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RECURRENT POLYPOSIS NASI

Plenary Session, held during the 12th Congress of the European Rhinologic Society including the VIIth I.S.I.A.N., Amsterdam (The Netherlands), June 1988

(Contents to be continued next page)

Fireside Conference on burning questions, held during the 12th Congress of the European Rhinologic Society including the VIIth I.S.I.A.N., Amsterdam (The Netherlands), June 1988

Free Contributions

This journal is cited in Index Medicus and Excerpta Medica

Preface

It has been a pleasure to edit these essays on such a controversial issue as recurrent polyposis nasi.
The articles emanate from Europe and Japan. All but two papers by R. Jankowski et al. and S. Jäntti-Alanko et al. were presented during the 25th Anniversary Congress of the European Rhinologic Society in Amsterdam, June 19–22, 1988.

The subsequent contributors illustrate the diversity of treatment modalities applied throughout the ORL world and our limited knowledge about the etiopathogenesis of nasal polyps.
The beneficial effects of medical therapy are extensively discussed, whereas endonasal (micro)surgical and laser techniques are presented.
Recurrent nasal polyposis is a typical human disease. It hampers an animal model. Additional fundamental and clinical research is still heavily needed before basic problems such as origin, growth and recurrency rate of nasal polyps can be understood.
The best treatment strategy remains to be individually determined, mainly based on clinical expertise and skills.

Utrecht, June 1989

Jan E. Veldman,
Guest-Editor

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Recurrent polyposis nasi. Documentation

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SUMMARY

After a short historical review a proposal is made for the definition of nasal polyposis. The authors studied 350 CT-scans of patients with nasal complaints. In a high percentage anatomical anomalies were observed. In 57.5% of the CT-scans sinus mucosal disease was visible. In all patients with maxillary sinus disease polyps (rounded structures) could be found; in 31% these polyps were mainly of grade 2. From a retrospective study of 111 biopsies of nasal polyposis (65 patients) it became clear that different polyps from the same patient showed substantial difference in cellular content, i.e. presence of eosinophils, neutrophils, plasma cells, glands, ducti and thickening of the basal membrane.

As oral acetylsalicylic acid provocation may be hazardous in ASA-sensitive patients, the authors developed a nasal aspirine provocation test. This nasal ASA test was carried out in 10 normal test subjects, 10 patients with aspecific hyperreactivity, 10 atopic patients and 16 patients with polyposis nasi. The reproducibility of the test, however, was so poor that the nasal ASA challenge test in its present form does not appear to be of any great clinical value.

Finally, the authors discuss the physiopathology of nasal polyposis.

Reports of nasal polyposis have appeared in the earliest medical writings of many countries. The cause of nasal polyps has been studied and debated since they were first recognised (Connell, 1983; Ogawa, 1986; Friedmann, 1986). Even in the early days, there existed surgical and medical approaches to the problem, a situation that still exists today. As early as one thousand B.C., a type of curette for "eradicating nasal polypi" was used in India, while Hippocrates (460-370 B.C.) developed a sponge method for their removal (Vancil, 1969). Cato the Censor

Paper presented in the Plenary Session 'Recurrent Polyposis Nasi'. 12th Congress of the European Rhinologic Society including the VIIth I.S.I.A.N., Amsterdam (The Netherlands), June 1988.

(232 B.C.) prescribed the inhalation of the breath of dry wild cabbage leaves to make the polyp fall away (Lederer, 1959). The medical profession proved to have a lot of fantasy in describing nasal polyps with extremes such as Celsus who likened the appearance of polyps to the nipples of a female breast and Avicenna who likened them to haemorroids (Lederer, 1959). The earliest objective evidence of nasal polyposis was presented recently by Pirsig et al. (1987). They described a skull from the baroque period with a broadened bony nasal pyramid probably due to massive nasal polyposis.

Most chapters in ENT text books give a description of nasal polyposis (Mygind et al., 1974; Albegger, 1977; Ballantyne, 1979; Paludetti et al., 1983; Ballenger, 1985) or discuss their pathogenesis (Pech et al., 1982; Ballenger, 1985) although it has not been possible to find a clear definition of nasal polyposis in the literature. According to Dorland's Illustrated Medical Dictionary a polyp is a protruding growth from a mucous membrane. One can also state that nasal polyposis is a disease. Again according to Dorland: "A disease is a definite morbid process having a characteristic train of symptoms, it may affect the whole body or any of its parts, and its etiology, pathology and prognosis may be known or unknown." As this can be applied to nasal polyposis the authors would suggest the following definition: "Nasal polyposis is a nasal disease characterised by the presence of solitary or multiple polyps – i.e. rounded structures of mucosa due to extreme oedema – in one or both nasal cavities and/or in one or multiple paranasal sinuses and which in an advanced stage can be seen by simple rhinoscopy, especially in the middle and superior meatus, resulting mainly in complaints of nasal obstruction" (Table 1).

Table 1. Initial complaints of 50 patients with nasal polyposis, prior to endonasal ethmoidectomy

nasal obstruction	84%
rhinorrhea	54%
headache	26%
asthma	18%
post-nasal drip	16%
anosmia	11%
middle ear pathology (drainage blocked; central perforation)	8%

According to Paludetti et al. (1983) nasal polyps originate mainly in the maxillary and ethmoidal sinuses. The pedunculated polyps that can be seen in the naked eye from the middle meatus (Frenkiel et al., 1982) hanging in the nasal cavity are probably the ultimate form of a disease. According to English (1985) nasal polyps may be solitary or multiple, unilateral or bilateral. With the introduction of

endoscopic nasal surgery one can often see, after the removal of the uncinate process, an infundibulum and ethmoidal cells filled with polyps while anterior rhinoscopy did not show any evidence of polyps (Stammberger, 1985). According to Pech et al. (1982) multidirectional tomography is not very informative. CT-scans are far superior to conventional tomography. According to the authors a CT-scan of an opaque sinus very often allows to differentiate between the presence of polyps and pus (Figure 1), whereas NMR studies, especially T_2 weighted images, very clearly show the extension of mucosal oedema in nasal polyposis (Figure 2).

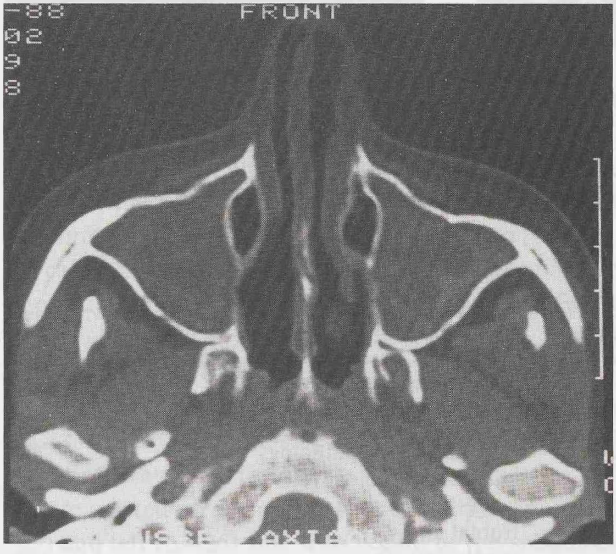

Figure 1. CT-scan shows complete blurring of the maxillary sinuses but a differentiation between the presence of polyps and secretions can be made (confirmed by sinoscopy).

Since an extensive CT-scan study on nasal polyposis has not been published yet, the authors studied the CT-scans of 350 patients with nasal complaints (Table 2): 149 (42%) of the CT-scans showed a normal translucency of the paranasal sinuses although there existed clear-cut anomalies (i.e. septal deviation, concha bullosa, "Haller" cells, processus uncinatus bullosus) in 100 (67%) of these translucent CT-scans (Table 3). Of the remaining 201 (57.5%) sinus disease was visible on the CT-scans. There existed no difference between the incidence of opacity between the left or right side of the paranasal sinuses, frontal recess or infundibulum. In these 201 cases of sinusitis the maxillary sinuses showed mucosal disease in 73%, the anterior ethmoidal cells in 35%, the posterior ethmoidal cells in 19% and the frontal and sphenoidal sinus each in 13% of the cases. Since the size of the frontal,

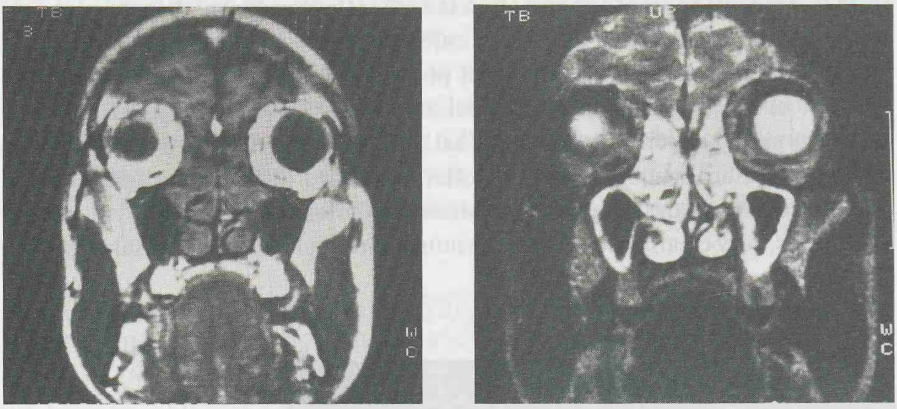

Figure 2. MRI of a patient with polyposis nasi. Oedema of the tunica propria especially clear on the T_2 weighted images.
A. T_1 weighted image
B. T_2 weighted image

Table 2. Findings in CT-scans of nose and sinuses in a population of patients with nasal complaints (N = 350)

without sinus disease (N = 149) 42.5%	with anatomical anomalies	67%
	without anatomical anomalies	33%
with sinus disease (N = 201) 57.5%	maxillary sinus pathology	73%
	anterior ethmoidal cells	35%
	posterior ethmoidal cells	19%
	frontal sinus	13%
	sphenoidal sinus	13%

Table 3. Number of cases with anatomical anomalies in 350 patients with nasal complaints

	A without sinus disease (N = 149)		B with sinus disease (N = 201)	
	number	percentage	number	percentage
septal deviation	68	45	152	75
conchal bullosa	66	44	66	32
"Haller" cells	15	10	3	1
processus uncinatus bullosus	3	2	2	1

maxillary or sphenoidal sinus is sufficient to recognise a rounded mucosal swelling (polyp) the authors were able to determine the incidence of polyposis in these structures (Table 4). In 31% of all sinusitis patients polyps were found in the maxillary sinuses. In all maxillary sinusitis cases polyps were recognised in 42% of them (38% left - 68% right side). For the frontal sinuses these percentages were respectively 1.5% and 11.5% and for the sphenoid sinuses 1.2 and 10%.

Table 4. Incidence of round structure (polyps) on CT-scans of patients with sinusitis (N = 201)

	total patient population	total sinusitis cases
maxillary sinus	31 %	42 %
frontal sinus	1.5%	11.5%
sphenoidal sinus	1.2%	10 %

Whenever the maxillary sinus mucosa shows slight signs of inflammation (grade 1 and 2) the right side is mainly involved (80 versus 60) while in grade 3 and 4 inflammation mainly the left side is involved (22 versus 10). In the vast majority of cases, however, the maxillary sinus shows only minor involvement. If polyps are found, they are mainly of grade 2 (Table 5, Figure 3). The total number of cases with grade 2 polyps is relatively small, with a slight predominance for the left side.

As to the ethmoidal labyrinth it was only possible to visualize polyps in four cases. Due to the small size of the cells it remains difficult to recognise a round swelling even on CT-scans.

There existed no clear difference in the presence of sinusitis between right (n = 25) and left (n = 26) side with regard to the sphenoidal sinuses. The number of clearly recognisable polyps is too small to draw any conclusion. This holds also for the frontal sinuses.

In another study of 16 patients with massive polyposis, confirmed by anterior rhinoscopy, the authors found an involvement of the maxillary, ethmoidal, sphenoidal and frontal sinuses in 100%, 93%, 69% and 53% of the cases respectively.

Ballantyne and Stokes (1974) state that the vast majority of polyps are simple polyps, i.e. pedunculated pieces of oedematous upper respiratory mucosa. In a retrospective survey of 65 patients with nasal polyposis we studied the histopathology of 111 biopsies of nasal polyps. It became clear that different polyps of the same patient showed a substantial difference in cellular content: 62 (63%) of these polyps had more than five eosinophils per microscopic field (magnification 40x). In the same polyp the distribution of eosinophils is not equal. In 13

Table 5. Incidence of involved sinuses and presence of polyps in sinusitis patients as observed by CT-scan (N=201).

	staging of sinusitis				staging of polyps		
grade	1	2	3	4	1	2	3
maxillary sinus (N=402)							
Ri(N)	52	28	6	4	7	40	9
Le(N)	39	21	11	11	10	52	6
total (N)	91	49	17	12	17	92	15
percentage (%)	23	12	4	3	4	22	3
anterior ethmoidal labyrinth (N=402)							
Ri(N)	55	16			1	0	
Le(N)	54	14			0	1	
total (N)	109	30					
percentage (%)	27	7					
posterior ethmoidal cells (N=402)							
Ri(N)	31	8			1	0	
Le(N)	28	7			1	0	
total (N)	59	15					
Percentage (%)	15	4					
sphenoidal sinus (N=402)							
Ri(N)	17	6	2	0	0	1	0
Le(N)	14	8	4	0	0	3	1
total (N)	31	14	6				
percentage (%)	8	4	2				
frontal sinus (N=402)							
Ri(N)	12	7	3	2	0	2	0
Le(N)	13	3	1	5	2	2	0
total (N)	25	10	4	7			
percentage (%)	6	3	1	2			

specimens they were found in the epithelial cell layer, although their preferential site was just underneath this epithelial layer. If neutrophils dominated, they were mainly located around blood vessels and in the epithelial cell layer. In certain areas of polyps inflammatory cells were mainly present. Plasma cells were found in all specimens. In 42% of the cases they even formed the majority of the cells present. In 70% of the cases glands were observed. In 32% of the cases there was a clear-cut cystic dilatation of these glands. Ducti were both short and long shaped. In most cases veins had a dilated aspect. The basal membrane of the epithelial layer was thickened in the majority of cases (73%). Rupture of the epithelial layer with granulation tissue formation was not observed. In the vast majority, the epithelial lining was a respiratory type of epithelium. There existed, however,

hyperplasia of goblet cells in 52% of the cases. Squamous metaplasia of the respiratory epithelium occurred in 81% of the cases.

