

THE JOURNAL OF
ALLERGY
AND
CLINICAL IMMUNOLOGY

VOLUME 88

NUMBER 2

Sheldon Memorial Lecture

Medical management of nasal polyps and sinusitis

Raymond G. Slavin, MD *St. Louis, Mo.*

Nasal polyps and sinusitis have come of age in the view of the allergist. Professional meetings, seminars, and abstracts abound related to nasal polyps and sinusitis. Allergy and immunology journals in the last decade have been replete with articles dealing with these subjects. The presence of sinusitis in some 31 million Americans, many of whom present to the allergist, mandates our interest and attention to this important entity.

NASAL POLYPS

Although nasal polyps were first described almost 3000 years ago, a great many questions still exist with regard to incidence, pathogenesis, and treatment.

Characteristics

Nasal polyps appear to be outgrowths of nasal mucosa and are typically smooth, gelatinous, semitranslucent, round or pear shaped, and pale. Most polyps are located in the middle meatus along the lateral wall of the nose and originate from the ethmoid sinuses. Histologically, the mass of a nasal polyp is chiefly made up of edema fluid with sparse fibrous cells and

a few mucus glands. Surface epithelium is pseudostratified, and the supporting structure is interspersed with masses of lymphocytes, plasma cells, eosinophils, and a few mast cells. Histochemical stains of nasal polyps and adjacent normal respiratory mucosa reveal the same characteristics.

Incidence

Men outnumber women two to one in occurrence of nasal polyps with the most polyps appearing after the age of 40 years. Settipane¹ demonstrates the frequency of nasal polyps, compiled in Table I, in various medical conditions. Note that the frequency of polyps is considerably less in nonallergic asthma and nonallergic rhinitis versus allergic asthma and allergic rhinitis.

Pathogenesis

The mechanisms that have been implicated in the formation of nasal polyps are listed in Table II. With this many possibilities, it is fair to say that no one theory explains why nasal polyps occur.²

Management

The management of nasal polyps may involve medical and surgical approaches. Antihistamines, decongestants, and cromolyn sodium are of little benefit. In the case of superimposed bacterial infection, appropriate antibiotics should be administered. Corti-

From the Department of Internal Medicine and Microbiology, St. Louis University School of Medicine, St. Louis, Mo.

Reprint requests: Raymond G. Slavin, MD, Professor of Internal Medicine and Microbiology, 1402 S. Grand St., R209, St. Louis, Mo 63104-1028.

1/1/29951

TABLE I. Frequency of nasal polyps in various conditions¹

Diagnosis	Frequency (%)
Aspirin intolerance	36
Adult asthma	7
Intrinsic	13
Atopic	5
Chronic rhinitis	2
Nonallergic	5
Allergic	1.5
Childhood asthma/rhinitis	0.1
Cystic fibrosis	20

TABLE II. Mechanisms implicated in the formation of nasal polyps²

Allergy
Infection
Autonomic imbalance
Mucopolysaccharide abnormality
Enzyme abnormality
Drug sensitivity
Mechanical obstruction
Histamine
Protooncogene

corticosteroids are extremely effective in reducing polyp size. Well-controlled studies have revealed a variety of intranasal preparations of corticosteroids to be effective in managing nasal polyps. These include beta-methasone nasal drops, beclomethasone nasal drops, aerosol or powder, budesonide aerosol, and flunisolide aerosol. Significant improvement in 80% of patients with moderate to severe polyposis occurs. In addition to decreasing polyp size and increasing nasal airway conductance, there is also a decrease in eosinophils in the nasal smear with a decrease in albumin, IgG, and IgE in the secretions.³

A fundamental effect of corticosteroids in inhibiting protein synthesis at the cellular level has led to fears that protracted use of intranasal steroids might lead to atrophic changes, as observed in the skin with protracted use of topical steroids. Examination of nasal polyp biopsy specimens after 5 years of local beclomethasone treatment demonstrated no change from pseudostratified to squamous metaplasia of surface epithelium that would be indicative of atrophic rhinitis. This is probably due to the rapid removal of beclomethasone from mucous membranes. The mucous membrane half-life of beclomethasone is 30 minutes in contrast to 6 to 10 hours in the skin.⁴

