Rhinology, 41, 220-230, 2003

Olfaction in patients with nasal polyposis: effects of systemic steroids and radical ethmoidectomy with middle turbinate resection (nasalisation)*

R. Jankowski and C. Bodino

Service d'O.R.L. et de Chirurgie Cervico-Faciale, Hôpital Central, 29 Avenue de Lattre de Tassigny, F-54035 Nancy Cedex, France

SUMMARY

Aim: *In this prospective study the effect of medical and surgical treatment on subjective olfaction was studied in patients with nasal polyposis (NPS). The effects on nasal obstruction, anterior and posterior rhinorrhea, sneezing and itching are reported in another article in this issue.*

Patients and Methods: *Protocol 1. Twenty-four patients with NPS who complained about anosmia were treated with a 7-days course of systemic steroids. Their subjective overall sense of smell was determined with a visual analog scale (VAS) before treatment, immediately after treatment, and two months later. Subsequently all patients underwent surgery bilaterally according to the nasalisation principles. The sense of smell was re-evaluated at 1, 3, 6, 9, and 12 months postoperatively.*

Protocol 2. Thirty-two patients with NPS not responding to medical therapy who, for different reasons, did not receive oral steroid treatment, received surgery only and were followed up during one year after nasalisation. Of these patients, 25 were anosmic and 7 normosmic.

Results: *Protocol 1. Following the 7-day treatment with systemic steroids the olfactory score increased significantly. During the waiting time for surgery (64±39 days) this score deteriorated again in a significant way. One month after nasalisation which included a depot injection of triamcinolone 80mg the day after surgery, the olfactory score ameliorated again and remained stable at 3,6,9, and 12 months. None of the patients reported any intake of systemic steroids during the one-year of follow-up. Statistically, there was a trend suggesting that the 12 month post-nasalisation score was better than the immediate post-oral steroid score. A good correlation between the improvement of the sense of smell after 7 days of systemic steroids and one year after nasalisation was found.*

Protocol 2 One month after the nasalisation protocol, olfaction in patients of the hypo-anosmic group had improved considerably. Scores at 3, 6,9, and 12 remained very stable. The sense of smell in the normosmic group did not change after surgery and remained stable during the year of follow-up.

In total, 49 patients with a severe loss of smell showed a significant improvement at 12 months after surgery.

Conclusion: *The presemt study shows that 1) long-lasting correction of polfactory dysfunction produced by nasal polyposis can be achieved through the combination of nasalisation and low dose of nasal steroids, 2) middle turbinate resection does not alter the possibilities to restore the sense of smell.*

Key words: olfaction, nasal polyposis, steroid treatment, radical ethmoidectomy, middle turbinate resection.

INTRODUCTION

Patients with nasal polyposis (NPS) demand effective treatment because of rhinitis symptoms, nasal blockage, and impaired sense of smell. This paper is focused on the rehabilitation of olfaction. Loss of the sense of smell, and with that "taste", is a very annoying symptom which can significantly compromise quality of life (Radenne et al., 1999; Miwa et al., 2001).

In 1956, Hotchkiss (Hotchkiss, 1956) reported that 30 patients with NPS who were treated with prednisone had an improvement in their sense of smell. He observed that this response

*Received for publication: February 25, 2003; accepted: August 4, 2003

was temporary and that when steroids were discontinued, the patients's olfaction deteriorated. He also observed that if patients continued to take low doses of prednisolone, they could maintain their sense of smell. This effect of systemic steroids on olfaction is well recognised today, but the fear of side effects limits their use.

The introduction of topically active steroids has been a remarkable therapeutic advance. Intranasal steroids are, by far, the best documented type of treatment for nasal polyposis, but unfortunately controlled studies have paid little attention to the sense of smell. Clinical experience indicates, however, that the effect of topical steroids, in contrast to systemic administration, seems to be poor (Lildholdt et al., 1997).

Despite a lack of controlled studies, surgical experience indicates that many patients with nasal polyps who are anosmic will have improvement of their anosmia after surgery (Delank and Stoll, 1998).

The aim of this paper was to approach the respective effectiveness of medical and surgical treatment on the subjective restoration of olfaction in patients with severe NPS.

The middle turbinate is thought to play a key role in olfaction, and many surgeons have cautioned against removal of the middle turbinate during endoscopic sinus surgery (ESS). However, the exact anatomical area covered by olfactory neuroepithelium and the location of the boundary between the olfactory and respiratory epithelium are not clearly established in humans (Biedlingmaier and Whelan, 1996; Feron et al., 1998; Leopold et al., 2000). The debate on appropriate management of the middle turbinate during ESS is characterizied by two schools of thought (Rice et al., 1998). Some favour the turbinate-sparing procedures popularised by Kennedy (1998), and others prefer partial or total middle turbinectomy, after the method of Friedman et al. (1986). Our experience in NPS is in favour of a systematic radical ethmoidectomy with middle turbinate resection, antrostomy, frontotomy and spenoidotomy, a procedure named nasalisation of the sinuses because it opens every sinus cavity into the nose (Jankowski et al., 1997).

PATIENTS AND METHODS

Protocol 1: Subjective evolution of the sense of smell after a 7 day treatment with systemic steroids and after nasalisation.

Twenty four consecutive patients with NPS, who complained about anosmia and fulfilled the selection criteria, were asked to participate in this protocol. These patients were referred to our department for surgery because medical treatment failed to control the symptoms associated with nasal polyposis, especially anosmia. For description of the protocol, please refer to our first paper in the same issue of the journal.

Protocol 2: Subjective evolution of the sense of smell after nasalisation in 32 consecutive NPS patients with (25 patients) and without (7 patients) severe olfactory loss.

During the selection period of protocol 1, 32 other patients were also referred to our department for surgical treatment of uncontrolled NPS. For different reasons, these patients did not want to take a short course of oral corticosteroids, but agreed to be followed up by mailed questionnaires during one year after surgery.

Among these patients were those who reported no loss in the sense of smell and who were excluded from Protocol 1 (7 normosmic patients). Subjective evolution of their sense of smell was compared to the one of the 25 anosmic other patients, using the same questionnaire as in protocol 1.

The first questionnaire they fulfilled was the day before nasalisation (QA). The second questionnaire (QB) was fulfilled one month after surgery, the day of the first post-op visit. The following questionnaires were returned by mail at 3 months (QC), 6 months (QD), 9 months (QE), and 12 months (QF) post-operatively.

Statistical analysis

Please refer to our first paper in the same issue of the journal. In addition, we used here the z-test to calculate the coefficient of correlation r.

