

**NWX-DISEASE CONTROL & PREVENTI**

**Moderator: Dale Babcock  
September 30, 2015  
11:00 am CT**

Coordinator: Welcome and thank you for standing by. At this time, all participants are in a listen-only mode. During the question and answer session, you may press star and then one on your touchtone phone if you would like to ask a question.

Today's conference is being recorded. If you have any objections, you may disconnect at this time. I'd now like to turn the meeting over to Dr. Andrew Kroger. You may begin.

Dr. Andrew Kroger: Thank you very much. Welcome to Current Issues in Immunization Net Conferences. I'm Andrew Kroger. I'm a medical officer in the Immunizations Services Division of the National Center for Immunization and Respiratory Diseases -- or NCIRD -- at the CDC. And I'll be the moderator for today's session.

To participate in today's program, you need a telephone connection and a separate internet connection.

The learning objectives for the session are: 1 -- to describe an emerging immunization issue; 2 -- be able to list a recent immunization

recommendation made by the Advisory Committee on immunization Practices, or ACIP; 3 -- to locate resources relevant to current immunization practice; and 4 -- to obtain, assess, and apply patient information to determine the need for immunization.

It is September 30, 2015 and today Ms. JoEllen Wolicki, Nurse Educator in the Communication and Education Branch in the Immunization Services Division in NCIRD, CDC will discuss HPV, which is an acronym for human papillomavirus, as presented in the CDC textbook Epidemiology and Prevention of Vaccine-Preventable Diseases; also known as the Pink Book, whose thirteenth edition was published this year.

A question and answer session will follow today's presentation.

Please make a note of the following information. If you have technical trouble, please dial star, zero on your telephone. If you'd like to ask a question when we get to that segment, please press star, one on the phone.

Continuing education, or CE, credit is available only through the CDC ATSDR training and continuing education online system at [www2a.cdc.gov/tceonline/](http://www2a.cdc.gov/tceonline/). CE credit for the session today expires on November 2, 2015.

CDC, our planners, and our presenters wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

Presentations will not include any discussion of the unlabeled use of a product or a product under investigational use, with the exception of Ms. Wolicki's discussion of the use of HPV vaccine in a manner recommended by the

Advisory Committee on Immunization Practices but not approved by the Food and Drug Administration.

CDC does not accept any commercial support. So now, I will turn the microphone over to Ms. Wolicki. You may begin.

JoEllen Wolicki: Thank you Dr. Kroger. Today I will discuss human papillomavirus disease and HPV vaccines, including the new, recently licensed nine-valent vaccine. This chapter begins on page 175 of the Pink Book, and these slides will be posted next week.

Human papillomavirus is the most common sexually transmitted infection in the United States. Human papillomaviruses are small, double-stranded DNA viruses that infect the epithelium. More than 150 HPV types have been identified. The relationship of cervical cancer and sexual behavior was suspected for more than 100 years and was established by epidemiologic studies in the 1960s. In the early 1980s, cervical cancer cells were demonstrated to contain HPV DNA. Epidemiologic studies showing a consistent association between HPV and cervical cancer were published in the 1990s. The first vaccine to prevent infection was licensed in 2006.

Most people with HPV do not develop symptoms or health problems from it. In 90% of cases, the body's immune system clears HPV naturally within two years; but sometimes HPV infections are not cleared and can cause cervical cancer and other less common but serious cancers including cancers of the vulva, vagina, penis, anus, and oropharynx; genital warts; and rarely warts in the throat, a condition called recurrent respiratory papillomatosis, or RRP. –There is no way to know who will go on to develop cancer or other health problems.

A small proportion of infected persons become persistently infected. Persistent infection is the most important risk factor for the development of cervical cancer precursor lesions. The most common clinically significant manifestations of persistent HPV is cervical intraepithelial neoplasia, or CIN. Within a few years of infection, low-grade CIN or CIN1 may develop, which may resolve spontaneously and the infection clear. Persistent HPV infections, however, may progress directly to high grade CIN, called CIN2 or CIN3. High grade abnormalities are at risk of progression to cancer. A small proportion of high-grade abnormalities spontaneously regress. If left undetected and untreated, years or decades later CIN2 or 3 can progress to cervical cancer. Infection with one type of HPV does not prevent infection with another type. Of persons infected with mucosal HPV five to thirty percent are infected with multiple types of the virus.

As noted earlier, most HPV infections are asymptomatic and result in no clinical disease. Clinical manifestations of HPV infection are outlined on this slide and include anogenital warts, RRP, cervical cancer precursors, and cancers including cervical, anal, vaginal, vulvar, penile, and oropharyngeal cancers.