A number of reasons might explain the failure of intranasal steroids to manage nasal polyps. One reason

would be total blockage of the nasal airway that would preclude the entrance of the drug. Systemic steroids should be administered first, to reduce polyp size. A second reason for topical corticosteroid failure would be concomitant infection of the nasal mucous membranes. In this instance, an antibiotic must be added. A third reason for topical failure would be nasal polyps that are rapidly growing. Systemic steroids must be administered in this case. Finally, involvement of the sinuses to the extent that this would account for the major part of symptoms would lead to a failure of topical steroids. The local application of corticosteroids to the nose is inadequate to control sinus inflammation. Therefore, definitive nasosinus surgery would be indicated.

One method for corticosteroid administration in treating nasal polyps is direct injection into the polyp. Although the technique is widely used, there are well-documented studies of unilateral visual loss after intranasal steroid injection.⁵ The mechanism for visual loss is believed to be both vasospastic and embolic with particulate material reaching the ophthalmic artery through anastomosis with the superficial temporal artery. These studies have prompted the Food and Drug Administration not to approve the use of steroids for this procedure.

In Table III, from work by Settignano,⁶ the folly is demonstrated of polypectomy alone in treating nasal polyps. In this table is illustrated the extraordinary recurrence rate of polyps after surgery. In a recent study from Scandinavia, surgical removal of nasal polyps was compared with the use of systemic steroids. After initial treatment with either surgery or systemic steroids, both groups of patients were administered topical steroids and followed for 1 year. Both groups experienced similar increase in nasal expiratory peak flow and sense of smell with a statistically significant increase in benefit from medication. The two major conclusions of the authors who were otolaryngologists were (1) "the continued postoperative use of topical steroids postpones or prevents recurrence of nasal polyps," and (2) "Surgical removal should be reserved for those few cases in which the presence of residual or recurrent polyps justifies the inherent risks and discomfort for the patient."⁷

Based on these and other studies, it would appear that a reasonable medical approach to management of nasal polyps would be a 10- to 14-day course of oral prednisone followed by intranasal beclomethasone or flunisolide.

SINUSITIS

To devise a logical approach to the medical management of sinusitis, it is important to consider the pathophysiology of sinusitis.

Pathophysiology of sinusitis

Protection against infection of the paranasal sinuses is largely provided by the mucociliary apparatus. Microorganisms, pollutants, irritants, and other foreign particles that escape the filtering apparatus of the nose are trapped in the mucus of the sinuses and then removed through the draining ostia by constant movement of the mucus blanket propelled by the underlying cilia. When this self-cleansing mechanism is impaired, bacterial infection occurs. Mucus accumulates and becomes infected by relatively harmless opportunistic bacteria normally found in the nose. In most instances of sinusitis, bacteria gain entrance to the sinuses via the ostia, but in some cases, such as dental abscess, bacteria can penetrate from contiguous structures. Nosocomial sinusitis can result from nasopharyngeal instrumentation in traumatized patients.⁸

Several factors may result in retention of secretions in the paranasal sinuses: (1) swelling of the mucous membrane, leading to reduced patency of ostia, (2) reduced transport capacity related to abnormalities of the cilia, including quantitative reduction, retardation of movement, and insufficient coordination of movement, and (3) overproduction of secretions.⁹

Of these three factors, patency of the ostia is the most important in the development of sinusitis.¹⁰ The ostia function primarily for drainage of secretions. Studies in normal subjects have demonstrated an inverse relationship between the functional diameter of the maxillary ostium and the time required for emptying of contrast material.¹¹ The cross-sectional area of the ostium is also the primary determinant of gas exchange in the human sinuses.¹²

