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Evolution of symptoms associated to nasal polyposis following oral steroid treatment and nasalisation of the ethmoid - radical ethmoidectomy is functional surgery for NPS*

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SUMMARY

Purpose: *The effects on the symptoms of nasal polyposis (NPS) of 1) a 7-day systemic steroid treatment and 2) radical ethmoidectomy (nasalisation) were compared.*

Patients and Methods: *Twenty-four patients with NPS whose symptoms failed to respond to medical treatment were included in the study. Symptoms were recorded on Visual Analog Scales (VAS) before (Q1) and the day (Q2) after a 7-day treatment of oral prednisolone (60mg/day), and a few weeks later the day before surgery (Q3). All patients were operated on bilaterally according to the nasalisation principles, i.e. endoscopic radical ethmoidectomy without mucosal preservation, with middle turbinate resection, antrostomy, sphenoidotomy and frontal ostium exposure, and a depot injection of triamcinolone 80mg the day after surgery. The fourth questionnaire (Q4) was fulfilled one month after surgery, the day of the first postop visit. The following questionnaires were returned by mail at 3 months (Q5), 6 months (Q6), 9 months (Q7), and 12 months (Q8) post-operatively. Patients stayed on topical steroids throughout the study.*

Results: *Nasal obstruction was a major complaint at entry in the study. Following the short-systemic steroid course the obstruction score improved significantly. However, at 2 months after the oral steroid treatment the obstruction score had deteriorated again. Following surgery, obstruction scores ameliorated again and remained stable over the full year of follow-up. Similar results were observed for anterior and posterior rhinorrhea, sneezing and itching. None of the patients reported any intake of systemic steroids during follow-up.*

Conclusion: *These data show that 'nasalisation' i.e. radical ethmoidectomy with middle turbinate resection and mucosa removal is effective functional surgery for patients with nasal polyposis if medical treatment fails.*

The subjective effects on the sense of smell are reported in a separate paper published in this issue.

Key words: nasal polyposis, steroid treatment, radical ethmoidectomy

INTRODUCTION

Nasal polyposis (NPS) is a chronic inflammatory disease of the nose and sinus mucosa, starting in the ethmoid sinuses, and leading to a protrusion of oedematous polyps in nasal and paranasal cavities. NPS causes symptoms such as nasal obstruction, anosmia or hyposmia, anterior and/or posterior rhinorrhea, sneezing, and itching. Patients are also bothered by sleep disorders, taste didorders, dry mouth, facial pressure or headache, recurrent boots of rhino-sinusitis with exacerbation of asthma, and irritability. Radenne et al. (1999) have demonstrated that the SF-36 questionnaire presents a high internal validity and reliability in patients with NPS, and that quality of life improvement after NPS treatment, either with nasal steroids or endonasal ethmoidectomy, is related to nasal symptom improvement.

The mainstay of treatment for NPS is medical, but surgery is now widely regarded as having a role to play in the majority of cases. If one applies the gold standard of a double-blind randomised placebo-controlled trial, there is a significant paucity of information in the literature to support surgery as opposed to medication, or indeed any particular surgical procedure of the many which have been described (Lund, 1997)

Intranasal steroids are, by far, the best documented type of treatment for NPS, but there are only placebo-controlled studies and no comparison between the different topical steroids themselves, or between medical and surgical treatments. Although systemic steroid treatment has not yet been studied in placebo-controlled trials there is no doubt that it is highly effective (Van Camp and Clement, 1994).

The only attempts at a randomised comparison of surgery and

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medication were performed by Lildholdt at al. In their first study (Lildholdt et al., 1988), they randomised 53 patients to either surgical removal of visible polyps with a snare or a depot injection of steroid (betamethasone 14 mg). All patients continued with topical steroid (beclomethasone aerosol, 400 µg/day) for 12 months. Both regimens caused substantial and equal increase in nasal expiratory peak flow and the improvement was maintained during the 1-year observation period. The sense of smell improved significantly in the systemic steroid group at 2 weeks but it was not maintained at 2-12 months during topical therapy. In a second study of 124 patients (Lildholdt et al., 1997), they randomised 33 patients who failed to respond to the initial treatment with topical steroid (budesonide powder 400 or 800 µg/day), to systemic steroid (depot injection of 14 mg betamethasone) or polypectomy with a snare. After 1 year of continuous topical therapy there was no difference between the two groups with regard to any effect parameter. The authors concluded that one injection of depot steroids was equivalent to polypectomy, that the primary treatment of nasal polyposis should be systemic and local steroids, and that surgery should only be reserved for those few cases in which the presence of residual or recurrent polyps justifies the inherent risks and discomfort for the patient.

