

Gardasil®: The New Vaccine for Human Papillomavirus (HPV)

Introduction

In June 2006, the federal Food and Drug Administration (FDA) approved Gardasil®, the first vaccine against human papillomavirus, or HPV. There are more than 100 strains of HPV, and about 30 infect the genital region. Some HPV strains have been implicated in a variety of cancers, including those of the cervix, anus, vagina, vulva, penis, mouth, and sinuses. Other strains cause benign, non-cancerous warts.

Gardasil protects against four strains of HPV: strains 6, 11, 16, and 18. Two of these strains, 16 and 18, cause approximately 70 percent of the cases of cervical cancer in the U.S. The other two strains in Gardasil, 6 and 11, cause genital warts.

Gardasil is produced by Merck. Another pharmaceutical company, GlaxoSmithKline, has filed for FDA approval of Cervarix™, a similar HPV vaccine.

Shortly after the FDA's approval of Gardasil, the Advisory Committee on Immunization Practices of the federal Centers for Disease Control and Prevention (CDC) recommended that all girls ages 11 to 12 begin receiving the vaccine, that the vaccine be included in the federal Vaccines for Children program (which pays for vaccines for low-income children), and that girls and women between the ages of 13 and 26 also receive the vaccine. These recommendations have been controversial, however, and several state legislatures have rejected measures to require Gardasil vaccination for school children.

The Institute for Women's Health's Dr. Erin N. Marcus interviewed Dr. Leo Twiggs, professor and chair of the Department of Obstetrics and Gynecology at the University of Miami Miller School of Medicine, about HPV vaccines. Dr. Twiggs has led numerous studies looking at Gardasil's effectiveness and has received research support from Merck.

Institute for Women's Health (IWH):

Thank you, Dr. Twiggs, for taking the time to speak with us today. Prior to the introduction of the Pap smear in the mid 20th century, cervical cancer was one of the top causes of death among women. Yet now, it is no longer a leading cause of cancer death in the U.S. Given that far fewer women die of cervical cancer than other diseases, such as heart disease and lung, breast, and colon cancer, why is there a need for an HPV vaccine?

Dr. Twiggs:

There's a need for this vaccine because we still have about 5,000 people who die of cervical cancer each year in this country.

Plus, for those who develop cervical cancer but don't die of it, the disease can cause many unpleasant side effects, because it usually stays localized between the bladder and the rectum.

It's also important to note that the vaccine protects against the two viral types that cause most genital warts. These are bothersome diseases that can be prevented by the vaccine. It's also a condition that's associated with a lot of stigma.

IWH:

Given that there are more than 100 strains of HPV, why did Merck decide to include strains 6, 11, 16, and 18 in the vaccine?

Dr. Twiggs:

There are many reasons why these strains were chosen. First of all, 16 and 18 cause more than 70 percent of cervical cancer, while 6 and 11 cause more than 90 percent of genital warts. The warts caused by 6 and 11 can masquerade as potentially precancerous conditions and cause a lot of expensive, invasive testing.

It is important to remember that the vaccine does not cover all of the strains of HPV that cause cervical cancer. If you have had the vaccine, you still need to be screened regularly, as specified in the ACOG (American College of Obstetrics and Gynecology) guidelines.

IWH:

Whom will this vaccine most benefit?

Dr. Twiggs:

Any person between the ages of 9 and 26 will benefit from this vaccine. It's best to be vaccinated between the ages of 9 and 13 because the immune system is exquisitely sensitive at that age. Also, from a practical point of view, it's easier to get children vaccinated at that age instead of later. And, it's best to receive the vaccine before the onset of sexual debut (according to estimates from the CDC, 24 percent of U.S. girls have become sexually active by age 15, 40 percent by age 16, and 70 percent by age 18).

IWH:

Some recent studies suggest the vaccine may also protect against several strains of HPV other than 6, 11, 16 and 18. Could you explain why this could be the case?

Dr. Twiggs:

The drug companies would love to use this claim (that there is cross protection) as a marketing tool, but it's important to remember that the cross-protection is not 100 percent. Most of the immune response is type-related. Strains 6 and 11, 16 and 18 are phylogenetically different from one another.

IWH:

Might the vaccine prevent against other types of cancer in which HPV plays a causative role, such as certain types of head and neck cancer?

Dr. Twiggs:

This has not yet been studied adequately and we need to study this more. But we can use the analogy of vulvar and vaginal cancer, in which 40 to 50 percent of cases are believed to be caused by HPV. It's possible some head and neck cancers can be prevented by HPV vaccine.

IWH:

Have you found that there has been a lot of patient demand for this vaccine? Is it expensive, and are most insurances covering it?

Dr. Twiggs:

There is a lot of demand. In South Florida, the total cost is about \$500. Most insurances are covering it, though some do not cover the entire cost.

IWH:

What are the risks of the vaccine? Do patients need a pregnancy test prior to receiving it?

Dr. Twiggs:

It would be prudent to have a negative pregnancy test prior to giving the vaccine. Patients shouldn't get the vaccine if they are pregnant but at this point (teratogenicity) is more of a theoretical risk. A patient registry has been created and we'll have more data on this in the future.

IWH:

The Commonwealth of Virginia and the District of Columbia require that girls entering sixth grade show proof of HPV vaccination prior to entering school, though both allow parents to "opt-out" of this requirement. Other state legislatures have rejected proposals to make HPV vaccination a school entrance requirement.

Given the big demand for this vaccine, do you think that mandating it for school entrance is necessary? Why do you think there is so much opposition to mandating it?

Dr. Twiggs:

I don't like the word mandate. I like the idea of making it universal, with an "opt out" option. The opposition is due to a feeling that the government is interfering in one's personal business, a feeling that there are too many vaccines already, and a parental denial of the age of sexual debut.

IWH:

Can men receive the vaccine? Would this make sense from a public health perspective?

Dr. Twiggs:

Men can receive it, and it is approved for use in men in Australia. Hopefully we will see more data in men.

Men can get infected with HPV, and they serve as a vector for infection, but we don't see the same kind of rates for penile cancer as for cervical cancer. That's because these viruses have tropism toward a specific type of tissue, as found in the transformation zone of the cervix.

IWH:

Are there any misconceptions surrounding the vaccine? Is there anything else that you think the public needs to know about it?

Dr. Twiggs:

I think it's very important to realize this is a 21st Century vaccine. It's a pure immunostimulant. It doesn't have viral DNA and should be safer than most other vaccines in terms of side effects.

In terms of cervical cancer, this is a sexually transmitted illness that can be prevented by vaccinating people. Up to 40 percent of people become infected with HPV, and it seems like a reasonable thing to do.

In terms of genital warts, as mentioned before, these can cause a lot of stigma and can inhibit people's sexuality. We want our kids to grow up to have healthy relationships, and we are trying to get people to feel good about themselves. It's women's health, not women's disease that we are promoting. This vaccine is something that promotes women's health.

IWH:

Thank you again, Dr. Twiggs, for taking the time to explain this important topic.