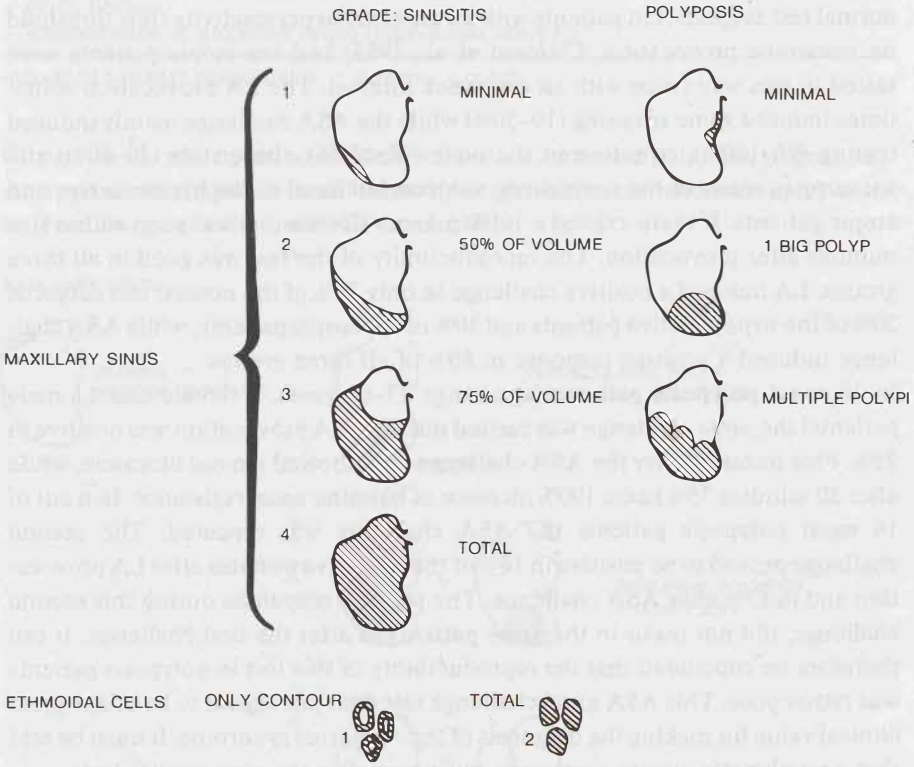

Figure 3. Grading of sinusitis and polyposis.

Patients with polyposis nasi can be very hazardous after an oral acetyl-salicylic acid (ASA) provocation test (Wayoff et al., 1979; Holopainen et al., 1979; Brown et al., 1979). Since a test to confirm ASA intolerance did not exist up to now, the authors developed a new nasal provocation test for this purpose. Normally, acetyl-salicylic acid is combined with lactic acid to form an aspirin tablet. In order to exclude an aspecific reaction of the mucosa due to irritation by powder the mucosa of both nasal cavities was first challenged with lactic acid (LA) powder via a De Vilbis insufflator (average 10 mg per side, spread 3–17 mg). Five minutes later ASA was blown into the nose (one puff in each nostril). The nasal patency of both sides was measured with passive anterior rhinomanometry (Clement et al., 1985) for the first time at time zero (i.e. baseline value), the second time five minutes later just before the LA provocation to reconfirm the baseline value a

third time just after the LA provocation, a fourth time after five minutes just before the ASA challenge, a fifth time just after the ASA challenge, a sixth time after 15 minutes and a seventh time after 30 minutes.
Every time the number of sneezes and possible rhinorrhea were noted. Ten normal test subjects, ten patients with an aspecific hyperreactivity (low threshold on histamine provocation, Clement et al., 1985) and ten atopic patients were tested in this way twice with an one week interval. The LA provocation sometimes induced some sneezing (10–50%) while the ASA challenge mainly induced tearing (90–100%), irritation in the nose (90–100%), rhinorrhea (40–80%) and sneezing in many of the normal test subjects but in all of the hyperreactive and atopic patients. If there existed a 100% patency decrease, it was seen within five minutes after provocation. The reproducibility of the test was good in all three groups. LA induced a positive challenge in only 20% of the normal test subjects, 20% of the hyperreactive patients and 30% of the atopic patients, while ASA challenge induced a positive response in 80% of all three groups.
In 16 nasal polyposis patients (age range 27–69 years, 5 female and 11 male patients) the same challenge was carried out. The LA provocation was positive in 25%. Five minutes after the ASA challenge 56% showed a nasal blockade, while after 30 minutes 75% had a 100% increase of baseline nasal resistance. In 6 out of 16 nasal polyposis patients the ASA challenge was repeated. The second challenge proved to be positive in 16% of the cases five minutes after LA provocation and in 83% after ASA challenge. The positive responses during this second challenge, did not occur in the same patients as after the first challenge. It can therefore be concluded that the reproducibility of this test in polyposis patients was rather poor. This ASA nasal challenge test does not appear to be of any great clinical value for making the diagnosis of the ASA triad syndrome. It must be said that no asthmatic attacks were seen during or after the provocation tests.

Modern technology (CT-scanning and endoscopy) enables us to make an appropriate diagnosis of nasal polyposis already in an early stage of the disease. The number of nasal polyposis patients is much larger than what could have been expected after simple anterior rhinoscopy. An early diagnosis will enable the clinician to restore nasal function through less extensive therapy.
The etiology of nasal polyposis still remains an enigma (Table 6). The common factor in all forms of polyposis (ASA, infection, cystic fibrosis, etc.) is extreme mucosal oedema. This extreme oedema is induced by inflammation and abnormal vasomotor responses (English, 1985). We did not find much histological evidence to support the hypothesis of Tos et al. (1977) where rupture of the epithelial layer and granulation tissue stand at the basis of formation of nasal polyposis. Localized oedema will induce the formation of spherical or pedunculated polyps

Table 6. Etiopathogenesis of polyp formation.

- chronic infection (bacterial, fungal)
- ASA intolerance
- Kartagener syndrome
- cystic fibrosis
- inflammation of unknown origin (non-atopic allergy?)
increased vascular permeability → oedema → polyp

(Figure 4a-c), while general oedema will induce a massive polyposis (Figure 4d). An appropriate diagnosis is still made by single rhinoscopy and endoscopy or by modern imaging techniques (CT-scan, MRI).

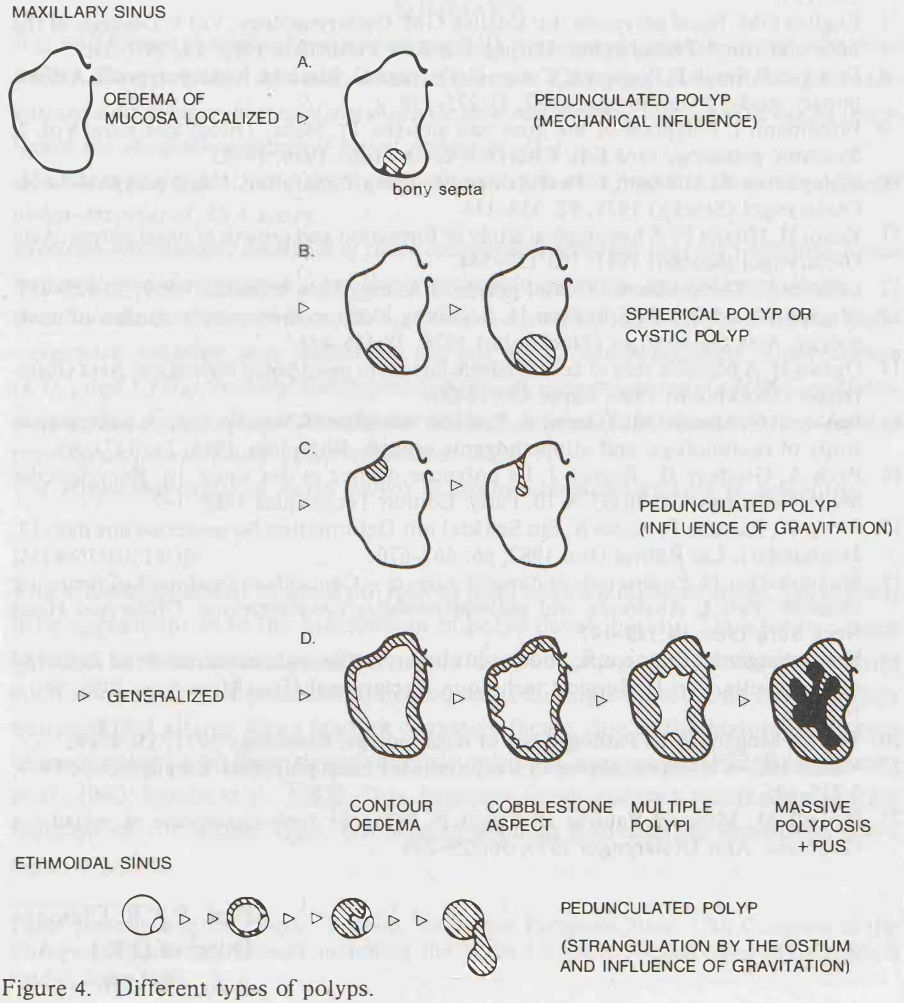

Figure 4. Different types of polyps.

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Etiology of nasal polyps associated with aspirin-sensitive asthma

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SUMMARY

It is well known that nasal polyps occur at high frequency in aspirin-sensitive asthma (ASA). Their etiology, however, remains obscure. Therefore, histopathologic observations and measurements of arachidonic acid metabolites were carried out to investigate the etiopathogenesis of nasal polyps in ASA.

Abundant eosinophils and degranulated mast cells were found in the tissue of nasal polyp-associated ASA cases.

Electron-microscopic analyses of these eosinophils revealed that high-electron-dense material had disappeared from the cytoplasmic granules' central crystalloids.

Arachidonic acid metabolites (PGE_2, PGF_2, 6-keto-PGF_1 and TXB_2) from the cyclooxygenase pathway were measured via gas mass-chromotography. Leukotrienes (LTC_4 and LTD_4) from the lipoxygenase pathway were measured via HPLC-radioimmunoassay. Especially noteworthy are the high level of leukotrienes and low level of prostaglandins in nasal polyp-associated ASA.

The etiopathogenesis of nasal polyps in aspirin-sensitive asthma is postulated.

INTRODUCTION

The etiopathogenesis of nasal polyps has long been a subject of study, yet there is little agreement as to the mechanism of polyp development. Thus far two main theories have emerged, the allergic and infectious. Recently, sensitivity to drugs such as aspirin has also been implicated as an etiologic factor. One has generally believed that allergy was a leading causative factor, due to the histologic picture of nasal polyps with their abundant eosinophilia (Cauna et al., 1972; Baumgarten et al., 1980; Jacobs et al., 1983). This, however, is not always a result of an allergic reaction of the atopic type, but is also seen in non-allergic aspirin-sensitive asthma (ASA).

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Some clinical findings regarding nasal polyps do not fit in well with diseases which are thought to be atopic in nature. Settipane (1977) reports very interesting data from records of patients with asthma and allergic rhinitis, i.e. the frequency of nasal polyps in the asthmatic patient was three times higher than in the allergic patient. Caplin (1971) reports nasal polyps as even occurring at frequencies as high as 96% in ASA patients. Given these histologic and clinical findings, it was thought important to clarify the etiopathogenesis of nasal polyps associated with non-allergic ASA, as being of value in discussing the pathogenesis of nasal polyps in general. To illucidate this issue we performed histopathology and measured arachidonic acid metabolites, i.e. prostaglandins (PGs) and leukotrienes (LTs) in nasal polyps of patients with ASA.

MATERIAL AND METHODS

Seven samples of nasal polyps were obtained from seven ASA patients; two samples were used for histopathological examination and five for arachidonic acid metabolite measurement. Ten samples of nasal polyps from five cases with chronic sinusitis and from five cases with allergic rhinitis were also examined to compare their arachidonic acid metabolite content with those of ASA cases.

Specimens for histology were immediately fixed in 10% formalin solution and embedded in parafin. Sections were cut at 5 microns, stained for one minute in 1% toluidine blue - alcohol solution (1 g of toluidine blue, 99 ml of 60% ethanol, pH 7.0) and mounted with glycerine.

Haematoxylin-eosin staining was also performed for routine light microscopy. For electron-microscopy, fragments of fresh nasal polyps from patients with asthma were fixed in Karnovsky's solution for two hours and subsequently rinsed three times in 0.1 M phosphate buffer for 10 minutes. Postfixation was performed for two hours in 1% O_sO_4, followed by triple rinsing. Routine alcohol dehydration was carried out and the samples were embedded in Spurr's low-viscosity resins.

For prostaglandine (PG) determination, samples of nasal polyps were homogenized in a polytron ® and centrifuged for 10–15 minutes at 2000 g. The supernatant was evaporated in a rotary evaporator. Each sample was dissolved by 15% ethanol and eluted through Sep-Pak C-18 for liquid solid extraction. The sample was methylated, methoximated, and then silylated. The sample was chromatographed over silica gel and then subjected to gas chromotographic and gas chromotographic-mass spectrometric analysis (Figure 1).

For leukotriene (LT) determination, samples of nasal polyps were homogenized in ethanol and centrifuged for 10 minutes at 2000 g. The LT containing ethanolic supernatant was then collected. Ethanol was removed by rotary evaporation under vacuum and samples were subjected to high performance liquid chromatography (HPLC). LTC_4 and LTD_4 purified by HPLC were further measured by radioimmunoassay (Figure 2).

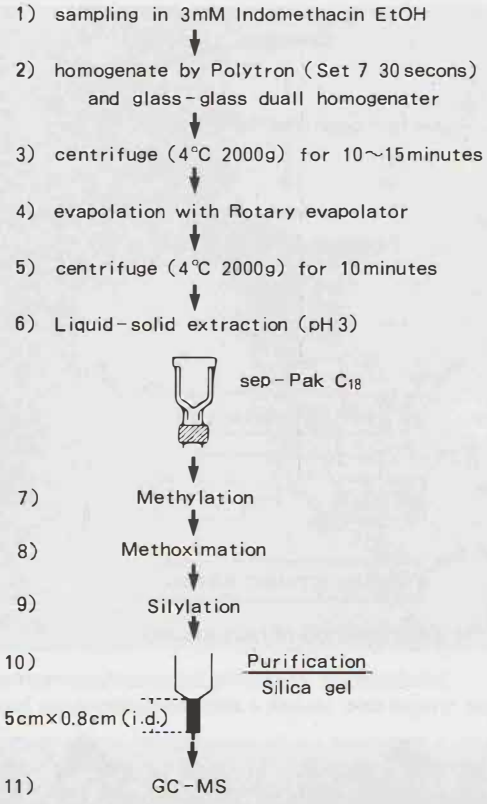

Figure 1. Methods for the determination of prostaglandins.

RESULTS

Morphology

At a light microscopical level numerous mast cells were found in nasal polyps of patients with ASA (ASA polyps). They were localized throughout the interstitium and around blood vessels. Most of the mast cells were extensively degranulated. A larger number of degranulated mast cells could be found deeper, inside the polyp, then at the surface (Figure 3).

In the electron-microscope mast cell degranulation was far more obvious. Only partly granulated, but also totally empty cells were found in all samples (Figure 4).

A quite high level of eosinophilic cell infiltration was observed in all cases of ASA polyps (Figure 5). Submicroscopical analyses revealed a special eosinophilic picture in ASA polyps. In normal eosinophils, highly dense cores of various shapes (central crystalloids) are embedded in a less dense matrix. The majority of eosinophils in ASA polyps lost this highly electron-dense material from their central crystalloids (Figure 6).

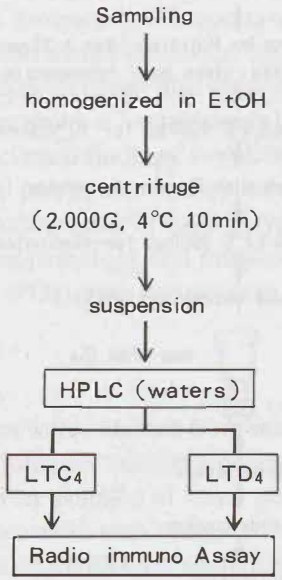

Figure 2. Methods for the determination of leukotrienes.