The advent of endoscopic sinus surgery has been developed in parallel with the concept of Functional Endoscopic Sinus Surgery (FESS). However, it should be stressed that an endoscopic approach can be as conservative or as radical as the surgeon wishes and ranges from removal of small polyps within the middle meatus, perhaps combined with uncinectomy, middle meatal antrostomy and opening of the bulla to a complete nasalisation of the sinuses with middle turbinate resection and extensive removal of the ethmoid mucosa. Our experience is that, when dealing with NPS, the more radical the surgery the more functional the results (Jankowski et al., 1991; Jankowski et al., 1997). In the FESS concept, the extent of dissection is determined by the extent of disease and the goals are to preserve as much as possible the ethmoid mucosa and the middle turbinate, even in a total spheno-ethmoidectomy (Lanza et al., 1992; Brent et al., 1998). Endoscopic radical ethmoidectomy (nasalisation) has therefore been regarded as non-functional surgery.
The aim of the present study is to compare the improvement of symptoms associated to NPS 1) after 7 days of systemic steroids and 2) during one year after nasalisation, in patients with NPS, and to show that endoscopic radical ethmoid surgery ('nasalisation') is Functional Endoscopic Sinus Surgery despite the fact that the concepts of FESS differ considerably from those of nasalisation.

PATIENTS AND METHODS

Twenty four consecutive patients with NPS were referred to our department for surgery because medical treatment failed to control the symptoms associated with nasal polyposis. Medical treatment inefficiency was considered in patients who reported daily topical steroid sprays for at least 6 months, and/or the need for more than 2 short courses of systemic steroids during the last year. Patients' eligibility was then considered if they were aged over 18 years, there was no contra-indication to a short course of systemic steroids and to general anaesthesia, no need for systemic steroids prescription for other pathologies in the year to come, and if they wanted or accepted to take one short course of systemic steroids before being operated, and to be followed up for one year after surgery.

Subjective estimates of symptoms' severity, i.e. nasal obstruction, sense of smell, anterior rhinorrhea, post-nasal drip, sneezing, and itching, were recorded on Visual Analog Scales (VAS). Based on literature of health measurements (Mc Dowell, 1987), patients were asked to evaluate their overall ability to smell by reference to events of the last week, and to cross a 10 cm line between 0 (absolutely no sense of smell) and 10 (normal sense of smell). For the other symptoms, estimates were asked to be made between 0 (no discomfort related to the symptom) and 10 (extreme discomfort). This was part of a questionnaire looking also at all medications (especially corticosteroids) that were taken during the last three months.

Patients fulfilled the first questionnaire (Q1) the day before they started a 7-day treatment of oral prednisolone (60mg once a day), covered with antibiotics (josamycine 1g twice a day). Patients who were on topical steroids were asked to continue without interruption until the day of surgery. Patients who had stopped the topical steroid treatment because of its inefficiency were asked to reintroduce it, in order to try to maintain the results of systemic steroids.

The second questionnaire (Q2) was fulfilled the day after the end of the systemic steroid treatment and mailed back to us in a pre-paid envelope. The third one (Q3) was fulfilled a few weeks later, the day before surgery.

All patients were operated on bilaterally according to the nasalisation principles (Jankowski et al.., 1995; Jankowski, 1997; Jankowski, 2000), i.e. a radical ethmoidectomy with middle turbinate resection, antrostomy, sphenoidotomy and frontal ostium exposure; the ethmoid mucosa is removed as much as possible, except around the frontal ostium and in very 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. To avoid a postop oedematous reaction of the mucosa in the large sinuses and to control the cicatrization of the ethmoid cavities, which probably starts from the remnant mucosa, we systematically recommend a depot injection of triamcinolone 80mg the day after surgery. In the nasalisation concept we also consider any septal deviation that could become symptomatic or could represent an obstacle to the diffusion of topical steroid sprays after the surgical cure of NPS and we do not hesitate to associate nasalisation with septoplasty when necessary. The day after surgery a nurse teaches the patient how to wash his nose with saline and a syringe, and patients are asked to do it at least three times a day for one month until the first postop visit. Topical steroids are also reintroduced the day after surgery and strongly recommended for the long term. We apply these principles in our daily practice

since 1987.
The fourth questionnaire (Q4) was fulfilled one month after surgery, the day of the first postop visit. Endoscopic cleansing of the surgical fields was achieved and patients were advised to continue to wash their nose on an as they needed basis, plus they were strongly recommended to stay on low dose of topical steroids for the long term (i.e. at least one year in the present study) under supervision of the family practitioner.

The following questionnaires were returned by mail at 3 months (Q5), 6 months (Q6), 9 months (Q7), and 12 months (Q8) post-operatively.

Statistical analysis
The statistical analysis was performed with a Macintosh computer (Apple Company, Cupertino, CA) using the StatView 4.5 Software (Abacus Concepts, Inc, Berkeley, CA, 1992). Data were expressed as mean ± standard deviation, and by the range. One factor analysis of variance for repeated measures (ANOVA) was used to compare the within-group VAS scores. When a significant F-test was obtained, Student's paired t-tests were carried out. For each test, a p value less than 0.05 was considered statistically significant.

RESULTS
Twenty four patients (17 men/7 women; mean age 44 years, range 24-61) completed the study until the 6th month, and 23 until the 12th month post-op. The patient lost to follow-up was a military who was sent in mission.