Another factor in determining gas exchange is nasal airflow. The sinus cavity air exchanges twice as fast during nasal breathing than during oral breathing.¹³ During normal nasal breathing with a patent ostium, 90% of the sinus air is exchanged in 5 minutes. The oxygen content of the sinus is dependent on several factors. A direct correlation between ostial size and oxygen tension has been demonstrated in humans. The most profound changes in oxygen tension occur when infection accompanies the occlusion. Purulent maxillary sinus aspirates have been demonstrated to have partial pressure of oxygen (tension) near zero, markedly elevated partial pressure of carbon dioxide (tension), and decreased pH.¹⁴ In vitro studies have demonstrated that growth of organisms, such as pneumococci, are inhibited by air exposure, compared with cultures grown with limited air access.¹⁵ In addition to favoring increased bacterial growth and purulence, low oxygen content in the sinuses may impair local defenses, such as granulocyte function.

Ciliary movement is also vital in protection of sinuses against infection. The cilia beat toward the os-

TABLE III. 167 patients with verified polyps and polypectomies⁶

Total patients	No. of polypectomies	No. of patients	%
167	1 or more	143	86
143	2 or more	57	40
143	3 or more	34	24
143	4 or more	22	15
143	5 or more	17	12
143	6 or more	11	8

tium in a radiating fashion to promote drainage. Even after surgical creation of a nasal antral window in the inferior meatus, which would favor gravitational drainage through the orifice, the cilia will still beat toward the natural ostium.¹⁶ Mucociliary transport in the sinus may be compromised by a combination of low oxygen content in the sinus and in the blood. In addition to local factors, several clinical disorders have been described associated with ciliary dysfunction with loss of dynein arms, including Kartagener's syndrome¹⁷ and immotile-cilia syndrome.¹⁸ Mucociliary activity of the sinuses is of such extreme importance in protection against sinusitis because spontaneous drainage of the maxillary sinus caused by gravity is nearly impossible for two reasons: First, the maxillary ostium is not simply an opening of 1 to 3 mm in diameter but rather a circuitous channel 6 mm in length that connects the maxillary antrum to the middle meatus. This is referred to as the ostio-meatal complex. Second, the maxillary ostium is located in the superior portion of the maxillary antrum. Therefore, for spontaneous drainage to occur into the nose in the upright position, the antrum must be completely filled before the contents can spill over or ciliary action must move secretions in a cephalad direction against the force of gravity. For these reasons, the maxillary sinus is by far the most common site of sinusitis. This is followed, in order, by the ethmoid, frontal, and sphenoid sinuses. Mucociliary activity is disturbed when purulent secretions are present because of changes in mucus property, structural damage to ciliated epithelium, and slower beating of the cilia. Generally, the cilia return to normal levels after infection, but with severe empyema and scarring, portions of the cilia may be converted to squamous epithelium. Thus, if mucociliary function is congenitally deficient or damaged by scarring from previous severe infections, spontaneous drainage of the sinuses cannot occur when ostial occlusion resolves.

A third local factor important in protection of the sinuses against infection is the nature and quantity of secretions. It should also be mentioned that in purulent

TABLE IV. Factors predisposing to sinusitis

Local	Systemic
Upper respiratory tract infection	Immune deficiency
Allergic rhinitis	Bronchiectasis
Overuse of topical decongestants	Dysfunctional cilio syndrome
Hypertrophied adenoids	
Deviated nasal septum	
Bone spurs	
Nasal polyps	
Tumors	
Foreign bodies	
Swimming and diving	
Cigarette smoke	
Barotrauma	
Dental extraction/injections	

secretion, there is a high content of proteases that come principally from granulocytes. These proteases are more harmful to the mucosa than are bacteria.