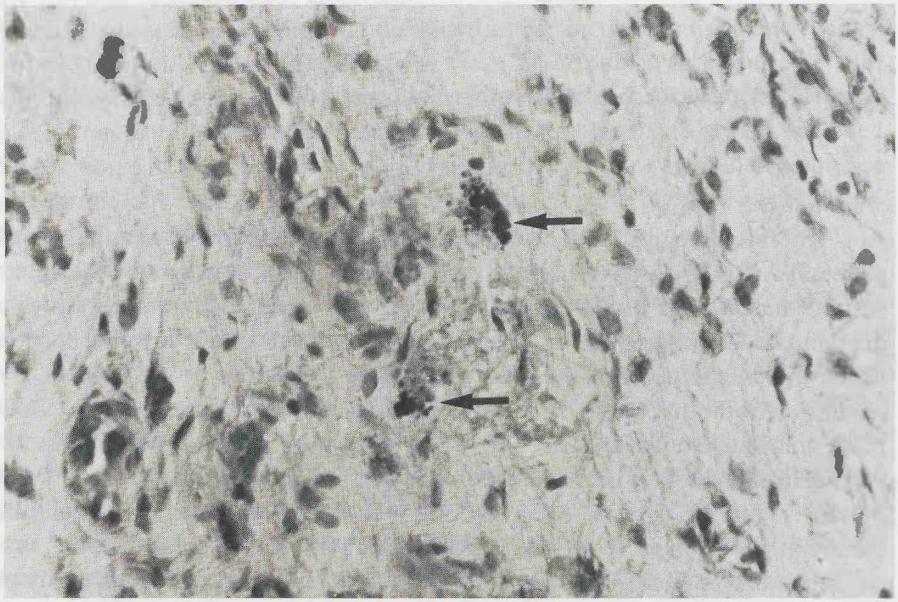

Figure 3. Degranulated mast cells (arrows) in a nasal polyp obtained from a patient with aspirin sensitive asthma (Toluidine blue, × 400)

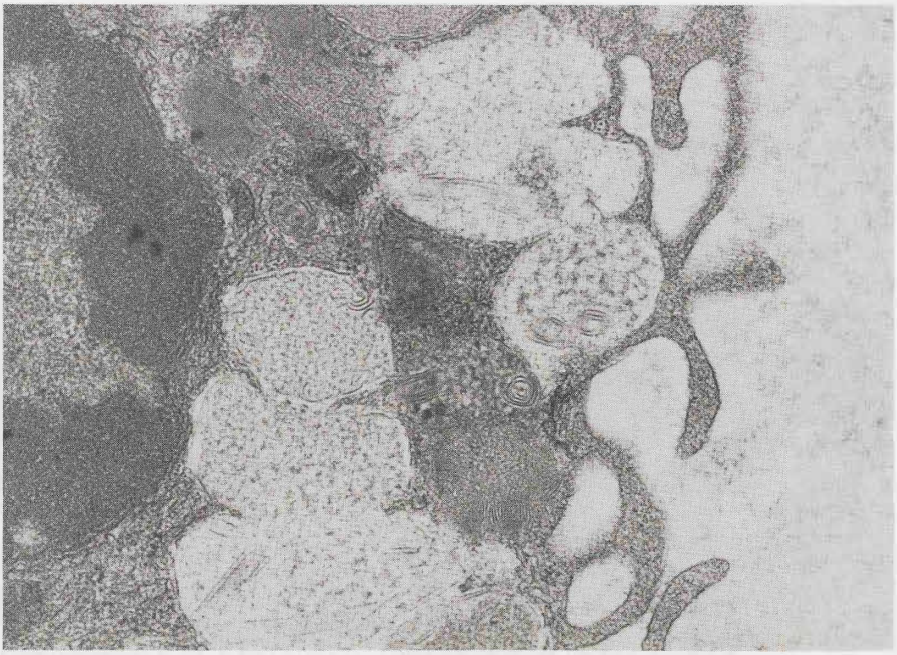

Figure 4. Electron-microscopical picture of degranulated mast cell in nasal polyp obtained from a patient with aspirin sensitive asthma (× 40,000).

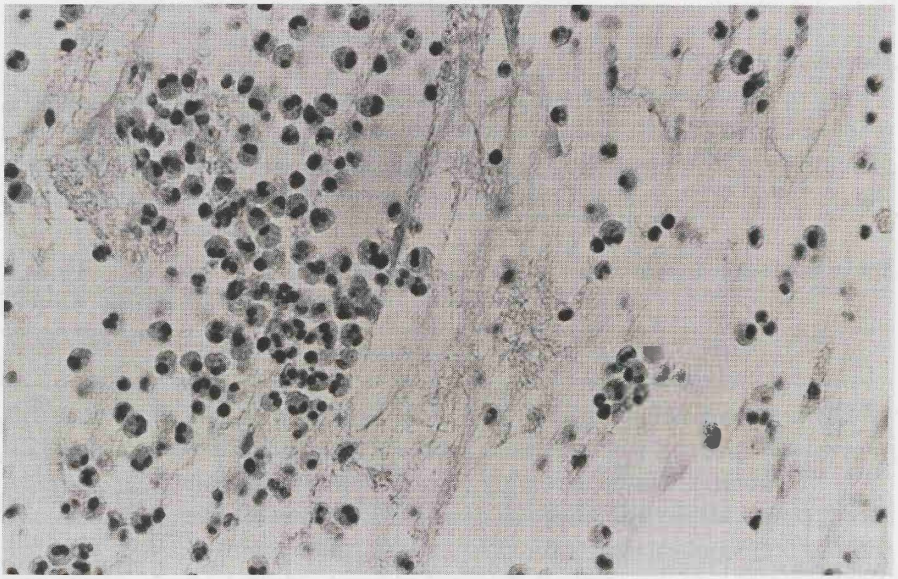

Figure 5. Large number of eosinophils distributed in submucosa of a patient with aspirin sensitive asthma (Haematoxyline-eosin, × 200).

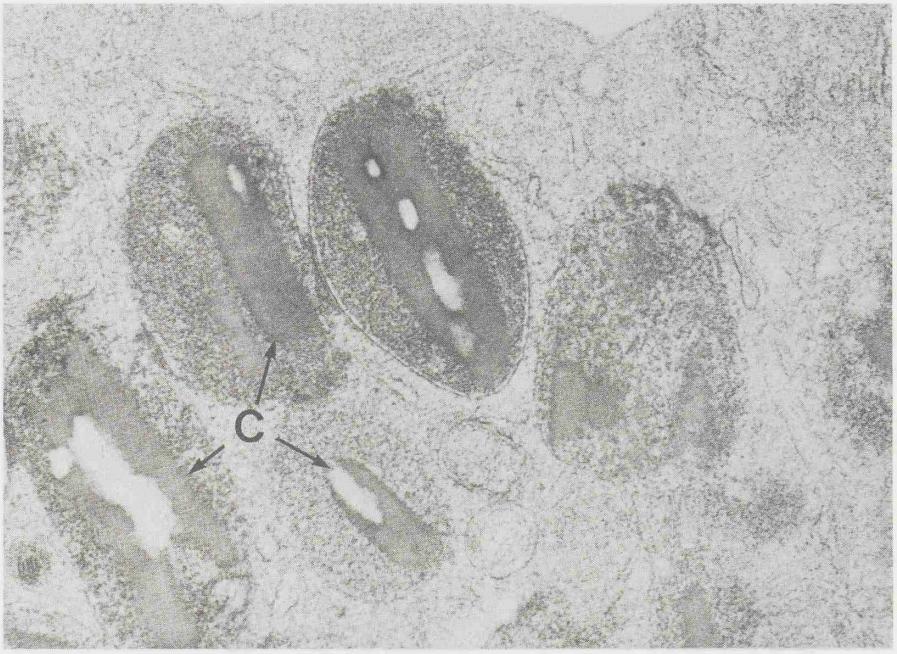

Figure 6. Electron-microscopical picture of eosinophils in the nasal polyps obtained from a patient with aspirin sensitive asthma. Note that high electron dense material in central crystalloid (c) disappeared (× 66,000).

Biochemistry

Values of mean concentrations of arachidonic acid metabolites (PGE_2, $PGF_{2\alpha}$, 6-keto-PG_1 and TXB_2) in the cyclooxygenase pathway of nasal polyps from patients with ASA, nasal allergy and chronic sinusitis are shown in Table 1 and Figure 7. The PGE_2 level was higher than those of the other three metabolites in

Table 1. Arachidonic acid metabolites in nasal polyps

	PG				LT	
	E_2	$F_{2\alpha}$	6-keto $F_{1\alpha}$	TXB_2	C_4	D_4
Sinusitis (n=5)	33.3 ±8.78	4.07 ±2.51	3.74 ±1.03	14.1 ±7.29	172 ±50	242 ±107
Nasal allergy (n=5)	28.6 ±10.21	6.45 ±3.23	4.56 ±2.13	8.96 ±6.84	336 ±327	211 ±158
Aspirin induced asthma (n=5)	7.33 ±2.28	1.45 ±0.66	3.77 ±2.94	4.56 ±1.48	1831 ±1719	1019 ±692
	10^{-9}g/g tissue				10^{-12} g/g tissue	

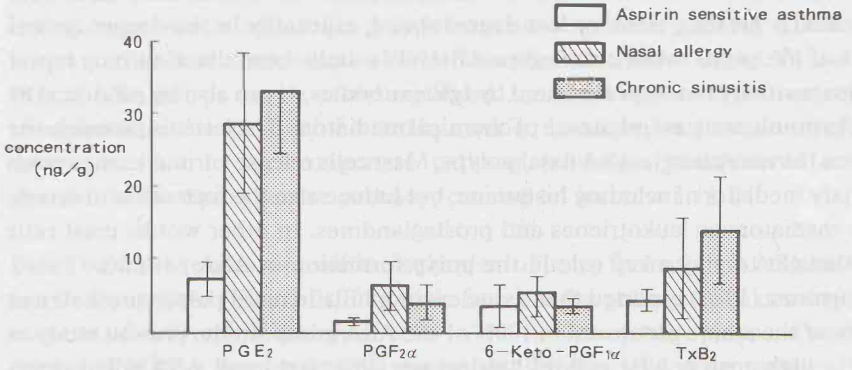

Figure 7. Mean concentrations of PGE_2, PGF_2, 6-keto-PGF_1 and TXB_2 in polyps from patients with aspirin sensitive asthma, nasal allergy and chronic sinusitis.

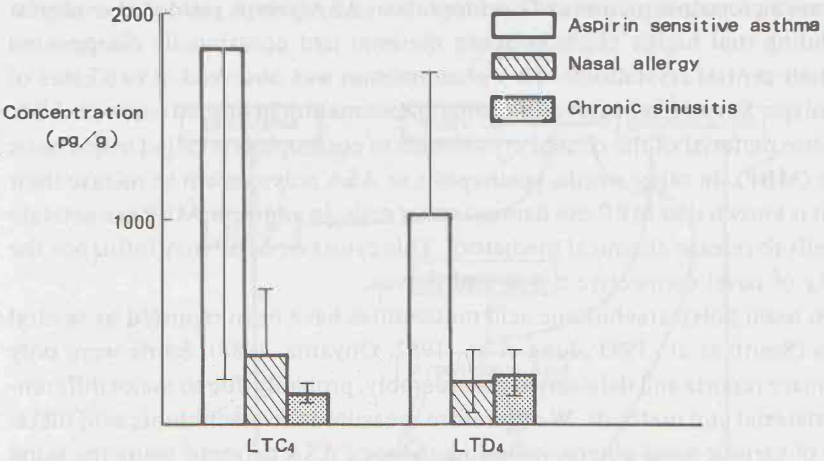

Figure 8. Mean concentrations of LTC_4 and LTD_4 in polyps from patients with aspirin sensitive asthma, nasal allergy and chronic sinusitis.

all types of nasal polyps. For all four metabolites holds that the mean concentration in ASA polyps is low as compared to the other clinical conditions. The differences between the nasal allergy and chronic sinusitis polyps are not significant.

The mean concentration of leukotrienes (LTC_4 and LTD_4) in the lypoxygenase pathway of nasal polyps from patients with ASA, nasal allergy and chronic sinusitis are shown in Table 1 and in Figure 8. Both metabolites increased predominantly in ASA polyps, as compared to the other two clinical conditions.

DISCUSSION

Light- and electron microscopy of ASA polyps revealed that mast cells were abundantly present, more or less degranulated, especially in the deeper central parts of the polyp. Mast cell degranulation is usually considered to be a type-1 hypersensitivity reaction mediated by IgE antibodies. It can also be produced by other stimuli, such as imbalance of chemical mediators. The latter is probably the case in the non-allergic ASA nasal polyps. Mast cells release various endogenous primary mediators, including histamine, but induce also the formation of secondary mediators as leukotrienes and prostaglandines. In other words, mast cells are thought to play a key role in the polyp formation in ASA patients.

Holopainen (1979) reported that tissue eosinophilia in nasal polyps presented in 88.9% of the atopic group and in 100% of the ASA group. In the present study as well, a high eosinophilic cell infiltration was observed in all ASA polyp specimens. These observations suggest that eosinophilia is not always a result of an allergic reaction, but can also be triggered through chemotactic factors such as LTs and platelet aggregation factors.

Electron-microscopic pictures of eosinophils in ASA polyps yielded the interesting finding that highly electron-dense material had occasionally disappeared from their central crystalloids. This phenomenon was observed in two cases of ASA polyps. Sasaki has observed a similar phenomenon in one patient with ASA. The dense material of the central crystalloids in eosinophils is called major basic protein (MBP). In other words, eosinophils in ASA polyps seem to release their MBP. It is known that MBP can damage other cells. In addition, MBP can activate mast cells to release chemical mediators. This cytotaxic MBP may influence the integrity of nasal connective tissue and nerves.

Data on nasal polyp arachidonic acid metabolites have been reported by several authors (Smith et al., 1981; Jung et al., 1987; Ohyama, 1988). Some were only preliminary reports and data varied considerably, probably due to major differences in material and methods. We therefore measured the arachidonic acid metabolites of various nasal polyps, including those of ASA patients, using the same method in all cases.

As to ASA polyps, Smith et al. (1981) reported that one patient with ASA showed a ten-fold increase in PGE_2 and PGF_2. Smith et al. (1981) also stated that they had no other tissue available in order to confirm that this was a consistent finding in patients with ASA. The significance of their findings remains therefore questionable. Jung et al. (1987) determined by radioimmuno-assay the LTC_4 levels of nasal polyps from four patients with a history of asthma and three patients with no history of asthma, and stated that polyps from patients with a history of asthma had higher levels of LTC_4. In our study, LTC_4 and LTD_4 in ASA polyps was predominantly increased, as compared to the levels in polyps from non-asthmatic

patients with allergic rhinitis or chronic sinusitis. These data are in agreement with Jung et al. (1987). We also showed that the level of PGs in ASA polyps was low as compared to the level in polyps from non-asthmatic patients. These data are in conflict with Smith et al. (1981). This phenomenon of high LTs and low PGs in ASA polyps can be easily explained: the cyclooxygenase pathway of the arachidonic acid cascade is inhibited by aspirin; therefore, the production of PGs decreases. Due to cyclooxygenase pathway inhibition, arachidonic acid is shunted to the lipoxygenase pathway, causing an increase in LTs.