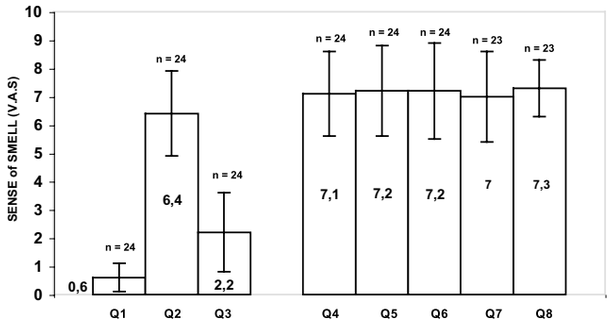

Figure 1. Subjective evolution of the sense of smell after a 7 day treatment with systemic steroids and after nasalisation in anosmic patients (ANOVA $p < 0.0001$).

V.A.S = Visual Analog Scale (0 = anosmia; 10 = normal sense of smell)

Q1 = the day before starting oral steroids

Q2 = the day after the end of the oral steroid treatment

Q3 = two months (64 ± 39 days) after the oral steroid treatment

Q4 = one month after the nasalisation protocol, which included the injection of a depot steroid the day after surgery

Q5 = three months after nasalisation

Q6 = six months after nasalisation

Q7 = nine months after nasalisation

Q8 = twelve months after nasalisation

Patients stayed on nasal steroids throughout the protocol. No patient received systemic steroids during the year of follow-up after nasalisation.

RESULTS

Protocol 1: Subjective evolution of the sense of smell after a 7 day treatment with systemic steroids and after nasalisation (Figure 1).

The day before starting the oral steroids (Q1) the mean olfactory score was 0.6 ± 0.5 cm (0-4.2 cm) (Figure 1). Fifteen patients were anosmic (score 0), and 9 scored under 5.

The 7-day treatment with systemic steroids significantly increased the Q2 olfactory score at 6.4 ± 1.5 cm ($p<0.0001$). Seventeen patients scored more than 5 and nine of them above 8. Seven patients stayed under 5.

The mean waiting time to being operated (interval Q2-Q3) was of 64 ± 39 days (14-195 days). The olfactory score significantly decreased after this mean interval of 2 months after the oral steroid treatment (Q3) and fell down to 2.2 ± 1.5 cm ($p<0.0001$). At time point Q3, only four patients still scored more than 5, with only two of them staying above 8.

One month after the nasalisation protocol (Q4), which included a depot injection of triamcinolone 80 mg, the olfactory score re-increased at 7.1 ± 1.6 cm ($p<0.0001$ over Q3). Nineteen patients scored more than 5, and among them 13 scored 8 or more. Interestingly three patients, who did not improve olfactory function after oral steroids, scored more than 5 after nasalisation. Among the five patients who scored less than 5, four had not improved after oral steroids too. Statistically, the one-month post-nasalisation Q4-score was not different from the immediate post-oral steroid Q2-score ($p=0.20$).

The following post-nasalisation scores at 3 months (Q5=7.2 ± 1.6), 6 months (Q6=7.2 ± 1.7), 9 months (Q7=7.1±1.6), and 12 months (Q8= 7.3 ± 1.6) remained very stable over the full year ($p=0.89$). No patient reported any intake of systemic steroids during this one-year follow-up. They all answered to continue topical nasal steroids on low recommended doses (1 or 2 sprays per nostril, once or twice a day). Statistically, the twelve-month post-nasalisation Q8-score was not different from the immediate post-oral steroid Q2-score, but there was a trend for Q8 to be better than Q2 (7.3 ± 1.6 versus 6.4 ± 1.5, $p=0.08$).

Looking at individual data (Table1), all patients who showed a good response after oral steroids improved also their sense of smell after nasalisation and for the full year of follow-up (n= 15), except patient N.16 who reported to be anosmic for more then 10 years, showed a good response to systemic steroids, reported only a very mild decrease 50 days later (the day before surgery), re-increased slightly one month after nasalisation, but thereafter decreased again and reported only poor remnants in her sense of smell twelve months after nasalisation. On the other hand four patients, who did not improve after oral steroids, improved after nasalisation (patients N.4, 10, 11, 17). Curiously patient N.12 did not improve after oral steroids, seemed to feel some remnants in his sense of smell one month after nasalisation (Q4), reported to be again anosmic during six months (Q5 and Q6), started to improve again after nine months, and finally scored 5.6 cm at twelve months (Q8). Two patients (patients N.18, 22) who did not improve after oral steroids did not either after nasalisation. Patient N.24 was lost to follow-up after Q6, but showed a typical good response both after oral steroids and after surgery up to six months.

Statistically we found a good correlation between the improvement in sense of smell after 7 days of systemic steroids, calculated as the difference between Q2 and Q1 scores, and the improvement one year after nasalisation, calculated as the difference between Q8 and Q1 scores (Figure 2, $r = 0.61$, $p=0.002$).

Interestingly olfaction in the four patients, who still scored more than 5 the day before surgery (Q3 of patients N.1, 14, 17, 21), was preserved and even slightly improved one year after nasalisation (Q3 = 10, 5.5, 5.5, 9.3 and, respectively, Q8 = 10, 9, 7.3, 9.8).

Protocol 2: Subjective evolution of the sense of smell after nasalisation in 32 consecutive NPS patients with (25 patients) and without (7 patients) severe olfactory loss.

Thirty two patients (18 men/14 women; mean age 47 years, range 18-78) completed the study until the 12th month post-op. All patients showed typical oedematous polyps in both nasal fossa. Fifteen were asthmatic, and ten reported aspirin intolerance (Widal's triad). Eleven patients reported previous surgery (4 one or more polypectomies, 6 an ethmoidectomy, 1 a middle antrostomy). No side effects or complications were reported during the protocol. In 17 cases a septoplasty was

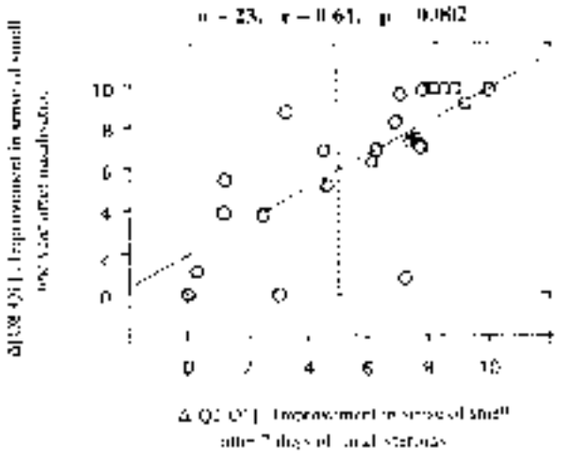

Figure 2. Correlation between the subjective improvement in sense of smell after 7 days of systemic steroids and the improvement one year after nasalisation

