



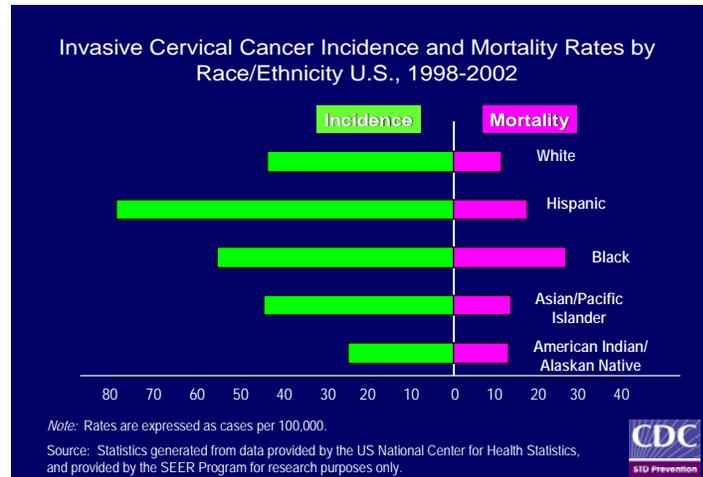
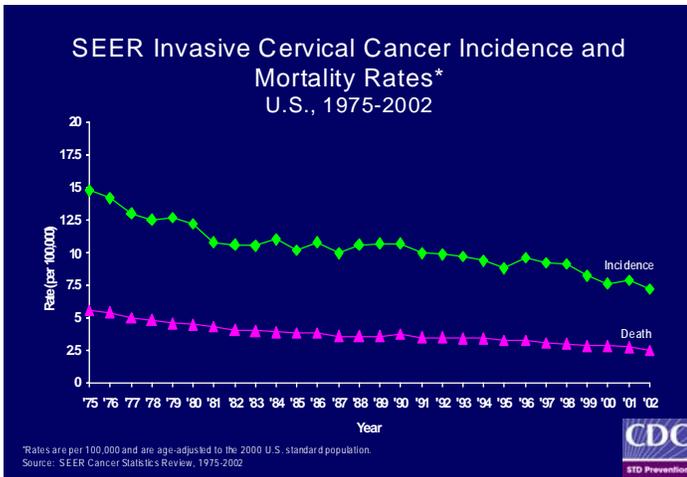
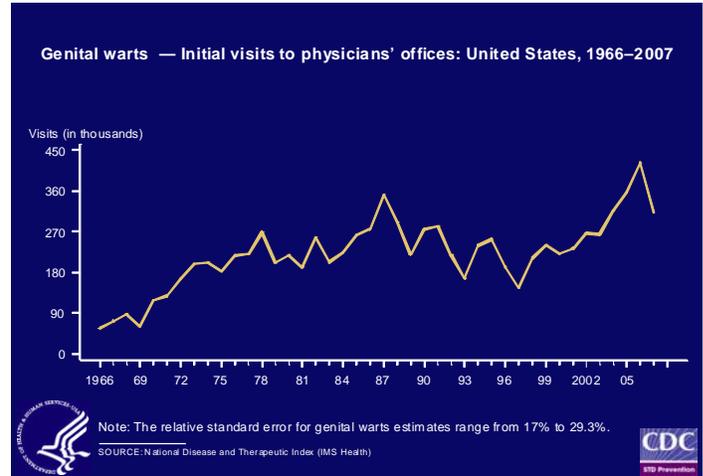
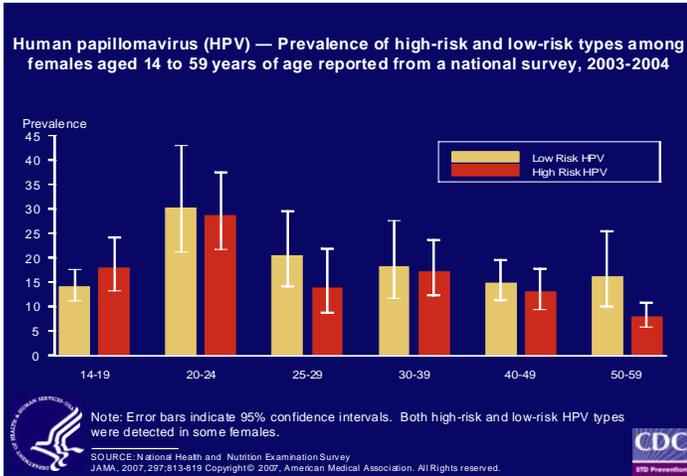
# County of San Diego Sexually Transmitted Diseases Quarterly Report



Issue No. 4

## The Spectrum of Human Papillomavirus Disease: Beyond Genital Warts and Cervical Dysplasia

February 20, 2009



HPV infections are the most prevalent of all sexually transmitted infections in the US, with an estimated 6.2 million infections annually. Up to 80% of sexually active persons acquire an anogenital HPV infection at some point in their lives. Studies of young women indicate that 10% are infected within 6 months of sexual debut, with 60% showing evidence of cervical HPV infection within 2 years.

