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Papillomas of the Larynx

Terminology:

Papillomas of the voicebox are called by a number of different names including papillomas or papillomatosis of the larynx, throat or vocal cords. In children, the disease is usually called RRP (Recurrent Respiratory Papillomatosis) and / or HPV (Human Papilloma Virus), after the virus which causes the condition. These terms tend to be used interchangeably, some more or less correctly than others. The larger problem is when papillomas are misdiagnosed or mislabeled as being other less-serious conditions. As you will learn, papillomas are a specific entity which tends to be very difficult to treat, have a well-defined behavior with no true "cure", and may be pre-cancerous.

The medical term for the voicebox is the *larynx*. The larynx begins at the "Adam's Apple" and extends down to almost the collar bones. The larynx is comprised of several sections, the vocal cords (or vocal folds) are only one part. The larynx is only one of the structures of the throat. Anything having to do with the larynx is termed *laryngeal*, therefore papillomas of the larynx are *laryngeal papillomas*.

Papilloma is the medical term for the common "wart" in laymen's terms. Papillomatosis is a condition of having multiple papillomas in one area, such as the larynx. ALL papillomas are technically growths, termed neoplasms. A neoplasm may be benign, pre-cancerous (termed dysplasia) or cancerous (termed malignant). The majority of papillomas are benign, including laryngeal. Papillomas can grow almost anywhere where there is a "skin surface" (termed epithelial or mucosal surface), both on the outside and inside of the body.

ALL papillomas are caused by a virus. The term *papilloma* is reserved for a growth caused by a virus. There are many viruses which cause papillomas. Most of these viruses cause papillomas in characteristic locations. For example, certain herpes-viruses cause papillomas on the genitalia. Laryngeal papillomas are caused by a family of viruses known as HPV, or human papilloma virus. This family of viruses has more than 100 members, but only 4 or 5 are usually found in the larynx. These same 4 or 5 also cause papillomas in the cervix in women. Unfortunately, in both the larynx and cervix, HPV related papillomas may be precancerous or cancerous, and are a major reason women are recommended to go for pap testing. It is estimated that about 4.3 children and 1.8 adults out of every 100,000 persons in the United States are affected by laryngeal papillomatosis.

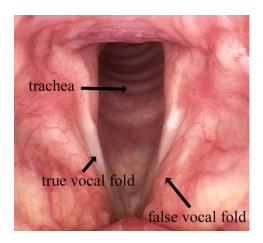
Polyps and nodules of the vocal cords are NOT growths, NOT caused by a virus, do NOT behave like papillomas, and are therefore NOT papillomas. Polyps and nodules are NOT the same as papillomas.

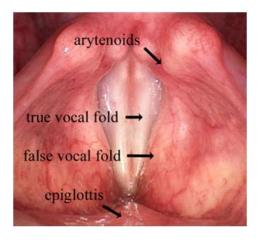
Diagnosis:

Hoarseness and voice changes are the most common presenting symptom of papillomas. Once papillomas are suspected, the patient should be referred to a center with expertise. The first step in diagnosing laryngeal papillomas is to examine the larynx in the clinic. Laryngeal papillomas have a characteristic appearance, as well as behavior. In our clinic, laryngeal examination is easily done with a small telescope that is placed into the mouth WITHOUT going down the throat, and causes no pain (see photograph). The vocal cords are recorded and examined under high magnification.

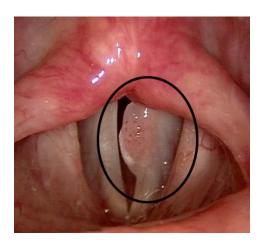


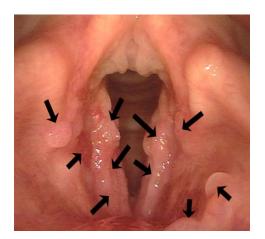
The following pictures show what normal vocal cords look like when examined in our clinic. Normal structures are highlighted. Imagine a lion-trainer has stuck his head into the lion's mouth and is looking down the throat ... that is the view we get with the same up-down, front-back orientation.





Now compare the following photographs in patients with papillomas. The first patient has just a single papilloma (which is more unusual), and the second patient has multiple papillomas with each involved area labeled with an arrow. Papillomas are most commonly described as looking like a "warty" bunch of grapes, or "clear cauliflower", characteristically with multiple red dots. These red dots are actually the papilloma's blood vessels, and the target of treatment.