Based on these results, a possible mechanism of polyp formation in ASA patients can be formulated (Figure 9). The basic facts are the presence of a considerable number of eosinophils and mast cells in the tissues of ASA polyps, a possible release of MBP, a low level of PGs and a high level of LTs. A decrease in PGE_2 level diminishes the membrane stability of mast cells with a release of primary chemical mediators such as histamine. An increased LTs level, especially of LTB_4 and histamine, leads to increased vascular permeability, edema and leakage of macromolecules from the vascular system. If such an imbalance of mediators

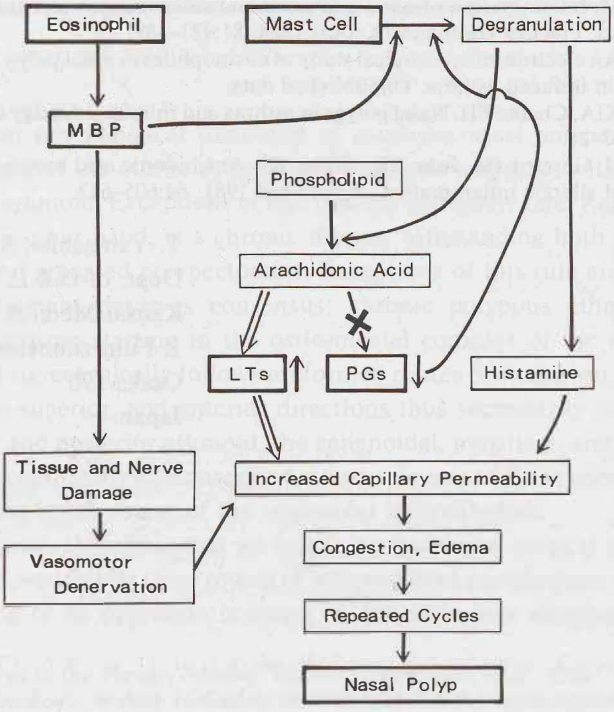

Figure 9. Possible mechanism of polyp formation in ASA patients.

persists, and the cycle continues the patient eventually develops nasal polyps. Another possibility is that the abundance of eosinophils in ASA polyps release a considerable amount of MBP, which stimulates mast cell degranulation. Since MBP acts also cytotoxic on nasal connective tissue and nerves by promoting vasomotor denervation and by increasing capillary permeability, the incidence of nasal polyps in ASA patients is especially high.

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Microsurgical treatment of recurrent nasal polyposis

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SUMMARY

Nasal polyposis has to be considered as an advanced form of chronic ethmoiditis requiring surgery. Its proliferation starts in the ostio-meatal complex of the lateral nasal wall, and follows typical routes. Depending on its extension endoscopical partial resections of the ethmoid may be carried out. For diffuse polyposis of all sinuses a complete endonasal ethmoidectomy together with the fenestration of the frontal, sphenoidal and maxillary sinuses (pansinus operation) is indicated. The importance of preoperative imaging by CT or polytomography, and of flanking measures, is stressed. Fair results concerning subjective relief and objective proof of lasting mucosal recovery are reported against the background of a low incidence of surgical complications.

To talk about microsurgical treatment of recurrent nasal polyposis means to discuss surgery of the ethmoid, because there is no polyposis without involvement of the ethmoid. Exceptions of this rule are extremely rare. Recurrent polyposis, on the other hand, is a chronic disease withstanding both conservative treatment and repeated polypectomies. Exceptions of this rule are also rare.

A third statement deserves consensus: chronic polypous ethmoiditis is a centrifugal process starting in the ostio-meatal complex of the middle nasal meatus, and stereotypically follows preformed routes of extension into the posterior, latero-superior, and anterior directions thus secondarily compromising the anterior and posterior ethmoid, the sphenoidal, maxillary, and frontal cavities. Only exceptionally circumscribed sinusitis in one of these compartments is found without involvement of the ethmoidal infundibulum.

It is only logical, therefore, that we orient our battery of surgical interventions at these facts, and follow these routes of inflammatory proliferation with surgery. The planning of an operation is based on the very clear imaging of chronic-

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mucositis utilizing CT-scans or polytomograms. According to what has been stated above the extent of microsurgery can be adapted to the individual case. For circumscribed pathology smaller interventions are indicated, while for advanced diffuse polyposis pan-sinus operations are at our disposal.

Surgical techniques

If we look at a list of generally accepted degrees of endonasal operations of the ethmoid (Table 1) we may discern between four main types:

1. Broadening of the ostio-meatal complex by hiatotomy or ethmoidal infundibulotomy, respectively, is a very delicate, circumscribed excision of the semilunar hiatus exposing the most important anterior inferior ethmoidal cells for better ventilation and drainage of the anterior ethmoid, the frontal sinus and of Highmore's cavity. It includes both an excision of the superior rim of the uncinate process and the opening of the ethmoidal bulla as far as necessary.

Table 1. Types of endoscopical ethmoidectomy.

Exposure of the ostio-meatal complex (Hiatotomy, Ethmoidal infundibulotomy)
Anterior partial ethmoidectomy
Posterior partial ethmoidectomy
Complete ethmoidectomy (with/without fenestration of the maxillary, frontal and sphenoidal sinuses)

2. It may be extended into an anterior partial resection of the ethmoid if the periinfundibular cells are obstructed by thickened mucosa or polyps.

3. If such pathologic abnormalities are found dorsally in the bulla one can easily perforate the ground plate of the middle turbinate and explore the posterior ethmoidal labyrinth. If necessary a posterior partial resection of the ethmoid may then be added. In case of diffuse polyposis a complete ethmoidectomy may result from this step-by-step advancement through the middle nasal meatus.

4. If preoperative tomography has visualized a severe diffuse polyposis of all the ethmoid and of all other sinuses one can select another approach. As we have suggested in 1981 a retrograde complete ethmoidectomy offers certain advantages. This procedure (Wigand, 1981) does not start according to the classical methods through the middle nasal meatus but begins with a partial resection of the posterior ethmoid, exposing the anterior face of the sphenoid sinus which is opened. After the exposure of the sphenoidal roof one follows the inferior surface of the anterior skull base and opens the ethmoid step by step from its posterior to its anterior compartments and continues with an exposure of the frontal sinus from below. Then follows a supraturbinal fenestration of the maxillary antrum

with subsequent removal of polyps and cysts but with utmost preservation of the mucosal lining. Thus a broad communication between all sinuses is established for the enhancement of ventilation and drainage. The parietal mucosa, even when severely diseased, is left in place.

While the initial opening of the posterior ethmoid and of the sphenoid sinus may be carried out with the unarmed eye or with the help of a microscope, for the management of the anterior ethmoid, the frontal and maxillary sinuses angled optics of at least 70° are utilized. Various instruments are prerequisite such as curved cup forcepses, punches, curettes etc. to work within the cavities.

Flanking measures

Some other preconditions exist: an excellent exposure of the surgical field is mandatory. For this purpose two flanking measures can be recommended:

1. A plastic septum correction with mobilization – not resection – of both the quadrangular cartilage and the perpendicular plate always helps considerably to enhance the visualization of the ethmoidal labyrinth.
2. And secondly, the middle turbinate can be trimmed according to the necessities of the individual case (Figure 1). A resection of the posterior third of the middle turbinate may be very helpful in polyposis. Also partial resection of the turbinate body itself can be carried out. Care should be taken, however, not to injure the olfactory rim. If the removal of the bulla and of intraturbinal cells has weakened the medial lamella of the middle turbinate its folding up may stabilize the remnants of the turbinate, and open the olfactory cleft at the same time.

Another precondition of success besides the complete opening of the ethmoid with total removal of all polyps but with preservation of the mucosal lining is the consequent endoscopical aftercare over 3–4 months. During this period crusts and secretions have to be removed, granulation tissue has to be etched in order to prevent recurrent polyposis, and the reobstruction of the anterior ethmoid has to be avoided by active removal of fibrin clots which often give rise to scar formation and synechia. The patient has to be informed before his operation that a long-range aftercare is as essential as a good operation. The end result should be an open ethmoidal bowl lined by moist mucosa, and having free communication with the frontal, sphenoidal and maxillary sinuses.

RESULTS

Regarding the results we have to distinguish between subjective relief of symptoms from polyposis and morphological recovery (Tables 2 and 3). The great majority of patients is satisfied by surgery. If we control the ethmoidal and antral lining endoscopically, however, there are often remnants of edema or micropolypi. If we count these changes as recurrencies, though they are usually

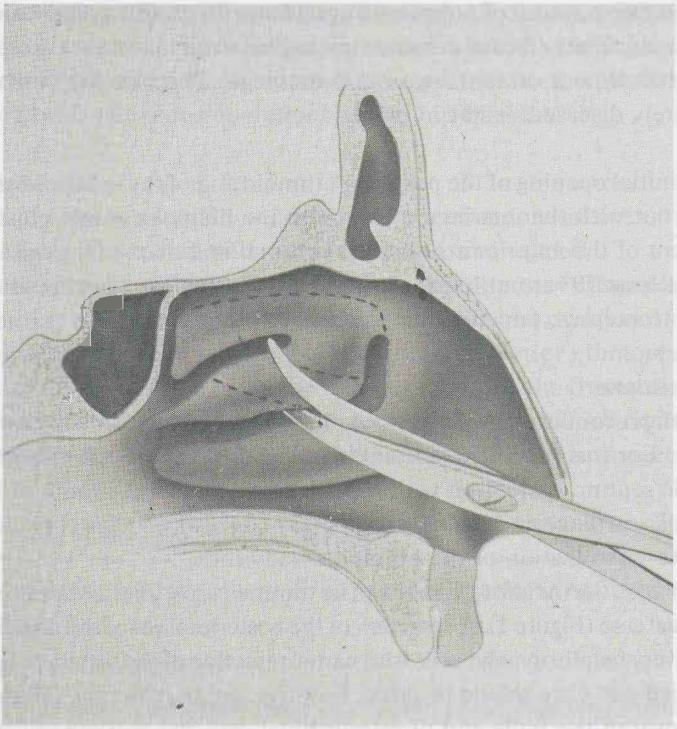

Figure 1. Resection of the dorsal third of the middle turbinate. The dotted lines above indicate a partial resection of the body of the middle turbinate (rarely necessary) and its subtotal resection (e.g. in case of tumour growth).

Table 2. Subjective evaluation of surgery for sinusitis polyposa.

	Number of patients	
Complete success	53	(24.1%)
Successful treatment	54	(24.5%)
Improvement	73	(33.2%)
No definite improvement	27	(12.3%)
Failure	13	(5.9%)
Total	220	(100.0%)

Table 3. Endoscopical findings after surgery for sinusitis polyposa.

	Ethmoid	Sphenoidal sinus	Maxillary sinus
Normal aspect	88 (52%)	123 (95%)	119 (72%)
Thickened mucosa	8 (5%)	–	22 (13%)
Humped hyperplasia	42 (25%)	6 (5%)	22 (13%)
Recurrent polyposis	30 (18%)	–	2 (1%)
Total	168 (100%)	129 (100%)	165 (100%)

neglectable, we arrive at a recurrence rate of 18%. It has to be emphasized, however, that this is not recurrent polyposis because these lesions do not grow.
With regard to possible complications (Table 4) it must be mentioned that within a series of more than 1600 ethmoidectomies, not one single serious complication was encountered. There were some circumscribed fistulas due to the rupture of olfactory fibres, but all of them were detected and immediately closed by mucosal grafting utilizing fibrin glue. There was not one involuntary perforation of the ethmoidal roof, and only few cases of postoperative meningism were observed which could be controlled within two or three days by antibiotic treatment. Ethmoidectomy for polyposis can be labeled, therefore, as a safe procedure.

Table 4. Complications of endoscopic endonasal ethmoidectomy (n = 600).

Loss of olfactory sensation	3.00%
Intraoperative csf-leak through olfactory fibre	0.30%
Obstruction of lacrimal duct	0.50%
Orbital complications, visual disturbance	0.00%
Postoperative meningitis	0.50%
Mortality	0.00%

One should always be aware of impending dangers. It must be admitted that during the last year a misfit in one case of transnasal sphenoidectomy happened. After simple puncture of the sphenoid sinus with a blunt aspirator a massive haemorrhage occurred from the internal carotid artery which in that case bulged into the sinus and was not covered by bone. The bleeding could be stopped rapidly but the patient who had a history of earlier vascular symptoms later died from the sequelae of a transient arterial hypotension. There was no cerebral haemorrhage found at autopsy.
This case is mentioned in order to emphasize that endoscopical surgery of the ethmoid and other sinuses is not hazardous but requires skill and utmost attention at every phase of the procedure.

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Surgical versus medical treatment of nasal polyps

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SUMMARY

Surgical removal of nasal polyps is associated with discomfort and risks for the patient, but is the treatment of choice to most otorhinolaryngologists. Medical treatment alone has been little investigated. In a prospective clinical trial surgical removal followed by continuous topical steroid treatment has been compared with a single dose of steroid deposit followed by continuous topical steroid treatment. During a study period of one year, expiratory nasal peak flow and sense of smell were monitored. In general, the course in the two groups was alike, with a tendency favouring the medically treated group.

In another study the clinical efficicacy of this medical regimen was further documented experimentally. By acoustic rhinometry the square area of the nasal passages was measured before and a few days after the injection of the steroid deposit. Increased volume was found, corresponding to the instant clinical improvement.

It is concluded that primary treatment of nasal polyps should be medical. Surgery is only recommended in cases, resistant to medical therapy.

INTRODUCTION

Most otorhinolaryngologists prefer surgical removal of nasal polyps, although this is associated with discomfort and certain risks for the patient. Medical treatment with steroids alone has been described, but is only occasionally recommended. Postoperative use of topical steroids postpones or prevents recurrencies (Pedersen et al., 1976). A combination of therapy of systemic and local steroids might even be more efficacious, which was supported both clinically (Lildholdt et al., 1988) and experimentally (Felding et al., 1988).

THE CLINICAL TRIAL

A prospective and randomized trial was performed of surgical removal versus a single dose of a 2 ml suspension of betamethasone dipropionate and beta-

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methasone disodium phosphate intramuscularly (Diprospan®, Essex Pharma, Denmark). In both groups a nasal spray of 100 micrograms of beclomethasone dipropionate (Aldecin Nasal®, Essex Pharma, Denmark) was applied twice daily during a study period of one year.

In 53 patients eligible for surgical removal of nasal polyps the diagnosis was documented by a mini biopsy. Symptoms and signs were recorded and smell was tested, as well as baseline nasal expiratory peak flow (NPF). After randomization 26 patients received medical treatment, while 27 received surgical removal. The clinical course was monitored at regular office visits during a 12 months follow-up period. At two weeks a considerable improvement in nasal passage was recorded in both groups. An intact smell was reported by 92% in the medical group versus 67% in the surgical group ($p<0.05$). However, in general the clinical course was alike in the two groups. Residual or recurrent polyps necessitated the initial treatment to be repeated in four patients in the medical group, and three in the surgical group.