**Anogenital warts** are a common complaint of young, sexually active persons; 90% of cases are caused by HPV types 6 and 11. Treatment of visible lesions is not curative and there is no consistent evidence that treatment reduces contagiousness. Although recurrence post-treatment occurs in 20% to 50% within six months, warts usually eventually resolve on their own (70% within one year, 95% within two years). Because the virus needs to reach the basal epithelium to infect cells, microtrauma from shaving, abrasions from sex and scratching increase susceptibility to infection, with autoinoculation not uncommon. Other factors linked to persistent warts include smoking, diets low in folate, and tanning (even of the non-genital area). Although genital warts may occur outside the condom-covered area, decreased transmission has been found in couples who routinely use condoms. Patients are often distressed by this diagnosis. Unwarranted concerns about infidelity may destabilize relationships, so the clinician should explain the high prevalence, long latency and usually asymptomatic nature of HPV infection. An excellent patient education resource may be found at <http://www.cdc.gov/STD/HPV/STDFact-HPV.htm>.

To report a STD case: 619-692-8520; fax 619-692-8541

STD Clinic: 619-692-8550; fax 619-692-8543

Virtually 100% of **cervical cancer** is caused by HPV infection; over 70% by types 16 and 18. In the US, an estimated 11,000 women will be diagnosed with and almost 4,000 women will die of cervical cancer in 2008.

Information is emerging about the disease burden of HPV at other anatomic sites. Studies in women have found that anal HPV infection is at least as common as cervical infection. Over the past 30 years, **squamous cell carcinoma of the anus** (SCCA) in the US has increased by approximately 96% in men and 39% in women. Detectable HPV occurs in 90% of SCCA cases. Among men who have sex with men (MSM), SCCA incidence is around 35 cases/100,000 population, comparable to cervical cancer incidence in the US before the institution of routine Pap smear screening. HIV-infected MSM have twice the risk for SCCA as non-HIV-infected MSM, with abnormal anal cytology inversely proportional to CD4 count. HIV-infected women and recipients of solid organ transplants are also at increased risk.

In the US, an estimated 35,000 people will be diagnosed with **cancer of the oropharynx** in 2008, and almost 8,000 will die from the disease. Squamous cell carcinoma of the head and neck (SCCHN) is the 7<sup>th</sup> most common cancer among men and the 4<sup>th</sup> most common cancer among African American men. Molecular evidence supports a causal role for HPV, particularly type 16, in the pathogenesis of SCCHN, with detection of oncogenic HPV types in 26% of SCCHN cases worldwide. A case-control study in Baltimore, controlled for tobacco and alcohol use, found that oral infection with oncogenic HPV types was 12 times higher in patients with SCCHN compared to age- and sex-matched controls (95% CI: 5.4 to 26.4). In this study, risk of disease was positively correlated with the number of oral sex partners ( $p$ -value for trend: 0.009), but vertical transmission at birth is another plausible mechanism for oral HPV infection. Additional cancers associated with HPV include **penile, vulvar, vaginal** and probably some cases of **esophageal cancer**.

Vertical transmission is also implicated in **recurrent respiratory papillomatosis** (RRP), which usually affects children. This rare condition often requires repeated surgery for growths affecting the airway and may undergo malignant transformation. One hundred percent positivity of oral HPV types 6 or 11 has been reported in RRP.

The quadrivalent HPV vaccine (Gardasil, Merck) has been shown to be highly effective in preventing high-grade cervical neoplasia associated with the targeted high-risk HPV types (16, 18). Efficacy was 98% to 100% in women who did not have type-specific HPV infection throughout the 3-dose vaccine course, but effectiveness was 29% to 50% in the intent-to-treat arm, because infection with types 16 and 18 is common even in young women, and the vaccine has no therapeutic value. Indeed, in women with a single lifetime partner, almost 1/3 test positive for HPV within one year of onset of sexual activity; hence the recommendation for vaccination to begin as early as nine years of age. High levels of HPV antibody have been found for up to 5 years post-vaccination. Recommendations for vaccine usage can be found at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5602a1.htm>.

While most modeling studies have concluded that vaccination of girls and young women is cost-effective, a controversial aspect is the potential cost-effectiveness of vaccinating boys and young men. When men are viewed solely as the vector of cervical cancer in women, cost-effectiveness analyses are not favorable. However, a growing awareness of the broader range of all genital and nongenital HPV-related disease (estimated to cost \$5 billion dollars in direct medical costs annually) is likely to alter this equation. The National Cancer Institute's Surveillance, Epidemiology and End Results Program (SEER) data reveal that approximately 150,000 cases of invasive HPV-associated cancer occurred nationally in men and women between 1998 and 2003. The burden of all cancers attributable to HPV in men is estimated to be 11,000 cases per year, equivalent to the number of annual cases of cervical cancer in women. Preliminary results from a randomized controlled trial looking at efficacy of quadrivalent vaccine in young men are favorable. Look for a rapidly evolving knowledge base and fluid recommendations on this topic in the future.