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### **HPV AND IMMUNIZATION**

Developed by Nia King and Dr. Kirk Leifso for PedsCases.com. July 22, 2021.

### Introduction

Hello, my name is Nia King and I am a third year medical student at Queen's University. This PedsCases podcast was developed with Dr. Kirk Leifso, a Pediatric Infectious Diseases Specialist and an Assistant Professor of Pediatrics at Queen's University. Today we are going to be exploring the human papilloma virus, or HPV, and it's vaccine.

### **Objectives**

Let's get started by reviewing our learning objectives for this podcast:

- 1) Describe the epidemiology and risk factors for the development of HPV;
- 2) Explore the health outcomes associated with HPV; and,
- 3) Discuss HPV-prevention strategies, including the HPV vaccine

## **Clinical Case**

Let's jump into our case. A nine-year-old boy and his father come into your practice for a well child visit. The father mentions that his twelve-year-old daughter just received a letter from school stating that her class will be receiving vaccines for cervical cancer next month, and he is wondering how it works, and if there is an equivalent vaccine for male-related cancers for his son. At the end of this podcast, we are going to discuss how you could approach this discussion.

#### **Introduction to HPV**

To start, let's dive into our first objective by exploring a brief overview of HPV. HPV, which stands for human papilloma virus, is a virus that is spread through physical contact. There are over 150 HPV genotypes, which can generally be divided into sexually transmitted and non-sexually transmitted types<sup>1,2</sup>. Today we will exclusively be discussing those that are sexually-transmitted, as these are targeted by the HPV vaccines. Sexually-transmitted HPV infections infect the anogenital region, oral cavity, and oropharynx<sup>1,2</sup>. HPV is not a notifiable condition in Canada<sup>2</sup>.

HPV is the most common viral sexually transmitted infection, or STI, in Canada: it is estimated that if not immunized, 75% of sexually active Canadians will have an HPV infection at some time<sup>1,2</sup>. It is readily transmissible between any sexual partners through direct skin or

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mucosal contact; this includes receptive and penetrative vaginal, anal, and oral sex, as well as non-penetrative sex<sup>1,2</sup>. It is important to note that transmission can occur from an asymptomatic individual<sup>2</sup>. It is estimated that intercourse with an infected partner will result in transmission of disease in two thirds of exposures<sup>3</sup>. It therefore makes sense that the main risk factor for HPV infection is a higher lifetime number of sexual partners.

Rarely, HPV can also be transmitted vertically to an infant exposed in the maternal genital tract<sup>1</sup>. This type of exposure can lead to a serious condition known as 'recurrent respiratory papillomatosis,' which results in recurrent benign tumours, or papillomas, within the respiratory tract<sup>1</sup>. Recurrent respiratory papillomatosis is rare and will not be the focus of this podcast. However, it is important to note that the HPV vaccination may prevent the development of this disease.

## Health outcomes

This leads us to our second objective, exploring HPV-related health outcomes. As mentioned earlier, there are over 150 types of HPV, of which approximately 40 can infect the anogenital tract<sup>1,2</sup>. Most HPV infections are asymptomatic, self-limiting, and resolve within 24 months without treatment, however in some people HPV infections can persist and lead to anogenital warts (also known as condyloma acuminata) and malignancies such as cervical, penile, anal, and oropharyngeal cancer<sup>1,2</sup>. Factors that may increase the risk of an HPV infection progressing to a negative health outcome include tobacco or cannabis use, immune suppression, and HIV infection<sup>1,2</sup>.

Different sexually-transmitted HPV types are associated with specific health outcomes<sup>2,4</sup>. For example, HPV types 6 and 11 are associated with anogenital warts, while types 16 and 18 are considered high-risk for the development of malignancies<sup>2</sup>. Persistent infection with a high-risk HPV type is the main cause of cervical precancerous and cancerous lesions, and also causes cancers of the vulva, vagina, penis, anus, mouth, and oropharynx<sup>1,2</sup>. Studies suggest that it takes approximately 10 to 15 years from the time of an initial high-risk HPV infection until a cancer develops<sup>1,2,5</sup>.