$\Delta[Q^2 - Q^1]$= difference between Q2 and Q1 scores

$\Delta[Q^8 - Q^1]$= difference between Q8 and Q1 scores

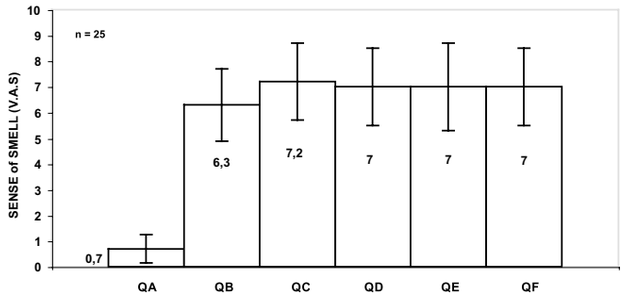

Figure 3. Subjective evolution in the sense of smell after nasalisation in 25 patients with severe olfactory loss, who were not tested pre-operatively with a short course of systemic steroids (ANOVA $p < 0.0001$).
V.A.S = Visual Analog Scale (0 = anosmia; 10 = normal sense of smell)
QA = the day before surgery
QB = one month after the nasalisation protocol, which included the injection of a depot steroid the day after surgery
QC = three months after nasalisation
QD = six months after nasalisation
QE = nine months after nasalisation
QF = twelve months after nasalisation
Patients stayed on nasal steroids throughout the protocol. No patient received systemic steroids during the year of follow-up after nasalisation.

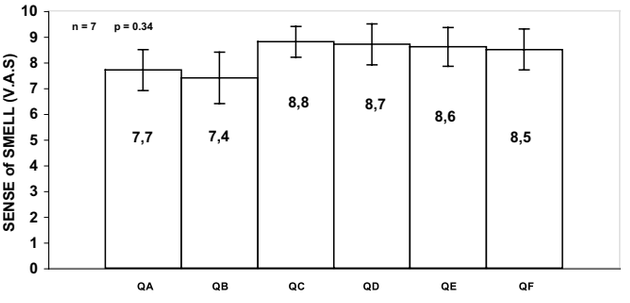

Figure 4. Subjective evolution in the sense of smell after nasalisation in 7 patients without severe olfactory loss, who were not tested pre-operatively with a short course of systemic steroids (ANOVA $p = 0.34$).
V.A.S = Visual Analog Scale (0 = anosmia; 10 = normal sense of smell)
QA = the day before surgery
QB = one month after the nasalisation protocol, which included the injection of a depot steroid the day after surgery
QC = three months after nasalisation
QD = six months after nasalisation
QE = nine months after nasalisation
QF = twelve months after nasalisation
Patients stayed on nasal steroids throughout the protocol. No patient received systemic steroids during the year of follow-up after nasalisation.

associated with nasalisation.
All patients accepted to fill in the questionnaire the day before surgery (QA). Loss in the sense of smell was reported by 25 patients with a mean duration of 5.2 ± 5 years (1 – 20 years) (hypo-anosmic group), whereas seven patients reported their sense of smell as correct (normosmic group). Visual analog scale scores are given in table 1 (protocol 2).

Patients of the hypo-anosmic group all scored QA between 0 and 3.5 cm (0.7 ± 0.6 cm). Patients of the normosmic group all scored QA between 5.5 and 10 (7.7 ± 0.9). The two groups were statistically different before nasalisation (Figure 5, $p<0.0001$).

Subjective evolution in the sense of smell in the hypo-anosmic group (n= 25) is presented in Figure 3. One month after the nasalisation protocol (QB), which included a depot injection of triamcinolone 80 mg and topical nasal steroids, eighteen patients scored more than 5 cm and among them seven scored 8 or more, six patients scored a slight improvement but stayed under 5 cm; only one patient remained anosmic. The mean score improved from 0.7 ± 0.6 (QA) to 6.3 ± 1.4(QB) ($p<0.0001$). Three months later (QC), the sense of smell was even a little better (7.2 ± 1.5) than at one month post-op (QB) ($p=0.008$). Twenty patients scored more than 5 cm, and among them fifteen scored 8 or more. The following post-nasalisation scores at 6 months (QD=7 ± 1.6), 9 months (QE=7 ± 1.5), and 12 months (QF= 7 ± 1.5) remained very stable over the full year ($p= 0.93$). Only five patients remained hypo-anosmic. No patient reported any intake of systemic steroids during this one-year follow-up. They all answered to continue topical nasal steroids on low recommended doses (1 or 2 sprays per nostril, once or twice a day).

Subjective evolution in the sense of smell in the normosmic group (n = 7) is presented in Figure 4. Statistically it did not change after surgery and remained stable during the one year of follow-up ($p = 0.34$). The mean score twelve months after surgery (QF) was even a little better than the day before surgery (QA) (8.5 ± 0.8 versus 7.6 ± 0.8, $p = 0.32$). Looking at individual data (Table 1), it should be noted that two patients (N.53 and 56) reported a decreased sense of smell one month after surgery. Whereas patient N.53 re-improved and completed the study with a sense of smell similar to the day before surgery, patient N.56 ended the study with a score a little below the pre-op score (5.1 versus 7.5 cm).

Twelve months after the nasalisation procedure the sense of smell scores (QF) of the hypo-anosmic patients were not statistically different from the scores of the normosmic patients, which also were not different from their pre-op scores (Figure 5).

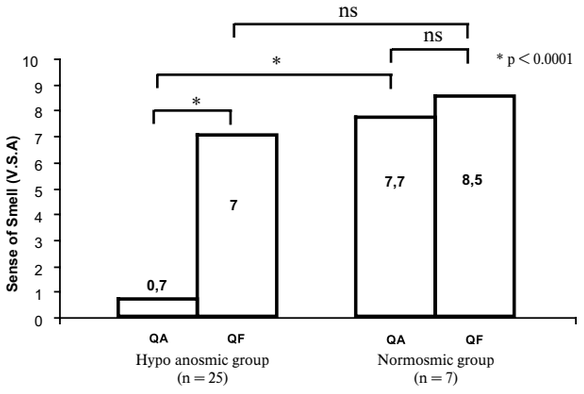

Figure 5. Comparison of the subjective sense of smell before (QA) and one year after nasalisation (QF) between the hypo-anosmic and the normosmic groups (* $p < 0.0001$).
V.A.S = Visual Analog Scale (0 = anosmia; 10 = normal sense of smell).