A 100% accurate diagnosis requires collaboration between a laryngeal surgeon (aka *laryngologist*) and pathologist. Because papillomas are growths caused by viruses, they have characteristic features that an experienced pathologist can identify from a biopsy specimen. The presence and exact HPV family member can be determined with advanced testing only in a few centers in the United States, and generally takes weeks. The diagnosis also rests on a number of clinical factors, including the appearance of the growths (as described above) and their clinical behavior. Laryngeal papillomas can NOT be cured as of yet, and the "recurrent" re-growth behavior of them lends some to term the disease "Recurrent Respiratory Papillomatosis" (the larynx is part of the breathing or respiratory organs). The characteristic behavior of laryngeal papillomas is recurrence after successful treatment. This behavior is one of the criteria for a diagnosis of laryngeal papillomatosis.

Clinical Behavior:

In children, papillomatosis is postulated to be *vertically transmitted* (infection from mother to child during the process of childbirth), and it seems plausible that the infection remains dormant until unknown factors stimulate viral activation. In adults, the mode of transmission is less clear, with researchers theorizing the same mother-child transmission that just remains quiet longer for unknown reasons. They have also suggested transmission through sexual contact from an infected person during oral sex. Almost all papillomas in the throat are caused by HPV *subtypes* (members of the HPV family) numbers 6, 11, 16 & 18. These same subtypes that appear in the cervix are a major reason that researchers believe that the throat can be infected during childbirth passage through the cervix or from oral-genital sexual activities. Types 6 & 11 are considered "lower risk" for the development of cancer whereas types 16 & 18 are considered "higher risk." The presence of the "higher risk" subtypes usually requires a more careful and frequent follow-up.

As previously stated, there is NO CURE for laryngeal papillomas. One criteria of the disease is recurrence after successful treatment. They are expected to return at some point! This does not mean that people are not free of all detectable disease for years or even decades (or longer). They can be. Treatments are becoming more and more aggressive and successful in producing long-term good results. Recurrence of disease does NOT indicate failure of treatment or expertise of the treating physician ... it is the expected behavior of the papillomas. Remission rates can vary widely from patient to patient, or even in the same patient whose papillomas were gone for years and have now returned. In general, experienced centers and physicians have much MORE success in achieving favorable long term results than others who see this disease less frequently.

Papillomas and Cancer:

There is emerging evidence that viruses can cause cancer to develop even in people who do not drink or smoke. This has been very well established in the cervix related to HPV. The relationship between HPV and cervical cancer is the main driving force for the HPV vaccine (more on the Gardasil vaccine later). The presence of "higher risk" HPV subtypes 16 & 18 are thought to be very significant. Cancer formation generally requires a combination of events beyond simply being infected with the HPV 16 or 18 subtype. Only a small percentage of persons infected with the higher risk subtypes of HPV will go on to form cancer. A lot is up to one's genetics and a host of factors including nutrition, general health and social factors, such as smoking and drinking.

Laryngeal papillomas have a tendency to have "dysplastic" features. In other words, the growths that they cause look abnormal to the pathologist under the microscope, ranging from slightly atypical, to precancerous (*dysplasia*) and very, very rarely, cancerous. Dysplasia is frequently a precursor to full-blown cancer. The goal is always to identify and treat dysplasia before it progresses to cancer. It is this verysame HPV-caused dysplasia that is being screened for in a pap test. Although no pap-test exists for the larynx per se, regular examination with the scope provides the best cancer surveillance. Finally, many physicians and researchers believe that the risk of cancer is also related to the length of time papillomas are left in place and untreated. For this reason, it is generally recommended to treat laryngeal papillomas, even if the person can "live with" the hoarseness.

Treatment:

Although no "cure" is known to exist, some centers have very successful therapies, including state-of-the-art lasers. These therapies can be broadly divided into "surgical" and "non-surgical." Surgical removal of the papillomas is the standard of care today. They will not go away with a pill or an antibiotic. Surgical removal also provides a specimen for the pathologist to analyze for the presence of any pre-cancer or cancer. The goal of any surgical procedure is to remove as much of the papillomatosis as possible without scarring the vocal cords, which may result in irreversible hoarseness. Too aggressive of a surgical procedure can result in a voice that is worse than before surgery. On the other hand, insufficiently aggressive surgery is not worth having if too much papillomatosis is left behind.

