CarraShield 9 Labs

Overview of Research on HPV, Cancer Prevention and Divine 9® with CarraShield®

Understanding HPV

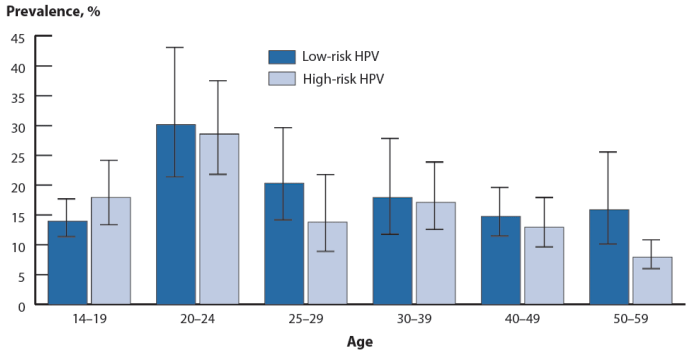
Human papillomaviruses (HPVs) are a diverse group of DNA viruses that infect the skin and mucosal tissues of humans. Some types of HPV have no effect. However, a subset of HPV types is responsible for most cases of cancer of the uterus and cervix, as well as a substantial fraction of other anal, genital and head-and-neck cancers. Another subset of HPV types is responsible for the development of genital warts.[1]

Genital infection with human papillomavirus (HPV) is the most common sexually transmitted disease in the United States today.[2] Sexually transmitted HPV in women is very common with an estimated lifetime risk of infection of about 75%.[3] HPV infections are also common in men who have sex with men (MSM) and women who have sex with women (WSW). HPV can be detected in the anal canal in over 50% of MSM.[4] Even people with only one lifetime sex partner can get HPV if their partner was previously infected with HPV.

Even though it is so common, HPV has historically been very hard to prevent. Recent studies have suggested that condoms are not effective in preventing HPV infection.[5] Because HPV is common, difficult to detect, and difficult to prevent, the Centers for Disease Control states that the only sure way to prevent it is not to have sex. Clearly, a recommendation few people will follow.

The figure to the right from the Centers for Disease Control shows the percentage of women who are carriers of HPV broken down by age group. A startling fact is how many women, once sexually active, can be infected and re-infected until well into their 50's.

HUMAN PAPILLOMAVIRUS (HPV) –
PREVALENCE OF HIGH-RISK AND LOW-RISK TYPES
AMONG FEMALES 14 TO 59 YEARS OF AGE FROM A NATIONAL SURVEY



Source: 2008 National Health and Nutrition Examination Survey,
Journal of the American Medical Association; republished by the Centers for Disease Control, Atlanta, GA

National Cancer Institute Studies

The work in the late 1990's by Harald zur Hausen showed HPV caused cervical and other cancers earned him the Nobel Prize in Medicine in 2008. His work launched a whole series of new research projects. The most well known projects were the development of vaccines. However, there were other less publicized projects looking at ways to block the transmission of infection.

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[1] Carrageenan Is a Potent Inhibitor of Papillomavirus Infection Public Library of Science, Pathogens, July 2006 | Volume 2 | Issue 7 | e69; submitted by the National Cancer Institute's Laboratory of Cellular Oncology

[2] Weinstock H, Berman S, Cates W, Jr. Sexually transmitted diseases among American youth: incidence and prevalence estimates, 2000. Perspectives in Sexual Reproductive Health. Jan-Feb 2004;36(1):6-10.

[3] Koutsky L (1997) Epidemiology of genital human papillomavirus infection. American Journal of Medicine 102: 3–8.

[4] Chin-Hong PV, Vittingholf E, Cranston RD, et al. Age-related Prevalence of Anal Cancer Precursors in Homosexual Men; the EXPLORE study, Journal of the National Cancer Institute 2005:97(12):896-905

[5] Holmes KK, Levine R, Weaver M (2004) Effectiveness of condoms in preventing sexually transmitted infection Bulletin of the World Health Organization 82: 454–461.

With the help of the National Cancer Institute (NCI), Merck began work to create a vaccine for HPV – later to be brought to market as Gardasil. Several years later, GlaxoSmithKline introduced their version of a vaccine, Cervarix. In spite of the commercial success both vaccines have had, they both have serious limitations. The most critical issue is the vaccines are not effective for men and women who are sexually active and may have had prior exposure to HPV. So while Gardasil is now a $2 billion business for Merck, they only market it to parents for use on their adolescents, not to sexually active adults. Cervarix has the same limitations.

