The human nasal mucosa after deprivation of airflow:
A study of laryngectomy patients

Edward W. Fisher[1], Valerie J. Lund[1], Andrew Rutman[2]

[1] The Royal National Throat, Nose and Ear Hospital, London, United Kingdom
[2] Host Defence Unit, National Heart and Lung Institute, London, United Kingdom

SUMMARY

The effects on the human nasal mucosa of ai,flow cessation can be studied conveniently in the laryngectomy patient. We studied 39 la,yngectomy patients and 50 healthy adults. Mucociliaty clearance was measured using the saccharin test, cifiaty beatfrequency (CBF) anafyzed in inferior meatal brushings and transmission electron microscopical observations made in similar nasal brushings.

Mucoci/ia,y clearance was no faster in laryngectomees (mean 15.4 ± 7.8 min); however, CBFwas higher in the latyngectomees (means 15.0 and 14.1 Hz; p < 0.05), especially in thefirst weeks after surge,y (mean 16.8 Hz; p < 0.01). Mucus-producing eells gradually decreased in proportion over thefirst postoperative year.

The changes in the nasal mucosa after aiiflow cessation are dynamic and require months to equilibrate. This has implications for the timing of postoperative assessment ofpatients undergoing airway surgery.

INTRODUCTION

The changes in nasal mucosal structure and function which occur in response to airflow are of importance since much of the rhinologist's surgical efforts are devoted to altering airflow.

Previous workers have examined experimental animals (Hilding, 1932; Hilding and Hilding, 1970) and considered the human model oftotal airflow deprivation - the laryngectomee (Moore-Gillon, 1985; Cvetnic et al., 1987). The consensus has been that nasal mucociliary function speeds up and is less variable after airflow cessation. We examine a somewhat larger group ofcases to clarify the issue, with the addition of ciliary beat frequency analysis.

METHODS

Subjects

Thirty-two laryngectomees were examined in a retrospective fashion (24 male, 8 female; ages 39- 78, mean age 66 yrs). Seven laryngectomees were examined prospectively (males aged 49-68, mean age 59 yrs).

Control subjects were 50 healthy adults (age range 20-77, mean age 45 yrs). Patients with a history of nasal disease or evidence of active sepsis were excluded.

Mucoci!ia,y clearance (MCC)

MCC was measured similarly as described by Andersen et al. (1974) using a saccharin particle. This was placed further posteriorly on the inferior turbinate than originally described (1.5-2 cm from the tip).

Ciliary beat frequency analysis (CBF)

The CBF of nasal mucosa! brushings was measured in vitro as described by Rutland and Cole (1980). Measurements were made at 37 °C on the warm stage of a Leitz Dialux 22EB microscope. Medium 199 with Earle's salts (Flow Laboratories Limited) was used as a culture medium.

Ten readings were taken from each sample in order to obtain a representative value.

Transmission electron microscopy (TEM)

The nasal mucosal brushings were fixed in cacodylate-buffered 2.5% glutaraldehyde and postfixed in 1% osmium tetroxide. After rinsing the sample was embedded in a drop of liquid 2% agar and allowed to solidify; it was then processed through to Araldite as is normal for transmission electron microscopy. All (90-300) epithelial cells per specimen were examined in detail for cell type (ciliated or mucus-producing) and also for mitochondrial damage, cilia loss and cell surface projection which are parameters of cellular "damage" (Read et al., 1991).

O/faction

Laryngectomees and age-matched controls were examined by threshold olfactometry for PM-Carbinol (Olfacto-Labs kit). Results were recorded in 'decismels'.

RESULTS

Mucociliary clearance

The saccharin times were not significantly different in the laryngectomees and control groups (Table 1). The wide variation in both groups is notable, and suggests that smaller populations produce misleading results.

Ci!ia,y beat f 'equency

The CBF values were raised in the postoperative laryngectomees compared to the control group (Table 2). The long-term (greater than six months) group had less elevated values (comparison with control group $p < 0.05$) than did patients in the early months after laryngectomy (comparison with control group $p < 0.01$). The appearance is that of an initial elevation in CBF which settles to a lower subsequent equilibrium value.

Electron microscopy

Samples from 8 control patients (preoperative laryngectomees) and 11 postoperative patients were analyzed. There were two principal trends seen:

1. a decrease in mucus-producing cells with the passage of time;
2. a small decrease in severity of the indices of cellular damage.

This is best exemplified by serial specimens taken from the same patient (Table 3). However, the wide scatter of values obscures the latter change when the total figures are reviewed (Table 4), and the differences do not reach statistical significance at $p < 0.05$. The picture is therefore one of small changes in these indices, rather than a gross transformation of the ultrastructure of the nasal mucosa.

Offaction

Comparison of laryngectomees and normal controls showed no significant differences in threshold to PM-Carbinol (Table 5). This confirms previous work (Moore-Gillon, 1985) and suggests that our patient group was not atypical.

Statistical analysis

Comparisons were made using a Student's t-test (MINITAB-St Thomas' Hospital).

DISCUSSION

The presumed influence of airflow on nasal structure and function is the basis of much of our current rhinological surgery. The laryngectomy patient provides a convenient model for the study of total airflow deprivation in man and has been the subject of several studies which complement the work of Hilding (1932, 1970) on experimental animals.