Anogenital warts typically present as multiple, asymmetrical growths on anogenital skin or mucous membranes; they vary in appearance from papular to cauliflower-like and they may fluctuate in size and number<sup>2</sup>. They may cause pruritis, local discharge, bleeding, and dyspareunia<sup>2</sup>. Anogenital warts typically resolve within 6 to 12 months, however in some people they may be diffuse and take up to 24 months to resolve.

Cervical cancer is the most common HPV-associated cancer and is typically asymptomatic<sup>2</sup>. Patients should therefore be counselled to follow their provincial or territorial guidelines for cervical cancer screening irrespective of their HPV immunization status<sup>2</sup>.

#### **Preventative measures**

For our third objective, let's review some HPV-prevention strategies. Fortunately, despite the widespread nature of HPV, precautions can be taken to lessen the risk of infection. As healthcare practitioners, when discussing STIs with adolescents, it is always important to educate on safe sexual practices. Abstinence is the only 100% effective way to prevent STIs, including HPV. Beyond abstinence, barrier contraception, including male and female condoms will not only reduce the risk of HPV transmission, but also decrease the risks of other STIs and unintended pregnancies<sup>2,4</sup>. Nevertheless, it is important to counsel patients that HPV can infect

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areas not covered by the condom, meaning that unlike some other STIs, condoms are not 100% effective in preventing HPV transmission<sup>4</sup>.

Consequently, patients can further protect themselves from HPV by getting vaccinated. Vaccines for the prevention of HPV have been approved in Canada since 2006. A bivalent, quadrivalent, and nonavalent vaccine are now authorized for use, each of which protects against a different number of HPV types<sup>1,4</sup>. To start, the bivalent vaccine protects against two HPV types, HPV-16 and HPV-18, which together are responsible for approximately 70% of all cervical cancers<sup>1,4</sup>. It has been approved for use in females aged 9 to 45 years<sup>1,4</sup>. The quadrivalent vaccine also protects against HPV-16 and 18, but adds protection against HPV-6 and 11 which cause approximately 90% of anogenital warts<sup>1,4</sup>. The nonavalent vaccine was approved most recently, and adds protection against another five HPV types (31, 33, 45, 52, and 58), which are responsible for 14% of anogenital cancers<sup>1</sup>. Both the quadrivalent and nonavalent vaccines are approved for use in females aged 9-45 years and males aged 9-26 years<sup>1,4</sup>. Because the vaccines prevent HPV infection, which is a necessary first step in cancer development, the vaccines can effectively prevent the development of cancer associated with specific HPV types<sup>1</sup>. When considering which vaccine to use, the Canadian Pediatric Society states that it would be prudent to ensure maximal coverage by using the nonavalent vaccine<sup>1</sup>.

These vaccines have demonstrated between 90 and 100% efficacy in preventing the types of HPV infection for which they are indicated<sup>6</sup>. However, they may not cure an existing HPV infection or associated health outcome<sup>6</sup>. Consequently, the vaccines have a maximum benefit if they are administered before acquisition of any HPV infection<sup>1,6</sup>. Nevertheless, if a patient is already infected with one HPV type, the vaccine will still protect against the other types in the vaccine; consequently, the vaccine should still be recommended to individuals who have previously had anogenital warts or an HPV-related cancer<sup>6</sup>.

Because infection can occur with the onset of any sexual touching, HPV vaccines are most beneficial if youth are vaccinated prior to their first sexual relationship<sup>1,6</sup>. The Canadian Pediatric Society states that nonavalent vaccine should be administered routinely to all youth between the ages of 9 and 13 years<sup>1</sup>. All provinces and territories have therefore implemented publicly funded school-based HPV immunization programs for both sexes<sup>1,7</sup>. The timing of the program varies between grades 4 and 7 depending on the province or territory<sup>1,7</sup>. Some provinces also offer time-limited catch-up programs for children who missed the vaccine at a younger age<sup>1,7</sup>. However, in other provinces and territories, if a child is not vaccinated at school, yet wants the vaccine, they may need to purchase the vaccine out of pocket<sup>8</sup>. This can cost between \$300 and \$500, which may be prohibitive especially for individuals without private insurance<sup>8</sup>. Thus, the Canadian Pediatric Society urges physicians to advocate for funding and implementation of a universal HPV vaccine program, regardless of when youth choose to be vaccinated<sup>1</sup>. Even though the vaccines are provided within a school-based program, the Canadian Pediatric Society recommends that physicians counsel patients and families about the HPV vaccine at well-child visits<sup>1</sup>.