NPF is an objective measure of changes in nasal patency. Figure 1 shows some differences between the mean values of the two groups. The relative gain in NPF at a two week check-up was statistically significantly higher in the medical group ($p<0.02$). In general, the clinical course was the same in the two groups. At the end of the study period the efficacy of treatment was rated excellent or satisfactory by three out of four patients in both groups.

EXPERIMENTAL STUDY

During the technical development of acoustic rhinometry (AR) the above mentioned clinical results emerged. Medical treatment of nasal polyps was a good model for testing the change in volume of the nasal cavities in the same subject prior to and after steroid application.

With AR the square diameter of one nasal cavity is calculated at every point between nostrils and pharynx. It is based on reflection of sound where signals are computer analysed (Felding et al., 1988). Initially, the narrowest area was found at each site of the nose, which corresponded to the most protruding part of the polyps. The medical treatment described above was performed and diameters were measured during the following weeks. It showed a dramatic increase in square diameter at the narrowest points in the nasal cavity, which occurred already within a few days of treatment and remained so for a study period of several weeks, although with considerable daily variations.

CONCLUSION

This study indicates that primary treatment of nasal polyps can as well be medical as surgical. Surgery can therefore be limited to those cases with residual or recurrent disease, including those patients where steroids are contra-indicated.

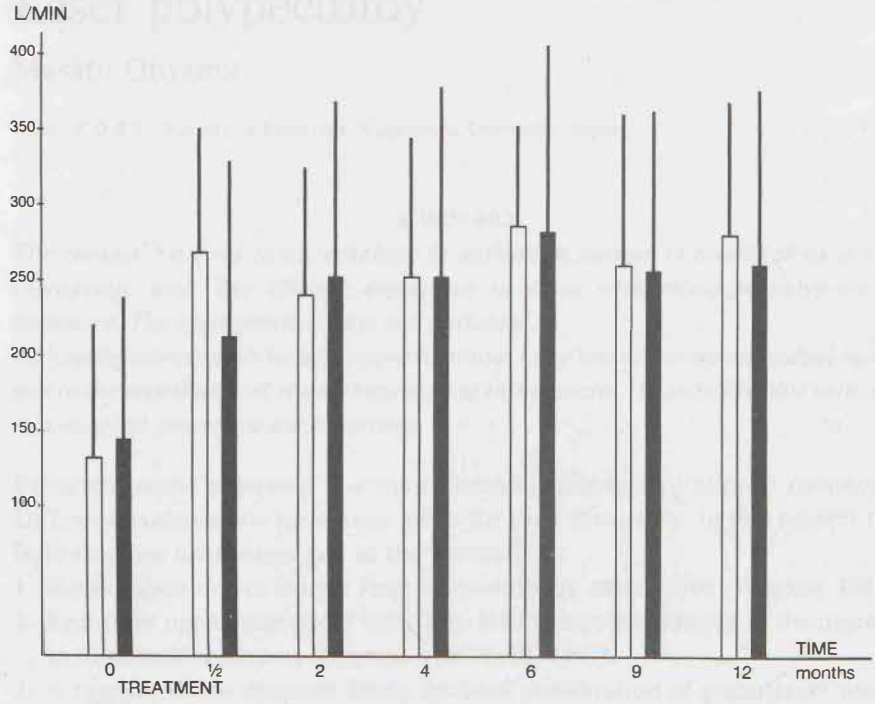

Figure 1. Mean nasal peak flows of two groups given different treatment modalities. White columns: medical treatment; black colums: surgical treatment; vertical barrs: SD. (Reprinted from Acta Otolaryngol (Stockh) 1988; 105:140–143.)

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Laser polypectomy

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SUMMARY

The contact Nd:YAG laser technique in endonasal surgery is presented as a new therapeutic tool. The clinical experience in cases with recurrent polyposis is presented. The therapeutic results are evaluated.

Although patients with nasal polyposis remain to be treated on an individual basis, due to the multifactorial etiopathogenesis of this disorder, the initial results with this new surgical procedure are promising.

Recurrent nasal polyposis is a most common problem in clinical rhinology. Different explanations have been given for their formation. In this respect the following has been suggested in the literature:

1. Nasal polyps derive from a form of necrotizing ethmoiditis (Woakes, 1985).
2. Recurrent upper respiratory infections lead to vascular damage of the mucosa in nose and/or sinuses (Eggston and Welff, 1947).
3. A rupture of the mucosal lining initiates proliferation of granulation tissue (Tos and Mogensen, 1979).
4. A local accumulation of an insulin-like growth factor stimulates the formation of nasal polyps (Petruson et al., 1988).
5. They develop from an expanding intramural cyst, such as antrochoanal polyps, and protrude through the sinus ostium into the nasal cavity (Berg et al., 1988).

In addition, inflammation, atopic allergy and occasionaly aspirin induced asthma play a role in their etiopathogenesis (Ohyama et al., 1985; Sasaki, 1987).

Nasal polyps have been histologically classified into three categories: the edematous, the glandular-cystic type (an active stage of connective tissue reaction) and the fibrous type (a healing stage of tissue matrix). Different treatment modalities have been proposed, based on their pathogenesis and macroarchitectural characteristics.

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The present paper deals with the application of the contact Nd:YAG laser technique for recurrent polyposis in the nose. The efficacy of this treatment is clinically evaluated.

CONTACT Nd:YAG LASER TECHNIQUE

The modality with conventional lasers is to coagulate, vaporize or incise soft tissues and requires that the laser beam travels a certain distance over the surface of the target tissue. Although the CO_2 laser is an useful instrument for vaporization or excision of tissues, it has also the disadvantage that it produces a carbonized layer on the tissue surface. Furthermore, it cannot be used for fine dissection as is required for functional surgery in the narrow and deep parts of the upper airway, including nose and sinuses.

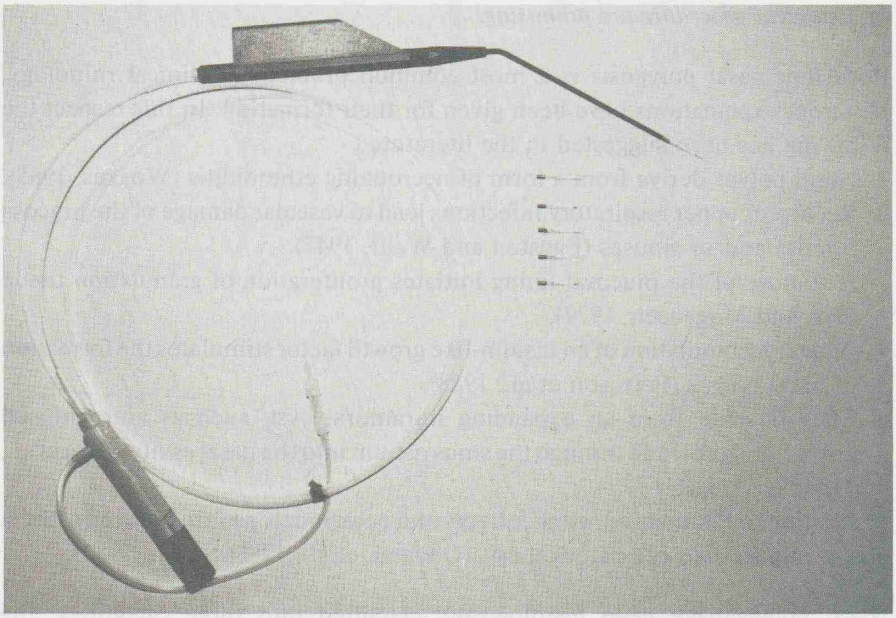

Figure 1. Surgical holder with different laser probes for contact Nd:YAG laser technique in endonasal surgery.

The beam of the Nd:YAG laser is scattered within the tissue surface even when its focus is concentrated on the target spot, thus leading to a dispersion of energy. The irradition from a Nd:YAG laser, however, causes a slow and gradual temperature rise when compared with the CO_2 laser. The latter produces an equal strength of laser energy resulting in a significantly more efficient coagulation. The laser covers a wide area. One has always to be cautious, since reflection on a surface of target tissue can be dangerous for the surgeon and his assisting person-

nel. To solve the above mentioned problems we have developed a new device which concentrates the laser beam on a target spot by attaching a new ceramic probe to the optical fiber tip (Ohyama et al., 1985, 1988) (Figure 1). Laser excision of soft tissue can now be performed through the same contact procedure as with the cold knife; however, with far less bleeding and with minimal injuries to the adjacent tissue. In this way Nd: YAG laser surgery can be remarkably controlled and is far superior to the conventional laser treatment.

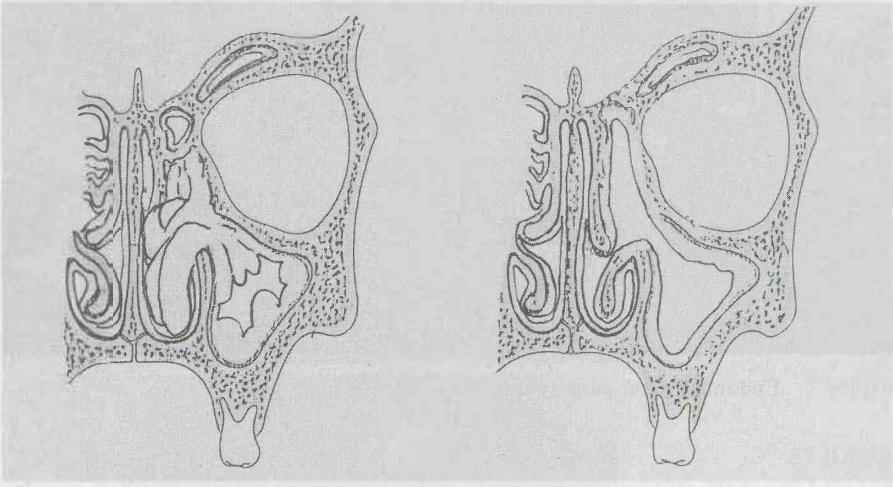

Figure 2. Schematic drawing of surgical procedure in contact Nd:YAG laser polypectomy.

SURGICAL PROCEDURE

Generally, surgery is performed with the patient in a supine position. After correct positioning of the nasal speculum with a rigid fiberscope local anaesthesia is given through injection of the mucous membrane around the polyps with a mixed solution of 2.0% xylocain and hydrogen peroxide in equal volumes. A good haemostasis is thus obtained at the site of surgery.

Figure 2 illustrates under which conditions the contact Nd:YAG laser technique is applied in the nose and sinuses in cases with polyposis. An essential part of the technique is that prior to laser surgery the polyps are irradiated and coagulated *interstitially* through insertion of the ceramic laser probe. This sequence in the procedure enables the surgeon an easy localization of the pedicle of any polyp, which can then be cut by the laser beam.

Recently, this laser surgery for treating nasal polyposis has been successfully performed with TV monitoring (Ohyama, unpublished data) (Figure 3). The small CCD TV camera system is in addition quite useful as teaching device for endonasal surgery.

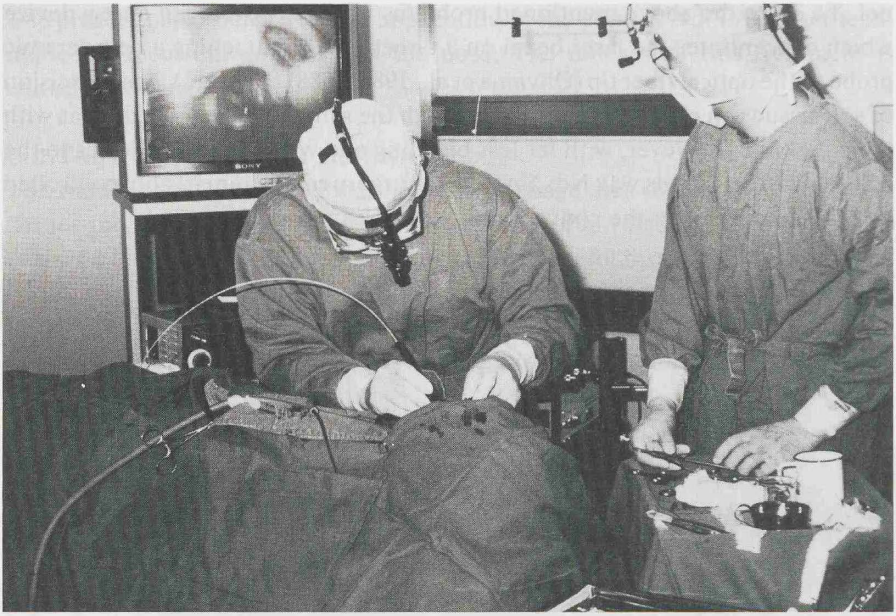

Figure 3. Endonasal laser surgery under TV monitoring.

RESULTS

Figure 4 shows the rhinoscopic finding in an 18 years old male patient with nasal polyposis before and after interstitial laser irradiation. The polyp shrinked and had been partly coagulated. Note the clear view of the pedicle after interstitial coagulation.

Figure 5 displays the results of the thermographic analysis of nasal patency in a case with allergic nasal polyps before and three months after laser polypectomy. The postoperative thermogram shows an increased dark colour area indicating low temperature after inspiration. Nasal patency is considerably improved after laser surgery.

The histological findings in a polyp resected by Nd:YAG laser surgery shows minimal tissue damage (carbonization and coagulation) at the contact site of the laser probe (Figure 6).

Table 1 shows the total number of cases treated with endonasal contact Nd:YAG laser surgery during the past four years. We have obtained quite satisfactory

Table 1. Number of cases treated with endonasal contact Nd:YAG laser surgery during the past four years (follow-up period over one year)

		male	female	total
turbinectomy	nasal allergy	21 (15)	25 (17)	46 (32)
	hypertrophic rhinitis	18 (17)	8 (8)	26 (25)
polypectomy		14 (13)	7 (6)	21 (19)

( ) indicates number of cases with improved nasal patency and less symptoms.

results. Nasal obstruction diminished considerably in most of our patients. Clinical symptoms as watery rhinorrhea and sneezing remained present, however, in those patients with a nasal allergy. In 19 out of the 21 cases who had laser polypectomy performed, the results were relatively good.

