# The prevention of post-laryngectomy olfactory mucosa degeneration

## Prevencija degeneracije olfaktorne sluznice nakon totalne laringektomije

Dubravko Manestar[1*], Goran Malvić[1], Blažen Marijić[1], Davor Čorak[2], Dražen Kovač[3], Radan Starčević[1]

[1] Clinic of Otorhinolaryngology, Head and Neck Surgery, University Hospital Rijeka, Rijeka

[2] Teaching Institute of Public Health of Primorsko-goranska County, Rijeka

[3] Department of Pathology, Faculty of Medicine, University of Rijeka, Rijeka

**Abstract.** Olfactory rehabilitation after a laryngectomy is based on establishing nasal airflow to allow odorant molecules to come into contact with the olfactory mucosa. Currently, the polite yawning technique (PYT) is the gold standard for post-laryngectomy olfactory rehabilitation, but it is usually introduced in patient's rehabilitation programs one month after the surgery. To prevent loss of valuable time and pathophysiological changes of the nasal and olfactory mucosa, a new device was developed, named the LaryScent. The timely establishment of nasal air flow with LaryScent would prevent histopathological changes and facilitate regenerative processes in olfactory mucosa.

**Key words**: laryngectomy; olfactory mucosa; rehabilitation

**Sažetak.** Olfaktorna rehabilitacija nakon totalne laringektomije temelji se na uspostavi protoka zraka kroz nos čime se omogućuje doticaj mirisnih molekula u zraku s olfaktornom sluznicom nosa. Trenutno je „Polite yawning" tehnika (PYT) *zlatni standard* u olfaktornoj rehabilitaciji nakon totalne laringektomije, ali pacijenti obično započinju s rehabilitacijom mjesec dana nakon operacije. Kako bi se prevenirao gubitak dragocjenog vremena i spriječio nastanak patohistoloških promjena sluznice nosa, razvijena je nova naprava nazvana LaryScent. Pravovremena uspostava protoka zraka kroz nos s LaryScent napravom prevenirat će histopatološke promjene olfaktorne sluznice i potaknuti regenerativne procese.

**Ključne riječi**: laringektomija; olfaktorna sluznica; rehabilitacija

[*]**Corresponding author:**
Dubravko Manestar, MD, PhD
Clinic of Otorhinolaryngology,
Head and Neck Surgery
University Hospital Rijeka
Krešimirova 42, 51 000 Rijeka
*e-mail*: dubravko.manestar1@gmail.com

http://hrcak.srce.hr/medicina

## INTRODUCTION

Olfactory rehabilitation of laryngectomees involves establishing nasal airflow to allow odorant molecules to come into contact with the olfactory mucosa. Two types of rehabilitation methods have been developed: appliances that temporarily connect the mouth and nose with the trachea, and techniques that establish nasal airflow using the muscular movement of the mouth, face, and neck. One of the first appliances was the laryngeal bypass[1-3]. It is comprised of a flexible tube with one end connected to a tracheostomy and firmly fixed onto a stoma to prevent airflow; the other end of the tube is flattened and put between the lips. During inspiration (i.e. dilation of the thorax), the airflow goes through the nose, into the mouth, and onwards through the tube in the trachea and the lungs. Patients must learn how to relax their soft palates to prevent obstruction of the epipharynx, which many patients have difficulties with[2]. Laryngeal bypass re-establishes nasal respiration; however, it is not practical for everyday use.

The PYT is the gold standard for post-laryngectomy olfactory rehabilitation, but it is usually introduced in a patient's rehabilitation programme one month after laryngectomy. A new device, named the LaryScent, was developed, which can be used to sample air for olfaction support either in patients being rehabilitated or in the few patients that do not respond to the PYT. This prevents the loss of valuable time and pathophysiological changes of the nasal and olfactory mucosa, which are limitations of the currently available devices and techniques.