All patients showed typical oedematous polyps in both nasal fossa. Fifteen were asthmatic, and 6 reported aspirin intolerance (Widal's triad). The diagnosis of nasal polyposis was known for 9 ± 7.3 years (2-26 years). Sixteen patients reported previous surgery (5 one or more polypectomies, 8 an ethmoidectomy, 2 a middle antrostomy, and 1 a Caldwell-Luc procedure).

No side effects or complications were reported during the protocol. In 8 cases, a septoplasty was associated with nasalisation.

1) Subjective evolution of the sense of smell
This specific result is reported and discussed in the accompanying paper in this issue of the journal.

2) Nasal obstruction (Figure 1)
Nasal obstruction was a major complain at entry in the study. Patients were asked to cross a 10-cm line between 0 (absolutely no sensation of nasal obstruction) and 10 (complete nasal obstruction). Twenty-two patients (92%) scored above 5, with among them nineteen above 8. The mean Q1-score was 8.5 ± 1.2.

The 7-day treatment with systemic steroids significantly decreased the Q2 obstruction score at 3.2 ± 0.6 cm ($p< 0.0001$). Only six patients still scored more than 5 with three of them more than 8.

After the mean interval of 2 months (64 ± 39 days) after the oral steroid treatment, the Q3 obstruction score deteriorated again and re-increased to 6.2 ± 0.7 cm ($p=0.0009$). At time point Q3, seventeen patients (71%) scored again more than 5, with ten of them more than 8.

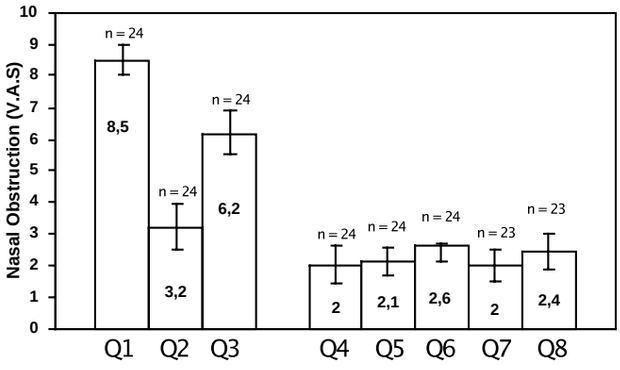

Figure 1. Evolution of nasal obstruction after 7 days of systemic steroids and during 1 year after nasalisation (ANOVA $p<0.0001$).
V.A.S = Visual Analog Scale (0 = absolutely no sensation of nasal obstruction; 10 = complete nasal obstruction)
Q1 = the day before starting oral steroids
Q2 = the day after 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 a depot injection of steroids 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.

One month after the nasalisation protocol (Q4), which included a depot injection of triamcinolone 80 mg and post-op topical steroids, the obstruction score re-improved and decreased to 2 ± 0.6 cm ($p<0.0001$ over Q3). Only four patients scored more than 5, and among them two more than 8. Interestingly 5/6 patients who poorly responded to oral steroid (score>5) scored between 1.5 and 2.5 after nasalisation. Only one patient scored 9.5 one month after nasalisation, but he improved on the next follow-up and ended the study scoring 3.6. Statistically, the one-month post-nasalisation Q4-score was not different from the immediate post-oral steroid Q2-score, but there was a trend for Q4 to be better than Q2 (2 ± 0.6 versus 3.2 ± 1.6, $p=0.13$).

The following post-nasalisation scores at 3 months (Q5=2.1 ± 0.5), 6 months (Q6=2.6 ± 0.6), 9 months (Q7=2 ± 0.4), and 12 months (Q8= 2.4 ± 0.5) remained very stable over the full year ($p=0.56$).

3) Anterior rhinorrhea (Figure 2)
Anterior rhinorhea was a major complain at entry in the study. Eighteen patients (75%) scored above 5, with among them thirteen above 8. The mean Q1-score was 7 ± 1.7.

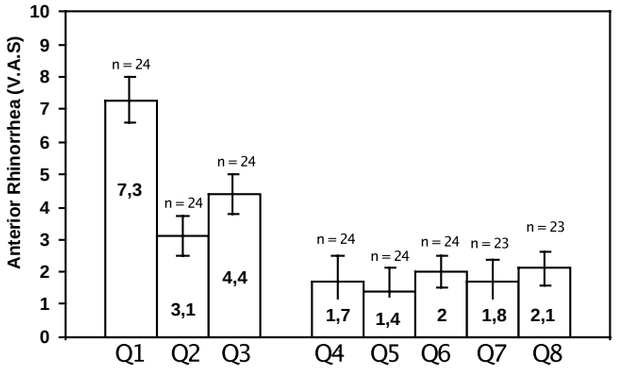

Figure 2. Evolution of anterior rhinorrhea after 7 days of systemic steroids and during 1 year after nasalisation (ANOVA p<0.0001). V.A.S = Visual Analog Scale (0 = absolutely no anterior rhinorrhea; 10 = severe anterior rhinorrhea).