This slide outlines the average number of cancers probably caused by HPV per year in the US. A large majority of cancers caused by HPV are brought about by one or two types -- HPV 16 or HPV 18. Together, these types cause about 22,000 cases of cancer in the United States each year. An HPV-associated cancer is a cancer that is diagnosed in a part of the body where HPV is often found, seen in the first column of the table. These parts of the body include the cervix, anus, penis, vagina, vulva, and oropharynx, or the back of the throat including the base of the tongue and tonsils. An HPV-attributable cancer is a cancer that is probably caused by HPV, shown in the

second and third columns of the table. We see here the disease burden related to HPV infection.

HPV infection occurs throughout the world. Humans are the only natural reservoir of HPV. It is transmitted by direct contact, usually sexual, with an infected person, even when the infected person has no signs or symptoms. It is important to note sexual intercourse is not required to acquire HPV infection. HPV is presumably communicable during the acute infection and during persistent infection. This issue is difficult to study because of the inability to culture the virus. Communicability can be presumed to be high because of the large number of new infections estimated to occur each year.

Studies of newly acquired HPV infection demonstrate that infection occurs soon after onset of sexual activity. In a prospective study of college women, the cumulative incidence of infection was 40% by twenty-four months after sexual intercourse and greater than 50% after four years.

As noted earlier, HPV infection is believed to be the most common sexually transmitted infection in the United States. An estimated seventy-nine million persons are infected and an estimated fourteen million new HPV infections occur annually, with half of these in persons fifteen to twenty-four years of age. About \$8 billion are spent each year to manage the outcomes of HPV infections, primarily for the management of abnormal cervical cytology and the treatment of cervical neoplasia. This exceeds the economic burden of any other sexually transmitted infection except human immunodeficiency virus.

Most cases and deaths from cervical cancer can be prevented through detection of precancerous cervical changes by a Pap test. Since 2012, all organizations have recommended that screening should begin at age twenty-one years.

While there are slight differences in other aspects of the recommendations, all groups recommend screening in women aged twenty-one to sixty-five years with a Pap test every three years.

For women aged thirty to sixty-five years who want to lengthen the screening interval, screening can be done with a combination Pap test and HPV co-testing every five years. HPV vaccination does not eliminate the need for continued Pap test screening since cervical cancer can be caused by HPV types not included in the vaccine.

Three HPV vaccines are licensed in the United States. These vaccines are noninfectious subunit vaccines. The antigen for the vaccine is the L1 protein of HPV, produced by using recombinant DNA technology. L1 proteins self-assemble into noninfectious, non-oncogenic units called virus-like particles, abbreviated VLP.

This table shown on the slide outlines the three vaccines currently available in the United States. In the first row, you see the three different vaccines with their brand names. And please note the new recommended ACIP abbreviations for each of the different vaccines. The bivalent vaccine is licensed for females nine through twenty-five years of age. The quadrivalent vaccine is licensed for females and males nine to twenty-six years of age. The recently licensed nine-valent vaccine is licensed for females nine through twenty-six years of age and males nine through fifteen years of age. All three vaccines protect against type 16 and 18. Quadrivalent vaccine provides protections to type 6 and 11 in addition to 16 and 18. The nine-valent vaccine is directed against the same four types as the quadrivalent -- 6, 11, 16, and 18 -- and five additional cancer-causing types. The quadrivalent and nine-valent vaccine are produced by the same manufacturer.

HPV vaccines are intended to prevent cancer, primarily cervical cancers, but cancer can take decades to develop following an HPV infection. Clinical trials using cancer as the endpoint would take many years to complete. So a clinical trial using cancer as the outcome is not very practical. Instead, other endpoints were used to determine vaccine efficacy, such as persistent HPV infection and cancer precursors. Bivalent and quadrivalent vaccines were studied in large efficacy and safety trials that included more than 15,000 females fifteen through twenty-six years of age. Half of the participants received vaccine; the other half received a placebo. Both vaccines were found to be highly effective. The vaccine efficacy was more than 95% reduction in cervical cancer precursors among the vaccinated group as compared to the unvaccinated group. Among females, efficacy against external genital lesions was 99% for the quadrivalent vaccine. Although high efficacy among persons without evidence of infection with vaccine HPV types was demonstrated in clinical trials for both HPV vaccines, there was no evidence of vaccine effectiveness or any therapeutic effect on existing infection or disease. Participants infected with one or more vaccine HPV type prior to vaccination were protected against disease caused by the other vaccine types. Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types.