A more practical appliance, at least for home use, is the scent-diffusing ventilator developed in 2006 by the Clinic of Otolaryngology, Head and Neck Surgery, University Hospital in Berlin, Germany. This appliance is similar to an oxygen mask; it covers only the nose, enabling the mouth and the tracheostomy to remain open for ingestion and respiration. It contains a small ventilator with a battery that insufflates air and olfactory molecules into the nose[4]. However, this device subjects the patient to the buzzing of the ventilator and constant pressure on the face; in addition, its physical appearance limits the users' social activities.

Some laryngectomised patients retain intact olfactory senses, even if they have not undergone olfactory rehabilitation. Laryngectomised patients that use oesophageal speech sometimes do not suffer from a decreased olfactory sense after surgery. The oesophageal voice is produced by swallowing and releasing air, thus vibrating the oesophagus mucosa. During this process, a small amount of air is pushed into the nasal cavity, allowing olfactory molecules to come into contact with the olfactory mucosa.

Other patients reportedly can "inhale" some air into the nose by moving the lower jaw, straining the neck muscles, and moving the mimic muscles in a manner that imitates the so-called forced olfactory sense. Some of these patients produce a sound similar to a shout, which probably results from separating the soft palate from the posterior wall of the pharynx. Schwartz et al.[5] called this the buccopharyngeal maneuver. Based on these earlier studies, Hilgers et al.[6] developed the "polite yawning" technique (PYT), previously called the nasal airflow-inducing maneuver.

## THE "POLITE YAWNING" TECHNIQUE

PYT is a technique in which the patient executes a yawn, but with the lips completely closed while lowering the tongue, soft palate, and jaw. For maximum effect, the patient repeats the movement several times in quick succession. This maneuver induces a negative pressure in the oral cavity and oropharynx, which generates a nasal airflow, enabling odorous substances to reach the olfactory epithelium again. PYT is widely accepted because of its simplicity and efficacy and is easily taught to patients by describing it as yawning with the mouth closed. The schematic drawing of PYT is presented in Figure 1.

## LARYSCENT – A DEVICE FOR POST-LARYNGECTOMY OLFACTORY REHABILITATION

Based on study entitled "Amount of airflow required for olfactory perception in laryngec-

