

## Increase in Head and Neck Cancer in Younger Patients Due to Human Papillomavirus, or HPV

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### Introduction

|                     | HPV(-)              | HPV (+)                |
|---------------------|---------------------|------------------------|
| INCIDENCE           | Decreasing          | Increasing             |
| COMMON RISK FACTORS | Tobacco, Alcohol    | HPV                    |
| MOST COMMON SITE    | Tonsil, Soft palate | Base of tongue, tonsil |
| AGE                 | Older               | Younger                |
| EDUCATION LEVEL     | Lower               | Higher                 |
| AFRICAN-AMERICAN    | Common              | Rare                   |
| TOBACCO USE         | High                | Low                    |
| SURVIVAL            | Poor                | Good                   |

**Figure 1. Comparison of HPV-related and non-HPV-related throat cancer**

The face of head and neck cancer has changed dramatically over the past 30 years. In the past, squamous cell carcinoma - the most common cancer in the head and neck - was most commonly seen in older adults who had a history of tobacco and alcohol use. As fewer people are smoking now than in the past, there has been a steady decline in the number of new diagnoses of this disease over the past 30 years. While smoking-related head and neck cancers have been declining overall, squamous cell carcinoma of the oropharynx (throat) has been increasing. Today, patients diagnosed with throat cancer are more likely to be younger adults in their 40s and 50s who have never smoked or used other tobacco products (**Figure 1**). The reason for these changes is the human papillomavirus, or HPV.

### What is HPV?

HPV is a virus. HPV can infect the mouth, back of the throat, cervix, anus, and penis. There are many different types of this virus. There are low-risk types (those which are known not to

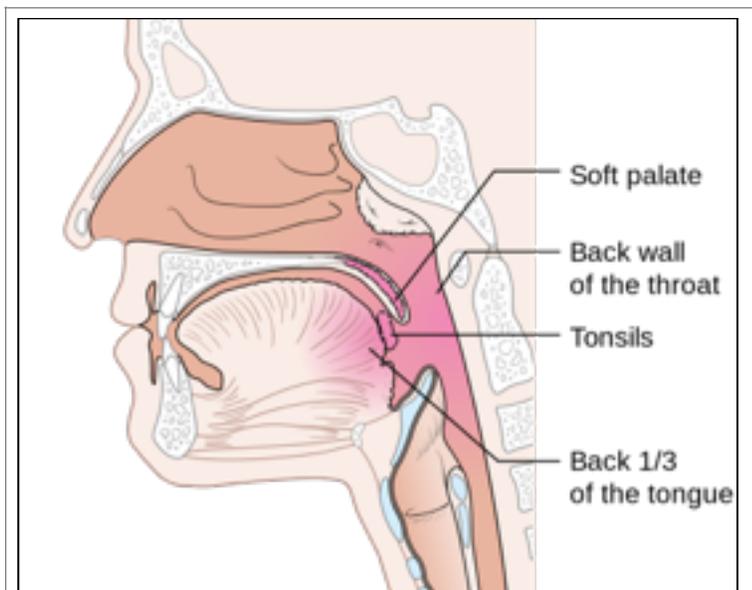
cause cancer). There are high-risk HPV types, those which have been shown to be associated with cancer.

### How is the infection transmitted?

HPV is a sexually transmitted infection. It can be transmitted through any kind of sexual contact including vaginal, anal, and oral sex.

### How common is HPV infection?

HPV is the most common sexually transmitted infection (STI) in the United States, making up over half of all new and existing STIs. The majority of adults will become infected at some point in life. Most of the time, the body's immune system removes the infection from the body. Approximately 1% of adults have detectable HPV-16, the type most commonly associated with throat cancer, in their saliva.



**Figure 2. Anatomy of the oropharynx** (Cancer Research UK / Wikimedia Commons)

### What can HPV infection lead to?

HPV infection can have no symptoms at all.

HPV can cause benign (non-cancerous) lesions such as genital warts or benign growths in the voice box of children born to infected mothers.