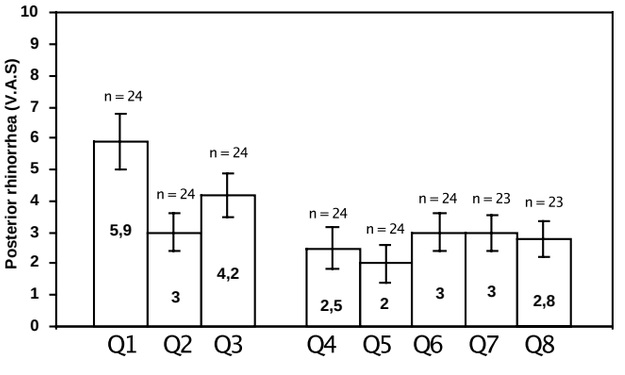

Figure 3. Evolution of poterior rhinorrhea after 7 days of systemic steroids and during 1 year after nasalisation (ANOVA p<0.0001). V.A.S = Visual Analog Scale (0 = absolutely no posterior rhinorrhea; 10 = severe posterior rhinorrhea).

The 7-day treatment with systemic steroids significantly decreased the Q2 score at 3 ± 1.6 cm (p<0.0001). Only six patients still scored more than 5 with three of them more than 8.

After the mean interval of 2 months (64 ± 39 days) after the oral steroid treatment, the Q3 score deteriorated again and re-increased to 4.4 ± 1.8 cm (p=0.07) despite topical steroid treatment. At time point Q3, eleven patients (46%) scored again more than 5.

One month after the nasalisation protocol (Q4), the score re-improved and decreased to 1.7 ± 1.2 cm (p=0.0005 over Q3). Only three patients (12.5%) scored more than 5, and among them only one more than 8. Statistically, the one-month post-nasalisation Q4-score was better than the immediate post-oral steroid Q2-score (1.7 ± 1.2 vs 3 ± 1.6, p=0.04).

The following post-nasalisation scores at 3 months (Q5= 1.4 ± 0.5), 6 months (Q6=2.1 ± 0.6), 9 months (Q7= 1.7 ± 0.6), and 12 months (Q8= 2.1 ± 0.6) remained very stable over the full year (p=0.32). 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 stay better than Q2 (2.1 ± 0.6 versus 3 ± 1.6, p=0.18).

4) Posterior rhinorrhea (Figure 3)

Posterior rhinorrhea was a major complain at entry in the study. Sixteen patients (66.5%) scored above 5, with among them eight above 8. The mean Q1-score was 5.9 ± O.9.

The 7-day treatment with systemic steroids significantly decreased the Q2 score at 3 ± 0.6 cm (p=0.004). Only six patients still scored more than 5 with three of them more than 8.

After the mean interval of 2 months (64 ± 39 days) after the oral steroid treatment, the Q3 score deteriorated again and re-increased to 4.2 ± 0.8 cm (p=0.05) despite topical steroid treatment. At time point Q3, twelve patients (50%) scored again more than 5.

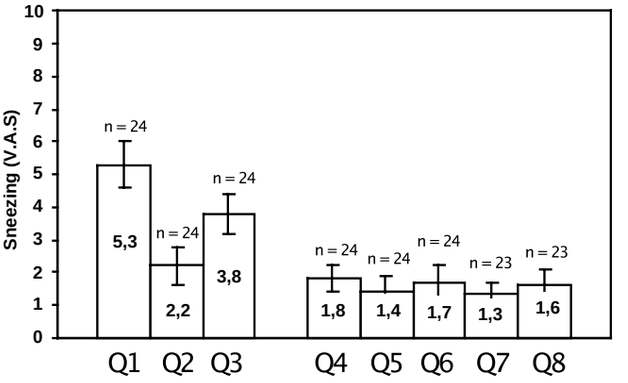

Figure 4. Evolution of sneezings after 7 days of systemic steroids and during 1 year after nasalisation (ANOVA p<0.0001). V.A.S = Visual Analog Scale (0 = absolutely no sneezings; 10 = severe sneezings).

One month after the nasalisation protocol (Q4), the score decreased to 2.5 ± 0.7 cm (p=0.02 over Q3). Only five patients (21%) scored more than 5. Statistically, the one-month post-nasalisation Q4-score was not different from the immediate post-oral steroid Q2-score (p=0.42).

The following post-nasalisation scores at 3 months (Q5= 2 ± 0.6), 6 months (Q6= 3 ± 0.6), 9 months (Q7= 3 ± 0.5), and 12 months (Q8= 2.8 ± 0.6) remained very stable over the full year.

5) Sneezing (Figure 4)

At entry in the study, thirteen patients (54%) reported a score above 5 for sneezing, with seven of them scoring more than 8.The mean Q1-score was 5.3 ± 0.7.

The 7-day treatment with systemic steroids significantly decreased the Q2 score at 2.2 ± 0.6 cm (p<0.0001). Only four patients still scored more than 5 with one of them more than 8.

