

The Human Papillomavirus vaccine: An oncology nursing issue

by **Catriona Buick and Dr. Kelly Metcalfe**

Abstract

In Canada, approximately 1,500 women are diagnosed with cervical cancer every year, and 581 will die of the disease (WHO/ICO Information Centre on HPV and Cervical Cancer, 2007). The importance of preventing cervical cancer is clear, as the effects that this disease has on the lives of women and their families regardless of culture, sex, nationality or country is evident. With the recent media attention and release of the Human Papillomavirus (HPV) vaccine in Canada, it is crucial that oncology nurses understand HPV, its role in the development of cervical cancer, and the HPV vaccine. A brief overview of HPV and its involvement in the development of cervical cancer will be discussed in this paper. In addition, information on the HPV vaccine and its implications, as well as the current policy for the vaccine in Canada will be addressed. It will become evident how the role of the oncology nurse, as an educator and advocate regarding the implementation of this vaccine is crucial for successful acceptance of this vaccine. Finally, future implications of the vaccine and avenues of research will be touched upon.

Introduction

“I think this will be a transforming vaccine for millions of women across the world,” reported Gynecologist Oncologist, Dr. Robert Ozols (cited by American Cancer Society, 2006, p. 2). The transformation that is being suggested is in regards to the morbidity and mortality associated with cervical cancer and the vaccine is the Human Papillomavirus (HPV) Vaccine. But what, exactly, does this mean for women in Canada and across the world? As oncology nurses, the importance of this vaccine in the prevention of cervical cancer is clear, as the effects that cervical cancer have on the lives of women and their families regardless of culture, sex, nationality or country is evident. It is crucial that oncology nurses worldwide band together and play a primary role in researching, educating, and advocating for its use in the prevention of cervical cancer.

Every year, approximately 510,000 women worldwide are diagnosed with cervical cancer. Of these women, 288,000 will die from this disease (American Cancer Society, 2006). So, the recent

landmark discovery that clearly links HPV as the main etiologic agent in cervical cancer (Sherman, Schiffman, Strickler, & Hildesheim, 1998) and then the discovery of an HPV vaccine was not only welcomed, but was needed by the international community (Moreira, Oliveira, Neves, Costa, Karic, & Filho, 2006).

Human Papillomavirus

HPV is a member of the papillomaviridae family. It is a sexually transmitted disease (Dunne & Markowitz, 2006). Worldwide, it is the most commonly acquired sexually transmitted infection (Moscicki et al., 2000; Ho et al., 1998; Tarowski et al., 2004; Brown et al., 2005, as cited in Zimet, 2006). There have been more than 100 types of HPV identified worldwide, 35 of which have a genital association (Kahn & Bernstein, 2005). These 35 include “low-risk” types of mucosal HPV, which are associated with warts and mild cervical

La vaccination contre le virus du papillome humain — un enjeu des soins infirmiers en oncologie?

Abrégé

Tous les ans, environ 1500 Canadiennes sont diagnostiquées du cancer du col de l'utérus et 581 d'entre elles mourront de la maladie (WHO/ICO Information Centre on HPV and Cervical Cancer (2007). La prévention du cancer du col de l'utérus est d'une énorme importance étant donné les effets évidents de cette maladie sur la vie des femmes et de leurs proches, quels que soient leur culture, leur sexe, leur nationalité ou leur pays de résidence. À la lumière de la récente attention portée par les médias au vaccin contre le virus du papillome humain (VPH) et de la récente mise en marché de ce dernier au Canada, il est crucial que les infirmières en oncologie aient une excellente compréhension du VPH, de son rôle dans le développement du cancer du col de l'utérus et du vaccin contre le VPH. Le présent article présentera un bref aperçu du VPH et de son implication dans le développement du cancer du col utérin. Il fournira également de l'information sur le vaccin contre le VPH, sur les conséquences de ce dernier et sur la politique actuelle du Canada concernant la vaccination. Il abordera le rôle déterminant que peut jouer l'infirmière en oncologie, à titre d'éducatrice et de porte-parole, sur le plan de la mise en œuvre de cette vaccination et de son acceptation généralisée. Finalement, il abordera les répercussions du vaccin et les voies de recherche de demain.