Nine-valent HPV, or Gardasil-9, was licensed in the United States in December 2014. As noted earlier, it is FDA approved for use in females nine through twenty-six years of age and males nine through fifteen years of age. Males sixteen through twenty-six years were not part of the original submission to FDA. Recently, data for males sixteen through twenty-six years of age has been submitted to the FDA. In addition to the HPV types in the quadrivalent vaccine, nine-valent vaccine targets an additional five types -- 31, 33, 45, 52, and 58 -- which are shown here on the slide in yellow.

Nine-valent HPV has been shown to have non-inferior immunogenicity to four-valent HPV for all serotypes and age groups, and approximately 95% effective against the five additional HPV types in the vaccine. In the United States, approximately 64% of invasive HPV-associated cancers are attributable to the HPV 16 or 18. All three vaccines protect against this type. 11% of HPV-associated cancers are attributable to the five additional types in nine-valent HPV. The five additional types account for 14% of HPV-associated cancers in females and about 4% of HPV-associated cancers in males. For cervical pre-cancer lesions -- or CIN2 or worse -- approximately 50% are caused by HPV 16 and 18, and 25% the five other HPV types. 9v HPV can be administered at the same clinical visit as other routine vaccines administered to adolescents -- Tdap and Men-ACWY, for example. The safety profile is similar to 4vHPV. The duration of protection following HPV vaccine is not known. A subset of participants who have received bivalent and quadrivalent vaccine have been followed for many years with no evidence of waning protection. Study populations including those that have received nine-valent HPV will continue to be followed for any evidence of waning immunity.

This is the childhood immunization schedule. CDC consolidated all of the HPV2 and HPV4 ACIP recommendations, and updated safety data in August 2014. Then, in March of 2015, CDC published new recommendations for the use of nine-valent HPV vaccine. HPV is highlighted on this schedule by the red box.

This is the adult immunization schedule. HPV immunization recommendations span both schedules. This schedule shows the adult immunization schedule age-related figure. HPV vaccine is highlighted by the red text box.

This slide shows Figure 2 of the 2014 adult immunization schedule, those at increased risk for disease, and immunization recommendations. Again, HPV is highlighted by a red box. We all know that the figures are very nice and easy to read, but the footnotes contain much more information that can be included in the figure. And of note - because HPV9 was approved for use this year, after the schedules were published, information about 9V HPV is not included in the footnotes of this year's schedule, but will be included in next year's schedule.

And here are the updated ACIP recommendations in detail. ACIP recommends routine vaccination at eleven to twelve years of age for boys and girls. The vaccination series can be started beginning at age nine years. Vaccination is also recommended for females aged thirteen through twenty-six years and for males aged thirteen through twenty-one years who have not been vaccinated previously or have not completed the three-dose series. Males age twenty-two through twenty-six may be vaccinated. Vaccination is recommended for males - for men who have sex with men and immune-compromised men, including those with HIV infection through age twenty-six. If females or males reach age twenty-seven before the vaccination series is complete, the second or third dose of the vaccine can be administered to complete the vaccination series. Females can be vaccinated with any of the three vaccine products. Males should be vaccinated with the quadrivalent or nine-valent vaccines. At the time of the first application to FDA, 9vHPV trials in males sixteen through twenty-six years had not been completed. Immunogenicity data in sixteen through twenty-six year olds are now available and were reviewed by ACIP. These data have now been submitted to the FDA. When ACIP deliberated on 9vHPV, they recommended use of 9vHPV in the currently recommended age group, including those for males

sixteen through twenty-six years of age. So this recommendation for males older than fifteen is an ACIP off-label recommendation.

Regardless of the HPV product used, the schedule is the same. The second dose should be administered one to two months after the first dose, and the third dose six months after the first dose. The minimum interval between the first and second doses of HPV vaccine is four weeks. The minimum recommended interval between the second and third dose of vaccine is twelve weeks. The minimum interval between the first and third dose is twenty-four weeks.

Following an accelerated schedule is not recommended. Accelerated schedules can be used to catch persons up that are lagging.. But once they have been caught up, the routine schedule should be followed.

There is one additional HPV vaccine interval issue. ACIP has not defined a maximum interval between HPV doses. If the vaccine schedule is interrupted and the interval between doses is longer than recommended, you should just continue the series where it was interrupted. It is not necessary to add doses or restart the series because of an extended interval between doses. Just pick up where the series left off and complete the needed doses.