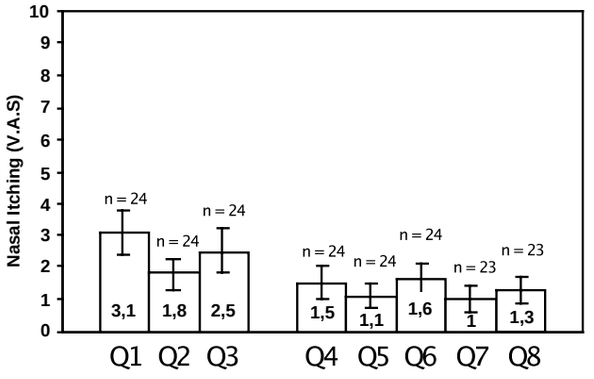

Figure 5. Evolution of itching after 7 days of systemic steroids and during 1 year after nasalisation (ANOVA $p<0.0001$).
V.A.S = Visual Analog Scale (0 = absolutely no itching; 10 = severe itching).

After the mean interval of 2 months (64 ± 39 days) after the oral steroid treatment, the Q3 score deteriorated again and re-increased to 3.8 ± 0.7 cm (p=0.01) despite topical steroid treatment. At time point Q3, nine patients (50%) scored again more than 5.

One month after the nasalisation protocol (Q4), the score decreased to 2.5 ± 0.7 cm (p=0.006 over Q3). Only five patients (21%) scored more than 5. Statistically, the one-month post-nasalisation Q4-score was not different from the immediate post-oral steroid Q2-score (p=0.4).

The following post-nasalisation scores at 3 months (Q5= 2 ± 0.6), 6 months (Q6= 3 ± 0.6), 9 months (Q7= 3 ± 0.5), and 12 months (Q8= 2.8 ± 0.6) remained very stable over the full year (p=0.47).

6) Itching (Figure 5)
Itching was not an annoying symptom at entry in the study (mean score Q1 = 3.1 ± 0.7). Six patients (25%) scored however more than 5, with four of them more than 8.

After 7 days of systemic steroids, only two patients still scored more than 5 (Q2 = 1.8 ± 0.5) (p=0.03 over Q1). Two months later, seven patients (29%) scored again above 5 (Q3 = 2.5 ± 0.7) (p=0.09 over Q2).

One months after nasalisation, only three patients (12.5%) scored above 5 (Q4 = 1.5 ± 0.5) (p=0.05 over Q3). The following post-nasalisation scores remained very stable over time (Q5 = 1.1 ± 0.4, Q6 = 1.6 ± 0.5, Q7 = 1 ± 0.4, Q8 = 1.3 ± 0.4). Only one patient scored constantly above 5.

DISCUSSION

The present study shows that after failure of medical treatment of nasal polyposis, nasalisation is able to alleviate nasal obstruction, anterior and posterior rhinorrhea, sneezing, and itching. The results on smell has been individualised in the accompanying paper, published in this issue. Quality of life has not been measured, but is certainly improved according to the satisfaction of patients who as soon as one month after surgery report their pleasure to rediscover the world of odors and with that taste, the pleasure to breath freely through the nose and to sleep well again, the pleasure of living without a handkerchief in the hand and of forgetting their nose. These data show that radical ethmoidectomy with middle turbinate resection and mucosa removal is functional surgery for patients with nasal polyposis.

These data, therefore, raise concerns about the current concepts of Functional Endoscopic Sinus Surgery (FESS). FESS principles stress the crucial role of sinus obstruction, especially of the ostio-meatal complex, in the pathogenesis of sinusitis: the restoration of ventilation and the re-establishment of muco-ciliary clearance are considered key to the resolution of disease. Moreover, in most of the papers sinusitis and nasal polyposis are considered as a continuum of the same disease, and are treated according to the same principles. The aim of functional ethmoidectomy in nasal polyposis is to remove the tissue source of the polyps, tailoring the extent of surgery to the extent of the disease, keeping as much ethmoid mucosa as possible (even in a total spheno-ethmoidectomy), and preserving the middle turbinate. As with chronic sinusitis, the concept is that removal of the obstruction will allow for adequate ventilation and drainage, and ultimately for reversal of the disease. According to Lanza and Kennedy (1992), once the healing is completed after surgery regularly scheduled follow-up appointments continue for the next year. During these visits any tiny polyps that might recur can undergo debridement before they become symptomatic. A more aggressive return of polyps can be met with a rigorous course of increased use of topical nasal steroids, oral antibiotics, and if appropriate systemic steroids. In our study, none of the patients had to undergo surgical debridement or needed rescue treatment with systemic steroids during the first year of follow-up. In our practice, we usually schedule only two follow-up appointments at one month and one year after surgery; of course patients stay under supervision of their family practitioner and we see them on demand if necessary. We followed our patients of a previous study (Jankowski et al., 1997) and found that the 5-year recurrence rate was 22.7 % after nasalisation versus 58.3 % after functional ethmoidectomy. Interestingly, only 1/22 patients (4.5 %) in the nasalisation group versus 7/18 patients (38.9 %) in the functional ethmoidectomy group had, meanwhile, to be reoperated on for symptomatic recurrence. The rest of the recurrences were diagnosed endoscopically at the 5-year check-up. The number of patients who reported at least one rescue treatment with systemic steroids during the fifth year after surgery was a little lower in the nasalisation group (5/22 for nasalisation vs 9/18 for functional ethmoidectomy, mainly asthmatic patients). The number of patients still taking nasal steroids was similar in both groups (approximately half of the patients in each group). However, the number of patients lost to follow-up after 5 years was high (17/39 in the nasalisation group versus 18/37 in the functional ethmoidectomy group), so that we could not get these data published (Pigret et al., 1997; Jankowski et al., 2000).

