

## HERPES SIMPLEX VIRUS TYPE 2 ANTIBODIES: HIGH PREVALENCE IN MONOGAMOUS WOMEN IN COSTA RICA

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**Abstract.** We studied the prevalence of antibody to Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) in 766 randomly selected Costa Rican women 25-59 years of age in a national household survey in 1984-1985. Overall, 97.1% were seropositive for HSV-1 and 39.4% for HSV-2. Only 1.1% of HSV-2 seropositive women gave a history of symptomatic genital herpes. HSV-2 virus antibody increased with age and with the number of lifetime sexual partners. HSV-2 seroprevalence among women who reported only 1 lifetime sexual partner was almost twice as high as the prevalence among women who denied sexual experience (30.5% vs. 17.7%) and reached 79.2% among women with  $\geq 4$  partners. HSV-2 seroprevalence was lower among women whose partners used condoms: 28.9% for those who had used condoms for at least 2 years vs. 44.3% for those who never used condoms.

Few population-based studies have examined the descriptive epidemiology and seroprevalence of herpes simplex virus (HSV) infection. Some of the obstacles to gathering such information are the difficulty in obtaining population-based serum samples, the lack of medical and sexual history data of patient populations in which seroprevalence studies have been done, and the lack of a highly specific serologic test to differentiate between antibody to type 1 and type 2 HSV.

The recent development of type-specific serologic techniques has made possible more precise estimates of the extent of infection with herpes simplex type 2 (HSV-2).<sup>1</sup> Between 1978 and 1980, the prevalence of antibody to HSV-2 in the white residential population of Toronto, Canada, was estimated as 15.5% by a precise method for distinguishing between HSV-1 and HSV-2.<sup>2</sup> Using another new, more specific serologic method, preliminary data from a U.S. national survey showed a prevalence of HSV-2 antibody of 16.4% among non-institutionalized civilian residents.<sup>3</sup>

We report the first nationally representative data from Costa Rica on the prevalence of antibody to types 1 and 2 herpes simplex virus (using the same specific serologic test used in the U.S. national survey) and the first population-based study that examines demographic char-

acteristics and medical and sexual histories in relation to the presence of HSV-2 antibody.

### MATERIALS AND METHODS

Compared with women in developed nations, Costa Rican women have a higher incidence of cervical cancer and a lower incidence of breast cancer.<sup>4,5</sup> In 1984-1985, the Costa Rican Demographic Association in collaboration with the Centers for Disease Control (CDC), the Costa Rican Social Security Administration, the Ministry of Health, and Family Health International conducted a case-control study of these 2 cancers. Details of the study design and population have been reported elsewhere.<sup>6-10</sup>

The current analysis is restricted to the population-based control series from that study and describes seroprevalence of HSV antibody rather than incidence. The control sample consisted of a cross-section of women in the 25-59 year age group. They were selected in a nationally representative cluster sample survey based on the June 1984 census. Sample points in sparsely settled areas, representing 5% of the population, were excluded. Of the 938 women eligible as controls, 92.8% were interviewed in their homes by trained female interviewers using a standard questionnaire modified from the CDC Cancer

and Steroid Hormone Study.<sup>11</sup> Interviews lasted an average of 40 min and focused on the women's reproductive, medical, and sexual histories.

After receiving informed consent, laboratory technicians obtained serum specimens from 88% of the interviewed control women. Sera were analyzed for antibodies to HSV-1 and HSV-2 (at the Division of Pediatric Infectious Diseases, Emory University) with a type-specific glycoprotein antigen,<sup>1</sup> and for antibody to *Chlamydia trachomatis*<sup>12</sup> (at the Chlamydia Laboratory, San Francisco General Hospital). The MHA-TP and RPR tests for syphilis were performed at the STD Laboratory, Center for Infectious Diseases, CDC.