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dysplasia, as well as the “high-risk” types (also known as oncogenic) and are associated with anogenital cancer, as well as low- and high-grade cervical dysplasia (Dunne & Markowitz, 2006). Eighteen types of high-risk HPV have been discovered, of these, two types HPV16 and HPV18 have been reported to account for 70% of all cases of cervical cancer (Saslow, Castle, Cox, Davey, Einstein, Ferris et al., 2007). A variety of other types account for the remaining 30%, and these vary internationally (Kahn & Bernstein, 2005). However, despite almost all cervical cancers being caused by HPV, not all high-risk HPV will develop into cervical cancer (Garnett & Waddell, 2000).

Research has shown that as many as 50% of sexually active women have been infected at one point with a form of genital HPV (Moreira et al., 2006) while others suggest as many as three out of four people who have been sexually active will have been exposed to HPV at some time (Cancer Care Ontario, 2004). Of these women, 70% to 90% will clear their high-risk infections of HPV within 12 to 30 months (Evander, Edlund, Gustafsson et al., 1995; Herrero, Hildesheim, Bratti, et al., 2000, as cited by Williamson, Passmore & Rybicki, 2005). However, for the remainder of these women who continue to have persistent high-risk HPV infections, this can substantially increase their risk for cervical intraepithelial neoplasia (CIN) and cervical cancer (Franco, Duarte-Franco & Ferenczy, 2001 as cited by Franco & Harper, 2005). In an International Agency for Research on Cancer (IARC) study that examined more than 1,000 women with invasive cervical cancer from 22 countries, the researchers found HPV DNA in 99.7% of the tumours, leading to the conclusion that HPV is a necessary cause of cervical cancer (Bosch, Manos, Munoz, Sherman, Janson, Petro, et al., 1995; Walboomers, Jacobs, Manos, Bosch, Kummer, Shak, et al., 1999, as cited in Munoz, Castellsague, Berrington de Gonzalez, & Gissmann, 2006). The research is currently ongoing to determine why certain women do not naturally clear their HPV infections (Moscicki, Schiffman, Kjaer, & Villa, 2006). However, there are a number of co-factors thought to be important in the development of cancerous lesions such as smoking (IARC, 2004, as cited in Munoz et al., 2006) and high parity (International Collaboration of Epidemiological Studies of Cervical Cancer, 2006).

The lifetime cumulative risk for cervical cancer is 1.3% (Parkin, Bray, Ferlay, & Pisani, 2005). Although the disease remains fairly rare in developing countries as a result of the implementation of recent screening programs (Parkin et al., 2005), HPV is still the most commonly acquired sexually transmitted infection (Moscicki et al., 2000; Ho et al., 1998; Tarowski et al., 2004; Brown et al., 2005, as cited in Zimet, 2006). Critiques of the HPV vaccine have highlighted that cervical cancer is not an epidemic and, therefore, widespread immunization may be unwarranted. However, this fails to take into consideration the burden of HPV. It is estimated that the number of women who have HPV-DNA is approximately 291 million and around 105 million will have the HPV-16 or-18 infections at least once in their lives (Burchell, Winer, de Sanjose & Franco, 2006). Furthermore, this disparagement fails to account for the psychological distress of an HPV diagnosis, such as the stigma of a sexually transmitted infection, anxiety and fears of cancer (Perrin, Daley, Naom, Packing-Ebuen, Rayko, McFarlane, et al., 2006).

Human Papillomavirus vaccine

The discovery of high-risk HPV and its association with cervical cancer is a unique and giant step in the research towards the cure for cancer, as, until recently, no human cancer had been so clearly linked to a cause (Franco & Harper, 2005). This

milestone discovery resulted in the development of the HPV vaccine. Currently there are two vaccines being manufactured: a bivalent and a quadrivalent (Newall, Beutals, Wood, Edmunds, & MacIntyre, 2007). The bivalent, which targets high-risk HPV-16 and -18, is manufactured by GlaxoSmithKline and is trademarked Cervarix (GlaxoSmithKline, 2006). The quadrivalent is the only vaccine currently available in Canada (Public Health Agency of Canada, 2007). This vaccine targets high-risk HPV-16 and -18, as well as low-risk HPV-6 and -11, which are primarily responsible for anogenital warts (Newall et al., 2007). This vaccine is trademarked Gardasil and was developed by Merck (Merck & Co, 2008). The FUTURE 11 (2007) study is a phase three randomized, double-blind trial involving more than 12,000 women between the ages of 15 and 26 years. The women were assigned to receive either three doses of the HPV-6, -11, -16, -18 vaccine or a placebo to evaluate the quadrivalent for the prevention of high-grade cervical lesions associated with HPV-16 & HPV-18. The vaccine prevented 98% of HPV 16/18-related high-grade cervical lesions in women who had not been previously exposed to either HPV-16 or HPV-18 (FUTURE 11 Study Group, 2007). Although prevention of cervical cancer is the main goal of the HPV vaccine, it is important to note that it is highly unethical to use invasive cervical cancer as an end point (FUTURE 11 Study Group, 2007).

