

Rise in Tonsillar Cancers Parallels HPV Positivity

BY NEIL OSTERWEIL
Contributing writer

CHICAGO — A threefold increase in the incidence of tonsillar cancer over 3 decades in Sweden was paralleled by a similar rise in the incidence of tumors positive for the human papillomavirus, the results of a cohort study indicate.

At the same time, however, survival rates in patients with tonsillar cancer also increased, possibly because of the higher proportion of HPV-positive cancers, which tend to have a better prognosis than other oral cancers, Dr. Hanna Dahlstrand said at the annual meeting of the American Society of Clinical Oncology.

The reasons for the increase in HPV-positive tumors are not known, although they could be related to a possible increase in sexual behaviors, particularly in urban centers, Dr. Dahlstrand said.

Sweden is a relatively small nation, but the results may be applicable to other countries, she noted. In the United States, for example, the incidence of HPV-related oropharyngeal squamous cell carcinomas has risen since 1973, whereas the incidence of squamous cell carcinomas at other oral sites has either remained constant or declined. In Finland, the incidence of tonsillar cancers doubled from 1956 through 2000.

HPV DNA has been shown to be present in 40%-75% of oro-

pharyngeal cancers, compared with about 25% of all head and neck cancers.

"It is only the high-risk types of HPV that are found, with at least 90% dominance of HPV-16, and the oncogenes on HPV, E6 and E7 are transcribed," she said, "And there is a temporal connection: Exposure to HPV-16 precedes by at least 9 years the diagnosis, and has been shown to be a strong risk factor for tumor development."

HPV-positive oropharyngeal cancers tend to occur more often in non-smokers and younger patients. Risk factors include multiple sexual partners, younger age at first intercourse, and oral sex. Several studies have shown that the presence of HPV positivity is associated with about a 50% reduction in 5-year mortality, said Dr. Dahlstrand of the department of oncology-pathology at the Karolinska Institute in Stockholm.

She and her colleagues conducted a nationwide cohort study using the exhaustive clinical and demographic databases available to Swedish investigators. Their goals were to see whether there has been an increase in the incidence of tonsillar cancer in Sweden; to determine whether such an increase, if present, could be linked to the proportion of HPV-positive tumors; and to see whether the incidence of HPV-

positive tonsillar cancers would have an effect on survival.

They identified a total of 2,165 incident cases of tonsillar squamous cell carcinoma from 1960 through 2003, using the Swedish National Cancer Registry.

To determine survival, the investigators used records from the Swedish Causes of Death Register, and checked them against

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the Swedish Emigration Registry from 1960 to 2001 to ensure that cohort members were not lost to follow-up. They identified a total of 1,800 survivors as of 2003.

The investigators also assessed the incidence of tonsillar cancer from 1970 to 2001 and survival in a Stockholm cohort, and used this cohort to control for treatment, tumor-nodes-metastasis stage, and cause of death. They identified 515 cases in this cohort, and 337 survivors as of 2001.

They were able to obtain 203 biopsy samples and screened them for HPV using polymerase chain reaction testing; they then typed and sequenced the HPV to determine expression of the E6 and E7 oncogenes and expression of HPV-16.

In the nationwide cohort, there was a 2.04-fold increase in the incidence of tonsillar cancers, from 1.2/100,000 population to 2.4/100,000, from 1960 to 2003. There was no parallel increase in cancers of the oral cavity (for example, mobile tongue or floor of the mouth), however.

In the Stockholm cohort, tonsillar cancers increased from 1.3/100,000 to 3.6/100,000, or 2.8-fold, from 1970 to 2002. There was also a 2.9-fold increase in the proportion of HPV-positive tonsillar cancers during that same time period. This increase

became significant for the 1990-1999 period, compared with 1970-1979 ($P = .0025$), and remained significant for 2000-2002 (P less than $.0001$). During the '70s, 23% of cases were HPV positive, which increased to 28% in the '80s, 57% in the '90s, and to 68% into the 21st century.

The mean 5-year relative survival rate in men with tonsillar cancer also increased in Sweden since the 1960s, from 32% to 53% in 1990-2001. The relative hazard ratio for death for the latest decade vs. the earliest was 0.50. Women had a slightly better survival rate than men then and now, with the rate increasing from 45% in the '60s to 60% in the '90s and into 2001. Because women had better survival early on, however,

the difference in relative hazard ratios was not quite as large as that for the cohort as a whole.

In the Stockholm cohort, in a Cox multivariate analysis adjusted for age, gender, stage, and treatment, the researchers found a similar significant rise in relative 5-year survival, with a relative hazard ratio of 0.54 for 1990-2001, compared with 1970-1979. A lower proportion of stage I and II tumors in the '90s, compared with the '70s, suggests the improvement in survival over the years can't be explained by earlier diagnosis, Dr. Dahlstrand said.