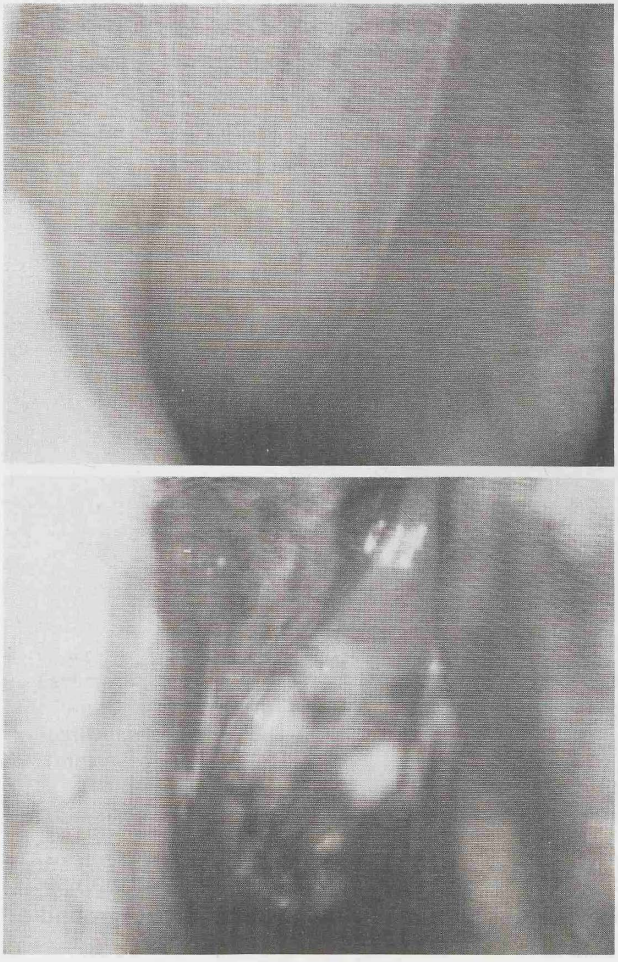

Figure 4. Rhinoscopic findings in a case with recurrent nasal polyposis. (Female, 18 years old)
A: before laser polypectomy
B: after *interstitial* laser irradiation

DISCUSSION

Chronic infection or allergy of the nose and sinuses may be considered as causative factors in the development of nasal polyps. It has not been possible to distinguish macroscopically between polyps in patients with or without allergy. Many patients experience that growth and recurrency of polyps are influenced by persistant upper respiratory tract infections. It is therefore very likely that the growth rate of polyps is variable, depending on the pathological conditions of the

mucosa in nose and sinuses. This holds especially for choanal polyps which have their origin in one of the sinuses.

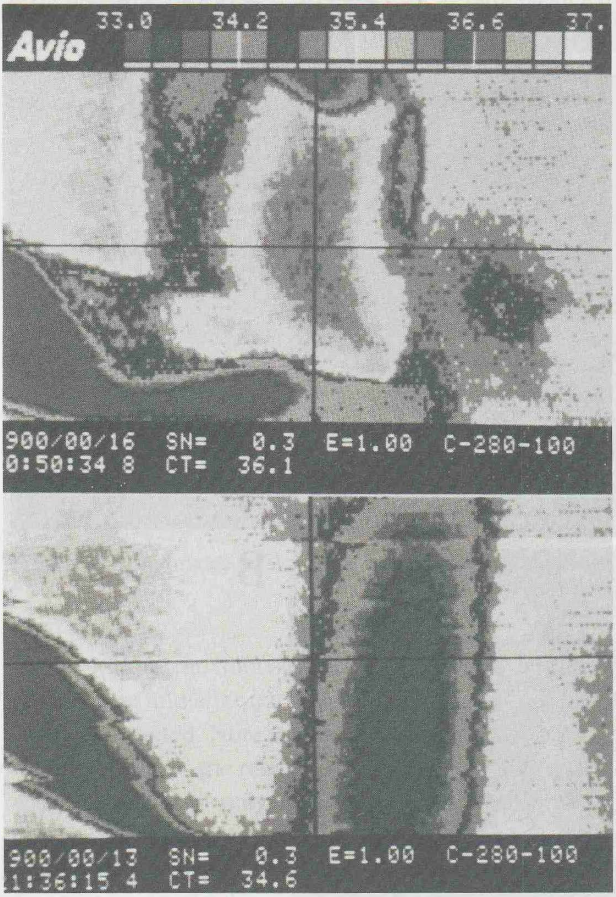

Figure 5.
Thermographic analysis of the right nasal cavity before (top) and three months after (bottom) laser polypectomy. (Female, 22 years old)

Two methods of treatment have been propagated in cases of nasal polyposis, either topical steroid application in those cases with an allergic background or surgical treatment.

Over the last decade it has been reported that topical aerosol therapy of beclomethasone dipropionate has a beneficial effect in about 80% of patients suffering from nasal polyps (Mygind et al., 1975; Pedersen et al., 1976). Such a steroid treatment should not be the method of choice for all patients. If surgical removal of polyps once or twice a year can keep the patient symptom-free, this treatment should be preferred and should not be replaced by permanent steroid therapy. Topical steroid therapy is meant to prevent polyp formation as well as to diminish frequent polypectomies not only in cases with polyps of an allergic origin but also

in those cases suffering from concomitant chronic sinusitis. However, patients with nasal polyps who belong to the infectious group do not respond very well to any steroid compound. It should further be pointed out that both topical steroid treatment and surgical removal of polyps are only symptomatic therapies.
We have performed endonasal surgery for treatment of nasal polyposis by using a contact Nd:YAG laser technique over the past years. It proved to be a very useful tool to reduce symptoms and appeared to be quite helpful in the treatment of chronic inflammatory disease of the nose (Ohyama, 1988). It should be noted that a conservative or radical ethmoidectomy in cases with recurrent nasal polyposis can also be performed in this way.

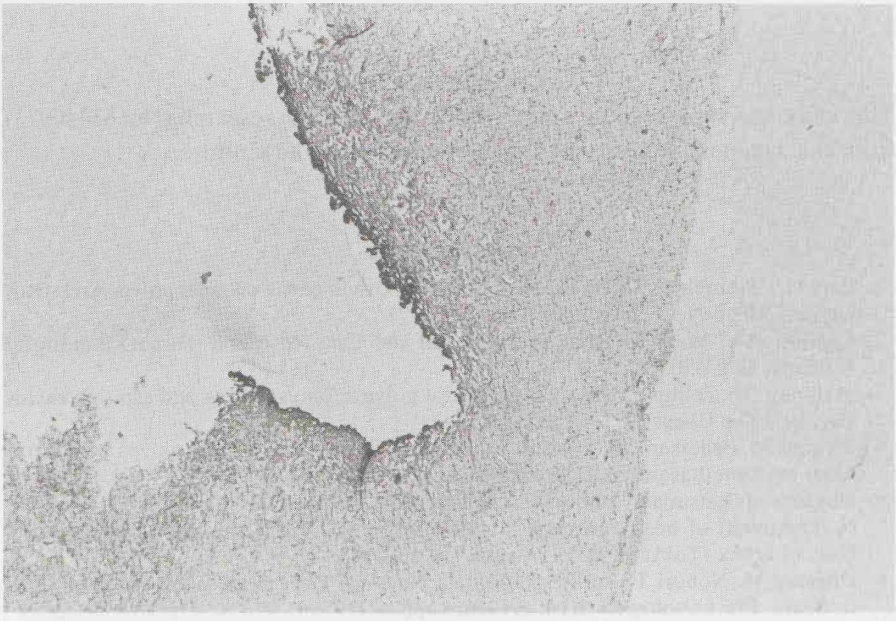

Figure 6. Histology of nasal polyp after *interstitial,* laser irradiation. Note edge with limited carbonization at laser contact site.

The advantages of this new technique can be summarized as follows:

1. Surgery can be performed with minimal bleeding and causes very little injury to the surrounding mucosa.
2. Postoperative pain is hardly present.
3. Nasal packing is not obligatory in most cases.
4. Interstitial laser irradiation may have a beneficial thermal effect on other target tissues such as turbinate mucosa or even tumour cells (Ohyama et al., 1988).

5. Laser irradiation can be expected to have an inhibitive effect on excessive tissue proliferation in the wound healing process and to a certain extent may prevent regrowth of polyps.
6. Surgery can be performed in patients with nasal polyps and turbinate hypertrophia as an one-day surgical procedure.

The following disadvantages should also be pointed out:

1. The technique requires occasionally a little longer operative time.
2. There is still considerable crust formation at the wound site after Nd:YAG laser surgery but limited to a period of two weeks.
3. The Nd:YAG laser beam, presently used, does not allow to cut bone yet.

ACKNOWLEDGEMENT

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Treatment of nasal polyps – Medication or surgery and which technique

In the chair: M. Tos (Copenhagen)
Participants: A.B. Drake-Lee (Birmingham), V.J. Lund (London), H. Stammberger (Graz)

Several case reports, some with few symptoms, some with severe and recurrent symptoms were presented and the panelists were asked to propose the evaluation to make the proper diagnosis and the treatment.

EVALUATION

The panelists agreed that the optimal initial evaluation of a patient with nasal polyps includes:

1. Anterior and posterior rhinoscopy
2. Endoscopy of the nose
3. X-rays of the sinuses, especially the ethmoid, eventually CT-scan
4. Allergic evaluation.

We are aware that the majority of patients with nasal polyps are seen and treated by general otorhinogologists in private offices outside hospitals and the proposed evaluation at the moment is usually performed in patients which fail the initial treatment, in recurrent and most severe cases.

TREATMENT

There was great disagreement how to treat the patients with nasal polyps. The panelists agree that the rational treatment should be based on understanding the disease process involved and tailoring the treatment accordingly. Bilateral nasal polyps are not a single disease but the end result of a number of pathological processes. Only rare cases have known aetiologies such as cystic fibrosis, immotile cilial syndrome and Young's syndrome. Most cases do not have an established cause but although allergy is frequently cited, the incidence is the same as in the normal population.

Fireside Conference on burning questions. 12th Congress of the European Rhinologic Society including the VIIth I.S.I.A.N., Amsterdam (The Netherlands), June 1988.

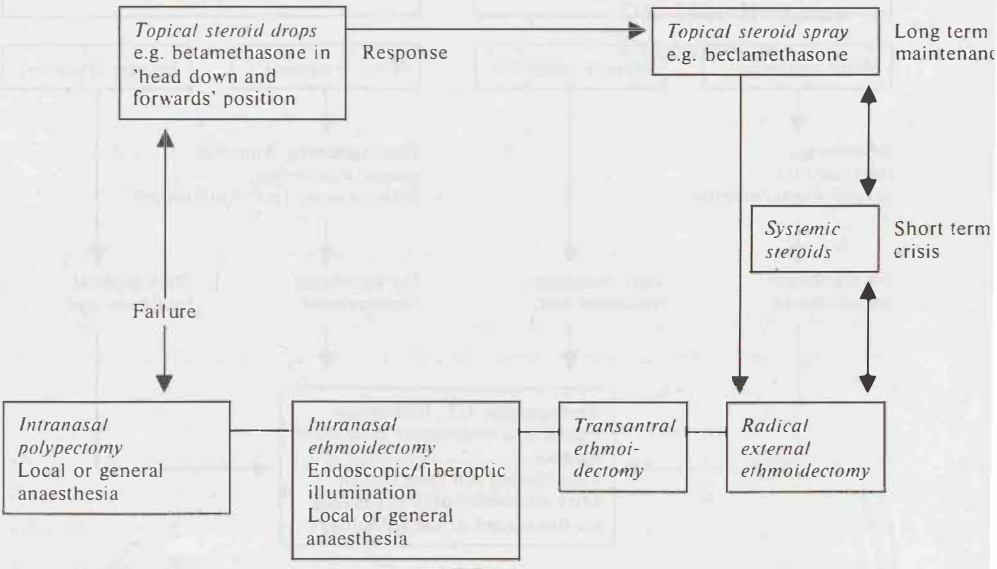
1. *The first panelist (D-L)* will apply medical treatment in all patients – those with minor and severe symptoms – with local steroids. He considers nasal polyps the nasal manifestation of an unstable respiratory mucosa. This means that the mucosa is diseased in itself and is not a normal mucosa that becomes diseased. The process may involve the whole of the nose, paranasal sinuses and may extent further down the respiratory tract into the lower respiratory tract. These patients have asthma as well as polyps. Published work suggests that mast cell reactions may be important in the development of nasal polyps. This explains both the therapeutic response to corticosteroids in half the patients and the non-specific action of acetyl acetic acid and the tartrazine dyes on mast cells.
Although surgery has been the mainstay of treatment since antiquity, no controlled trials have ever been undertaken to show that nasal polyps are cured by more extensive surgery than simple nasal polypectomy with a snare. Unsupported statements such as "I get good results", are to be condemned in the latter twentieth centuary. Since patients respond to corticosteroids, they now have a place in the management of the condition.
D-L treats polyps initially be either an aqueous solution of a corticosteroid such as beclomethasone diproprionate or flunisolide, two puffs each nostril twice a day or betamethasone nose drops, two drops each side twice a day. If the polyps do not respond after a month then surgical removal with a snare is indicated. Oral corticosteroids may be used in very refractory cases that have not responded to either surgery or nasal medication. Very occasional oral corticosteroids may be used in patients with severe nasal obstruction where it is impossible to introduce nasal medication.
One of the false concepts of surgery is that of making the ethmoid sinuses a single unit will prevent recurrence. The maxillary sinus is already a large unit and polyps readily form here. If an antrostomy is created then polyps will prolapse through it in severe recurrent cases. In addition, extensive surgery to the ethmoids may make the middle turbinate unstable and if it is removed the main landmark of polyp surgery is lost. This may make subsequent surgery very difficult even for the experienced surgeons.
Drake-Lee concludes that the aim of treatment is to provide a simple and safe approach to the management of nasal polyps that can be practised as widely as possible. Preliminary medical treatment will prevent surgery in over half the cases and subsequent surgery should leave the nose anatomically as normal as possible. Simple removal with a snare is adequate.

2. *The views of the second panelists (V-L)* can be summarised in Table 1. It is, however, important to establish a tissue diagnosis prior to commencing therapy as occasionally neoplasms such as inverted papilloma and mucus-secreting adenocarcinoma can masquerade as "benign nasal polyps". Initial medical treat-

ment is with topical steroid drops such as betamethasone sodium phosphate administered in the "head down and forwards" position for 4–6 weeks. If the patient is symptomatically improved, they are maintained with a topical steroid spray such as beclomethasone diproprionate. If the initial medical treatment fails, the polyps are removed, usually under local anaesthesia using a snare. This can be repeated as necessary in combination with a topical steroid preparation but after a number of procedures (5–6) it would be appropriate to perform the polypectomy under general anaesthesia if this has not already been done and to consider an intranasal ethmoidectomy using fibre-optic illumination or under endoscopic control. Ethmoidectomy is not commonly resorted to as although it may delay recurrence, it does not cure the condition. In a recent series of 10 patients with 20 years follow-up who had undergone between 2–10 intranasal polypectomies and external ethmoidectomy, although the interval between external ethmoidectomy and subsequent polyps was significantly longer, only two patients have had no recurrence following radical surgery. The average interval between external ethmoidectomy and next polypectomy was 73 months ($p = < 0.05$).