In Canada, the HPV vaccine is recommended and licensed for females between the ages of 9 and 26 years regardless of their previous HPV status (Public Health Agency of Canada, 2007). The most common side effects reported include swelling, pain and erythema at the injection site (Zimmerman, 2007). A recent study (Brotherton, Gold, Kemp, McIntyre, Burgess, & Campbell-Llyod, 2008) in New South Wales examined cases of anaphylaxis following the quadrivalent HPV vaccine. There were seven classified cases of anaphylaxis identified from 269,680 HPV vaccines administered, using the Brighton Case Definition (Brotherton et al., 2008). There were no cases of anaphylactic shock or casualties that occurred and five of the cases were reported after the first dose of the vaccine and two from the second dose (Brotherton et al.). Four of the cases received allergy skin-prick testing, which were negative for baker's yeast, polysorbate 80 (vaccine components) and the vaccines (cervarix, gardasil) (Brotherton et al.). The cases of anaphylaxis identified from this study are significantly higher than those identified in comparable school-based vaccination programs (Brotherton et al.). Brotherton et al.'s interpretation of these findings highlights that this could be a result of a number of factors: the allergenicity of the components of the vaccine, the enhanced passive adverse surveillance of vaccines or the current use of the Brighton case definition for anaphylaxis. Another potential factor is that from mid-adolescence, women have higher rates of anaphylaxis than males (Poulos, Waters, Correll, et al., 2007; Sheikh & Alves, 2001, as cited by Brotherton et al.). The small number of cases identified and other reports of anaphylaxis make the estimates imprecise and a misclassification of only one or two cases would substantially alter the estimates of fold differences (Brotherton et al.). In conclusion, WHO (2008, as cited by Brotherton) highlights that anaphylaxis is a rare event. This should not curtail the population-based vaccine programs. Further research is needed to report on the long-term effects of this vaccine and the research is still unclear as to whether these women will require a follow-up booster vaccine in the future (Public Health Agency of Canada, 2007).

The Canadian federal government announced in March of 2007 that 300 million dollars has been allocated to assist with the implementation of the vaccine across Canada (Canadian Cancer Society, 2007). Currently, in Ontario the vaccine is publicly

insured exclusively for young women in grade eight only (Cancer Care Ontario, 2007). In fall 2007, the provincial government announced a \$117-million investment over three years to provide HPV vaccines to these grade eight women exclusively on a volunteer basis (CCO, 2007). Therefore, for those women who do not fall under the current criteria, the vaccine will cost each individual approximately \$404 for a series of three vaccines (Comeau, 2007). It is important that the intended goals of the vaccination program be to vaccinate women who have not been exposed to the virus (Sideri & Mariani, 2008). However, there may also be a case for individual vaccination of women who fall outside the grade eight criteria (Sideri, 2008, as cited in Sideri & Mariani, 2008). Although the vaccine is available throughout Canada, due to the lack of universal coverage, it may not be feasible for all women to be vaccinated (Cain, Denny, & Ngan, 2007). For these reasons, we must continue to be cautious not to create further avenues for health inequalities between the rich and poor, as the research notes that up to 80% of cervical cancer occurs in the lower resource settings (Cain et al., 2007).

Vaccines are arguably the most cost-effective instruments in health care, with the first goal being to protect the individual and the second being to protect the community and cause a reduction in morbidity and mortality (Kane, 2006). There have been few studies looking at the cost-effectiveness of the HPV vaccine on the under-resourced health care systems. However, a model-based analysis suggests that, indeed, implementing a vaccine combined with a screening program for HPV vaccine that allows for a later age of screening and with less frequent screening once immunity has been established will likely be a cost effective use of the health care resources (Goldie, Kohli, Grima, Weinstein, Wright, Bosch, Franco, et al., 2004). Furthermore, a recent meta-analysis stresses that a few studies are likely to have underestimated the cost-effectiveness of a HPV vaccine program (Sanders & Taira, 2003; Kulasingam & Myers, 2003; Goldie, Kohli, & Grima, 2004, as cited in Newall et al., 2007). It must be noted that most of these reviews were conducted in developed countries where established screening programs already exist (Newall et al., 2007) and more research is needed in developing countries where screening programs are not always utilized.