HPV vaccine should be administered or can be administered at the same visit as other age-appropriate vaccines. And this was mentioned earlier on an earlier slide. Administering all indicated vaccines at the single visit increases the likelihood that adolescents and young adults who receive each of the vaccines on schedule and when they're needed. HPV vaccine is an IM injection. Pre-vaccination testing such as Pap tests, screening for high risk HPV DNA, type-specific HPV tests or HPV antibody, or pregnancy testing is not needed or recommended to determine if HPV vaccine can be

administered. Patients should be advised the vaccine will not have a therapeutic effect on existing HPV infection, genital warts, or cervical lesions. And it's also important to note that women should be instructed that HPV vaccination does not mean that they should not get regular Pap tests. Pap tests and cervical screening are still recommended, as we know that there are cervical cancers caused by HPV types that are not included in any of the vaccines.

There are no data on the schedules that include multiple products or different products, or what we sometimes refer to as a mixed product series. The response to type 16 and 18 are likely to be similar when different products or multiple products are used to complete the series. Protection against types other than 16 and 18 is probably reduced if fewer than three doses of quadrivalent or nine-valent vaccine is received. ACIP recommends providers use the same products for all three doses whenever possible.

ACIP recognizes that providers may not know or have the product that was previously administered. If providers do not know or have the previously administered product available, or are transitioning to 9vHPV, ACIP recommends providers administer the product they have available based on the product indications. Females may receive any of the three HPV products and males should only receive the quadrivalent or nine-valent HPV vaccines. And this is an ACIP off-label recommendation.

The HPV workgroup recognized that many questions will come up during this transition period and developed supplemental information and guidance for providers, in addition to the published ACIP nine-valent vaccine recommendations that were published in the MMWR. So they identified other clinical areas where there may be additional questions or guidance needed for the use of nine-valent HPV. This FAQ document is posted on the ACIP

webpage. I recommend that you share this helpful document with staff. I know that I find it very helpful when answering questions about nine-valent vaccine and its use.

There are a variety of what ACIP call “special situations” for HPV vaccine. Vaccine can be administered to females twenty-six years of age or younger with abnormal Pap tests or equivocal Pap tests, positive HPV DNA tests -- meaning they’re currently infected -- or those with genital warts.

Remember, as earlier, even though it will not treat the existing infection, they will mount a response to the vaccine types that they have not been exposed to.

Remember, as noted earlier, these women should be informed that the vaccine will have no effect on existing disease or infection. Females twenty-six years of age or younger who are breastfeeding may be vaccinated. HPV is an inactivated vaccine, so immune-compromised person for whom vaccination is recommended may be vaccinated. And this includes persons with HIV.

HPV vaccine should not be administered to persons with a history of severe allergic reaction to a vaccine component or following a prior dose. HPV4 is contraindicated with persons with a history of severe allergy to yeast. Anaphylactic allergy to latex is a contraindication to the bivalent HPV vaccine because latex is included in the tip cap for the prefilled or the manufacturer-filled syringes.

A moderate or severe acute illness is a precaution to vaccination, and vaccination to be deferred until symptoms of the acute illness improve. A minor acute illness like diarrhea or a mild upper respiratory tract infection with or without a fever is not a reason to defer vaccination.

Although HPV is an inactivated subunit vaccine, ACIP prefers a conservative approach to vaccination of pregnant women. The vaccine has not been causally associated with adverse pregnancy outcomes or with adverse effects on the developing fetus. The data on vaccination during pregnancy are limited. HPV is not recommended for use during pregnancy. If a woman is found to be pregnant after initiating the vaccination series, completion of the series should be delayed until after the pregnancy. If a vaccine dose was inadvertently administered during pregnancy, there is no indication for medical intervention. The vaccine series should just be stopped and completed after the pregnancy. A pregnancy registry has been established for 9vHPV. Also of note, the bivalent registry was closed earlier this year with concurrence from FDA. And the quadrivalent vaccine pregnancy registry was closed in 2013. Vaccination during pregnancy with any of the three vaccine products can be reported to the respective manufacturer and to the Vaccine Adverse Event Reporting System, or VAERS.

The most common adverse event reporting during clinical trials for HPV vaccines were local reactions. These included pain, redness, or swelling at the injection site. Local reactions generally increase in frequency with subsequent doses. A similar proportion of placebo recipients reported an elevated temperature as those that received the vaccine. However, reports of fever did not increase significantly with subsequent doses. A variety of systemic adverse reactions were reported by vaccine recipients, including nausea, dizziness, myalgia, and malaise. No serious adverse events have been associated with HPV vaccination based on monitoring by CDC and the Food and Drug Administration, or FDA.