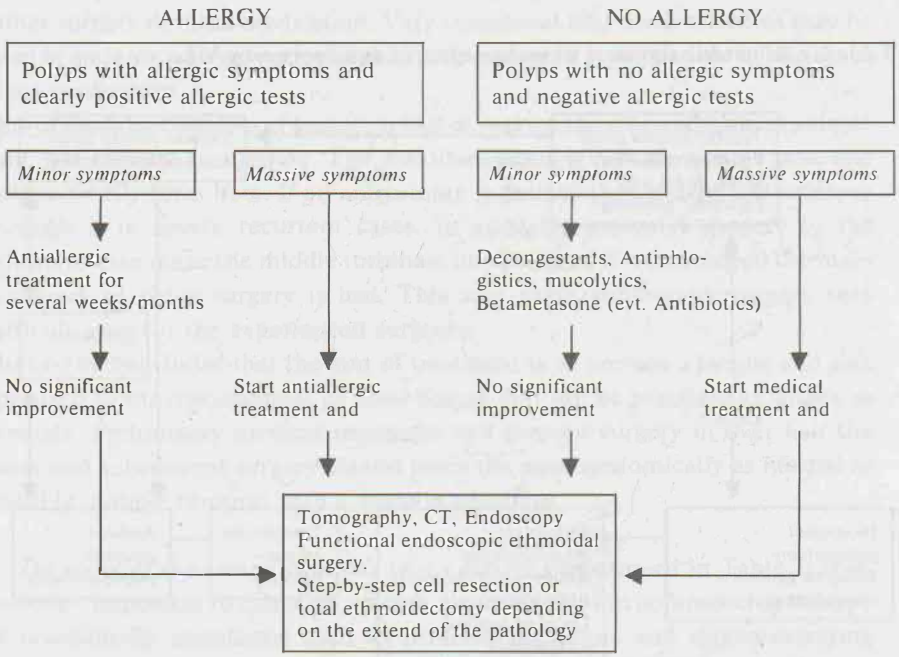
Topical steroids are recommended for maintenance therapy and between surgical procedures.

Table 1. Schematic summary of management of nasal polyps by V-L.



3. *The third panelist (H-S)* never uses a snare and all surgery performed by him for nasal polyps is "endoscopic clearing of the ethoidal disease" - that comprises partial ethmoidectomy in most cases. He believes that most polyps are originating from the ethmoids and that all polyps are associated with ethmoidal sinusitis. He distinguishes between patients with polyps having allergic symptoms and positive allergic tests and patients with negative allergic tests (Table 2).
If there is a positive allergy history and positive allergy test (skin test, RAST, RIST, provocation test) with minor symptoms he will use local steroids. If there is no improvement H-S will perform adjunctive limited, partial endonasal, endoscopic ethmoidectomy. Before ethmoidectomy tomography or/and CT-scan as well as endoscopy should be performed.
If there is positive allergy with massive symptoms from the polyps he will start anti-allergic treatment and perform functional endoscopic partial or total ethmoidectomy with removal of all polyps with their roots. In patients with negative allergy the above mentioned surgery is performed in an earlier stage of the treatment period (Table 2).

Table 2. Schematic summary of management of nasal polyps explained by H-S.



The disagreement among the panelists conserning the treatment of nasal polyps reflects the disagreement on ethiology, patogenesis and origin of nasal polyps. These problems which are not solved at all, were also discussed during the fireside conference. In the literature there are no reports on the origin of nasal polyps. It is not documented if they originate from the nasal mucosa or from the ethmoidal sinus mucusa or from both regions. If they originate from the nasal mucosa we need to define the exact place in the nasal cavity and we need to distinghuish between the medial and lateral walls of the middle and superior turbinates and between the medial and superior middle meatus especially the ostia of the maxillary and ethmoidal sinuses.
If the polyps originate from the ethmoidal cells we have to investigate how do they come to the nasal cavity. There was never e.g. documented how a polyp starting in the most anterior or most posterior cell reaches the ostium of the cell, passes the ostium, and eventually even passes the ostium of the next cell in order to be visible in the nasal cavity.

It was a privilege for me as the moderator of this Fireside Conference to put forward these provoking but unsolved questions and hereby hopefully initiate some new research about the many unsolved problems concerning nasal polyps.

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Rhinology, Suppl. 8, 51-58, 1989

Immunohistological characteristics of nasal polyps

A comparison with healthy mucosa and chronic sinusitis

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SUMMARY

Immunohistological investigations were performed on a series of samples from 37 patients with nasal polyps, 22 with chronic sinusitis, and 15 controls with healthy nasal and sinusal mucosa. Mean numbers of plasma- and mast cells were not different in the various groups. Immunoglobulin isotypes were always predominently IgA and IgM; IgE were scarce. Deposited immune complexes were always absent. A statistically significant difference, however, was observed in the number of eosinophils within the mucosa. Patients with nasal polyps had up to ten times more eosinophils per surface unit than patients with sinusitis or healthy mucosa.

INTRODUCTION

Nasal polyps are a common pathological condition developing spontaneously or in patients suffering from chronic sinusitis. The clinical and histological features of these mucosal proliferations are rather similar although various etiologies can be suspected in these disorders. Allergy, bacterial or viral infections, autonomic dysfunction and hormonal imbalance have been suggested as possible initiating factors. The variety of theories proposed in the literature sustains the fact that no clear picture has yet emerged regarding the pathogenic mechanisms of nasal polyps.

Evidence for the participation of local immunological mechanisms has been obtained in a limited number of studies. However, the results of these studies are somewhat contradictory. For instance, while some authors (Bass et al., 1974) never detected IgE, others demonstrated significant levels of IgE (Drake-Lee et al., 1984; Frenkiel et al., 1985) suggesting that polyposis could be a manifestation of a local allergic phenomenon (Jones et al., 1987). Immunohistological methods, however, may provide a wider array of information, than more evidence for immediate hypersensitivity mechanisms.

The present study was designed to attempt a thorough definition of the immunohistological features of nasal polyps in three groups of well defined patients. The results obtained were compared with those of nasal and sinus mucosae from healthy subjects and patients with chronic sinusitis. The numbers of eosinophils, mast cells and plasma cells producing the various isotypes of immunoglobulins were quantified. The presence of deposited immune complexes was also investigated. This study demonstrated a significant difference in the numbers of eosinophils in nasal polyps, and similar characteristics in the different groups studied for other components of immune mechanisms.

MATERIALS AND METHODS

1. Patients

A. Thirty seven patients with nasal polyps were entered at random into the study (27 males and 10 females, mean age 44.9 years, range 16–67 yrs). Each patient underwent a complete assessment by a rhinologist and a clinical immunologist. These patients were classified clinically into three groups:

1. Group PI included 12 patients (seven males and five females, mean age 46.2 yrs, range 19–67 yrs) who presented with the classical triad of polyps, asthma (clinical history and/or detected by pulmonary function testing) and aspirin intolerance (clinical history and/or ASA challenges).
2. Group PII included 10 patients (seven males and three females, mean age 42.3 yrs, range 26–64 yrs) exhibiting nasal polyps and asthma without any sign or history of aspirin intolerance.
3. Group PIII included 15 patients (thirteen males and two females, mean age 46.2 yrs, range 16–67 yrs) suffering from nasal polyps only.

Immediate hypersensitivity was established on the basis of skin testing in two patients of the first group, two of the second and four of the third.

B. Twenty two patients suffering from chronic maxillary sinusitis were divided, on the basis of endoscopic findings, into two groups:

1. Group SI included 13 patients (eight males and five females, mean age 45 yrs, range 21–61 yrs) with retention of purulent secretions (chronic purulent sinusitis).
2. Group SII included 9 patients (seven males and two females, mean age 35.1 yrs, range 17–56 yrs) without purulent secretions but exhibiting an edematous hyperplasia of the mucosa (chronic edematous sinusitis).

C. Fifteen subjects without clinical symptoms and radiologic findings provided representative samples of healthy nasal mucosa (group HI, five males and four females, mean age 30.1 yrs, range 20–44 yrs) and healthy maxillary sinus mucosa (group HII six males, mean age 49.2 yrs, range 34–67 yrs).

2. Tissue specimen

All patients suffering from polyposis underwent bilateral polypectomy with ethmoidectomy under general anaesthesia.

Chronic sinusitis specimens were removed from maxillary sinuses with endoscopic control, under local or general anaesthesia. Healthy nasal mucosa was easily obtained from the external side of the middle turbinate in nine volunteers. Specimens of healthy maxillary sinuses were obtained under endoscopic control with the informed consent of patients submitted to throat cancer surgery. All samples were snap frozen in liquid nitrogen immediatly after biopsy, and stored at –80 °C until study. Serial 3 micrometer thick frozen sections were obtained with a cryomicrotome (Slee, London, UK), air dried and processed without further fixation.

Mast cells were detected according to their tinctorial metachromatic properties after staining with toludene blue in distilled water.

Direct immunofluorescence was used to investigate the presence of deposits and/or cells containing IgA, IgG, IgM, IgE, and the presence of complement factors C1q, C3, C9, fibrinogen (antihuman proteins monospecific antisera from Behring, Marburg, FRG). Indirect immunofluorescence was used for the detection of C9 deposits (anti-C9 antiserum from Behring; second-step reagent: FITC anti-rabbit antiserum, Institut Pasteur Productions, Paris, France). Incubations were performed at room temperature for 30 mn, and followed by three washes in pH 7.2 phosphate buffered saline (PBS), at room temperature. Stained sections were covered with PBS-glycerol, stored in humid chambers at +4°C and examined within 48 hours. All observations were performed without knowledge of the pathology, by two examiners using microscopes equipped with Ploem systems of UV light epi-illumination. Eosinophils were analysed according to their optical properties in phase contrast and their non-specific labelling with irrelevant fluoresceinated reagents. The number of cells per surface unit were enumerated in a minimum number of five representative areas using a graticule.

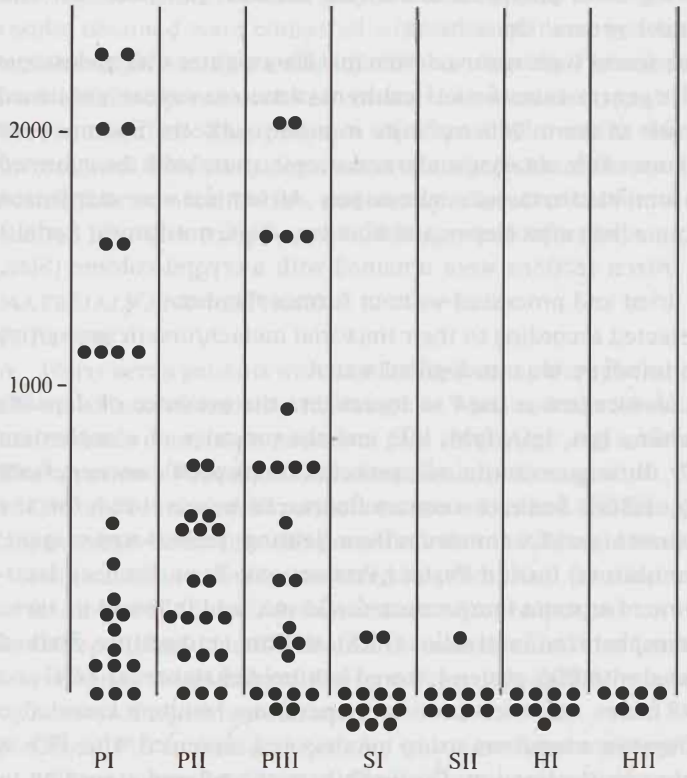
3. Statistical analysis

A one way analysis of variance test was used to compare quantitative data between the various groups studied.

RESULTS

1. Eosinophils

Eosinophils were not present in the healthy mucosa of the nose or sinuses. Small numbers (80/mm^2) were unfrequently seen in chronic edematous (1/9 cases) as well as purulent (1/13 cases) sinusitis. Numerous eosinophils were frequently observed in nasal polyps: 87% of the patients in group PI, 85% in group PII, 71% in group PIII. The mean numbers of eosinophils were 920/mm^2 in group PI, 520/mm^2 in PII, 880/mm^2 in PIII (Figure 1).



Mean numbers of eosinophils per square mm in tissue samples from patients in the various groups studied:
PI: nasal polyps, asthma and aspirin intolerance; 12 patients, 23 samples.
PII: nasal polyps and asthma; 10 patients, 19 samples.
PIII: nasal polyps alone; 15 patients, 23 samples.
SI: chronic purulent sinusitis; 13 patients and samples.
SII: chronic edematous sinusitis; 9 patients and samples.
HI: healthy middle turbinate mucosa; 9 patients and samples.
HII: healthy maxillary sinus mucosa; 6 patients and samples.

2. Mast cells

Mast cells were observed in healthy and diseased tissue specimens. Mean numbers were 40/mm^2 in healthy nasal mucosa, 60/mm^2 in chronic oedematous sinusitis, 80/mm^2 in chronic purulent sinusitis, 40/mm^2 in group PI nasal polyps, 20/mm^2 in group PII nasal polyps, 20/mm^2 in group PIII nasal polyps.

3. Immunoglobulin-producing cells

Plasma-cells predominantly produced IgA and IgM.

In healthy nasal mucosa, many IgA- (140/mm^2) and IgM-plasma cells (80/mm^2) were seen, while only a few were evidenced in healthy sinus specimens (less than 1 cell/section).

In chronic sinusitis, IgA- and IgM-plasma cells were numerous in purulent cases (140 cells/mm^2 for IgA- and 60 cells/mm^2 for IgM in group SI) while in chronic edematous sinusitis (group SII) and in control sinuses plasma cells were extremely scarce (less than 1 or 1 cell/slide).

In nasal polyps, IgA- and IgM-plasma cells were present in the same proportion as in purulent sinusitis, or as in healthy nasal mucosa. No difference was apparent between the three subgroups.

Plasma cells stained with fluorescent antiserum to IgE were noted in only two specimens of chronic purulent sinusitis and eight of the 64 polyps: 1/21 in group PI (5%), 4/19 in group PII (21%), 3/24 in group PIII (12%). In the specimens where these cells could be detected, their numbers were always low (1 or 2 cells/-section). A history of allergy was elicited in only one patient with IgE-plasma cells in the polyps, while IgE-secreting cells could not be observed in seven patients with polyps and positive skin testing. Great care was taken in the identification of IgE-producing cells, in order to make sure that the nonspecific staining of eosinophils was not mistaken for positive plasma cells.

IgE-secreting cells were seldom encountered in both healthy or in diseased mucosa of the upper respiratory pathway. These cells could only be seen in three polyps: one in group PI and two in group PII, always in very low numbers.

4. Deposited immune complexes

The use of antiimmunoglobulins and anticomplement factors antisera could have evidenced deposited immune complexes. These were obsered in none of the specimens studied, neither around the vessels or in subepithelial areas.

5. Statistical analysis

A statistical analysis demonstrated that a significant difference was only observed in eosinophil counts. The presence of infiltrating eosinophils thus appears characteristic of nasal polyps. Eosinophils numbers were similar in groups PI and PIII, but significantly higher in these two groups than in group PII ($p < 0.05$).

DISCUSSION

The present study confirms that the most striking histological feature of nasal polyposis is the tissue eosinophilia (Harlin et al., 1988). As emphasized previously (Holopainen et al., 1979; Krajina et al., 1987), accumulation of eosinophils is not specifically related to allergy. Indeed, the nasal polyps we studied were not obtained from patients with allergic rhinitis. Stimuli leading to the

accumulation of eosinophils in polyps are not known. It is also unclear why the eosinophil count was lower in group PII than in the other two groups. There appears to be no similar report in the literature. Some patients with nasal polyposis also have a significant eosinophilia in nasal secretions (Holopainen et al., 1979; Jacobs et al., 1983). In 1980, a new subgroup of rhinitis called "non-allergic rhinitis with secretion eosinophilia" was characterized (Mullarkey et al., 1980; Jacobs et al., 1981; Mullarkey, 1982). There was unfortunately no description of histological features in mucosa of these patients. The correlation between secretory eosinophilia and a significant presence of eosinophils inside the mucosa is not very well documented. Personal investigations in a small group of patients did not show any specific correlation between these two features. In sensitized patients, secretory eosinophilia follows natural or provocative allergen stimulation, and may be absent in resting periods. Mucosal eosinophilia could be linked with chronic and/or irreversible histological damages. This would explain why resident eosinophils are generally more numerous in polyposis than in rhinitis. A mechanism possibly related to cyclooxygenase inhibition has been suggested in aspirin intolerance (Szczeklik et al., 1975). LTC_4, produced by eosinophils, is a potent mediator of bronchoconstriction and increases microvascular permeability (Frigas et al., 1986). However in our study, mucosal eosinophilia did not correlate with aspirin intolerance. This suggests that eosinophil accumulation and aspirin intolerance could result from two independant mechanisms, both involved in the pathogenesis of nasal polyposis.