Because the social and demographic characteristics of women who had a serum specimen drawn did not differ from those of women who did not,<sup>13</sup> the analysis was restricted to those women for whom a serum specimen was obtained. Sampling fractions used in selecting controls varied by age group in order to match the age distribution of the cancer cases for the original case control study. In order to obtain population estimates of seroprevalence, the results for the current analysis were age-weighted by the inverse of the sampling fractions to compensate for the over-sampling of women in certain age groups.<sup>14</sup> Demographic and reproductive history variables were cross-tabulated with age and with the number of lifetime sexual partners to characterize seropositivity. Cells with <25 women are not presented. Since the population survey was based on a multi-stage, cluster sample methodology, confidence intervals were calculated using a Taylor series approximation of the variance.<sup>14</sup>

## RESULTS

Fewer than 1% of the women reported a history of oral herpes lesions. The prevalence of HSV-1 antibody was 97.1% with minimal differences by population subgroups. When analyzed by age, region, or education level, >90% of the women in each subgroup were seropositive for HSV-1.

Very few women reported a history of sexually transmitted diseases. Antibody to HSV-2 was detected in 39.4%, but only 1.1% of seropositive women reported a history of genital herpes lesions. More than half the women had antibody to *Chlamydia trachomatis* (56.1%) and 6.4% had

a reactive syphilis (MHA-TP) serology. Women who had serologic evidence of past syphilis infection were almost twice as likely to have antibody to HSV-2 as women nonreactive for syphilis (77.5% vs. 36.8%). Similarly, women with serological evidence of past chlamydial infection were almost twice as likely to be seropositive for HSV-2 as women with no evidence of chlamydial infections (50.3% vs. 25.9%). Of 44 women who had serological evidence of both syphilis and chlamydial infection, 85.1% were seropositive for HSV-2; only 26.7% of the 313 women who were seronegative for both syphilis and chlamydia had serological evidence of HSV-2 infection.

When analyzed by geographic region, the prevalence of HSV-2 antibody was highest (48.7%) in urban areas outside the central valley, chiefly the port cities of Limón and Puntarenas (data not shown). Education was inversely related to seroprevalence of HSV-2, even when controlled for age or for the number of lifetime sexual partners (Table 1). Previously married women had a seroprevalence almost twice as high as that of currently married women (62.3% vs. 35.2%).

The number of lifetime sexual partners was a strong predictor of seropositivity for HSV-2 for both older and younger women (Table 2). Seroprevalence among women who reported only 1 sexual partner in their life was almost twice as high as the prevalence for the 36 women who denied having coitus (30.5% vs. 17.7%). Seroprevalence again doubled for women with 2 sexual partners compared to 1 partner (57.7% vs. 30.5%). Similarly, 61.6% of women with 3 sexual partners during their life and 79.2% of women with  $\geq 4$  partners were seropositive.

Seropositivity increased with age, even when controlled for the number of lifetime sexual partners (Table 1). However, in each age group, the prevalence of HSV-2 antibody among women with  $\geq 2$  lifetime sexual partners was approximately twice as high as that of women with 1 or no partners.

Although women who reported a young age at first coitus had a higher seroprevalence, this difference diminished when controlled for the number of lifetime sexual partners (Table 2). Seropositivity increased with the number of pregnancies, but this relationship was pronounced only for women with  $\geq 2$  lifetime sexual partners. HSV-2 seroprevalence was not related to use of specific contraceptives, except for con-

TABLE 1  
Percentage of women with HSV-2 antibody by selected demographic characteristics