Subjective evolution of the sense of smell in the 49 hypo-anosmic consecutive patients one year after nasalisation.
Forty nine patients joined the study with a subjective severe loss in sense of smell (mean score = 0.7 ± 0.6, range 0 – 4.2 cm); forty (82%) ended the one-year follow-up with a significant improvement of their subjective sense of smell (mean score = 7.2 ± 1.5, range 5 – 10) ($p < 0.0001$); in addition the patient lost to follow-up scored 8.2 cm on the last check-up at 6 months after nasalisation.

DISCUSSION

The present study shows that 1) long-lasting correction of olfactory dysfunction produced by nasal polyposis can be achieved through the combination of nasalisation and low dose of nasal steroids, 2) middle turbinate resection does not alter the possibilities to restore the sense of smell.

The concept of steroid dependant anosmia in nasal polyposis was individualised by Jafek (1987) who reported two cases and observed that both surgery and systemic steroids were able to temporary restore the sense of smell, but to get a long-term reversal of anomia a combined treatment with surgery and low doses of daily oral steroids (5 mg) was necessary. This concept was fully illustrated in the paper by Stevens (2001), who conducted a prospective study of 24 patients with nasal polyposis who were anosmic prior to surgery; those who remained anosmic after surgery (12 patients) were treated first with and were found to be unresponsive to nasal steroids; these patients were thereafter started on 40 mg prednisone per day, and 9 reported restoration of a normal sense of smell based on the UPSIT score, 2 no response at all to steroids, and one refused them; attempts at alternate dosage resulted in deterioration of the sense of smell during the day they were off medication; the longest time any patient in this series remained on oral steroids was three years; many who stopped were fearful on the long-term effects of oral steroids despite being on 5 mg per day.

The place and role of surgery is, however, a matter of debate in this concept. Fifty percent of Stevens' patients regained a correct sense of smell by surgery alone, but this was one month after surgery and there was no follow-up data. Among the eleven remaining anosmic who received oral steroids, only two did not regain sense of smell but nine did it. Our data show that patients who are able to restore their sense of smell under oral steroids are those who will also restore their sense of smell after surgery, with a good correlation between the post-oral-steroid improvement and the post-nasalisation improvement (Figure 2). According to our experience, nasalisation might have been able to bring back the sense of smell of these nine patients, without need of post-op daily low dose of oral steroids. Unfortunately there is no clear description of Stevens' surgical procedure, which is only reported as "endoscopic nasal and sinus polypectomy" or "endoscopic nasal and sinus surgery".

In an another paper by Blomqvist et al. (2001) evaluating medical versus surgical treatment of nasal polyposis in a randomised controlled study, it is concluded that when hyposmia is the primary symptom no additional benefit seems to be gained from surgical treatment. In this study, thirty-two patients with nasal polyposis and symmetrical nasal airways were randomised to unilateral endoscopic sinus surgery after pre-treatment with oral prednisolone for ten days and local nasal budesonide bilaterally for one month; postoperatively patients remained on nasal steroids and were followed for 12 months. The sense of smell was improved by the combination of oral and local steroids, and surgery had no additional effect. Surgery had, however, additional beneficial effects on nasal obstruction and secretion, and twenty-five percent of the patients (8/32) were willing to undergo an operation also on the unoperated side at the end of the study, twelve months later. The authors have only published their mean results and no range of values or individual data are known. For instance, the mean score in sense of smell at entry in the study is about 70 mm on their visual analogue scale (VAS) (with, as far as we can expect, 0 meaning normal sense of smell and 100 anosmia), but the authors do not give the range of values and we do not know how many patients are anosmic and how many normosmic; nevertheless, the mean score improves to 50 mm after oral + nasal steroids; interestingly, three months after surgery the score has improved to 30 mm on the operated side and to 40 mm only on the unoperated side, this difference being statistically significant according to the authors; at twelve months post-op, however, the scores are similar on both sides (40 mm). As a consequence, the mean olfactory improvement can be estimated to be 30 mm of VAS.

In our study, the mean sense of smell score at entry was 6 ± 5 mm (range 0 – 42 mm) (with 0 meaning anosmia and 100 normal sense of smell); it increased to 64 ± 15 mm after seven days of oral steroids, but despite maintenance of nasal steroids

decreased to 22 ± 15 mm two months later; one month after nasalisation it re-increased to 71 ± 16 mm and remained stable until the end of our study, twelve months later. As a consequence our conclusion is completely different: when hypoanosmia is the primary symptom, a big benefit can be gained from surgical treatment. The mean olfactory improvement in our study is of 65 mm of VAS.

Of course, our patients were probably different from Blomqvist et al.'s patients (perhaps our patients were in a later and more severe stage of the disease), but our impression is that the difference, which could explain the apparently contradictory results of these two studies, could be found in the type of surgery performed. Fortunately, Blomqvist et al. very clearly describe their surgical procedure performed under general anesthesia: "the extent of surgery was determined by the disease but always included uncinectomy, anterior ethmoidectomy, and exploration of the posterior ethmoids; if the posterior cells were involved, surgery was continued posteriorly with posterior ethmoidectomy and in some cases with sphenoidotomy; the ostium to the maxillary sinus was enlarged, and diseased mucosa from the fronto-nasal recess was removed; if there was a pneumonized concha bullosa, the lateral mucosa and bone were usually removed to decompress the ostiomeatal complex; care was taken to preserve an intact mucosa". The nasalisation procedure is different: the extent of surgery is not determined by the disease but by the anatomy of each patient and the aim of surgery is in every patient to perform a radical anterior and posterior ethmoidectomy, with middle turbinate resection, antrostomy, sphenoidotomy and frontal ostium exposure; the ethmoid mucosa is removed as completely as possible, except around the frontal ostium and in inaccessible areas, proper to the anatomy of some patients, that could make the surgery hazardous; secretions, polyps or cysts of the maxillary and sphenoid sinuses are removed, and if possible of the frontal sinus too, but the mucosa on the walls of the large sinuses is preserved.