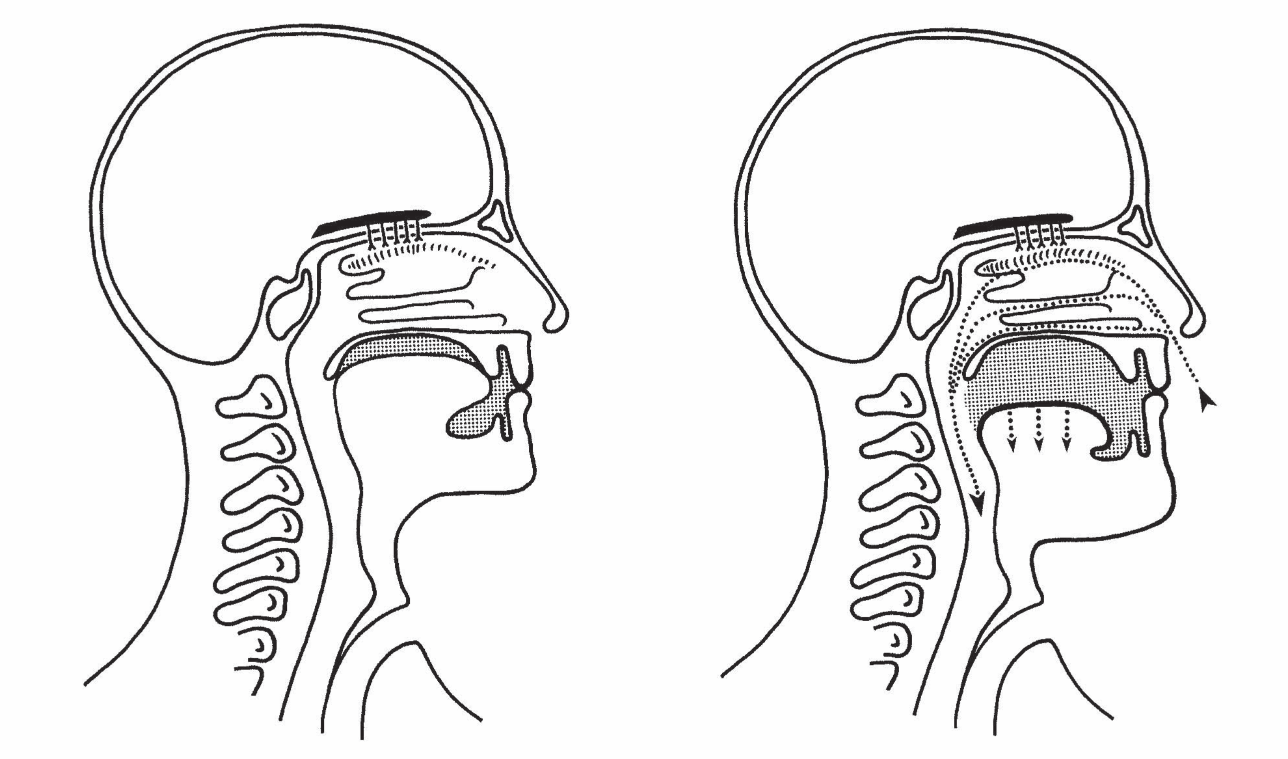

**Figure 1.** Schematic presentation of situation before and after nasal-airflow inducing maneuver

tomees: a prospective interventional study", an artificial device was developed, named the LaryScent, which can be used to sample air for olfaction support either in patients being rehabilitated or in the few patients who do not respond to the PYT[7]. The device is a low cylinder (7 cm wide and 2.2 cm in height) with a raised part on the upper plane for the nose and a spring inside. The spring is attached to the inside of the lower plane, and air is pushed out or sucked into the device by pressing or releasing this plane. In addition, the lower plane is connected to the sidewall, which prevents popping of the spring. The technical design is presented in Figure 2. One second is sufficient for squeezing the lower plane and pushing out 85 ccm of air.

## THE OLFACTORY NEUROEPITHELIUM

The olfactory neuroepithelium is pseudostratified columnar epithelium composed of at least six morphologically and biochemically different cell types. Bipolar receptor cells (neurons) are the first type and begin in the nasal cavity and end in the brain without a single synapse. Olfactory receptor cells are 5-7 µm wide and are located in the lower two-thirds of the epithelium.

**Figure 2.** Schematic model of the LaryScent device for post-laryngectomy olfactory rehabilitation

The cilia of these cells are organized in a classic 9+2 microtubule arrangement, but differ from the cilia of the respiratory epithelium because they are longer and lack dynein arms. They contain seven domain transmembrane receptors that interact with odorant molecules. Supporting (sustentacular) cells are the second type. These cells insulate the bipolar receptor cells from one another, are involved in deactivation of odorant molecules, and assist in protecting the epithelium from foreign agents. They have microvilli instead cilia. The third type is microvillar cells, which are located at the epithelial surface and structurally resemble the so-called brush cells of the upper and lower airway. Their function is not fully understood. The fourth cell type lines the Bowman's glands and ducts; whereas, the fifth and sixth cell types are the horizontal (dark) and globose (light) basal cells[8].

Prior to total laryngectomy, the nasal mucosa plays an essential role as the initial part of the respiratory system; air is inhaled into the nose and prepared to reach the alveolus in the form most suitable for inspiration and expiration. Following total laryngectomy, the nasal mucosa stops being part of the respiratory system, affecting functions such as air sponging, air heating, air filtration, and immunity.

Olfactory receptor cells and basal cells have the ability to regenerate; therefore, damaged olfactory neuroepithelium may regenerate, although it rarely does. Usually, the damaged mucosa is replaced by metaplastic respiratory epithelium[9].

Since the nasal mucosa loses the physiological stimulus normally incited by airflow, it becomes thinner and changes its colour over time. In addition, the nasal mucosa is no longer homogeneous in structure and has no ability to regenerate. This results in areas of degeneration, neuroepithelial cells being replaced by abnormal alcophilic clusters, and exposure of the nasal mucosa's lamina propria to external influences[10]. Pseudostratified columnar epithelium changes and the number of goblet cells and submucosal glands decrease. Fibrosis occurs in the stroma, as well as myxoid degeneration and neovascularisation[11].