It has long been recognized that HPV causes cervical cancer. This is why HPV is part of cervical cancer screening. HPV also causes other cancers such as penile, anal, and vulvar cancers. HPV is now the most common cause of cancer of the oropharynx (cancers of the back of the throat, tonsils, and back of tongue)(Figure 2).

### How does HPV cause cancer?

Once the HPV virus comes into contact with tissues in the throat, it forces its way into the individual cells. All cells in the body have multiple defense mechanisms in place that prevent it from becoming a cancer, but the types of HPV that cause cancer can disable some of these defenses, making it more likely for that cell to become cancer. Things like smoking or drinking alcohol can add to the problem by causing further damage to cells and increasing the likelihood of developing cancer.

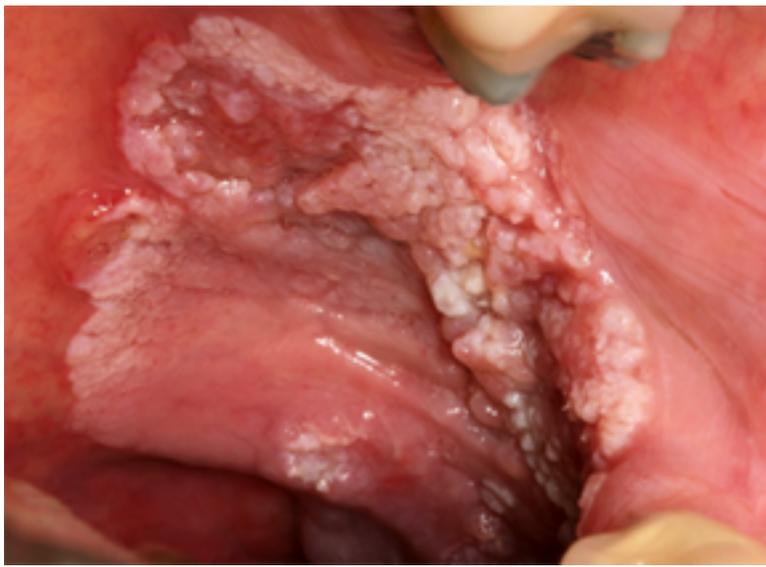
| SYMPTOM               | Percent of Patients |
|-----------------------|---------------------|
| Neck Mass             | 51 %                |
| Sore throat           | 28 %                |
| Visible oral lesion   | 14 %                |
| Difficulty swallowing | 10 %                |
| Lump in the throat    | 9 %                 |

**Figure 3. Most common symptoms of HPV-related throat cancer**  
(adapted from McIlwain, et al: JAMA Otolaryngology Head Neck Surg. 2014;140(5):441-447)

### What are the symptoms of HPV-related throat cancer?

Throat cancers caused by HPV may be present for some time before causing any symptoms. Recent evidence suggests that throat cancers caused by HPV present with different symptoms than those caused by smoking (Figure 3).

The most common presentation of throat cancer caused by HPV is a mass in the neck. Other common presenting symptoms include a sore throat that doesn't go away, ear pain, pain with swallowing, or bleeding in the mouth. Some people may notice a sore or ulcer in their mouth or their dentist may notice it during an exam (Figure 4).



**Figure 4. Classic appearance of HPV-related throat cancer in a non-smoker**

#### **How common is HPV-related throat cancer?**

Approximately 12,400 people in the United States are diagnosed with throat cancer each year. While most cases used to be caused by tobacco and alcohol use, the number of smoking-related cases is actually declining as fewer people are smoking today than in the past. Today, most new cases of throat cancer are caused by HPV infection. Some estimates suggest that 70-90% of new throat cancers have evidence of HPV. This epidemic has changed the face of throat cancer. These new cancer patients are younger and healthier than in the past and may have no other identifiable risk factors.

Both men and women are at risk for HPV-related throat cancer, though it appears to be more common in men. While smoking-related mouth cancers are more common in African-Americans, HPV-related throat cancer is more common in Caucasians. Studies have shown that a higher number of lifetime oral sex partners (>5) as well as a higher number of lifetime vaginal sex partners (>25) have been associated with increased risk of HPV-related throat cancer.