The ethmoid sinuses are obviously the site where nasal polyps of the nasal polyposis disease originate. In 1882, Zuckerkandl (Zuckerkandl, 1882) already stated that the most common site of origin of these polyps was the clefts of the ethmoids. Only a few studies have been done since then. Larsen et al. have performed three authopsy studies (Larsen and Tos, 1991; Larsen and Tos, 1995; Larsen et al., 1998) and have observed that 1) polyps are found in the meatus, most of them in the middle meatus (67%) and the rest in the superior meatus, 2) that all polyps are related to the ethmoidal sinus clefts, most of them to the anterior ethmoidal sinus clefts, the remaining to posterior ethmoidal sinus clefts, and 3) that genuine polyps are not observed inside the ethmoidal cells and other paranasal sinuses. However, it was not registered in the charts of these patients that they had symptoms from their nasal polyps during life. It is therefore hard to say whether these cadaver specimens are representative of patients having suffered from nasal polyposis or other kind of polyps (many specimens showed, for instance, unique unilateral polyps). Moreover, at the time of death the underlying pathology may have long been resolved, and the observed polyps could only represent vestiges. A clinical study performed by Stammberger (1991) showed slightly different results. Polyps origination was described in 200 patients undergoing functional endoscopic sinus surgery. In more than one third of the patients polyps were only discovered after endoscopes were introduced directly into the middle nasal meatus; in these early stages most polyps arose from the clefts of the ostiomeatal complex. Most of the polyps were, however, visible in the middle meatus and these polyps originated from the mucosa of either outside or inside the ethmoidal cells. Polyps which were visible medially between the nasal septum and the turbinates, usually protruded from the superior meatus or from contact areas between the turbinates and the septum (especially in recurrent cases following surgery) or – very rarely – from the olfactory ridge. A few polyps were also observed, protruding from the sphenoethmoidal recess. We have also a long experience with nasal polyposis surgery and nasalisation, which means that we open all the sinuses in every case. It seems to us that nasal polyposis is a disease of the ethmoid labyrinth, affecting the ethmoid mucosa either diffusely or multi-focally. In some cases polyps can be found in the maxillary, frontal or sphenoid sinuses, but these polyps usually have their pedicle in the ethmoid and prolapse into a large sinus or, very rarely, have their pedicle inside the large sinus but very close to the natural ostium or the adjacent ethmoidal cells (ex: Haller cell). The mucosa of the large sinuses appears either normal (sometimes despite a complete oedematous obstruction of the ethmoid labyrinth, the best example being a normal mucosa inside the frontal sinus despite a complete blockade of the ethmoido-frontal recess) or oedematous with more or less secretion retention, but the cases in which a large sinus is completely filled by an oedematous swelling of the mucosa are exceptions in primary patients. The reasons why the disease starts and develop into the ethmoid sinuses are unknown, but the complex anatomy of the ethmoid labyrinth could be one. In the nasalisation concept, the goal is to transform the ethmoid labyrinth into a large unique cavity opened into the nose.

The most striking histologic feature of nasal polyposis is inflammation with eosinophil infiltration. For many years allergy to inhalant allergens, food allergens and even allergy to bacterial and more recently to fungal products (Katzenstein et al., 1983) has been advocated. We have to admit to the patient that although his/her disease has similarities to allergic diseases, we do not, at present, know the cause and a search of an allergic aetiology will usually be futile (Keith et al., 1994; Mygind and Lildholdt, 1997). The aetiology of nasal polyposis is still unknown (Lildholt et al., 1994). However, considerable progress has been recently made in the description of the immunopathogenic factors at work, and one of the most seducing hypothesis is that the disease could be based on a self-perpetuating immune inflammation characterized by Th2 lymphocytes, mast cells and eosinophils (Otsuka et al., 1987; Ohnishi et al., 1988; Ohtoshi et al., 1991; Ohno et al., 1991; Bachert et al., 2000). Most of the data indicate that the disease is orchestrated by the eosinophils (Jankowski, 1996; Jankowski et al., 2002). Once they have been attracted in the ethmoid mucosa, their migration, viability, and effector functions could be maintained by an autocrine pathway. It is now clear that eosinophils can synthetize and secrete several important inflammatory and regulatory cytokines, in particular IL-3, IL-5 and GM-CSF. These three cytokines have been shown to prolong eosinophil survival in vitro and to enhance various metabolic functions. They are also involved in migration of eosinophils toward specific tissue sites (Kayab, 1995). As a consequence, the ethmoid could be compared to a sequestrating structure for the eosinophils, which come from the bone marrow via the blood.

