

# Methylene Blue Staining Test in Assessing *Safe Margins* in Laryngeal Papillomatosis

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*Laryngeal papillomatosis, although a viral and benign disease, poses a great challenge for the ENT surgeon from a therapeutical point of view. The lack of a curative treatment and the tendency of the papillomatosis to recur in an extensive manner require an aggressive treatment. Although multiple medical therapies are available, their results are not always the desired ones. That is why nowadays the focus of the therapy is on the surgical approach. The best results may be obtained thru multiple surgeries, with resection of all papilloma foci. Although this approach may impact the quality of life of the patients due to the multiple interventions required, the overall result translates into a physiologic airway. Because the site where the lesions first appear is at an epithelial level, tendency to use methods of early diagnosis, that make the disease recognizable before extensive lesions, is the natural tendency. Also, it is extremely important to remove all papilloma lesions during surgery, thus minimizing the chances of recurrence or at least increasing the interval between interventions. The aim of this paper is to present the methylene blue staining test as an adjuvant method of evaluating the resection margins during surgery for laryngeal papillomatosis. This method can improve the results of surgery and increase the patient's adherence to treatment, by decreasing the number of interventions required.*

*Keywords: methylene blue, laryngeal papillomatosis, safe margins, surgery*

The exposure to the human papilloma virus can be quite common, thru sexual intercourse, and most often causes genital papillomatosis. However, it can affect the larynx as well, causing laryngeal papillomatosis. This can be acquired during adulthood by exposure the virus, but also the child may be affected if delivered naturally by a mother with genital papillomatosis. The last case associates a poorer outcome, with more often recurrences and more extensive lesions [1]. The most often encountered subtypes are HPV 6 and HPV 11.

Because of the viral nature of the disease, multiple medical therapies have been considered. The intralesional injection of Cidofovir was thought to be a breakthrough due to the success reported by Van Cutsem in 1995 [2], but side effects such as dysplasia of the mucosa or malignant turn-over were afterwards reported [3,4]. The highest alarm was signaled by studies that showed an important risk of malignant degeneration [5]. Although other results were more promising, not linking the procedure with mucosa degeneration [6], the overall attitude was more temperate.

With the technological revolution, we now have a wide range of surgical options for these patients. It is less and less necessary to perform a tracheotomy for patients with laryngeal papillomatosis, exception being the cases with a low adherence to treatment. Attempts to associate the local resection with adjuvant therapy have also been considered [7], with good results.

Today, one of the most widely used means of therapy is the surgical resection of laryngeal papilloma lesions with CO<sub>2</sub> laser under microscopic control. This allows a complete resection, with a good hemostasis. The results are superior to open approaches and the patients require a shorter period of recovery. When needed, in office procedures of resection using a diode laser may be associated.

As such, we must keep in mind that this disease can not be completely cured. It is only by multiple interventions that we can maintain a proper airway. The extensive and recurrent nature of the disease requires that all resection be performed having in mind the complete resection of the lesion and all recurrence be diagnosed as soon as possible. Only by achieving these two desiderates can we expect good results.

That is why all adjuvant method that allow the surgeon to perform a complete resection of the papilloma lesions can be extremely valuable. The papilloma foci can be spread in the entire larynx and hypopharynx and small lesions can be easily overlooked even under microscopic control. These can lead to early recurrence, which will increase the number of interventions necessary to maintain the natural air passage.

The aim of this paper is to present the adjacent use of the methylene blue staining test in assessing the resection margins during surgery for laryngeal papillomatosis. Because this test emphasizes the changes that occur at

an epithelial level, all lesions are easier to detect and resect during the same intervention. The method could prove useful due to the fact that, if alone translates into good results, the need for systemic medication and the associated known side effects [8,9] will decrease.

### Experimental part

Our study was conducted in The Prof. Dr. Dorin Hociota Institute of Phonoaudiology and Functional ENT Surgery. We included a number of 19 patients, males and females, with an age ranging from 34 to 68 year old. The diagnosis of laryngeal papillomatosis was confirmed by transnasal fibroscopy under normal white light. We included both patients that had underwent previous interventions and patients that were recently diagnosed.

With the patient under general anesthesia, using a laryngoscopy tube, we performed a complete evaluation of the lesions under microscopic control. This allows a more thorough evaluation of the extension of the lesions, especially in patients that do not tolerate easily the endoscopic examination.