Removal of papillomas usually takes place under general anesthesia in an operating room. Once the patient is fully asleep, a special scope holds open the mouth until the throat can be seen under a microscope (see photograph below). The involved areas should be carefully inspected and mapped out. A biopsy is generally taken, especially if an area looks suspicious. A combination of lasers, microinstruments and injections are used to treat the involved areas. In advanced centers, the ideal laser to treat papillomas is the KTP LASER. This opinion is supported by dozens of published articles in the medical journals. The photograph shows an area of papillomas being treated with the KTP laser.



The KTP laser targets the blood supply to the papillomas and "chokes-it-off", killing the papilloma while being as gentle as possible on the vocal cord to limit scarring. Finally, injection of an anti-viral medication into the infected vocal cords is performed, except in patients with previous pre-cancer or cancer of the voicebox from their papillomas.

The unique risks and side effects of this procedure include (but are not limited to) chipped or broken teeth. Note in the photograph how the metal scope rests against, and causes pressure on the teeth. Rarely (less than 5%), the pressure is enough to chip or break one or more teeth. This risk is higher if you have bad teeth to begin with, caps, or a small mouth. A standard mouth guard is always used, however many dentists can create a custom tooth guard to reduce this risk in overly concerned individuals. After the surgery, people *may* complain of a sore throat, altered sense of taste, tongue

weakness, tongue discomfort, or prolonged hoarseness. These are all normal and should resolve completely within a few days to weeks. Rarely, the altered sense of taste and tongue weakness can last for several months. This is due to a "Charlie horse" the scope gives the muscles of the tongue, especially in difficult or long cases.



POST-OPERATIVELY: you are on seven complete days of <u>absolute voice rest</u>. This means NO whispering either. You would not ski the day after having your knee reconstructed, so why would you talk after throat surgery? Talking and whispering after surgery significantly delays healing and may result in irreversible scarring and hoarseness! For the second week, you may begin to use the voice for 5-10 minutes per hour. It is still expected to be hoarse, and again, the more it is overused at this phase, the longer the ultimate healing will take. Diet is usually anything soft if the tongue is bothering you; or no restrictions if it is not. There are no activity restrictions once the general anesthesia has worn off. Tylenol extra strength or ibuprofen may be used for any discomfort. Sometimes a course of antibiotics or steroids are recommended.

Prevention:

Laryngeal papillomas are not thought to be transmitted by kissing an infected person. The role of oral-genital contact in infected persons has not been fully elucidated. The role of the HPV Gardasil vaccine in preventing laryngeal papillomas is not yet known. It is *expected* to be beneficial in the preventing HPV infection in the larynx, just as it does in the cervix, but it will be years before the data is conclusive either way. The role of the vaccine in persons already infected is also interesting. Here again, there is a *theoretically expected* benefit for laryngeal papillomatosis, but there is no data to support or refute any claim. The vaccine was designed and intended to reduce cervical HPV infection, and HPV-related cervical cancers in pre-sexually active girls. Its role in adults (male or female, infected or not) is simply not known.

Research does seem to indicate that there is some benefit to taking acid suppression medications in reducing recurrence rates of papillomas in the larynx. This does not replace surgical removal. It is though that asymptomatic stomach acid in the throat stimulates the virus to produce papillomas even in persons who do not experience heartburn. The data is scant and weak, however most physicians do recommend the use of these medications in many patients. Finally, there is also evidence that the

naturally occurring compound indole-3-carbinol (found in cruciferous vegetables, like broccoli) acts as an anti-growth, and anti-cancer agent. For those not eating several large servings of cruciferous vegetables weekly, the indole-3-carbinol can be purchased as a nutritional supplement. Routine surveillance is one of the keys to long-term disease control and cancer prevention, especially in persons infected with higher risk HPV strains, or having had papillomas displaying dysplasia on biopsy. The timing of office visits and overall duration of surveillance vary greatly depending on the patient, pathology and other clinical factors.

Contact:

If you have any general questions regarding laryngeal papillomas you may contact us at the Center. Please note: under no circumstances can or will a personal medical consultation occur over the telephone or via e-mail without an office visit and examination in person.