Knowing the vaccines would have limitations, the NCI began searching for a way to block infections using a topical gel. In doing so, they found CarraShield Labs' Divine 9, made with the company's proprietary CarraShield™ seaweed extract. In 2006 and 2007, two studies were performed by the National Cancer Institute (NCI) using Divine 9. Published in peer reviewed journals "Public Library of Congress - Pathogens"[1] and "Nature Medicine"[6], these studies examined the ability of carrageenan to prevent HPV infections. Led by Dr. John Schiller, department head in the Laboratory of Cellular Oncology at NCI, the research team found carrageenan to be an extremely potent inhibitor of HPV infection. Dr. Schiller's team found Divine 9, made with CarraShield, to be the most potent HPV inhibitor in the study, better than using pure carrageenan.

In their next set of tests in 2009, NCI used monkeys to determine if performing a PAP smear increased the odds of HPV infection due to irritation of walls of the vaginal track and the cervix. The results of the unpublished study are disturbing. Using Surgilube[7] as a lubricant for the procedure, HPV infection rates increased by a statistically significant amount. However, when the researchers used a carrageenan lubricant, infection rates dropped to virtually zero. While Divine 9 wasn't specifically used in this particular study, it is the same carrageenan mixture that Divine 9 outperformed in the earlier studies.

Leading the World in HPV Prevention Research on Humans

While laboratory and animal studies are vital in the initial research stages, the next step in any medical research is to determine the effectiveness on humans. Today, there are only two human clinical studies in the world on HPV prevention using a topical microbicide and Divine 9 with CarraShield is used in both. These studies are led by renowned specialists in cancer epidemiology and are extremely large scale experiments, each involving hundreds of volunteers over several years.

McGill University Clinical Trial Involving Four Hundred Women

Because of the success of Divine 9 in the NCI animal studies, McGill University's Division of Cancer Epidemiology launched a large-scale, double-blind human trial on the ability of Divine 9 to prevent the transmission of HPV in women in 2013. The study is called CATCH an acronym for *Carrageenan-gel Against Transmission of Cervical HPV*, and is designed to track HPV infections in over four hundred female volunteers for a one year period. CATCH is funded by the Canadian Institutes of Health Research.

The McGill University research team is led by Dr. Eduardo Franco, Director of the Division of Cancer Epidemiology. Dr. Franco, a renowned expert on the prevention of cervical cancer and HPV-associated diseases, has published over 300 scientific articles and spoken at over 300 conferences worldwide.

The primary aim of CATCH is to evaluate the efficacy of Divine 9 in reducing genital HPV incidence, i.e., in preventing new HPV infection, in young sexually active women as well as to evaluate the efficacy of carrageenan in reducing genital HPV prevalence, i.e., in accelerating clearance of existing infections, in these same women.

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[6] Genital Transmission of HPV in a Mouse Model is Potentiated by Nonoxynol-9 and Inhibited by Carrageenan**,** Roberts, J.; Buck, C.; Thompson, C.; Kines, R.; Bernardo, M.; Choyke, P.; Lowy, D.; Schiller, J. (2007). *Nature Medicine* **13** (7): 857–861

[7] Surgilube, a brand from Fougera, is widely used in medical clinics for procedures. The use of Surgilube is standard practice in gynecology exams.

Participants are randomized to use either Divine 9 or a placebo lubricant that does not contain CarraShield via a variable block randomization algorithm and blinded intervention. Study participants will continue using the assigned intervention for the complete follow up period (1 year), independent of any other methods of contraception and/or STI prevention (e.g., condoms).

McGill University Clinical Trial on Two Hundred Gay Men

In May 2016, CarraShield Labs announced the launch of an entirely new study at McGill University's Division of Cancer Epidemiology on the ability of the CarraShield in Divine 9 to prevent the transmission of HPV among gay and bisexual men. The new McGill study is called LIMIT-HPV, an acronym for *Lubricant Investigation in Men to Inhibit Transmission of HPV*. LIMIT-HPV will involve tracking the presence of HPV infections of over three hundred male volunteers for a one year period. As with the earlier CATCH with female volunteers, LIMIT-HPV research will focus on determining the protective capabilities of Divine 9 with CarraShield as compared to a placebo lubricant. Dr. Eduardo Franco will also be the principle investigator on this latest study.

Conclusion

The excellent results in the NCI laboratory studies have led to the launch of two large scale human clinical trials using Divine 9. These are the only human clinical trials in the world on HPV prevention using a topical gel and Divine 9 is featured in both.

While no conclusive evidence exists yet that Divine 9 with CarraShield will block HPV in humans, the results of the NCI tests were compelling enough to justify multi-million dollar investments in these two Phase 2 human trials. CarraShield Labs will provide updates as the data collection continues. At this time CarraShield Labs makes no medical claims about Divine 9 and provides this information strictly for educational purposes.