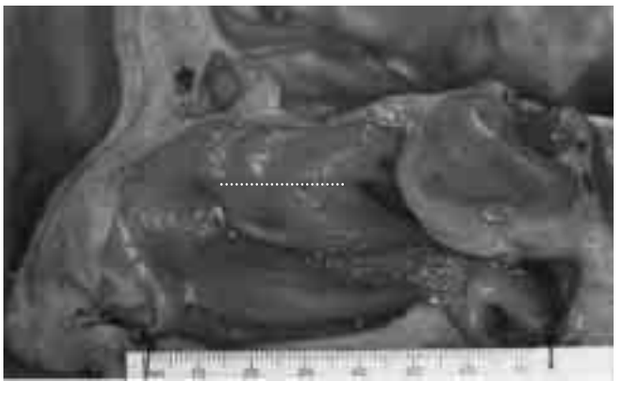

Figure 6. Anatomy of the turbinate (medial) wall of the ethmoid. Above the dotted line is the conchal lamina (and a very small superior turbinate in this specimen); below the doted line is the middle turbinate, which is resected in the nasalisation procedure.

Our experience is that middle turbinate resection and removal of the ethmoid mucosa both help to correct the olfactory dysfunction produced by nasal polyposis. The middle turbinate (Figure 6) is attached anterior to the lateral edge of the cribriform plate by a piece of bone which has been termed concha lamina (Mouret, 1922; Lang, 1989). This conchal lamina also gives attachment to the superior, and in a few patients to the supreme ethmoid conchae, and forms a continuous bony lamella that separates the cribriform plate and the ethmoidal cells lying beneath the ethmoidal roof. An axial CT-scan (Figure 7) clearly shows that the nasal fossa at this level appears as narrow parallel clefts a few millimetres wide on both sides of the nasal septum, which are laterally limited by a continuous bony wall, namely the conchal lamella (Teatini et al., 1987). The free-hanging parts of the middle, superior and supreme turbinates originate successively from anterior to posterior from the concha lamina. We start the resection of the middle turbinate at the apex of the middle meatus, where the anterior margin of the middle turbinate abuts the lateral nasal vault. We use left-curved scissors hold horizontally, so that the line of section can be directed towards the lower free margin of the superior turbinate, which is preserved (Figure 6). Once the superior meatus has been reached, the middle turbinate can be mobilized and it becomes easy to detach the posterior end of the middle turbinate from the lateral wall. So, in the nasalisation procedure, the free hanging part of the middle turbinate is resected, but the conchal lamina and the superior turbinate are left intact. We have measured in a cadaver study of twelve specimens that removing the middle turbinate in this way corresponds to an amputation of 49 ± 6% (range 38 – 60%) of the medial wall of the ethmoid (Bodino et al., in press). Removing the middle turbinate is actually a major step to perform a radical ethmoidectomy, because it opens the route to a very precise dissection of all ethmoid cells located between the ethmoidal roof and the concha lamina. Our hypothesis is that chronically inflamed mucosa left in this area could disturb the electrophysiology of the olfactory mucosa, especially nerve conduction. The work by Havas and Lowinger (2000) gives actually some support to the hypothesis that resection of the middle turbinate without removing the mucosa of the ethmoidal surface of the concha lamina and adjacent cells below the roof seems insufficient to restore olfaction. They have conducted a prospective study of 1233 subjects, including 88 subjects having objective evidence of preoperative hyposmia; before surgery, the patients were randomly divided in two groups; 509 patients, with among them 36 hyposmics, had partial middle turbinate resection (MTR) as part of their FESS procedure, and in 597 cases with among them 52 hyposmics the middle turbinates were preserved (MTP); 22 of 36 patients (61%) remained hyposmic in the MTR group, compared with 32 of 52 (61%) in the MTP group. These data suggest that resection of the middle turbinate with preservation of the