## THEORIES ABOUT HYPOSMIA AND ANOSMIA IN LARYNGECTOMEES

There are two main theories about the occurrence of hyposmia and anosmia in laryngectomees. The first theory by Ritter et al. states that disruption of nasal airflow causes a decrease in olfactory function because odorant molecules do not come into contact with the olfactory mucosa[12]. Reduced air flow also causes histological changes in the olfactory neuroepithelium[5,13]. Mozzell et al.[14] and Tatchell et al.[15] concluded, based on their research using a larynx bypass device, that laryngectomees have intact olfactory mechanisms that function normally when adequate airflow is provided.

Welge-Luessen et al.[16] recorded olfactory chemosensory potentials evoked after stimulation with hydrosulfuric acid and carbonic anhydride in 11 laryngectomees. Potentials could not be detected in one third of patients after stimulus with hydrosulfuric acid. They concluded that anosmia is due to impaired airstream transport of odorant molecules to the olfactory area and possible damage to the olfactory neuroepithelium.

The second theory about the loss of sense of smell after total laryngectomy was suggested by Henkin et al. They claimed that the operation itself damages the sensory nerves of the larynx and significantly impairs olfactory function by interrupting feedback mechanisms between the larynx and nose[17]. The theory was partly confirmed by studies in animal models by Netzer et al. The neuroepithelium was examined in two groups of dogs. One group of dogs underwent total laryngectomy; while, the trachea was separated from the larynx in the second group, without cutting the neurovascular supply of the larynx. The histological changes in the nasal mucosa found in the first group of dogs were similar to those in the nasal mucosa of laryngectomies[18].

Most of the scientific community currently accepts the first theory, that reduced air flow is the cause of hyposmia and anosmia after total laryngectomy; although, the histopathological findings of Henkin and Netzer are taken into account. The structural changes of the olfactory mucosa that occur with time would explain why it is impossible to restore normal discrimination to the olfactory function in laryngectomees in spite of restored airflow in the olfactory cleft. Karaca et al. found, in their study of 11 laryngectomees, changes in the nasal mucosa after airflow cessation were dynamic and required months to equilibrate; however, they did not find a relation between progression of the histopathologic findings and the duration of cessation[11].

On the other hand, studies have shown that the olfactory mucosa, because of its regenerative capacity, could be used in the treatment of spinal injuries. Recently, highly proliferative olfactory ecto-mesenchymal stem cells (OE-MSC) were identified in the lamina propria of olfactory mucosa. These cells are similar to bone marrow mesenchymal stem cells, which tend to differentiate into neural cells[19]. In addition, the permanent regeneration of olfactory receptor neurons is due to bi-compartmental stem cells of the mucosa, namely the basal cells of the olfactory neuroepithelium and OE-MSCs in the underlying lamina propria. There are also olfactory ensheathing cells in the lamina propria, which share similar phenotypic properties with both astrocytes and Schwann cells. These cells are potential candidates for transplant-mediated repair in injuries of the spinal cord[20,21]. The regenerative ability of olfactory mucosa could also explain the transient anosmia described after treatment with certain antibiotics or irradiation of the pituitary gland[22,23]. Use of the LaryScent on the first postoperative day may preserve nasal airflow before the histopathological changes of mucosa occur, especially considering the regenerative ability of the olfactory mucosa.

## CONCLUSION

There are still many open questions related to the regenerative ability of the olfactory mucosa. It is unclear how the olfactory mucosa can be used for treating cerebral spinal injuries because of its regenerative capacity, while it does not completely regenerate after restoring nasal air flow. The timely establishment of nasal air flow with LaryScent could prevent histopathological changes or facilitate regenerative processes in the olfactory mucosa. The purpose of LaryScent is to supplement, not substitute for the PYT in certain social situations. During the short period after surgery when the straining of neck and mimic muscles is not recommended, LaryScent would be used to prevent changes in the nasal mucosa and to preserve the patient's mental health.

**Conflicts of interest statement:** The authors report no conflicts of interest.

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