Recent histological and biochemical studies have stressed the presence of high numbers of mast cells in nasal polyps (Sasaki, 1986; Takasaka et al., 1986), as well as this of a variety of vasoactive compounds, such as histamin (Drake-Lee et al., 1982). Other studies (Frenkiel et al., 1982; Drake-Lee et al., 1984; Jones et al., 1987) have reported a considerable local production of IgE in polyps. Therefore it was suggested that nasal polyp formation could be IgE-mediated, through local phenomena, and that conventional skin or serum testing might not detect this local allergic process (Frenkiel et al., 1985; Jones et al., 1987). In our study, mast cells were observed in similar proportion in healthy mucosae, chronic sinusitis and in nasal polyps. IgE-producing cells were extremely scarce. These data do not support this seducing hypothesis of a local allergic process.

The numbers and localization of immunoglobulin-secreting cells appeared to be similar in our three series of nasal polyps, chronic purulent sinusitis and healthy nasal mucosae. This observation indicates that immunoglobulins probably play no specific role in the pathogenesis of nasal polyps (Nakashima et al., 1980). Similarly, the absence of deposited immune-complexes in our samples rules out the participation of humoral immunity through type III reactions in nasal polyposis. No study had yet specifically investigated for immune complex deposits in nasal polyps. However, some authors suggested from indirect data that an

immune complex mediated, Arthus-type, reaction might be involved (Ogawa, 1986). Our study also invalidates this hypothesis.

In conclusion, this analysis in depth of immunohistological features of nasal mucosa in polyposis, sinusitis and normal nasal mucosa shows that the most significant feature in nasal polyposis is tissue eosinophilia. Further studies have to focus on a better understanding in the pathophysiology of this cell, in order to elucidate its participation in the etiology of nasal polyposis.

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Recurrence of nasal polyps after surgical treatment

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SUMMARY

Recurrence of nasal polyposis after polypectomy or ethmoidectomy was studied in 85 patients four years after surgery. The patients were classified into one of three groups according to clinical findings: an atopy group (history confirmed by skin test or nasal provocation), an acetylsalicylic acid intolerance (ASA) group (confirmed by provocation), or an "intrinsic" group (no specific diagnosis). The risk of recurrence was significantly greater in patients with ASA intolerance than in the other two patient groups; the frequency of reoperations during the follow-up period was significantly higher in the ASA group and the need for topical corticosteroid treatment had also been more frequent. Bronchial asthma was diagnosed in 40% of all patients. Asthma was significantly more often associated with ASA group (91%) vs 46% at AT and in only 16% at INTR group.

INTRODUCTION

The etiology of nasal polyposis is still unclear. Traditionally, mucosal allergy has been regarded as a causative factor (Blumstein, 1966) but according to several studies at least atopic allergy does not seem to play a major role in the etiology (Caplin, 1971; Lanoff, 1973; Delaney, 1976). Nasal polyps are common in patients with acetylsalicylic acid intolerance, the frequencies varying between 35 and 96% (English, 1983) and in asthmatic patients occurrence rates between 20 and 42% have been reported (Weille, 1936; Spector et al., 1979). In patients with allergic rhinitis, however, the frequency of nasal polyps was found to be only 4% (Binder, 1981).

There are not many reports on the recurrence of nasal polyps. In a study by Blumstein and Tuft (1957) recurrence of polyposis after polypectomy and allergy management was diagnosed in 53% during follow-up for 4.3 years. The recurrence of polyps may be slowed down by long-term topical corticosteroid treatment. Pedersen et al. (1976) reported a marked reduction in the degree of nasal obstruction in 80% of patients after treatment with beclomethasone dipropionate aerosol. At one year after ethmoidectomy, Virolainen and Puhakka

(1980) found a recurrence rate of 46% in the patient groups treated with intranasal steroids while the corresponding figure was 87% in the placebo group. In a similar study by Drettner et al. (1982) the figures after polypectomy were none out 11 for the steroid group and three out of 11 for the placebo group. According to Dingsør et al. (1985) flunisolide was significantly more effective than placebo in preventing recurrence of nasal polyposis during one year's treatment after polypectomy. The present report describes a 4-year follow-up study of 85 patients with nasal polyps. The following aspects were given particular attention:

1. Frequency of repolypectomy in different clinical groups.
2. Need of symptomatic treatment.
3. The effect of nasal surgery on asthmatic symptoms.

PATIENTS AND METHODS

The basic series consisted of 109 patients with nasal polyposis diagnosed by clinical examination. The polyps of the patients have been verified with polypectomy or ethmoidectomy in 1977–78 at the Department of Otolaryngology, University Central Hospital, Helsinki. Of these 109 patients, 85 attended a follow-up examination four years after surgery. To 56/85 patients (66%) polypectomy or ethmoidectomy has been performed before the follow-up period.

The patients have been classified into one of three groups according to the results of clinical and allergological investigations. To classify the patients, the following examinations had been performed to all patients: skin prick tests, nasal smears for eosinophils, blood eosinophil count and serum IgE and oral aspirin provocation test on patients with a history of ASA intolerance. History was taken with special emphasis on atopy and aspirin intolerance. Prick tests have been performed to all patients. If there was a discrepancy between anamnestic data and prick test nasal provocation tests have been performed. The patients were classified into one of three groups based on the results of these investigations (Holopainen et al., 1979):

1. Patients who had a history of atopy (AT) confirmed by positive skin test or nasal provocation.
2. Patients who had a definite history of acetylsalicylic acid intolerance (ASA) intolerance or positive aspirin provocation test, or
3. Patients in whom the diagnostic procedures revealed no specific factors and the disease was classed as intrinsic (INTR).

The patients included in the follow-up study were distributed among the three groups as follows: the AT group 13 patients, the ASA group 22 patients, and the INTR group 50 patients. Polypectomies or etmoidectomies had been performed before the present study on 82% in the ASA group, on 69% in the AT group and on 58% of the patients in the intrinsic group ($p = n.s.$). At the follow-up examination four years after surgery, the nasal status was examined by rhinoscopy. Data were

collected from the follow-up period on the occurrence of nasal and asthmatic symptoms, and on the use of medication for nasal symptoms. The number of reoperations performed because of nasal polyps was recorded.

RESULTS

Recurrence of nasal polyps during the follow-up period

In case of recurrence of nasal polyps patients were treated surgically. The operation was primarily ambulatory re-polypectomy or in extended cases with opacity in ethmoid sinus X-ray, an anterior ethmoidectomy was done by endonasal approach. Repolypectomies had been performed during the follow-up period on 8% (1/13) in the AT group, on 22% (11/50) in the INTR group and on 59% (13/22) in the ASA group. These differences were significant ($p<0.01$) (Figure 1). There was a significant difference between the groups in the frequency of reoperations during the follow-up period. None of the patients in the AT and INTR groups had required more than two repolypectomies during the follow-up period. Most of them, 78% in the INTR group and 92% in AT group, had not needed a repolypectomy during four years. In contrast, 23% of the patients in the ASA group had had three or more repolypectomies to relieve nasal obstruction during the four years (Figure 2). The proportion of patients in whom ethmoidectomy had been necessary since the onset of polyposis was 59% (13/22) in the ASA group, 62% (8/13) in the AT group and 28% (14/50) in the INTR group.

Present medical treatment

Medical treatment at the time of the follow-up examination is presented in Figure 3. Topical corticosteroids were used by 55% of ASA patients but only by

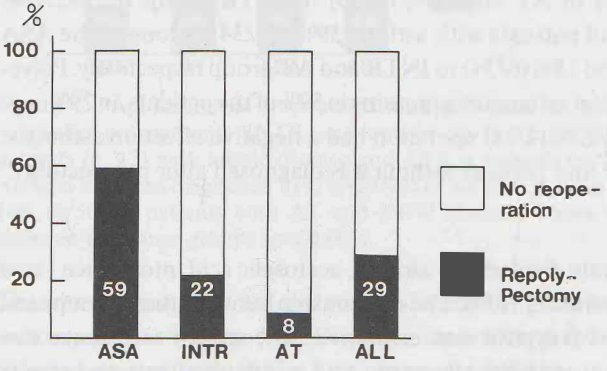

Figure 1. Repolypectomies during four years in 85 patients with nasal polyps. Proportion of repolypectomized patients was 13/22 (59%) in aspirin intolerance (ASA) group, 11/50 (22%) in the group with so-called intrinsic disease (INTR) and 1/13 (8%) in the atopic (AT) group. The differences between ASA, INTR and AT groups were significant ($p<0.01$).

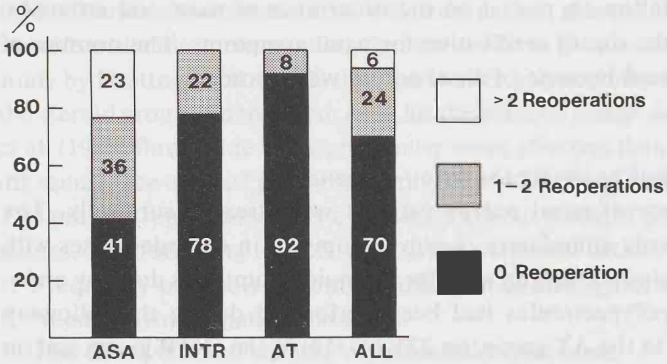

Figure 2. Number of repolypectomies in 85 patients followed for four years after polypectomy or ethmoidectomy. Proportion of repolypectomized patients in the aspirin intolerance (ASA) group, the group with so-called intrinsic disease (INTR) and atopic (AT) group. 78% (39/50) in the INTR group and 92% (12/13) in AT group had not needed a repolypectomy, whereas 23% (5/22) of the patients in the ASA group have had three or more repolypectomies ($p < 0.001$).

31% and 23% of patients belonging to the AT and INTR groups. There was a nearly significant difference between ASA, AT and INTR groups ($p < 0.055$).

Polyposis and asthma

Bronchial asthma has been diagnosed in 40% (34/85) patients. Mean duration of asthma was 13 years. Asthma has has been diagnosed before nasal polyposis in most of the cases 30/34 (88%), however in four patients it appeared after diagnosis of polyposis. Three of these four cases belonged to the ASA-group.

Bronchial asthma is significantly often associated with the ASA-group 91% (20/22) versus 46% (6/13) in AT and 16% (8/50) in INTR group respectively ($p < 0.001$) (Figure 4). Of all patients with asthma 59% (20/34) belonged the ASA group versus 24% (8/34) and 18% (6/34) to INTR and AT group respectively. Polypectomy has a positive effect on asthmatic symptoms in 59% of the patients, in 29% operation had no effect and in 12% (4/34) operation had a negative effect on asthmatic symptoms. In two of these four patients asthma was diagnosed after polypectomy.

DISCUSSION

85 patients were prospectively divided into atopy –, acetosalic acid intolerance – and intrinsic groups (Holopainen et al., 1979). The relationship between these groups and the clinical course of nasal polyposis was examined. The risk of recurrence was significantly higher in the patients belonging to the ASA group, because these patients had significantly more reoperations than the patients in the AT and INTR groups. These patients also used significantly more corticosteroids than the patients in the other groups and they also have a significantly higher prevalence of bronchial asthma.

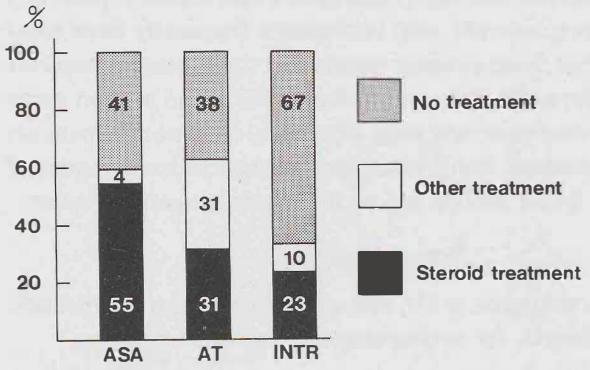

Figure 3. Medical treatment at the time of the follow-up examination in 85 nasal polyposis patients followed for four years after polypectomy. ASA = patients (n. 22) with aspirin intolerance, AT = patients (n. 13) with atopic disease, and INTR = patients (n. 50) in whom, the disease was intrinsic. Steroid treatment was used by 55% (12/22) of ASA patients but only by 31% (4/13) and 23% (11/49) of the patients belonging to the AT and INTR groups. There was a nearly significant difference in relation to use of steroid treatment between ASA, AT and INTR groups ($p < 0.055$).

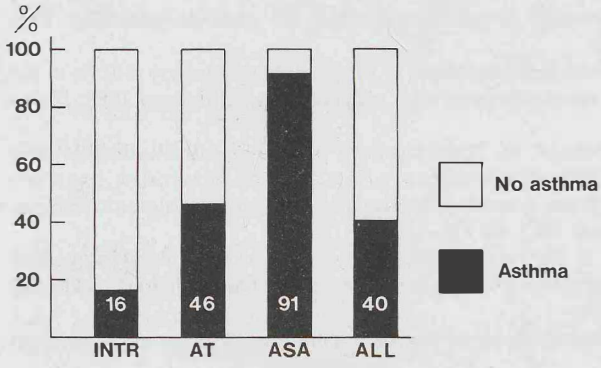

Figure 4. Appearance of bronchial asthma in 85 nasal polyposis patients followed for four years after polypectomy. INTR = patients (n. 50) in whom, the disease was intrinsic, AT = patients (n. 13) with atopic disease and ASA = patients (n. 22) with aspirin intolerance. Asthma has been diagnosed in 91% (20/22) of patients in ASA group versus 46% (6/13) and 16% (8/50) of patients with AT and INTR disease. There was a significant difference between the three groups ($p < 0.001$).

The recurrence of nasal polyps has been little studied. In a previous study, recurrence was reported in 53% of patients after a follow-up period of 4.3 years (Blumstein and Tuft, 1957). Virolainen and Puhakka (1980) observed recurrence in 87% of the patients who used no topical steroids after ethmoidectomy, whereas it was 46% of the group using corticosteroids. Patients with nasal polyposis have not earlier been classified and the tendency to recurrence and the need of surgical

treatment in different groups have not been examined. From earlier reports it is known that patients with acetylsalicylic acid intolerance frequently have nasal polyps (English, 1983) and that these patients require 2–3 times more operations than other patients with polyps (Enzman and Rieben, 1983). The present study supports earlier studies on recurrence and need of surgical treatment of patients with acetylsalicylic acid intolerance. It may also be stated that clinical grouping of patients into ASA, AT and INTR groups has an important prognostic value.

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