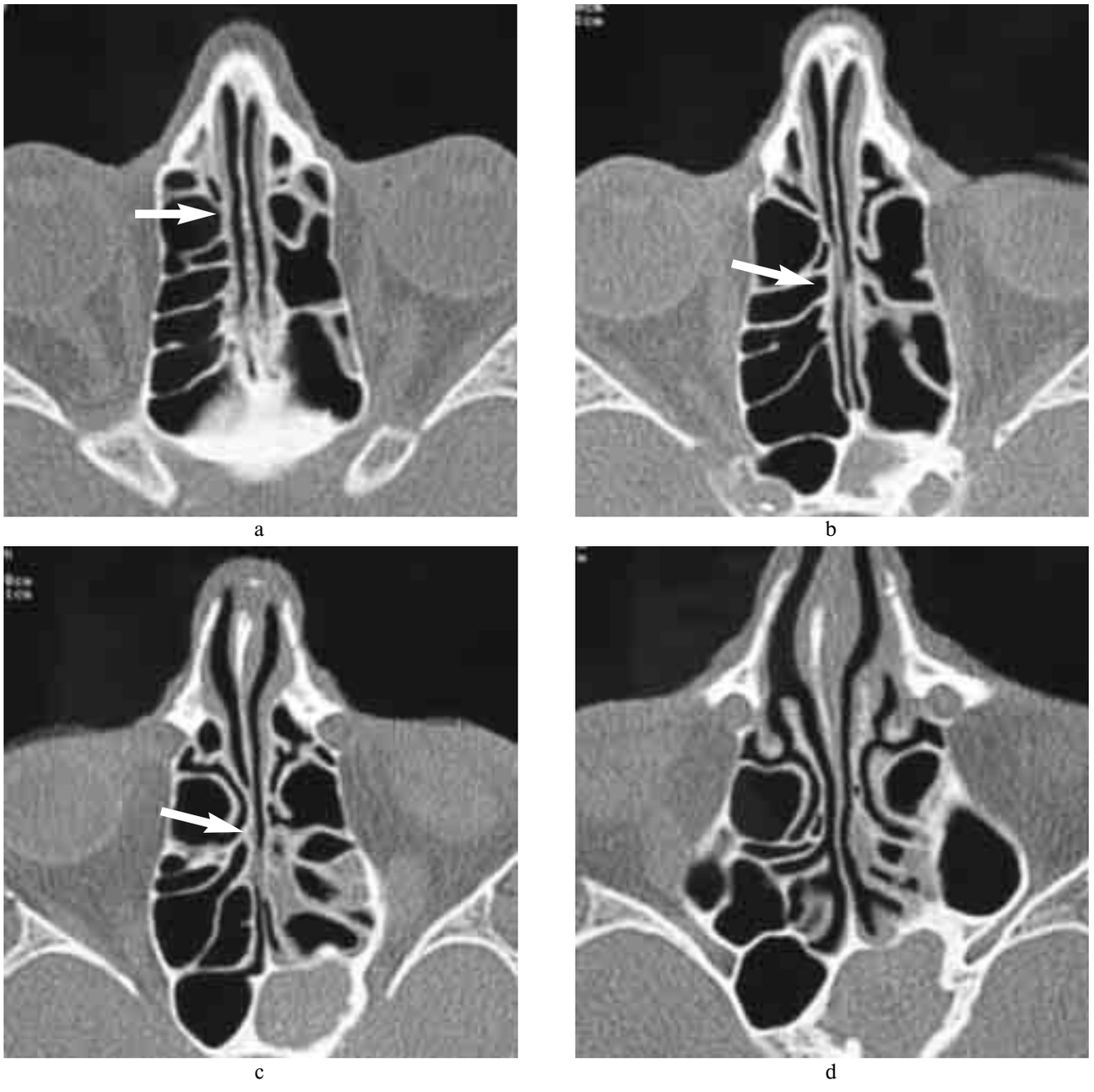

Figure 7. Axial CT-scans at the level of the olfactory clefts shows that the nasal fossae are laterally limited by a continous bony wall named conchal lamina (arrow) (a = superior, d = inferior).

mucosa as recommended in FESS is apparently not sufficient to restore the sense of smell. In the nasalisation procedure, we always try to remove as completely as possible the inflamed mucosa of the ethmoidal roof and adjacent surface of the concha lamina.

According to classical knowledge, the human olfactory neuroepithelium is located predominantly on the dorsal aspects of the nasal vault, the septum, and the superior turbinate. Resection of the middle turbinate should, therefore, not have deleterious effect. Feron et al. (1998) have, however, observed that the probability of finding olfactory epithelium in a biopsie specimen ranged from 30 to 76%, depending on its location; that the dorsoposterior regions of the nasal septum and the superior turbinates provided the highest probability, but, surprisingly, that olfactory epithelium could also be found anteriorly and ventrally on both septum and middle turbinate in approximately 50% of 12 specimens. Leopold et al. (2000) have confirmed by means of the electro-olfactogram and anatomically located biopsy specimens that the mucosa of the middle turbinate near its insertion to the lateral wall contained olfactory tissue in 7 of 12 subjects. These data are in conflict with the

Table 1. Visual Analog Scale data on the Sense of Smell; 0 = anosmia; 10 = normal sense of smell.

			NAME	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Protocol 1		1	Mme OLI.L	2,6	10	10	10	10	10	10	10
		2	Mme AUB.MF	0	10	0	10	10	10	10	10
		3	Mr BRE.B	0	7	0	8,4	10	9,8	9,5	9,1
		4	Mr PER.C	0	1,2	0,2	7,7	6,5	5,5	6,5	5,5
		5	Mme AMA.S	0	8,9	0	10	10	10	10	10
		6	Mr GER.Y	0,1	9,3	0	8	7	9,4	9,3	10
		7	Mr BOH.C	0	7,5	0,2	5,6	7,6	7,5	6,4	5
		8	Mr THI.JN	2,1	9,8	1,2	10	8,7	9,2	8,6	9,4
		9	Mr BAR.G	0,1	6,2	1,5	9,4	8,7	6,5	6,3	6,8
		10	Mr SAC.M	0	2,5	1,7	2	4,5	3,8	4,5	5,7
		11	MmeDIE.MJ	0	3,2	1,7	7,5	8,6	8,8	9,5	9,1
		12	Mme KEL.M	0	0	0	2	0	0	1,8	5,6
		13	Mr ZIE.R	0	6,2	1,8	6	6,7	7	7,4	8,8
		14	Mr HAN.P	0,3	7,2	5,5	8	8,3	8,7	8,4	9
		15	Mr BAR.F	0	7,8	0	9,7	9,7	10	8,7	9,6
		16	Mme FEY.M	0	7,2	5	6,5	3,2	0,8	2,5	0,3
		17	Mr MOR.J	3,7	4,8	5,5	7,4	7,5	7,6	7,8	7,3
		18	Mr HAB.S	0,2	0,5	0	0,4	0,6	1,3	1,2	1,2
		19	Mr SAN.D	4,2	8,8	3,7	9,4	9,6	9,4	10	8,5
		20	Mr WAL.C	1,5	6	1,4	8,2	8,5	8,4	1,8	7,5
		21	MrGOD.E	0	8,5	9,3	9,5	9,7	10	10	9,8
		22	Mme GUI.V	0	3	0	0	0	0	0	0
		23	Mr DALL.D	0	8,1	0,2	9,8	9,7	10	9,8	9,7
		24	Mr GIN.S	0	9,8	5	3,8	7,5	8,2	-	-
			NAME			**QA**	**QB**	**QC**	**QD**	**QE**	**QF**
Protocol 2	**Anosmic patiens**	25	Mr SPA.P	-	-	0	9,2	8,8	9	9	8,2
		26	Mr WEB.A	-	-	0	7,3	7,5	7,8	8,2	8,2
		27	Mr MAR.A	-	-	0,5	5,2	9	8	9	9
		28	Mr BRU.A	-	-	0,5	10	10	10	9,6	10
		29	Mr WUL.B	-	-	0	1,2	2	0,5	0,5	1,2
		30	Mme SCH.A	-	-	0	2	0	2	0,9	2
		31	Mme GIN.C	-	-	0	9,5	0,2	7,8	8,8	9,9
		32	Mr NAU.JL	-	-	0,7	8,7	9	8,5	7,5	8,2
		33	MrHOM.F	-	-	0	7,2	9,5	8,4	9,4	8,4
		34	Mr GRI.F	-	-	3	7	9	9	10	10
		35	Mme PIE.C	-	-	0	9,7	9,7	8,2	7,4	7,1
		36	Mr SCH.D	-	-	0,2	7,2	10	9,8	9,8	9,6
		37	Mme GAU.M.O	-	-	2,8	3,7	8,2	8,4	8,4	7,9
		38	Mr HEN.C	-	-	0,5	10	10	9,4	10	9,4
		39	Mr BIS.B	-	-	3,5	7,5	7,5	8,6	8,5	8,3
		40	Mme DOR.MP	-	-	2,3	4,5	3,5	3	4,2	1,9
		41	Mr ROB.P	-	-	0	2	2,7	0,8	1,8	1,5
		42	Mme VET.V	-	-	0	10	10	10	10	10
		43	Mme LAR.R	-	-	0,5	0,5	0,5	0,2	0,5	0,7
		44	Mr MEL.JL	-	-	0,2	5,6	8,5	8	7,2	7,9
		45	Mr CHO.M	-	-	0	5,5	7,5	10	10	10
		46	Mme KIE.S	-	-	3,2	6,5	8,7	8,8	8,7	9
		47	Mr DIA.G	-	-	0	2,8	6	5,1	5	5,2
		48	Mme GER.MT	-	-	0,3	7,4	8,6	7,2	6,2	7
		49	Mme STE.M	-	-	0,3	7,6	7,4	6,2	4,6	5,6
	os	50	Mme PEC.Y	-	-	7	9	9,3	10	10	10