The entire region that had to be examined was washed with saline solution and 1% acetic acid. Afterwards, using a moist sponge, we colored it with 1% methylene blue solution (fig. 1). We waited for three minutes, then washed away the excess methylene blue with the same acetic acid solution.

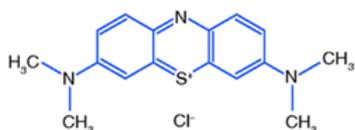


Fig. 1. Chemical formula of methylene blue

Next, we examined the entire area, taking into account all the papilloma foci that were more intensely colored, a darker shade of blue, compared to the adjacent light blue areas. The shape and size of the papillomatous areas were observed, with emphasis on the aspect of the epithelial layer (fig. 2 and fig. 3).



Fig. 2. Laryngeal papillomatosis - lesion of the vocal fold dark blue after methylene blue staining.

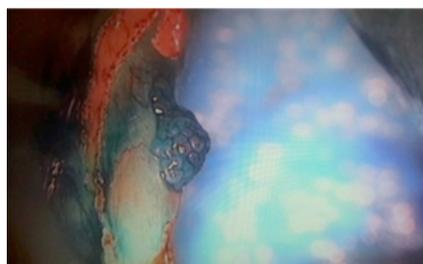


Fig. 3. Laryngeal papillomatosis - the lesion is enhanced and the vascular design more visible



Fig. 4. Intraoperative view after the complete removal of the laryngeal papillomatosis lesions.

All papilloma was removed, using the CO<sub>2</sub> laser under microscopic control. As a second step, the same coloring process was repeated, paying special attention to the immediately surrounding areas of the surgery site (fig. 4). If an abnormal pattern of coloration was revealed, suggesting that papilloma foci are still present, the resection limit was increased.

The removed tissue was sent for histopathological examination, to confirm the diagnosis of papillomatosis and infirm any malignant degeneration.

### Results and discussions

The methylene blue staining test is already method for assessing the resection margins when a tumoral pathology is concerned, although it has so far been used when malignancies were concerned [10]. Another advantage when using this substance is the fact that it helps in the scaring process and it has a local bacteriostatic and antioxidant effect [11-13].

However, the method proved to be useful in the assessment of laryngeal papillomatosis as well. As a first step, when the first coloring is performed, it emphasizes small papilloma foci that could otherwise be overlooked, thus aiding the surgeon in the complete removal of all present lesions.

The second important advantage is that we could better evaluate the resection margins. If the coloring test raised the suspicion of remnant papilloma, the resection margins were widened, until healthy tissue was reached. This could be done in the same intervention, ensuring a better result for our patients.

The coloring pattern is easy to observe. The change of color intensity easily draws the attention on the suspected areas. It is true that a more thorough evaluation requires experience with the method, but it can be applied by surgeons that are still in the beginning with safe results.

One of the main problems raised by laryngeal papillomatosis is the risk of malignant degeneration. If a wide range of local systemic therapies are available for malignancies [14], our desiderate remains a local control that will prevent such degeneration.

### Conclusions

Laryngeal papillomatosis is a benign viral disease, with no known curative treatment. Taking into account this two facts, we must also remember that it's extensive and recurrent character make the management of this pathology quite challenging. It can lead total obstruction of the airway with acute respiratory failure, requiring tracheotomy. Even in cases where the lesions are less extensive, the need for multiple interventions can impose a decrease in the quality of life of our patients.

The results of the medical therapy, although promising, are not always entirely reliable. That is why the therapeutic strategy requires surgical interventions that must ensure the normal airway. The so-called *one step ahead* strategy requires multiple interventions with the complete removal of papillomas and a new intervention whenever other lesions appear. Although somewhat more difficult to accept by the patients, it had so far good results in our experience. Our patients were able to maintain a physiological airway and lead a normal life.

The method we present uses the methylene blue staining test as adjuvant tool for the complete removal of laryngeal papillomatosis lesion. It is an easy, cheap and available method, that does not require too much experience for the surgeon and does not increase significantly the surgery time. Moreover, it has almost no side effects and it can be reproduced with every intervention.

Overall, we consider that any method that helps us ensure the complete removal of papilloma foci is a tool that must be taken into account. In this case, we had good results, with no papilloma recurrence in the immediate period following surgery. Considering that these patients will face multiple interventions as a premises, and that a complete removal of the lesions in the first interventions will translate into an increase of the period of time between interventions, we must recognize the potential of this method, although further comparative studies are necessary to assess the exact benefit.

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