The present study shows that systemic steroids are highly effective to relief symptoms associated to nasal polyposis, but that their efficacy disappears over time despite the maintenance of topical steroids. We have observed (Jankowski et al., 1995) in histopathological analysis of surgically removed specimens 1) that the number of eosinophils was significantly lower in patients treated with systemic steroids within two months before surgery (22 ± 3 %) than in untreated patients (50 ± 2 %), 2) that the number of eosinophils in specimens of patients who were only on topical steroids before surgery was unchanged compared to untreated patients (47 ± 2 % versus 50 ± 2 %), and 3) that the number of eosinophils was significantly higher in untreated patients with asthma (58 ± 3 %) and even more in Widal's triad (75 ± 4%). These data suggest a relationship between the charge in eosinophils of the ethmoid reservoir and the evolution or severity of the disease. The way by which systemic steroids improve nasal polyposis could be by depleting the ethmoidal reservoir in eosinophils. In patients, who are failure of medical treatment, topical steroids might not be effective to stop the re-colonisation by eosinophils. The present study shows that in such patients, nasalisation + topical steroids are able to control the disease for at least one year. In fact, surgery could act on nasal polyposis as systemic steroids might, by depleting the ethmoidal reservoir in eosinophils, and by this way help to control the disease, in particular by permitting a better penetration of topical steroids into the ethmoid reservoir to prevent re-colonisation by eosinophils. If this hypothesis is true, one can understand that polypectomy might be less effective than ethmoidectomy, and functional ethmoi-

dectomy less effective than radical ethmoidectomy (Jankowski et al., 1997).

The question why eosinophils do accumulate into the ethmoid structures is also of fundamental interest. An interesting answer, based on mediator studies, has been proposed by researchers of Mc Master University, Ontario, Canada (Otsuka et al., 1987; Ohnishi et al., 1988; Ohtoshi et al., 1991; Ohno et al., 1991). The theory is that tissue micro-environments (epithelial cells, fibroblasts) are inductive compartments in which inflammatory cell functions are modulated. The starting point was that these authors could demonstrate the presence of inflammatory progenitor cells in human nasal mucosa (Otsuka et al., 1987). They further investigated the potential contribution of epithelial cells and fibroblasts to the accumulation of eosinophils and metachromic cells in polyp tissue. They further examined the cytokine content of different epithelial culture mediums and found that among the different mediators only GM-CSF (granulocyte/macrophage colony-stimulating factor) was produced in significantly higher amount by nasal polyps. Looking at fibroblasts, they found that fibroblasts derived from nasal polyp tissues express the gene and release the product GM-CSF at greater level compared to normal fibroblasts. As a conclusion, these authors suggested 1) that epithelial cells and fibroblasts might be up-regulated in vivo and be the cause of the perpetual inflammatory reaction that characterizes nasal polyposis, and 2) that GM-CSF, a cytokine with powerful biologic effects including the regulation of survival, proliferation, and activation of granulocytes as well as differentiation of hematopoietic cells, could play a central role. However, they further demonstrated that approximately 30% of eosinophils infiltrating the polyp tissues expressed the GM-CSF gene, suggesting that the eosinophils themselves could be the main source of GM-CSF. This was confirmed by another group (Hamilos et al., 1993) who found a correlation between the number of activated eosinophils and of cells expressing mRNA for GM-CSF. These data indicate that GM-CSF is mainly produced by the eosinophils themselves, and support the central role of eosinophils and the autocrine hypothesis of eosinophil accumulation in the pathogenesis of nasal polyposis. More recently, Wei et al. (2003) have elegantly shown ex-vivo that nasal tissue obtained from patients with chronic rhinosinusitis (CRS) and asthma have the ability to attract both the peripheral blood eosinophils from CRS patients and healthy control subjects, but significantly more the eosinophils from CRS patients, suggesting that in CRS + asthma patients the peripheral blood eosinophils are already distinctly activated in the systemic circulation. These data also clearly suggest that the attractant for eosinophils is located in the sinus mucosa. However, we still do not know the nature of the attractant and the reason(s) why eosinophils are attracted in the ethmoid mucosa, and keep being attracted even after treatments able to deplete the ethmoïd reservoir of eosinophils, like steroids (Jankowski et al., 2002). An interesting hypothesis has been proposed by Ponikau et al. (1999; Taylor et al., 2002) suggesting that a large variety of fungi found in the nasal mucus could be a permanent trigger for eosinophil accumulation in the sinus mucosa, leading to the concept of eosinophilic fungal rhinosinusitis. If this hypothesis is true, surgery would certainly have a minor or no place in the treatment of nasal polyposis, and our results are hard to explain. On the contrary, nasal polyposis can be regarded as an intrinsic and self-sustained inflammatory disease of the ethmoid mucosa (Moneret-Vautrin et al., 1992) with some specific intrinsic attractant and activator for eosinophils in this mucosa. In the nasalisation concept, the ethmoid mucosa is removed as much as possible: does it help to better control the disease by removing more extensively the source of this hypothetic attractant?

