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Re: Debate on the Link Between SV40 and Human Cancer Continues

The news article by Nancy J. Nelson (1) repeats the current scientific dogma that simian virus 40 (SV40) was removed from all oral polio vaccine sold and administered in the United States. In a recent article (2), however, I have challenged this accepted "fact" based on legal documents and the absence of test results from at least one of the principal vaccine manufacturers, Lederle. As noted in that article, internal Lederle documents indicate that the company has not been able to document that it tested all vaccine seeds to confirm the absence of SV40 contamination. Therefore, statements in Nelson's article, such as "[p]eople most likely to have received contaminated vaccines were born from 1941 through 1961," are inaccurate and potentially misleading.

Dr. Strickler's statement that "[m]esotheliomas are developing in people who are too old to be vaccinated, and brain tumors [are developing] in children that are too young to have been vaccinated," may be explained by the presence of SV40 in the oral polio vaccine and the fact that oral polio vaccine can spread from the recipient to those who come in contact with the excretions (oral and fecal) of the recipient within a defined period of time (3). There has been no investigation of whether SV40 can be transmitted from individuals vaccinated with the live oral polio vaccine to unvaccinated individuals because everyone has assumed that SV40 was never in that product from the inception of its being sold in the United States.

Every scientist who is attempting to determine the role of SV40 as a cause of cancer in humans and every news reporter who is interested in this issue should demand all of the records of both the government and the vaccine manufacturer so that there can be a full scientific and independent investigation as to whether there was full compliance

with the removal of SV40 from all oral polio vaccine used in the United States from 1962 until 2000. Oral polio vaccine is no longer sold in the United States, and only enhanced inactivated vaccine is now allowed for routine immunization.

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Overall, Nancy Nelson's news article about simian virus 40 (SV40) and human tumors (1) was well balanced. We would like to make some additional comments. (More information can be found in the February 2001 issue of *Seminars in Cancer Biology*.)

First, the statement in the sidebar that SV40 causes "abnormalities" in human cells underestimates the extent of damage. Human cells infected by SV40 *in vitro* develop extensive genetic damage [(2), reviewed in (3)] and have grown as tumor nodules when injected into volunteers (4). The susceptibility of human cells to SV40 is cell type dependent, with mesothelial cells the most susceptible (2,3,5). SV40 is the only known carcinogen that, by itself, causes malignant transformation and immortalization of human mesothelial cells in tissue culture (2,3,5).

Second, the incidence of mesothelioma in the United States has increased from nearly none in 1955 to approximately 2500 cases per year, and SV40 may be one of the contributing factors.

Third, the hypothesis that most mesotheliomas occurred in an age group that could not have been exposed to SV40-contaminated polio vaccines (1) reflects a common but mistaken belief that, during the "contamination" period (1955 through 1961), only newborns

and children were vaccinated. In the United States, 34.7 million people aged 20-59 years were vaccinated with potentially contaminated polio vaccine during this period (3). This is the cohort in which most mesotheliomas have developed in the past 20 years (3). Furthermore, administration of the oral attenuated polio vaccine in the early 1960s exposed both the recipient and his contacts to the poliovirus and to SV40 because both viruses were infectious. There is also evidence that SV40-contaminated vaccines were produced and distributed after 1961 (6). Finally, even if polio vaccines contributed to the spread of SV40, other mechanisms of transmission presumably exist because SV40 has been detected in nonvaccinated individuals (3).

Fourth, epidemiology studies [reviewed in (3)] have measured the association of the polio vaccine with the overall increase in cancer. However, one would not expect increases in rare cancers such as mesotheliomas to affect overall cancer rates. Two independent studies of cohorts vaccinated in early childhood with potentially contaminated polio vaccines (3) suggested an increased risk of mesothelioma (relative risk, ≥ 3). However, the number of cases was small because mesotheliomas are rare in people younger than 50 years; thus, it is premature to make definitive conclusions about an increased risk of mesothelioma in individuals vaccinated with SV40-contaminated polio vaccines (3).

Fifth, several groups have used various technical approaches (immunostaining, messenger RNA *in situ* hybridization, and primed *in situ* hybridization) to demonstrate that SV40 is present in malignant mesothelioma cells but not in nearby normal cells (3). Moreover, SV40 has been detected in mesothelioma cells and not in nearby nonmalignant cells microdissected from the same slide (3).

Sixth, SV40 is not always lost when mesothelioma cells are cultured (5); accordingly, treatment with an antisense construct to the SV40 T antigen arrests SV40-positive mesothelioma cells in tissue culture [reviewed in (7)]. Also, Epstein-Barr, another episomal virus, is often lost when human nasopharyngeal tumor cells are put in tissue culture.

Seventh, it has recently been shown that a small number of mesothelioma

cells infected with SV40 can induce the growth of nearby noninfected cells (5).

Eighth, enzyme-linked immunosorbent assay tests are not reliable to distinguish among SV40 and the human polyomaviruses JC and BK. However, DNA sequencing can reliably distinguish these three viruses (3).

Finally, experts from around the world in the fields of virology, molecular genetics, mesothelioma, brain and bone tumors, and oncology, including many skeptical of the association between SV40 and human cancer, discussed it at a consensus meeting at the University of Chicago, IL, on April 20-21, 2001. The scientists who chaired the final panel discussion (and who are not directly involved with this research) concluded that "the presence of SV40 in some human tumors has been convincingly demonstrated . . . the possible role

of SV40 in the pathogenesis of mesothelioma has been considerably strengthened since the 1997 NCI conference" (7).

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