Legend: see next page

Protocol 1: Evolution of the sense of smell after a 7 day treatment with systemic steroids and after nasalisation.
Q1 = the day before starting oral steroids
Q2 = the day after the end of the oral steroid treatment
Q3 = two months (64 ± 39 days) after the oral steroid treatment
Q4 = one month after the nasalisation protocol
Q5 = three months after nasalisation
Q6 = six months after nasalisation
Q7 = nine months after nasalisation
Q8 = twelve months after nasalisation
Protocol 2: Evolution of the sense of smell after nasalisation in 32 consecutive NPS patients with (25patients) and without (7 patients) severe olfactory loss.
QA = the day before surgery
QB = one month after the nasalisation protocol
QC = three months after nasalisation
QD = six months after nasalisation
QE = nine months after nasalisation
QF = twelve months after nasalisation

work by Biedlingmaier and Whelan (1996) who investigated the presence of olfactory tissue on 36 sections from 12 endoscopically resected turbinates and did not find neither olfactory epithelium nor olfactory receptor cells. However, Biedlingmaier's technique involves removing only a window from the anterior one third of the lower one half of the middle turbinate. These authors furthermore reviewed 110 patients having 198 middle turbinate resections and found that only one patient complained of post-operative anosmia (0.9%). Friedman et al. (1996) have published a prospective non-randomized study comparing the UPSIT scores of 38 normosmic patients who underwent partial middle turbinate resection and 26 normosmic patients in whom the middle turbinate was preserved; all patients were re-evaluated approximately eight weeks after surgery by UPSIT test. No modification of the sense of smell was observed in both groups. Friedman's technique involves removing approximately the anterior half of the middle turbinate, keeping a stub of the vertical attachment to serve as a landmark. In our small series of 7 normosmic patients, only one reported a discrete decrease in his sense of smell one year after nasalisation: his pre-op score was of 75 mm, his one-year post-op score of 51 mm (patient N.56). The mean pre-op score was, however, not different from the mean post-op score in this small series. In addition, five patients of our protocol 1 (Subjective evaluation of the sense of smell after systemic steroids and nasalisation) reported a score still above 50 mm the day before surgery (Q3); in four patients the one-year post-op score was improved (see Table 1, patients N. 1, 14, 17, 21), but one patient (N.16) slowly decreased his sense of smell from 50 mm to 3 mm; this patient was, however, anosmic before the oral steroid treatment (score Q1 = 0). Once more, the mean pre-op score of these five patients was not different from the mean post-op score. It is difficult to know whether or not the sense of smell of these two patients deteriorated because of middle turbinate resection or natural evolution of the disease. Our data show, however, that in the large majority of cases resection of the middle turbinate does not alter the possibilities to restore the sense of smell of patients with nasal polyposis, but a surgeon facing a patient should always discuss the risk.

It is not known, and we have not found data in the literature, how long after the first episode of anosmia related to nasal polyps patients will 1) develop steroid dependant anosmia, and 2) irreversibly loose their sense of smell. In our series of 49 hypo-anosmic patients we count 6 patients (12%) who remained irreversibly anosmic despite systemic steroid and/or surgical treatment (patient N. 18, 22, 29, 30, 41, 43).

Daily low-dose oral steroid therapy seems controversial to keep a sense of smell, and the concerns may be the same as those reported with corticosteroid therapy in rheumatoid arthritis (Saag, 1997). Some observational studies suggest that mortality might be increased with steroid use, and several large retrospective reviews indicate that long-term low-dose steroid use is a significant independent predictor of numerous, potentially serious adverse events. Both cumulative and average steroid dose are independent important adverse-event predictors. Even at low doses, steroids can lead to skin thinning and ecchymoses, acne, hirsutism and striae. Development of a cushingoid appearance can be troubling to patients, but is uncommon at doses below physiologic range. Steroid psychosis is uncommon at doses < 20 mg/day of prednisone, but symptoms of akathisia, insomnia, and depression are observed in patients taking low-dose therapy. Steroid-induced osteoporosis is the most worrisome of all steroid-related toxicity, and it has been estimated that $> 50\%$ of steroid users will develop bone loss. Changes in spinal bone mineral density (BMD) have been observed within the initial 5 months of low-dose therapy. Prednisone doses as low as 2.5 mg/day may suppress osteocalcin, a biochemical marker of bone formation. Avascular necrosis of bone is a significant and common problem in patients receiving high steroid doses, but is seldom

noted when the prednisone dose is maintained <20 mg/day. The incidence of myopathy in patients receiving low-dose steroids is rare, but of note, myopathy has been reported to occur at a dose as low as 8 mg/day of fluorinated steroid preparations after only 3 months of treatment. Steroids increase the risk of adverse gastrointestinal events such as gastritis, ulceration, and bleeding. In addition, there are anecdotal reports of intestinal rupture, diverticular perforation, and pancreatitis believed to be caused by low-dose steroids. Moderate- to high-dose steroid therapy can lead to an increased risk of serious infections, but few studies have rigorously explored the risk of infection in patients treated with low-dose and this risk is uncertain. Posterior subcapsular cataracts are well-described complication of prolonged corticosteroid use. Although some clinicians believe there is no minimal safe dose with respect to this complication and report exist of cataract formation even with inhaled preparations, others note that cataracts rarely occur in patients taking <10 mg/day for < 1 year. The development of frank glaucoma, particularly with low-dose therapy, is rare and tends to appear in patients who are otherwise predisposed to the condition. However, a recent report suggests that glaucoma may occur with inhaled steroids as well (Garbe et al., 1997). It is uncommon for frank diabetes to develop de novo as a result of steroid therapy, but patients with diabetes mellitus and glucose intolerance may have higher blood glucose levels while taking low-dose steroids. Patients with essential hypertension require closer surveillance of blood pressure and may need modification of their antihypertensive regimens while on low-dose steroid therapy. An additional concern of chronic steroid use is hypothalamic-pituitary-adrenal (HPA) insufficiency. HPA insufficiency appears to be both dose- and duration-specific. High-dose therapy can result in protracted suppression of adrenocorticotropic hormone (ACTH) release and adrenal hyporesponsiveness in as little as 5 days. Spontaneous recovery of the HPA axis is usual in patients on 5 mg of prednisone, however, subphysiologic doses (< 7.5 mg/day) given for long-term periods may lead to HPA blunting. HPA suppression is worsened if steroids are given twice daily. The last risk, which is not well documented but we have had it observed in our practice, is the patients' dependence to systemic steroid therapy. Abrupt withdrawal often results in dramatic flares in nasal polyposis activity, and many of these patients, even after surgery and sometimes despite good anatomical results, will continue to need and to ask for steroid treatments to feel good.