Syncope after vaccination has been reported among adolescents who received HPV and other vaccines recommended for this age group. 70% of the fainting episodes occurred within fifteen minutes of vaccination. Recipients should be

seated during vaccine administration and ACIP recommends clinicians should consider observing patients seated for fifteen minutes after vaccination.

And although it does indicate on the slide that most of the increase was noted among females eleven to eighteen years of age, males have been known to faint also after vaccination.

Only local reactions occurred more frequently among vaccine recipients than those among placebo recipients. Serious reactions following an HPV vaccine have not been reported. Syncope precautions should be observed when vaccinating all adolescents and young adults, and monitoring of this will continue.

All HPV vaccines should be stored in the refrigerator between thirty-five and forty-six degrees Fahrenheit, or two to eight degrees Celsius. HPV vaccine should be protected from light and stored in the original packaging, as we recommend for all other vaccines.

I'd like to turn now to talk a little bit about our immunization rates and how well we're doing vaccinating against - with HPV vaccine. Despite increases, coverage estimates for HPV vaccine or vaccination have remained low in 2014 and continue to lag behind rates for Tdap and quadrivalent meningococcal conjugate vaccines as noted in the National Immunization Survey for Teens.

Four out of ten adolescent girls and six out of ten adolescent boys haven't started the HPV vaccine series and are vulnerable to cancers caused by HPV infection. And this and more detailed information were recently published in an MMWR this past summer.

Unfortunately, I think the first thing that comes to mind with this vaccine is sex rather than cancer. This vaccine does not increase sexual activity among young people, but it does prevent cancer. There are twenty-six million girls under thirteen years of age in the United States. If none of them are vaccinated with HPV vaccine, it is estimated that more than 168,000 will develop cervical cancer and more than 54,000 will die from it over the course of their lives.

If we continue with vaccination rates around 30% for twelve year old girls, we will prevent 44,500 of these cases and about 14,600 deaths. Those numbers would increase to preventing over 98,000 cases and more than 31,000 deaths if we reached vaccination coverage rates of 80%. And as you can see in this last bullet, the cases and deaths each year that will remain while we remain at 30% coverage.

Talking about HPV vaccine during a healthcare encounter is very important to vaccine acceptance. Several qualitative evaluations have been done regarding this issue. Common themes found around these studies show that the vaccine is often presented as optional whereas other vaccines indicated for adolescents were recommended. Also, some providers expressed mixed or negative opinions about the vaccine. When parents expressed reluctance to the vaccine, providers were hesitant to engage in a discussion. Finally, some providers shared the parents' view that it was acceptable to delay vaccination until the teen was older.

A strong recommendation for vaccination with HPV is very important. Recommend HPV when discussing other adolescent vaccines, making it part of your standard procedure. Consider standing orders if they are appropriate in you practice.

Implementing standing orders and sending out reminders and recalls for those who miss appointments have all been shown to increase immunization rates. We don't want to miss any opportunities to vaccinate.

Also, it's very important to talk about this with your staff and know that everybody is on board with the same messages and are saying the same things and giving the same strong recommendation to patients about vaccination with HPV vaccine.

The last bullet on this slide - I've included a web address where you can find many tools to help you with HPV vaccination when talking with your teens and parents and, again, also with staff. It's very important that everybody is providing the same consistent message to your patients.

Last but not least, we have updated the HPV web portal where all our materials can be found, and we encourage all of you to visit this site and make use of the multiple items there and educational materials for both staff and - which are outlined here on this slide where you see on the right tips and time-savers when talking to parents about HPV vaccine. It's a really good piece to use when discussing HPV vaccine messaging with your staff. And there's also patient educational materials on this site as well.

Included on this slide are some additional HPV resources that you can see here where we have links to the recommendations, the HPV infection Web page, the vaccination Web page, and then materials from the Immunization Action Coalition and the Children's Hospital of Philadelphia Vaccine Education Center.

And with that, I'd like to thank everyone for their time and listening today, and turn it back to Dr. Kroger.

Dr. Andrew Kroger: Thank you very much JoEllen. We're now going to move to a question and answer session. And while the queue fills, I'm going to give you some information about continuing education.

If you do have a question, please dial star, one to get in the queue for the operator. And please be sure your question is related to today's content.

We will have a recast of this program available on the internet on our Web site at [www.cdc.gov/vaccines](http://www.cdc.gov/vaccines)

[/ed/ciinc](http://ed/ciinc). This will be available the week of October 5, 2015. The slides will be there as will the audio portion and other resource information.