	Age (years)						No. sexual partners*			
	Total		25-39		40-59		0-1		≥ 2	
	%	No. women	%	No. women	%	No. women	%	No. women	%	No. women
<b>Age (years)</b>										
25-29	32.8	(122)†	—	—	—	—	25.6	(86)	50.0	(36)
30-39	38.5	(270)	—	—	—	—	26.7	(187)	65.9	(82)
40-49	44.6	(194)	—	—	—	—	32.6	(126)	66.0	(67)
50-59	46.1	(180)	—	—	—	—	37.7	(138)	73.8	(42)
<b>Education</b>										
None	54.9	(79)	—‡	—	55.5	(56)	34.8	(43)	77.2	(36)
Primary incomplete	46.1	(258)	50.8	(89)	42.5	(169)	32.9	(173)	71.5	(84)
Primary complete	37.9	(187)	34.1	(113)	46.8	(74)	29.8	(129)	57.0	(57)
Secondary	33.1	(172)	28.9	(123)	50.3	(49)	26.7	(132)	52.4	(40)
University	26.7	(70)	25.8	(44)	28.9	(26)	25.0	(60)	—‡	—
<b>Marital Status</b>										
In union	35.2	(542)	33.1	(299)	39.3	(243)	28.1	(423)	59.4	(117)
Sep/wid/div	62.3	(106)	65.9	(28)	60.3	(78)	50.8	(54)	73.9	(52)
Single	41.2	(118)	36.4	(65)	50.3	(53)	24.0	(60)	60.0	(58)
<b>Total</b>	39.4	(766)	35.9	(392)	45.3	(374)	29.6	(537)	62.5	(227)

\* Two women with unknown numbers of sexual partners excluded.

† Numbers in parentheses refer to the unweighted number of women in each cell.

‡ Less than 25 cases.

doms. Women whose partners had used condoms were less likely to have antibody to HSV-2 than those whose partners had never used condoms (Table 3). Women whose partners had used condoms for ≥ 2 years had a lower prevalence

than women whose partners had used condoms for < 2 years. An apparent protective effect of condom use also occurred when stratified by age or by the number of lifetime sexual partners (Table 4).

TABLE 2  
Percentage of women with HSV-2 antibody by age at first intercourse, number of sexual partners, and number of pregnancies

	Age (years)						No. sexual partners*			
	Total		25-39		40-59		0-1		≥ 2	
	%	No. women	%	No. women	%	No. women	%	No. women	%	No. women
<b>No. sexual partners</b>										
0	17.7	(36)†	—‡	—	—‡	—	—	—	—	—
1	30.5	(501)	27.6	(251)	35.1	(250)	—	—	—	—
2	57.7	(133)	54.4	(65)	62.7	(68)	—	—	—	—
≥ 3	68.8	(94)	64.0	(53)	78.0	(41)	—	—	—	—
<b>Age at first intercourse§</b>										
None	17.7	(36)	—‡	—	—‡	—	17.7	(36)	NA	—
16	49.3	(112)	44.9	(66)	59.5	(46)	33.8	(49)	60.8	(63)
16-19	42.2	(280)	41.4	(134)	43.3	(146)	28.5	(178)	65.7	(102)
≥ 20	35.8	(336)	30.9	(169)	43.6	(167)	30.9	(273)	58.2	(61)
<b>Number of pregnancies</b>										
0	25.1	(70)	19.1	(42)	41.6	(28)	23.1	(60)	—‡	—
1-2	32.6	(161)	27.6	(117)	55.1	(44)	26.7	(120)	51.4	(41)
3-4	43.9	(222)	41.8	(152)	50.2	(70)	33.9	(150)	63.1	(71)
≥ 5	44.8	(313)	50.2	(81)	42.1	(232)	30.6	(207)	70.4	(106)
<b>Total</b>	39.4	(766)	35.9	(392)	45.3	(374)	29.6	(537)	62.5	(227)

\* Two women with unknown numbers of sexual partners excluded.

† Numbers in parentheses refer to the unweighted number of women in each cell.

‡ Less than 25 cases.

§ Two women with unknown age at first intercourse.

TABLE 3  
*Percentage of women with HSV-2 antibody by condom use and age group*

Age	Never used condoms	Used condoms 1-23 months	Used condoms $\geq 24$ months	Total
		Percent $\pm 1.96$ SE*		
25-39	40.6 $\pm$ 6.3	33.0 $\pm$ 8.8	24.6 $\pm$ 11.2	35.9 $\pm$ 5.0
40-59	48.9 $\pm$ 6.2	35.6 $\pm$ 12.8	36.1 $\pm$ 12.0	45.3 $\pm$ 5.3
Total	44.3 $\pm$ 4.9	33.5 $\pm$ 7.8	28.9 $\pm$ 8.7	39.4 $\pm$ 3.8

\* CI = 95%.