The most common local and systemic factors predisposing to sinusitis are presented in Table IV. Although systemic factors may play some role, particularly hypogammaglobulinemia,¹⁹ far and away the most common factors predisposing to sinusitis are local. Heading the list are viral upper respiratory tract infections and allergic rhinitis in which the mechanism for the development of sinusitis would appear to be similar. Acute rhinitis of either infectious or allergic etiology results in edematous obstruction of the nasal ostia, decreased paranasal sinus ciliary action, and increased mucus production. With the subsequent accumulation of mucus in the sinus, the stage is set for secondary bacterial infection and the conversion of mucus to mucopus. Mucopus further impairs ciliary function and increases swelling around ostia when it discharges into the nose, creating a vicious cycle.

Management of sinusitis: Medical approach

Sinusitis should be considered as an abscess, that is, an infection within a closed anatomic space. The medical approach to managing infectious sinusitis is presented in Table V. Saline nasal spray or douches are useful to liquify secretions and also decrease blood flow to the nose with a resultant decongestant effect. It is vital to increase the diameter of the maxillary ostium and promote mucociliary activity. In this way, purulent secretions are removed with an associated increase in sinus O₂, a decrease in sinus PCO₂, decrease in lactate content, increase in ciliary movement, and decrease in proteolytic enzymes. Phenylpropanolamine, orally, has been demonstrated to increase the

TABLE V. Medical management of sinusitis

Steam and saline
Prevents nasal crusting
Liquifies secretions
Mild decongestant effect
Decongestants: phenylpropanolamine, phenylephrine, oxymetazoline, increase ostial diameter
Topical corticosteroids: beclomethasone, flunisolide
Mucoevacuants: guaifenesin, potassium iodide, thin secretions aiding drainage
Antibiotics

functional diameter of the maxillary sinus.²⁰ There would also appear to be benefit in reducing mucosal inflammation, allowing host-clearance mechanisms to recover. One controlled study²¹ demonstrated that a nasal spray incorporating beclomethasone and a decongestant was more effective in treating sinusitis than a topical antibiotic. There is no controlled study demonstrating the efficacy of mucoevacuants in treating sinusitis. It appears reasonable, however, based on the above discussion, that thinning of sinus secretions would increase drainage and promote the recovery of host-clearance mechanisms.

The bacteria responsible for acute sinusitis are largely aerobic. *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Haemophilus influenzae* are the most common. Anaerobic bacteria are largely responsible for chronic sinusitis. Common pathogens include alpha streptococci and species of bacteroides, *Veillonella* and *Corynebacterium*.

Organisms generally considered to be opportunistic and of low virulence, particularly the gram-negative variety, may be of significant concern in elderly patients who may be immunocompromised by coexisting illnesses or medications. A good example is *Klebsiella ozaenae* sinusitis occurring in an elderly diabetic.²²

Viral infections of sinuses have not been well studied. Rhinovirus, influenza virus, and parvovirus have all been cultured from sinuses, but their significance is not known.

Fungal infection of the paranasal sinuses may occur in both immunocompromised and immunocompetent individuals.^{23, 24} *Aspergillus fumigatus* is the most common fungus responsible for sinusitis. Other fungi causing sinusitis include *Actinomyces*, *Nocardia*, *Mucor*, *Sporothrix schenckii*, and *bipolaris*. Mucormycosis is particularly associated with diabetes mellitus. Fungal sinusitis should be suspected in any case of antibiotic-resistant sinusitis. The sinus exudate is generally thick, of a peanut butter-like consistency. The management of invasive fungal sinusitis includes extensive debridement and parenteral antifungal

TABLE VI. Antibiotic treatment of sinusitis

Drug	Dosage	
	Children	Adults
Amoxicillin	40 mg/kg/day	500 mg t.i.d.
Trimethoprim-sulfamethoxazole	8/40 mg/kg/day	1 Septra* DS b.i.d.
Erythromycin and sulfizoxazole	50/150 mg/kg/day	
Amoxicillin-clavulanate	40 mg/kg/day	500 mg t.i.d.
Cefaclor	40 mg/kg/day	500 mg t.i.d.
Cefuroxime	125 mg b.i.d. <2 yr	500 mg b.i.d.
	250 mg b.i.d. >2 yr	

t.i.d., Three times a day; b.i.d., twice daily; DS, double strength.