For continuing education credit, go to [www2a.cdc.gov/tceonline/](http://www2a.cdc.gov/tceonline/). The course number for this program is E as in Edward, C as in cat, 2064-093015. Note that 093015 is today's date and that this course number is specific to today's course. You will need this course number when completing CE requirements.

You also need the verification code, which is HPV13. And this also applies to today's program only. I'll repeat the verification code. HPV and then the numerals one and three with no space.

CE credit for this program expires November 2, 2015. I'll repeat this information at the end of the question and answer period as well. So let me now turn it over to the operator to please let us have our participants ask the questions they wish to ask. Operator?

Coordinator: Hello. Our first question comes from ().

(XXXXXXXXXX): Hi. Thank you for the presentation. Can you clarify vaccinating during pregnancy? I thought that one slide said that we can vaccinate pregnant women and the immunosuppressed, and then there were other slides about delaying vaccination during pregnancy.

JoEllen Wolicki: Hi (. Thank you for that really important question and the opportunity to clarify any confusion. Vaccination with HPV is not recommended during pregnancy.

What ACIP indicates is that if a pregnant woman has started the series before pregnancy or maybe a dose was inadvertently given during that time period when we're all - like maybe we think we might be pregnant but we're not sure that we're pregnant.

That early time period, the vaccine - nothing needs to be done but we stop the series and we wait and vaccinate after the pregnancy. So vaccination during pregnancy is not recommended.

(XXXXXX): Thank you.

JoEllen Wolicki: Does that help?

(XXXXXXXXXX): It does, thank you.

JoEllen Wolicki: Thanks.

Dr. Andrew Kroger: Thank you. We'll take the next question in the queue.

Coordinator: Our next question comes from Ms. (.

(XXXX): Yes. Thank you for the presentation. I have two questions. The first question is if you started the patient on HPV9, HPV quadrivalent for the first and second dose, what would you do? Would you give HPV9 as the third dose?

And the second question is - at our clinic here I've seen that when we were using the HPV quadrivalent, we had no problems. But now we've given the HPV9 and in a month we've seen two patients came back with syncope, complaining of syncope twenty-four hours after the vaccine. I just wanted to know if any studies were done on that.

And I have one more question. The third question is that if a patient is pregnant and you give the vaccine, do you have to report it to VAERS after? Do you report it in the registry if it's given and actually the patient is pregnant?

JoEllen Wolicki: Okay, Ms. (-. Thank you so much for those questions, and I'm going to repeat them to make sure that I got them right. I was writing but I was writing furiously while you were talking.

So I think your first question had to do with - if you have a person who started with either HPV4 or - I'm sorry. I'm using the old abbreviations. I'm still trying to train myself to use the new ones. Four-valent HPV or bivalent HPV - can you use the nine-valent HPV to complete this series?

And the answer is yes, you certainly can. We don't want you to miss an opportunity if you have nine-valent vaccine in your inventory, go ahead and use the nine-valent vaccine to complete the series.

Now your second question was about syncope twenty-four hours after vaccination. I have not heard of this and Dr. Kroger is looking at me with a blank expression also. I haven't heard about reports of this.

So we all know that adolescents faint, and usually when - and we know that because of this we have them sit down when we vaccinate them and we have them sit and wait for fifteen minutes afterwards just to make sure they're not going to fall on the way out the door and hit their heads or hurt themselves in some way.

Twenty-four hours after vaccination - I'm just not aware of any studies or any information that has been done about that. And I would suggest that you would report those to VAERS. And Dr. Kroger has something to add.

Dr. Andrew Kroger: In the vaccine safety data link study -- this is Dr. Kroger -- that was published in 2011, they looked at a number of conditions -- Guillain-Barré syndrome, stroke, appendicitis, seizures, allergic reactions, anaphylaxis, venous thromboembolism. And syncope was one of those conditions that was looked at, which - and VSD found no association with any of these conditions and HPV4 vaccine.

Now, I don't know the timing exactly of when that syncope occurred in that study, but what JoEllen mentioned is definitely correct that apart from anything that could be associated with the vaccine per se, syncope is something you've got to think about with every vaccine. IN that circumstance, syncope - right, during the administration period.

Ms. (xxxxxxx): Okay, during the administration period. I did report it.

JoEllen Wolicki: Thank you XXXXXXXX for reporting that to VAERS and taking the time. We really appreciate that you did that. And then your third question was about inadvertently administering vaccine to a pregnant woman and whether you should report. You can report that - I'm sorry.

Ms. (\_: So like to a registry or anything set up?