The nurse's role in education

Success of vaccine programs will strongly depend on effectiveness of the vaccine, which has been shown in the case of the quadrivalent (Canadian Communicable Disease Report, 2007), and the coverage of immunization obtained or the public's acceptance of the vaccine (Moreira et al., 2006). This is where the oncology nurse's role of health care education and advocacy is imperative. A key responsibility of the oncology nurse is to educate individuals, families and communities with the relevant and accurate information in order for them to make an informed choice that is right for them. The Canadian Association of Nurses of Oncology (2001) acknowledges that individuals have the right to self-determination, the right to access information and the right to make decisions about their health. In keeping abreast of these rights, it is essential that appropriate and accurate information that allows for and supports informed decisions around HPV and the vaccine is provided to women, families and communities.

This area of health promotion is a key element in the nurse's role (Casey, 2007). The World Health Organization (1986, as cited by Casey, 2007) defines health promotion as the process of enabling people to increase control over their health and to improve their health. The focus here is on the health and empowerment of the individual, family and community (Naidoo & Wills, 1998, as cited in Casey, 2007). This could translate into

such interventions and activities as providing culturally sensitive and relevant information (at a fifth-grade reading level) to women and their families or collaborating with community leaders and other organizations in order to reach out with education and information to diverse populations (Gullatte, 2001).

Without proper education and universal coverage, complete acceptance and immunization will be difficult to obtain. Moreira et al. (2006) reported on a cross-sectional study, which assessed the attitude and knowledge of uninsured women in Brazil. They found that 69% of the women were unaware that HPV may lead to cervical cancer. However, once educated, 72% of women decided to enroll in the HPV vaccine trial. These findings were also established in Canada where only 13% of adolescents reported to have heard of HPV (Dell et al., 2000 as cited by Zimet, 2006). This clearly indicates the need for oncology nurses to take the lead on education surrounding the HPV vaccine and its role in prevention of cervical cancer in these young women.

Furthermore, Moreira et al.'s (2006) study established that 89% of women reported that a recommendation from a physician would positively contribute to the acceptance of the vaccine. This places a considerable emphasis on the importance of training health care providers around the vaccine, as the lack of education, policy and provider education can severely hinder one's ability to advocate for the vaccine (Cain et al., 2007). This is emphasized in a study that surveyed 207 Fellows of the American College of Obstetricians and Gynecologists with 13 vaccine scenarios to evaluate their HPV acceptability. It was noted that doctors were reluctant to recommend the vaccine to patients younger than 13 years (Raley, Followwill, Zimet, & Ault, 2004, as cited by Zimet, 2006). These findings were similar to a study that examined pediatric nurse practitioners' attitudes to recommending a vaccine for a sexually transmitted disease (Mays & Zimet, 2004, as cited by Zimet, 2006). In order to see a reduction in and/or elimination of HPV-16 and HPV-18, females should be immunized prior to first sexual activity to maximize vaccine efficacy (Kahn & Bernstein, 2005) and provide the best opportunity to prevent HPV infections (Sherman et al., 1998). One study has demonstrated that 48 months after the initial sexual encounter, more than 50% of adolescent women had developed an HPV infection (Winer et al., 2003, as cited by Dunne & Markowitz, 2006). According to a national survey of adolescents in the United States, 7% reported being sexually active before the age of 13 (Grunbaum, Kann, Kinchen, et al., 2004, as cited by Saslow et al., 2007) and 24% of females reported having sexual intercourse by the age of 15 (Amba et al., 2004, as cited by Saslow et al., 2007). A Canadian Community Health Survey (CCHS, 2003, as cited by Canada Communicable Disease Report, 2007), asked participants to indicate whether they had sexual intercourse and at what age, specified that 1.1% of females indicated they had sexual intercourse by the age of 12, 3.3% by the age of 13, and 9.0% by the age of 14. In 2007, Statistics Canada estimated there were approximately one million females in Canada between the ages of 10 and 14. Therefore, based on these results, approximately 90,000 female adolescents are sexually active. It is evident that if vaccine efficacy and acceptance is to occur, then oncology health care providers must be confident and knowledgeable in educating and recommending the vaccine to its target population.