*Burroughs Wellcome Co., Triangle Park, N.C.

drugs. The allergic form of fungal sinusitis most commonly caused by *Aspergillus* is treated by debridement and systemic steroids.

The antibiotic of choice in managing acute or chronic bacterial sinusitis is ampicillin or amoxicillin. The responsible organisms are generally sensitive to these antibiotics, and adequate mucosal and sinus fluid concentrations of these antibiotics are obtained. For patients who are penicillin sensitive, an adequate alternative is trimethoprim-sulfamethoxazole.

It is estimated that approximately 20% of bacteria responsible for sinusitis have become resistant to penicillin and to cephalosporins by producing β -lactamase enzymes that destroy the β -lactam nucleus of these antibiotics. Clavulanic acid, an inhibitor of the β -lactamases, has been introduced in combination with some penicillins, and these drugs have proven to be useful in patients with β -lactamase-producing organisms. Other antibiotics useful in such instances are Cefaclor and cefuroxime axetil (Ceftin; Glaxo, Inc., Research Triangle Park, N.C.). A number of antibiotic programs to treat sinusitis are summarized in Table VI.

The duration of treatment is as important as the choice of antibiotics. Two weeks of antibiotic therapy is generally adequate for acute sinusitis, with chronic sinusitis requiring 3 to 4 weeks or longer.

Special mention should be made of the diagnosis and management of nosocomial sinusitis in the nasotracheally intubated patient. The diagnostic approach to these patients should be aggressive with maxillary sinus aspiration. Appropriate antibiotics are then administered, guided by culture and sensitivity studies along with sinus lavage.²⁵

Aspirin desensitization

Sweet et al.²⁶ have recently reported the effects of aspirin desensitization on aspirin-sensitive patients

with rhinosinusitis and asthma. These patients were desensitized with aspirin and then maintained on daily aspirin. They experienced significant improvement in sense of smell, nasal symptoms, and numbers of episodes of upper respiratory tract infections and sinusitis per year. They had impressive declines in nasal polypectomies and sinus operations. The authors conclude that long-term aspirin treatment prevents or retards ongoing inflammation in the nose, sinuses, and bronchial tree.

I thank Maria J. Weingartner for her excellent secretarial assistance.

REFERENCES

1. Settipane GA. Nasal polyps. *Immunol Allergy Clin N Am* 1987;7:105.
2. Slavin RG. Nasal polyps and sinusitis. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, eds. *Allergy: principles and practice*, vol 2. 3rd ed. St. Louis: CV Mosby, chap 54, 1988:1291-1303.
3. Sorensen H, Mygind N, Pedersen CB, Crytz S. Long-term treatment of nasal polyps with beclomethosone dipropionate aerosol. III. Morphological studies and conclusions. *Acta Otolaryngol* 1976;802:260.
4. Mygind N, Prytz S, Sorensen H, Pedersen CB. Long-term treatment of nasal polyps with beclomethosone dipropionate aerosol. I. Treatment and rationale. *Acta Otolaryngol* 1976;82:252.
5. Guntert VG. A serious complication (blindness) after intranasal injection of hydrocortisone. *HNO* 1963;11:77.
6. Settipane GA. Nasal polyps. In: Settipane GA. *Rhinitis*. 1st ed. Providence, RI: Brown University, 1984:133-40.
7. Lildholdt T, Fogstrip J, Gamelgaard N, Kortholm B, Ulsoe C. Surgical versus medical treatment of nasal polyps. *Acta Otolaryngol* 1988;105:140.
8. Caplan ES. Nosocomial sinusitis. *JAMA* 1982;247:639.
9. Reiner A, von Mecklenburg G, Toremalam NG. The mucociliary activity of the upper respiratory tract. III. A functional and morphologic study on human and animal material with special reference to maxillary sinus disease. *Acta Otolaryngol* 1978;(suppl 355):1.