JoEllen Wolicki: Alright. When the vaccines first came out, the FDA and the manufacturers created a registry to report doses administered to pregnant women. And when they did enough data, they closed those registries.

So the registries for the bivalent vaccine and the registry for the quadrivalent vaccine have been closed. One closed this year. I think it was the bivalent one that closed earlier this year and the quadrivalent one has been closed for some time.

Nine-valent vaccine has its own registry now. So if nine-valent vaccine is administered to a pregnant woman, Merck has established a registry and they have a telephone number that you can report it to. You can call the manufacturer and you should report that to the manufacturer.

Whenever HPV vaccine is administered to a pregnant woman, you have the option of reporting it to VAERS. You don't have to, but you can. Does that make sense?

MsXXXX): So much. I do appreciate it.

Dr. Andrew Kroger: Thank you very much. We'll take the next question in the queue.

Coordinator: The next question comes from (XXXX).

XXXXXXXX): Hi. I have a follow-up question regarding pregnancy. It was stated in one of the slides that you did not have to screen for pregnancy, but you're saying you do not want the person to be pregnant and receive the vaccine. And secondly, under adolescents under eighteen, do they need a guardian or parent permission to receive the vaccination?

JoEllen Wolicki: Thank you for those questions. So you are right ACIP does not recommend routine administration of this vaccine during pregnancy, but it also does not recommend for pregnancy testing. This is inactivated vaccine. We don't recommend vaccination during pregnancy because we're very cautious with pregnant women, but both of the registries for the bivalent and the nine-valent vaccine have not shown anything that we need to be concerned about.

So we don't recommend that pregnancy testing. We're afraid that pregnancy testing prior to vaccination could be considered a barrier for some people. Now, your next question was about...

(XXXXXXXX): Permission.

JoEllen Wolicki: Oh, consent. Thank you. Dr. Kroger just wrote that down for me -- consent. Consent varies from state to state. You're certainly going to want to look into your state's laws, but there is no federal requirement for signed consent for vaccines.

(XXXXXXXX): Okay. Alright, thank you.

JoEllen Wolicki: But I really encourage you to contact your state immunization programs because we all know that these laws can vary from state to state.

(XXXXXX): Okay, thank you.

Dr. Andrew Kroger: Thank you. We'll take the next question.

Coordinator: The next one comes from ().

(XXXXXX): Hi, thank you. My question is to follow-up again on if you start with HPV4. I work at a college health center and so I understand that it's okay to continue with the 9V HPV. But what do you recommend? Are these women and guys going to get adequate coverage by switching? Or is it just better to give them three doses of the same type of vaccine?

JoEllen Wolicki: So thank you very much, ( for that question. And I know that is actually a really good way for me to put in another promo, for lack of a better word, for the supplemental information and guidance document that I talked about earlier, because it addresses a lot of these issues.

ACIP recommends that nine-valent vaccine be used to continue or complete a series that was started with a different HPV vaccine product. We don't want anybody to miss an opportunity. We know it's hard enough to get three doses into them, let alone if you can't give them what you have on hand.

Most of the cancers are caused by types 16 and 18, and those are in all three of the vaccines. So we're not - they're not so much worried about making sure that they're covered or protected against those types. Obviously, types that aren't contained in the vaccine -- so like for HPV2 is missing two of the types that are in four, four is missing five of the types that are in nine.

When you have those additional types and you don't have all three doses, you're not going to be able to say that they are fully protected because we do

not have data on mixed product series when you don't have all three of those vaccines given. Does that make sense?

(XXXXXX): Yes. Okay.

JoEllen Wolicki: Thank you for that question because we get that question a lot.

(XXXXXX): I know. Okay, thank you.

JoEllen Wolicki: It's a confusing time when you're transitioning between vaccines.

(XXXXXXXX): Okay. Thanks.

Dr. Andrew Kroger: Thank you. We'll take the next question.

Coordinator: The next question comes from ().

(XXXXXXXXXX): Yes, hello. I have two questions. One - when giving Tdap and MCV4 and HPV at the same time, it's recommended that you give them in different anatomical sites. How do you pair them up? Tdap with MCV or HPV with Tdap? What is your recommendation?

And my second question is can you explain the newborn-to-mom transmission of HPV? Is that during the acute infection or is there a carrier? That's it.

JoEllen Wolicki: Alright. So we're going to tag team your question. Thank you very much for them. I'm the nurse, so I'm going to answer the administration questions. And then Dr. Kroger is going to do your second question.

