. Furthermore, genital ulcer disease due to HSV is a risk factor for sexual acquisition and transmission of HIV infection.

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 asymptomatic or unaware of their infection. However, since the 1980s, serological methods have made it possible to study the epidemiology 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. 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; 33.3% 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 IgG-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 (Enzymost Diagnostica, Austin, TX, USA). 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 specificity of the two HSV type specific tests have been demonstrated in previous studies.

Statistical analysis

The χ² 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.
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 1991. 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).

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

<table>
<thead>
<tr>
<th>Age Group</th>
<th>HSV-1</th>
<th>HSV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>35–40 years</td>
<td>64.5</td>
<td>66.4*</td>
</tr>
<tr>
<td>40–45 years</td>
<td>69.0</td>
<td>68.5</td>
</tr>
<tr>
<td>45–50 years</td>
<td>69.0</td>
<td>70.0</td>
</tr>
</tbody>
</table>

* p<0.01.

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

<table>
<thead>
<tr>
<th>Education Level</th>
<th>HSV-1</th>
<th>HSV-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No diploma or undergraduate</td>
<td>72.2</td>
<td>73.5</td>
</tr>
<tr>
<td>Graduate or postgraduate</td>
<td>62.5</td>
<td>61.1</td>
</tr>
</tbody>
</table>

p Value ns ns 0.001 0.001

Married | 66.0 | 66.8 |
| Single | 64.8 | 54.0 |
| Widowed/separated/divorced | 68.4 | 62.9 |

p Value ns ns 0.001 0.001

Female 15.7 18.8 18.1 17.0 19.5

Male – – 12.5 14.2 15.0

p Value <0.001 <0.001 ns ns
REFERENCES


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