#### DISCUSSION

The high prevalence of specific HSV-2 antibody in Costa Rican women is consistent with the limited previous studies from Central America. One previous Costa Rican study reported that 10 of 20 selected clients in a family planning clinic had neutralizing antibody to HSV-2.<sup>15</sup> In Guatemala City, Guatemala, 45 of 60 selected outpatients were seropositive for HSV-2 as determined by an ELISA test (Juan Manuel and Amaya Ferman, University of San Carlos, Guatemala City, Guatemala, personal communication). A more specific serological test was used in Herrera Province, Panama. There, 33% of control subjects in a cervical cancer case-control study had HSV-2 antibody.<sup>16</sup> None of these Panamanian women reported a history of genital herpes.

The seroprevalence of HSV-2 increased with age and varied by marital status and educational level. However, the number of lifetime sexual partners demonstrated the most dramatic gradient for seropositivity. Two-fold differences in seroprevalence were observed between women with 1 sexual partner and women with no sexual experience and for women with 2 partners as compared to women with 1 sexual partner. Women with  $\geq 4$  lifetime sexual partners had a seropositivity of 79.2%, compared with 17.7% among women with no history of coitus. This latter group included only 6 seropositive women and may have reflected perinatal infection, inaccurate sexual histories, oral transmission of HSV-2, or residual cross-reactivity with HSV-1.

Since most women in this study (65.4%) reported only 1 sexual partner in their life, the seroprevalence estimate for the total population is primarily determined by the prevalence in this subgroup. Yet the seroprevalence among these monogamous women was high (30.5%). This strongly suggests that risk factors related to male sexual behavior, which were not measured in this study, are responsible for the high seroprevalence of HSV-2 in Costa Rican women.

Very few women reported a history of genital herpes or any other sexually transmitted disease (STD). Some Costa Rican women may have been hesitant to report symptomatic genital herpes infection, or may not have been informed of the diagnosis by a clinician. But most genital herpes infections in Costa Rica are probably asymptomatic, as in other countries.<sup>16,17</sup> Women with serological evidence for syphilis or chlamydial infection were twice as likely to have HSV-2 antibody than women with no serologic evidence for these diseases. These results suggest that women who had 1 STD were likely to have  $> 1$ .

Condom use has been associated with a decreased risk for several sexually transmitted diseases.<sup>18</sup> In this study, the pattern of condom use (Tables 3, 4) is consistent with a protective effect against HSV-2. Women whose partners used condoms had a lower prevalence of HSV-2 antibody in both age groups as compared to non-users. Among younger women and women with only 1 sexual partner, the long-term use of condoms ( $\geq 2$  years) had a slightly lower HSV-2 seroprevalence than short-term users. However, since this is a prevalence rather than an incidence

TABLE 4  
*Percentage of women with HSV-2 antibody by condom use and number of sexual partners*

No. partners	Never used condoms	Used condoms 1-23 months	Used condoms $\geq 24$ months	Total
		Percent $\pm 1.96$ SE*		
1	34.6 $\pm$ 5.8	27.7 $\pm$ 8.4	21.2 $\pm$ 8.4	30.5 $\pm$ 4.1
$\geq 2$	68.5 $\pm$ 7.4	49.8 $\pm$ 16.0	52.9 $\pm$ 21.4	62.5 $\pm$ 7.1
Total	44.3 $\pm$ 4.9	33.5 $\pm$ 7.8	28.9 $\pm$ 8.7	39.4 $\pm$ 3.8

\* CI = 95%.

study, condom use could have occurred before or after HSV-2 infection.

The cross-sectional study design<sup>19,20</sup> and the restriction to women 25–59 years of age impedes our ability to identify risk factors for HSV-2 infection.

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