So when administering vaccines, we all know when we're administering injectable vaccines we need to give them in different anatomical sites. And when we're giving multiple vaccines, we want to make sure that those sites - while they can be in the same limb, we want to make sure that they're at least an inch apart so that we can differentiate between local reactions.

We know that Tdap and meningococcal conjugate vaccine can cause a fairly sore local reaction or a local site days later. ACIP does not have a preference as to where you place the vaccines. That becomes your personal practice preference how you do that.

One of the things that is noted about HPV vaccination, though, is HPV vaccine stings when you administer it. Anybody who's given HPV knows it stings pretty good and they'll look at you like you really gave them something that they felt.

So when you look at procedural pain strategies or strategies to decrease the actual injection pain itself, administering the vaccine that stings or hurts when you give it is one of the evidence-based strategies that will help them perceive less pain. So giving HPV vaccine last is going to help decrease the pain associated with those three injections for the adolescent.

Dr. Andrew Kroger: And then this is Dr. Kroger. With respect to current respiratory papillomas, yes, it's thought that transmission causing that condition is thought to occur based on acute infection late in pregnancy. So that's the answer to that question.

Okay, why don't we take one more question - one last question if there's one in the queue?

Coordinator: Our last question comes from ().

(XXXXXXXXXX) Hi. My question is more related to a term that you used at the beginning of the presentation where HPV is cleared. Can you elaborate on what that means? Does that mean that it's gone? Latent? Is it cured, or what does that mean?

JoEllen Wolicki: It means that - cleared means it's sort of gone, but I think that Dr. Kroger probably has a more technical explanation for it.

Dr. Andrew Kroger: It's a challenging distinction because HPV cannot be cultured. So for testing you're relying on either PCR tests, which are indicators of current infection, or there are serologies that can be done. But that doesn't distinguish as well between current and previous infection.

But it is thought that 91% of HPV infections do clear, in which the person is no longer considered to have current infection with HPV. But it is a complicated issue that I think - I recommend - there's a great discussion of this in the August 29, 2014 MMWR.

They talk about how you use laboratory diagnostics to do this type of epidemiology. So it is very complicated. And if you have any follow-up questions based on that, you can definitely send that to [Nipinfo@cdc.gov](mailto:Nipinfo@cdc.gov).

(XXXXXXXXXX): Thank you.

Dr. Andrew Kroger: Thank you. Well thank you everyone for all the questions. And thank you, JoEllen. That's all the time we can devote to them now, so now I'm going to repeat the CE information that I gave previously.

For CE credits, you can see the Web site, [www2a.cdc.gov/tceonline](http://www2a.cdc.gov/tceonline). The course number is E as in Edward, C as in cat, 2064-093015. Please note 093015 is today's date and this code applies to today's program.

The verification code is HPV13. Write this down. HPV and then the numerals one and three with no space. CE credit expires November 2, 2015.

For help with the online system, available eight AM to four PM Eastern Time, please dial 1-800-41TRAIN. This corresponds to 1-800-418-7246. Or you can email [CE@cdc.gov](mailto:CE@cdc.gov).

You can email immunization questions to us if you did not get to ask them today at [Nipinfo@cdc.gov](mailto:Nipinfo@cdc.gov). And we'll try to respond to those as quickly as possible. You can also call immunization questions at 1-800-CDC-INFO -- 1800-232-4636 -- from eight AM to eight PM Eastern Time, Monday through Friday.

Additional resources that we have include the Pink Book, and the Web site for the Pink Book is [www.cdc.gov/vaccines/pubs/pinkbook/index.html](http://www.cdc.gov/vaccines/pubs/pinkbook/index.html). The Pink Book is available online or you can purchase a hard copy at the link for the Public Health Foundation Learning Resource Center on that Web site.

Our CDC vaccines and immunizations home page is [www.cdc.gov/vaccines/default.htm](http://www.cdc.gov/vaccines/default.htm). Our resource guide for healthcare personnel titled "CDC Immunization Resources for You and Your Patients" is listed at [www.cdc.gov/vaccines/ed/downloads/immz-resources.pdf](http://www.cdc.gov/vaccines/ed/downloads/immz-resources.pdf).

Follow us on Twitter for immunization news, information, and resources for private and public healthcare personnel. That's [@cdcizlearn](https://twitter.com/cdcizlearn) on Twitter.

So this concludes our program. I want to thank Ms. JoEllen Wolicki for the presentation covering the topic in great detail, and for answering all of the questions. Thank you very much and have a great day from Atlanta. Goodbye.

Coordinator: This concludes today's conference. Thank you for joining us. You may now disconnect.

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