International agenda

During the last 50 years, cervical screening programs in developed countries, such as Canada, have drastically decreased the morbidity and mortality rates for cervical cancer. However, in a vast majority of developing countries, implementation of effective screening methods has yet to reduce these rates (Franco

& Harper, 2005). There are direct correlations between investments in screening programs and the declines in cervical cancer (Cain et al., 2007). With the addition of the HPV vaccine to screening, the disease can be largely prevented (Cain et al.). The investment in the vaccine is urgent, especially where cervical cancer is the leading cause of death, as in many of the low-resource countries where widespread screening is unavailable (Saslow et al., 2007). The highest risk areas are Sub-Saharan Africa, Central and Latin America and parts of Asia (Plummer & Franceschi, 2002) where cervical cancer has exceeded breast cancer as the leading cancer in women (Parkin et al., 2005). There are approximately 510,000 cases of cervical cancer a year (Saslow et al., 2007) with 80% of these cases in developing countries (Parkin et al., 1984, as cited by De Vuyst, Steyaert, Renterghem, Claeys, Muchiri, Sitati, et al., 2003).

Unfortunately, the time gap between the use of current treatment measures in the industrial world and the developing world often leads to many cohorts of people not receiving the treatment or, in this instance the vaccine, that they need (Kane, 2006). This lack of access to the HPV vaccine (primary prevention) or even screening (secondary prevention) in underdeveloped countries represents a failure to address international goals and targets set in relation to women's health issues (Cain et al., 2007). Cain et al. have argued that the basic human rights of these women are being violated. It is the responsibility of oncology nurses worldwide to explore, advocate, educate and research new ways to make the vaccine and cervical cancer screening accessible for women from all walks of life.

Vaccine potential

This vaccine provides tremendous hope for prevention of cervical and possibly other cancers. It is unclear as to the other positive effects the HPV vaccine may have on cancers such as anal, penis and vulvar (Cogliano et al., 2005, as cited by Arbyn & Dillner, 2007). There is much still to be determined. It is also important to recognize the benefits that this vaccine may have on the prevention of women diagnosed with pre-cancerous lesions of the cervix. In Ontario in 2000, approximately 54,000 women were diagnosed with an abnormal pap test, with many requiring further follow-up for these abnormalities (Cancer Care Ontario, 2002).

It is vital to note that the tumour risk would decrease drastically, but will not be eliminated entirely (Sherman et al., 1998). Therefore, screening must continue for both vaccinated and

unvaccinated women because the vaccine is not 100% effective in all scenarios, as it only protects for the high-risk HPV-16 and HPV-18. In addition, some women are already affected with an HPV infection (Saslow et al., 2007). It is also important to realize, however, that this vaccine will not have an impact on cervical cancer rates until the girls reach the median age of 48 years (Ries, Harkins, Krapcho, et al., 2006, as cited by Saslow et al., 2007). There is still an obligation to address, provide, advocate and educate women nationally and internationally surrounding cervical cancer control services (Cain et al., 2007). It is clear that investment in this area of women's health is pressing and essential in order to reduce morbidity and mortality, as well as to eventually prevent cervical cancer in future generations (Cain et al.).

Further investigations into education focusing on women who already have a diagnosis of HPV is needed and education on the impact the vaccine will have on the prevention of CIN and cervical cancer is also required. As Goldie et al. (2004) suggest, more research also is needed to uncover a better understanding of the persistent cases of high-risk HPV in women who are not vaccinated and those that go on to develop cancer.

Summary

Oncology nurses are in a unique role to observe firsthand the effects the implementation of the HPV vaccine will have on women across the world. It is within this position that nurses can play a large role in cancer control and prevention by educating and advocating for and on behalf of individuals, families and communities around HPV, its links with cancer and the HPV vaccine. Nurses can strive to ensure that patients, women, communities and countries have the most appropriate care, education and treatment surrounding this life-threatening disease. Cervical cancer is exclusive to women and, as the research highlighted, very few women have identified the link between HPV and cervical cancer. Nurses are in a privileged and essential role of teaching and educating this unique population about HPV and the HPV vaccine in order to make the choice that is right for them. It is also critical that information about HPV, the HPV vaccine and its implications is advocated and shared with other health care providers. Furthermore, the limited availability and coverage of vaccine provides unique opportunities for nurses to create innovative approaches to advocate and research this under-invested and under-researched area of women's health in order to make the vaccine accessible for women around the world. 🌱

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