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Ethnic differences in polyomavirus simian virus 40 seroprevalence among women in Houston, Texas

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Summary *Objective:* To examine the prevalence and distribution among racial/ethnic groups of polyomavirus SV40 antibodies in women in Houston, Texas.
Methods: Women in three different cohorts reflecting the evolving demographics of Houston were evaluated for frequency of SV40 antibodies using a plaque-reduction neutralization assay.
Results: Women in cohort A (enrolled 1972—1973) were 68% (145/212) African-American and 32% Caucasian; the overall frequency of SV40 neutralizing antibodies was 7%. Women in cohort B (enrolled 1975—1977) were Caucasian with an overall frequency of SV40 neutralizing antibodies of 18% (37/211). Women in cohort C (enrolled 1993—1995) were 50% (199/400) African-American, 25% Caucasian, and 25% Hispanic; the overall frequency of SV40 neutralizing antibodies was 10%. Logistic regression analysis for cohort A showed no difference in SV40 neutralizing antibodies with respect to race/ethnicity, pregnancy status, number of previous pregnancies, or history of sexually transmitted diseases. For cohort C, race/ethnicity was identified as a significant factor associated with SV40 neutralizing antibodies, with Hispanics having a seroprevalence of 23% compared to 5—6% in the other two groups ($p = 0.01$).
Conclusions: A significantly higher SV40 seroprevalence was found among Hispanics than other racial/ethnic groups in the city of Houston. Findings are compatible with a model that certain population groups potentially exposed to SV40-contaminated oral poliovaccines have maintained cycles of SV40 infections.

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Introduction

Simian virus 40 (SV40) is a member of the family Polyomaviridae that establishes persistent infections in susceptible hosts.[1,2] Introduction of the virus into humans is linked to the development and distribution of early forms of the poliovaccine.[3–8] Both inactivated and live attenuated preparations of the poliovaccine were produced using primary rhesus monkey kidney cells, some of which were naturally infected with SV40. Infectious SV40 survived the vaccine inactivation treatments, and data indicate that some children and young adults in the United States likely were administered SV40-contaminated poliovaccines from 1955 through 1962.[3] Precise records do not exist, but it is believed that the distribution of SV40-contaminated inactivated poliovaccine lots varied by state in the United States and that Texas was estimated to have received lots with a low level of contamination.[9] SV40-contaminated candidate live attenuated oral poliovaccines were tested in large field trials outside the United States prior to licensing, especially from 1958 to 1960.[5] Both inactivated and live attenuated SV40-contaminated poliovaccines were administered in several countries in Latin America and other regions of the world.[5,6,10,11]

The transmission, pathogenesis, and current prevalence of SV40 infections in humans are largely unknown, but it appears that infections have occurred in target populations in different geographic regions.[12–16] Studies with enzyme-linked immunosorbent assays (ELISAs) using virus-like particles have estimated SV40 seroprevalences of 2—10%,[17–19] based primarily on serum samples obtained from the United States and the United Kingdom, both highly developed countries. SV40 seroprevalences estimated by neutralization assays have similarly ranged from 2% to 10%, with some population groups reaching 16%.[13–15,18,20–22] An immunoassay based on SV40-specific peptides from the viral capsid proteins detected SV40-specific antibodies in 18% of Italian blood donors.[23] The polyomaviruses JCV, BKV and SV40 can be differentiated serologically by hemagglutination and neutralization assays,[24] with neutralization assays based on abrogation of virus infectivity recognized as a highly specific measure of virus antibodies.[25]

While some SV40 infections in humans are related to direct exposure to early forms of the contaminated poliovaccines, markers of infection have been detected in individuals too young to have been exposed to the contaminated vaccines.[4,5] This suggests there are other sources of exposure to the virus. In addition to the recognized excretion of polyomaviruses in urine, polyomaviruses are found in human stool samples,[26–30] in sewage,[31] and in human feces-contaminated waters,[32,33] highlighting the potential for fecal—oral transmission by these agents. It was shown previously that 19% of newborn children and 15% of infants 3- to 6-months-old in the United States at the time of receiving the original contaminated oral poliovaccine excreted infectious SV40 in their stools for up to 5 weeks after vaccination.[34] Maternal—infant transmission has also been shown to be a possible route of transmission in animal models.[35] SV40 DNA has been detected in the blood in numerous studies, suggesting a possible mode of spread within a host.[36–46] A model has been proposed that SV40 human infections were established primarily by the use of contaminated live oral poliovaccines and that infections persist today in regions where living conditions allow transmission of virus by a fecal/urine—oral route.[5]

This investigation was designed to explore the prevalence of SV40 neutralizing antibodies and to seek insights into parameters of infections in three distinctive cohorts of women in Houston, Texas, one of the largest and more ethnically diverse cities in the United States. The cohorts reflect the evolving demographics of this large metropolitan area and allowed an assessment of whether race/ethnicity, year of birth, pregnancy status, number of previous pregnancies, or history of sexually transmitted diseases is associated with infections by polyomavirus SV40. A comparison of members of one cohort with mothers of the cohort addressed potential familial transmission of the virus.

Methods

Subjects and study criteria

Cohort A in this study included women enrolled between 1972 and 1973 to assess seroepidemiologic features of herpes simplex virus type 2 (HSV-2) infections and pregnancy, as part of a study of HSV-2 associations with cervical cancer.[47] Women in cohort B were enrolled between 1975 and 1977 to monitor adverse outcomes in women exposed to diethylstilbestrol in utero.[48,49] Mothers of subjects in cohort B were included to compare SV40 infections in mothers and children. Women in cohort C were enrolled between 1993 and 1995 for a study of human papillomavirus and cervical carcinoma.[50] Women from cohorts A and C were recruited from patients of the public hospital that provides care for the uninsured and indigent of Harris County, Texas. At the time of enrollment, subjects signed informed consent and provided information related to demographics, pregnancy status, number of previous pregnancies, and history of sexually transmitted diseases (STD). The subjects self-identified their race/ethnicity from options listed on the questionnaire. Women from cohort B were recruited from private physician practices caring for middle and upper-middle class patients in Harris County. At the time of enrollment, subjects signed informed consent. Blood samples were collected from participants of all three cohorts at the time of enrollment and sera were stored at −20 °C. Only women with available archival serum samples were included in the present study; the serum bank had been moved several times and some sera could not be located. Women were designated to have been potentially exposed to SV40-contaminated poliovaccines if born before December 31, 1962 and non-exposed if born on or after January 1, 1963.

Serum neutralization assay

SV40 seroprevalence was determined using a specific plaque-reduction neutralization assay that has been described.[13,14,20] Briefly, heat-inactivated serum samples were diluted in Tris-buffered saline (TBS; pH 7.4) and mixed with equal volumes of SV40 diluted to contain 50—100 plaque-forming units per 0.1 ml. The virus—serum mixtures were incubated at 37 °C for 30 min prior to inoculation onto