A 7-day treatment with oral steroids seems actually a good test to know whether or not the sense of smell of one patient is reversible. Moreover, we have found a good correlation between systemic steroids restoration and surgical restoration in the sense of smell (Figure 2). The difference between steroids' and nasalisation's restoration in the sense of smell is a matter of time. Our data demonstrate that the sense of smell remains stable for at least one year after nasalisation in the large majority of patients. We know also from our practice that many patients have kept their sense of smell for more than 10 years, but that others have lost it after months or years, not always because of recurrence of polyps. Nasal polyposis certainly weakens the olfactory mucosa, but we do not know if the natural history would bring all patients to irreversible anosmia and after how many years. The only fact we know is that we have effective treatments to restore the sense of smell in these patients. Topical steroids are effective in a few patients. The combination of short-courses of systemic steroids and long-term nasal steroids is a second possibility. The third therapeutic option is either daily low-dose systemic steroids or surgery. Our opinion is that there are no more risks (and probably even less risks) to propose the patient the nasalisation procedure than daily low-dose systemic steroids. It has been proven that surgical complications are experience-dependant, and that safe ethmoidectomy surgery can be performed once experience is gained (Stankiewicz, 1989). There are today, throughout the world, a lot of experienced surgeons able to perform radical ethmoidectomy as we do in the nasalisation procedure, and a lot of instructional courses for inexperienced sinus surgeons to gain expertise. Moreover, computed-assisted surgery might be very helpful in the learning curve to perform such procedure.

In conclusion, our experience indicates that the sense of smell of patients with hypo-anosmia produced by nasal polyposis can be restored, after failure of medical treatment, by the combination of nasalisation and long-term nasal steroids.

REFERENCES

1. Blomqvist E, Lundblat L, Anggard A, Harraldson P, Starne P (2001) A randomized controlled study evaluating medical treatment versus surgical treatment in addition to medical treatment of nasal polyposis. J Allergy Clin Immunol 107: 224-228.
2. Bodino C, Grignon B, Jimenez A, Braun M, Jankowski R (2004) Surgical Anatomy by the Turbinate wall of the ethmoid. Rhinology (in press).
3. Delank K, Stoll W (1998) Olfactory function after functional endoscopic sinus surgery for chronic sinusitis. Rhinology 36: 15-19.
4. Feron F, Petry C, McGrath J, Mackay-Sim A (1998) New techniques for biopsy and culture of human olfactory epithelial neurons. Arch Otolaryngol Head Neck Surg, 124: 861-866.
5. Friedman W, Katsantoni G, Rosenblum B (1996) Endoscopic sinus surgery with partial middle turbinate resection: effects on olfaction. Laryngoscope 106: 977-81.
6. Garbe E, Lelorier J, Bolvin J, Sulssa S (1997) Inhaled and nasal glucocorticoids and the risks of ocular hypertension or open-angle glaucoma. JAMA 277: 722-727.
7. Havas T, Lowinger D (2000) Comparison of functional endonasal sinus surgery with and without partial middle turbinate resection. Ann Otol Rhinol Laryngol, 109: 634-640.
8. Hotchkiss W (1956) Influence of prednisolone on nasal polyposis with anosmia. Arch Otolaryngol 6: 478-479.
9. Jafek B, Moran D, Eller P, Rowley J, Jafek T (1987) Steroid-dependent anosmia. Arch Otolaryngol Head Necck Surg 113: 547-549.
10. Jankowski R, Pigret D, Decroocq F (1997) Comparison of functional results after ethmoidectomy and nasalisation for diffuse and severe nasal polyposis. Acta Otolaryngol (Stockh) 117: 601-608.
11. Kennedy D (1998) Middle turbinate resection: evaluating the issues--should we resect normal middle turbinates? Arch

Otolaryngol Head Neck Surg 124: 107.
12. Lang J (1989) Clinical anatomy of the nose, nasal cavity and paranasal sinuses. Georg Thieme Verlag, Stuttgart-New York.
13. Leopold D, Hummel T, Schwob J, Chen Hong S, Knecht M, Kobal G (2000) Anterior distribution of human olfactory epithelium. Laryngoscope 110: 417-421.
14. Lildholdt T, Dahl R, Mygind N (1997) Effect of corticosteroids on nasal polyps. Evidence from controlled trials. In: N. Mygind and T. Lildholdt, Editors. Nasal polyposis - An inflammatory disease and its treatment. Munksgaard: Copenhagen. pp 160-169.
15. Miwa T , Furukawa M, Tsukatani T, Costanzo R, Dinardo L, Reiter E (2001) Impact of olfactory impairment on quality of life and disability. Arch Otolaryngol Head Neck Surg 127: 497-503.
16. Mouret J (1922) Le schema des masses laterales de l'ethmoide. Rev Laryngol 43: 9-22.
17. Radenne F, Lamblin E, Bandezande L, Tillie-Leblond J, Darras J, Tonnel A (1999) Quality of life in nasal polyposis. J Allergy Clin Immunol 103: 79-84.
18. Rice DH (1998) Middle turbinate resection: weighing the decision. Arch Otolaryngol Head Neck Surg 1241: 106.
19. Saag K (1997) Low-dose corticosteroid therapy in rheumatoid arthritis: balancing the evidence. Am J Med 103: 31S-39S.
20. Stankiewicz J (1989) Complications in endoscopic intranasal ethmoidectomy: an update. Laryngoscope 99: 686-690.
21. Stevens M (2001) Steroid-dependent anosmia. Laryngoscope 111: 200-203.
22. Teatini G, Simonetti G, Salvolini H, Nasala W, Meloni F, Rovasio S, Dedola G (1987) Computed tomography of the ethmoid labyrinth and adjacent structures. Ann Otol Rhinol Laryngol 96: 239-250.

Professor R. Jankowski
Service O.R.L.- Hôpital Central
54035 Nancy
France

E-mail : r.jankowski@chu-nancy.fr
Fax : +33-(0)3-885-2258