#### **What is the prognosis for HPV-related throat cancer?**

| Time in years | HPV - Positive | HPV - Negative |
|---------------|----------------|----------------|
| 1             | 97%            | 90%            |
| 2             | 95%            | 62%            |
| 3             | 86-93%         | 58%            |
| 4             | 84%            | 50%            |
| 5             | 79-82%         | 46%            |

**Figure 5. Differences in overall survival between HPV(+) and HPV(-) throat cancer**

HPV-related throat cancer carries a more favorable prognosis than non-HPV throat and mouth cancers (Figure 5). This is likely due to HPV-related throat cancers being more responsive to treatment. The prognosis for any given patient will depend on the stage of disease and HPV status. Overall survival for HPV-positive throat cancer after 2 years is 95%, compared with HPV-negative throat cancer which has a 2-year survival of 62%. HPV-related throat cancer has a 5-year survival rate of 79%, compared with 46% for HPV-negative Patients.

### What are the treatments for HPV-related throat cancer?

HPV-related throat cancer can be treated in a number of ways and the optimal treatment may vary with each patient's unique situation. In general, most patients with throat cancer will undergo a combination of chemotherapy and radiation. Others may have surgery alone or surgery in combination with chemotherapy and radiation. Modern advances in surgical technique including transoral robotic surgery (TORS) and transoral laser microsurgery (TLM) can be used for select tumors.

### What are the side effects of treatment?

The side effects associated with treatment will also vary depending on the type of treatment decided by the patient and his or her physicians. Some of the more common side effects include dry mouth, difficulty swallowing, and neck pain. Some patients may experience changes in how they taste food or lose their sense of taste altogether. Still others may experience hoarseness or other voice changes that may be permanent. Patients who undergo chemotherapy may experience side effects such as mucositis (severe mouth ulcers), hearing loss, nausea and vomiting, diarrhea, weakness, and fatigue.

## **Will the vaccine prevent throat cancer?**

There are two FDA approved vaccines currently in use in the U.S. to prevent HPV infections. These vaccines are approved for prevention of cervical cancer and anogenital warts. However, use of the vaccine also creates immunity against HPV16, the type of HPV responsible for >95% of HPV associated head and neck cancers. Therefore, it is likely to reduce future burden of head and neck cancers.

The vaccines are safe and have now been given to millions of people with no or minimal side effects.

Currently, the Gardasil® and Cervarix® vaccines are recommended for all girls and women ages 11 to 26, and the Gardasil® vaccine is also recommended for all boys and men age 12 to 21. In order for it to be effective, it must be administered before being exposed to the virus, which means it should be given before the start of sexual activity. While some parents have expressed concern that giving the vaccine amounts to their endorsement of sexual activity, studies have shown that vaccinated teens are no more likely to engage in sexual behavior than teens who are unvaccinated.

Since the HPV virus is sexually transmitted, people may reduce their risk of HPV infection by practicing safe sex and limiting their number of partners. People should be aware that HPV can be transmitted via oral sex and that this is presumed to be how most adults with HPV of the throat were initially infected.

Finally, people can reduce their risk of throat cancer by not smoking and limiting their intake of alcohol.

## **Summary**

Most new cases of throat cancer today are caused by infection with the human papilloma virus (HPV) and occur more often in non-smokers in their 40s and 50s. Risk factors include increased number of oral sex partners and increased number of vaginal sex partners. The most common symptoms are a neck mass, sore throat, or ulceration in the mouth that does not go away. Depending on the location and stage of the disease, treatment options may include a one or more of the following: surgery and/or radiation, with or without chemotherapy. HPV-related throat cancer has a better prognosis than non-HPV throat cancer. People can reduce their risk of this type of cancer by receiving the HPV vaccine series prior to becoming sexually active, limiting the number of oral and vaginal sexual partners, and practicing safe sex.

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