The vaccines are given intramuscularly and can be given simultaneously with other age appropriate vaccines at different injection sites, using separate needles and syringes<sup>6</sup>. It is suggested that the HPV vaccine be administered after other vaccines as it is known to cause more injection pain<sup>6</sup>. For healthy, immunocompetent children aged 9 to 14, a two-dose schedule is used; the doses must be given at least 6 months apart<sup>1,6</sup>. For immunocompromised patients, or those 15 and older, a three-dose schedule is used over 6 months<sup>1,6</sup>. The duration of protection following HPV vaccination is not known, however research suggests that there is no evidence of waning protection for at least 10 years; studies are ongoing to determine if a booster dose is needed for continued protection<sup>4</sup>. All three vaccines are very safe, with the most common adverse events being pain at the site of vaccination, swelling, or redness<sup>1</sup>. In one in

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one million cases, serious allergic reactions may occur<sup>1,9</sup>. The HPV vaccines are only contraindicated in persons with a history of anaphylaxis after previous administration of the vaccine and in persons with proven immediate or anaphylactic hypersensitivity to any component of the vaccine or its container<sup>6</sup>. The HPV vaccines are not given during pregnancy, and studies on the safety and efficacy in this population are ongoing<sup>6</sup>.

## Screening and treatment

Guidelines on HPV-related screening and treatment are outside the scope of this podcast. However, it is important to counsel patients that HPV immunization does not protect against all cancer types, therefore cervical cancer screening guidelines should continue to be followed regardless of immunization status<sup>4</sup>.

## Specific populations

There are a couple populations that should be specifically mentioned when discussing HPV. Firstly, in children over the age of 18 months presenting with anogenital warts, sexual abuse should be considered as a possible cause and referral to a specialist with expertise in this area should be considered<sup>2</sup>. Secondly, while not recommended at a population level, individuals who were fully vaccinated with the bivalent or quadrivalent vaccines may wish to be reimmunized with the nonavalent vaccine to gain added protection<sup>1</sup>. If a patient requests this, the vaccine can be administered on a catch-up schedule<sup>1</sup>.

# Clinical case

Let's get back to our case with the father of the nine-year-old boy asking about his daughter's vaccine for cervical cancer. In this case, it would be important to educate the father about the pathogenesis of HPV-related cancers and how a persistent HPV infection is the major risk factor. Therefore, by immunizing against several HPV-types, ideally prior to the initiation of sexual activity, his daughter would be immune to the HPV types that cause over 90% of cervical cancers. It would also be important to discuss that HPV infections are not only responsible for cervical cancer, but can also cause several other negative outcomes in both sexes, such as anogenital warts and other types of cancer. Therefore, it is recommended that his son also receive the vaccination within the school-based program. In getting vaccinated, his son would not only reduce his own risk of infection, but would also reduce the risk of transmitting an HPV infection to a future sexual partner. As your patient matures, additional HPV and STI preventative counselling should include education on safe sex practices and using barrier protection methods.

# <u>Review</u>

That concludes our PedsCases podcast on HPV and vaccination. Let's go over a brief review of main points from this podcast:

1) HPV is the most common viral STI in Canada and is readily transmissible through direct skin or mucosal contact<sup>1,2</sup>

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- 2) While most HPV infections are asymptomatic and self-limiting, persistent HPV infections can lead to anogenital warts and several malignancies including cervical, penile, anal, and oropharyngeal cancer<sup>1,2</sup>
- 3) Condoms are not 100% effective in preventing HPV infection<sup>4</sup>
- 4) There are three HPV vaccines available in Canada, and the Canadian Pediatric Society states that the nonavalent vaccine should be administered routinely to all youth between the age of 9 to 13 years<sup>1</sup>

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