Finally, when the investigators looked at survival by HPV status in the Stockholm cohort, they found that independent of age, gender, and tumor stage, the hazard ratio for patients with HPV-positive tumors was 0.17.

In all, 49% of cases from 1973 to 2008 were HPV positive, and the E6 and/or E7 mRNA were found in 94% of assessable HPV-positive samples, Dr. Dahlstrand noted.

The findings show that about a threefold increase in the incidence of tonsillar cancer was accompanied by about a threefold rise in the rate of HPV-positive tonsillar cancers. The presence of the E6 and E7 oncogenes provides further evidence linking HPV to tonsillar cancers, she said.

The study funding source was not provided. Dr. Dahlstrand said she has no relevant financial disclosures. ■

HIV Testing, Treatment Are Most Warranted in Minority Populations

BY JOEL B. FINKELSTEIN
Contributing Writer

WASHINGTON — Widespread testing would likely blunt the high HIV infection rate in African Americans and Latinos, but little money and effort have been put into prevention, experts said at the National Minority Quality Forum's 2008 Leadership Summit.

"African Americans and Latinos suffer disproportionately from the HIV/AIDS epidemic," said Dr. Madeline Sutton, of the Heightened National Response to the HIV/AIDS Crisis Among African Americans, a program of the Centers for Disease Control and Prevention. She is the latest director of the \$45 million effort to expand the use of HIV testing. But that effort, say some in the AIDS community, has suffered from revolving leadership, and has so far not had overwhelming impact.

"Test everyone and treat everyone," said Dr. John Bartlett, chief of the division of infectious diseases at Johns Hopkins University, Baltimore.

The test is relatively inexpensive at about \$15, he said. It's a "dream test" that's highly accurate and detects a disease that is lethal if not treated and manageable when it is, yet it's not being used.

And its underuse translates to more trans-

mission. The rate of infection is notably higher in those who don't know they have the disease. In those testing positive, 40% have been infected for 8-10 years, he said at a meeting sponsored by the Alliance of Minority Medical Associations, the National Association for Equal Opportunity in Higher Education, and the Department of Health and Human Services.

For African Americans, it's not clearly genetics or behavior that is leading to the rise in the infection rate, Dr. Sutton said. The CDC's effort is based on better understanding the barriers to testing. "A lot of issues have to do with stigma."

Latino patients face similar barriers and more, given the stigma fuelled by the immigration debate, said Britt Rios-Ellis, Ph.D., director of the Center for Latino Community Health, Evaluation, and Leadership Training, a partnership between the National Council of La Raza and California State University, Long Beach "They are the only minority group to see a doubling of HIV infection [from] heterosexual contact, from 5% to 12% for males and from 23% to 67% for females between 2001 and 2006. In rural Mexico, most women with AIDS are married. We're seeing the same pattern here. If we could get everyone into testing and care, [it] would make a difference." ■

HIV/AIDS Diagnoses Soar in Men Who Have Sex With Men

From 2001 through 2006, the number of HIV/AIDS diagnoses in men who have sex with men increased by nearly 9% in 33 states, with particularly high increases in black men and Asian/Pacific Islanders under age 25 years, according to the Centers for Disease Control and Prevention.

The CDC analysis of trends in HIV/AIDS diagnoses in men who have sex with men (MSM) estimated that 214,379 people were diagnosed with HIV/AIDS, of which 46% were among MSM and 4% were among MSM who also injected illicit drugs. Diagnoses during this time period dropped in all transmission categories except for MSM (MMWR 2007;57:681-6).

Of the cases diagnosed among MSM, 64% were in men who were aged 25-44 years. There was a 12% increase in diagnoses in all black MSM. Diagnoses in black MSM aged 13-24 years increased by 93%, a rate that was about twofold greater than the rate of increase in

white MSM in the same age group.

Asian/Pacific Islanders aged 13-24 years saw the largest proportionate increase in HIV/AIDS diagnoses. In this group, HIV/AIDS diagnoses increased by 256% (an estimated annual increase of almost 31%). Among MSM in this younger age group, the annual percentage increases in diagnoses were statistically significant in all racial/ethnic populations, with the exception of American Indian and Alaska Natives.

"These findings underscore the need for continued effective testing and risk reduction interventions for MSM," particularly for those younger than age 25 years, according to the report.

Among the limitations of the report, the 33 states are not representative of all HIV-positive people in the United States. However, the racial and ethnic disparities observed are similar to those observed for AIDS cases in all the states.

—Elizabeth Mechtat