With regard to nasal mucociliary clearance, there have been reports that laryngectomy patients have faster clearance with less variability (Dixon et al., 1949; Moore-Gillon, 1985) and that they have no slow clearance as judged by the saccharin test (Proctor, 1983). However, Sakakura et al. (1983) report no such increase in the speed of clearance except in the early months following laryngectomy. Quinlan et al. (1969), using a radioactive tracer, found that mean

Table 1. *Mucocilia,y clearance* (saccharin time - minutes).

patients		time postoperative	mean± SD
controls	(n = 50)	–	13.3 ± 5.6
laryngectomees	(n = 5)	< 1 month	16.2 ± 8.6
laryngectomees	(n = 8)	1-6 months	11.5 ± 3.9
laryngectomees	(n = 13)	< 6 months	13.3 ± 6.3
laryngectomees	(n = 27)	> 6 months	15.4 ± 7.8

Table 2. Ciliary beat frequency of nasal brushinqs (beats per second).

patients		time postoperative	mean± SD
controls	(n = 40)	–	14.1 ± 1.5
laryngectomees	(n = 7)	< 1 month	16.8 ± 1.9
laryngectomees	(n = 7)	1-6 months	14.9 ± 2.4
laryngectomees	(n = 14)	< 6 months	15.9 ± 2.3
laryngectomees	(n = 29)	> 6 months	15.0 ± 1.9

Table 3. Transmission electron microscopical findings in one laryngectomy patient examined serially (%).

parameter	preoperative	1 month	9 months	1 year
loss of cilia	15	10	13	8
cell projections	26	11	7	11
mitochondrial damage	14	6	5	7
mucus cells	18	12	7	8

Table 4. Transmission electron microscopical findings in controls and laryngectomy patients (mean ± SD %).

parameter	preoperative n = 8	early postoperative (less than 1 year) n = 9	late postoperative (over 1 year) n = 8
loss of cilia	15.5 ± 3.3	12.7 ± 4.0	13.1 ± 2.8
cell projections	19.9 ± 5.6	20.2 ± 10.7	15.6 ± 3.7
mitochondrial damage	12.1 ± 5.2	16.2 ± 10.2	9.6 ± 4.8
mucus cells	18.3 ± 10.3	13.4 ± 5.8	11.5±4.0

Table 5. Olfactory thresholds to PM-Carbinol (decismels).

	ll	mean± SD
controls	28	31.4 ± 13.4
laryngectomees	28	2.5 ± 14.8

transport rates were similar in laryngectomy cases and controls. The laryngectomees did differ, however, in that rates were uniform throughout the antero-posterior extent of the nasal cavity, rather than showing the normal increase in this direction.

Our study shows no statistically significant change in the saccharin time postoperatively, and in this respect the validity of the saccharin test must be considered. Recent anatomical and physiological work has stressed the variability of the transition zone at the anterior end of the inferior turbinate (Davis, 1990). This makes the placement of the saccharin particle crucial, since too anterior a placement will result in values which simply reflect structural changes in the anterior turbinate epithelium (which are known to change radically after airflow change (Davis, 1990)), rather than any overall change in transport rate. Thus our more posterior placement circumvented this problem.

The addition of ciliary beat frequency analysis has suggested that beat frequency is enhanced, perhaps in a dynamic fashion, and this may relate to the findings of Sakakura et al. (1983), since the beat frequency and saccharin time have been shown to correlate to some degree (Duchateau et al., 1985). However, it must not be forgotten that the method is in vitro and is to be interpreted with some caution until a more convenient in vivo method can be devised (Reimer et al., 1977).

Studies of nasal mucosa! structure after airflow cessation in experimental animals (Hilding, 1932; Hilding and Hilding, 1970) demonstrated an increase in goblet cells on the closed side and loss of cilia with squamous metaplasia on the open side with doubling of airflow. There was increased ciliogenesis on the closed side within a few days, which continued for months. Mogensen and Tos (1978) confirmed these findings and found that the change was dynamic, with a particularly marked increase of goblet cells on the occluded side in the first 16 days.

Scanning electron microscopy (Moore-Gillon, 1985) has confirmed the light-microscopical findings of increased mucus and ciliated cells in laryngectomy patients, in agreement with Proetz (1941), who even suggested that mucus cells became predominant. However Dixon et al. (1949) found no such increase in goblet cells in humans, and the changes in ciliated epithelium were complete by three months. The longer-term cytological and histological studies on laryngectomees by Cvetnic et al. (1987, 1988) showed a decrease in goblet cells and degenerative changes in the epithelium which are complete by two years and correlate well with their animal studies. There is, therefore, substantial disagreement in the literature.

Our work tends to support the findings of Cvetnic et al. (1987, 1988) with a decrease in goblet cells over time in patients followed serially. However, this is statistically obscured in the analysis of the total specimens due to wide scatter between individuals, and hence changes must be modest in degree.

Airflow changes have effects on nasal mucosa! structure and function, and our studies suggest that this is a dynamic process which takes many months to complete. This is of relevance to the postopera.tive assessment of patients undergoing surgery to alter the nasal airway.

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E.W. Fisher, M.A., F.R.C.S.
The Royal National Throat, Nose and Ear Hospital
Gray's Inn Road
London WClX 8DA
United Kingdom