The reasons why the ethmoid mucosa is extensively removed in the nasalisation procedure are, however, more practical. By contrast to FESS procedures, which propose a centrifugal dissection that starts in the heart of the ethmoidal labyrinth (bulla and uncinate process) and progresses outwards trying to preserve at least mucosa on the orbital wall, the ethmoidal roof, and the middle turbinate, the nasalisation procedure proposes a centripetal dissection. A middle antrostomy is first performed to identify the roof of the maxillary sinus, which is the floor of the orbit and a drive to find the medial wall of the orbit (which is the lateral wall of the ethmoid). The orbital floor is hard bone and it is not hazardous to remove pieces of mucosa on its inner part to clearly expose the bone. The dissection progresses gently medially and upwards, keeping close tangential contact with the bony landmark, and invariably leads to an easy and clear identification of the lamina papiracea. Anteriorly, the best place to find the under-periosteum plane of dissection is on the frontal process of the maxilla, where the bone is hard, just anteriorly to the uncinate process and at the level where the anterior margin of the middle turbinate abuts the lateral nasal vault. The mucosal flap elevated in this area can easily be further detached from the bone in two directions: 1) posteriorly and inferiorly in direction of the upper edge of the inferior turbinate; this delimitates the lower edge of the middle antrostomy 2) posteriorly and laterally in direction of the orbital wall; the under-perioteum flap first reaches the uncinate process attachment on the frontal process; removal of the uncinate attachment leads into the spaces that Grunwald has named sinus lateralis (which is considered by Stammberger as the lateral wall of the infundibullum) (Stammberger, 1991) and that Terrier has named "unciformian" cells (Agrifolio et al., 1990); whatever the name, the mucosa can be removed in this space by careful dissection of the bony structures; junction of this space and the orbital walls is best found at the level of the natural ostium of the maxillary sinus. Posteriorly, the safest landmark for a complete marsupialisation of the ethmoid is probably the sphenoid cavity. The safest way to enter the sphenoid sinus is probably to puncture its anterior wall with a thin, straight suction tube which is slipped along the nasal septum and inserted a few millimetres above the choanal arch, close to the midline, at the level where the anterior wall can be fractured by a very light pressure. Very often this is the way to enter the natural ostium when it is not visible. A large sphenoidotomy can then be performed, which helps to localise both the ethmoidal roof and the apex of the medial orbital wall. However, a clear identification of the connection between these two structures can only be achieved by a meticulous removal of the mucosa. In our experience resection of the middle turbinate is necessary to perform a radical ethmoidectomy, because it opens the route to a very precise

dissection of all ethmoidal cells located between the ethmoid roof and the conchal lamina. The conchal lamina is the continuous bony wall described by Mouret (1922), which is attached antero-posteriorly to the junction between the cribriform plate and the roof of the ethmoid, and which gives attachment anteriorly to the middle turbinate and posteriorly to the superior, and in a few patients to the supreme ethmoid conchae. Finally, marsupialisation of the anterior ethmoid is performed centripetally towards the frontal ostium, the dissection following the well identified bony structures of the conchal lamina, ethmoidal roof, medial orbital wall, and frontal process of the maxilla. This centripetal technique can be applied whatever the size or volume of the polyposis; it is also applicable in revision cases, whatever the type of the previous surgery, because most of the landmarks can be found again. All the landmarks are easy to recognise and the procedure can be performed safely without need of sophisticated tools. This is not true in centrifugal techniques because a dissection starting in the heart of the ethmoid labyrinth can not be based on invariable and secure landmarks, especially when pathology like nasal polyps can modify these landmarks, or make them difficult to be identified.

In conclusion, the present study shows that nasalisation, i.e. radical ethmoidectomy with middle turbinate resection and mucosa removal, can be considered as functional surgery for nasal polyposis. Our results are based on one year of follow-up, which is not a long term result. Therefore we will try to collect these patients again at a later time to give some conclusions about long-term results, late scarring and sinus obstruction, development of mucoceles. These results raise concerns about the application of current Functional Endoscopic Sinus Surgery principles (i.e. the restoration of ventilation and the re-establishment of muco-ciliary clearance) to the surgical treatment of nasal polyposis. In the nasalisation concept the goal of surgery is to transform the ethmoid labyrinth in a unique cavity, largely opened into the nose so that it can be reached by topical steroids. The key points to achieve a nasalisation procedure are 1) to perform large antrostomy and spenoidotomy 2) to resect the middle turbinate 3) to remove as much as possible the ethmoid mucosa, but without hazards, in order to follow the bony walls of the ethmoid box 4) to progress centripetally in the dissection towards the frontal ostium. Surgery, as well as systemic steroids, probably act by depleting the ethmoid reservoir in eosinophils. Eosinophils appear as the main actors of a self-perpetuating inflammation and are probably entrapped in the ethmoidal mucosa via an autocrine pathway. Cadaver study and surgical observations indicate that nasal polyposis is mainly a disease of the ethmoids. Could it be that the ethmoidal mucosa contains specific attractants for eosinophils? In this hypothesis it is understandable that the best control of the disease would be obtained by radical surgery.

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