10. Drettner B. The permeability of the maxillary ostium. *Acta Otolaryngol* 1965;60:304.
11. Aust R, Drettner B, Hemmingson A. Elimination of contrast medium from the maxillary sinus. *Acta Otolaryngol* 1976;1:468.
12. Aust R. Oxygen exchange through the maxillary ostium in man. *Rhinology* 1974;12:25.
13. Aust R. Measurements of the ostial size and O₂ tension in the maxillary sinus. *Rhinology* 1976;14:43.
14. Carenfelt C, Lundberg C. Purulent and nonpurulent maxillary sinus secretions with respect to Po₂, PCO₂ and pH. *Acta Otolaryngol* 1977;84:138.
15. Carenfelt C, Lundberg C. The role of local gas composition in the pathogenesis of maxillary sinus empyema. *Acta Otolaryngol* 1978;85:116.
16. Drettner B. Pathophysiology of paranasal sinuses with clinical implications. *Clin Otolaryngol* 1980;5:277.
17. Elverland HH. Kartagener's syndrome—a reappraisal. *Acta Otolaryngol Suppl (Stockh)* 1979;360:219.
18. Afzelius BA. A human syndrome caused by immotile cilia. *Science* 1976;193:317.
19. Stiehm ER. Immunodeficiency disorders: general considerations. In: Stiehm ER, Fulginiti VA, eds. *Immunologic disorders in infants and children*. Philadelphia: WB Saunders, 1980:183-219.
20. Melen I, Friberg B, Andreasson L, et al. Effects of phenylpropanolamine on ostial and nasal patency in patients treated for chronic maxillary sinusitis. *Acta Otolaryngol* 1986;101:494.
21. Sykes DA, Wilson R, Chan KL, et al. Relative importance of antibiotic and improved clearance in topical treatment of chronic mucopurulent rhinosinusitis: a controlled study. *Lancet* 1986;2:359.
22. Siegel JD. *Klebsiella ozaenae* sinusitis, otitis media, and meningitis in an elderly diabetic woman: a case report. *J Am Geriatrics Soc* 1987;35:685.
23. Washburn RG, Kennedy DW, Begley MG, et al. Chronic fungal sinusitis in apparently normal hosts. *Medicine* 1988;67:231.
24. Morgan MA, Wilson WR, Neel HB III, Robert GD. Fungal sinusitis in healthy and immunocompromised individuals. *Am J Clin Pathol* 1984;82:597.
25. Linden BE, Aguilor EA, Allen SJ. Sinusitis in the nasotracheally intubated patient. *Arch Otolaryngol Head Neck Surg* 1988;114:860.
26. Sweet JM, Stevenson DD, Simon RS, Mathison DA. Long-term effects of aspirin desensitization—treatment for aspirin-sensitive rhinosinusitis-asthma. *J ALLERGY CLIN IMMUNOL* 1990;85:59.

AVAILABLE NOW! The PROCEEDINGS OF THE INTERNATIONAL CONGRESS OF ALLERGOLOGY AND CLINICAL IMMUNOLOGY can be purchased from the Publisher. This collection of "state-of-the-art" presentations from the XII Congress held October 20-25, 1985, in Washington, D.C., brings together the current advances in basic and applied aspects of allergy and allergic diseases. It includes 528 pages covering such topics as IgE, roles of the different cell types and their products, clinical problems, asthma, rhinitis, and reactions to foods and drugs and occupational agents, collected and reviewed by Editor Charles E. Reed, MD (USA) and Associate Editors Joseph Bellanti, MD (USA), Robert J. Davies, MD (UK), Sidney Friedlaender, MD (USA), Albert Oehling, MD (Spain), and Raymond G. Slavin, MD (USA).

To purchase, call or write: Mosby-Year Book, Inc., 11830 Westline Industrial Dr., St. Louis, MO 63146-3318, or telephone FREE 1-800-325-4177, Journal Fulfillment, ext. 4351 (in Missouri call collect at 314-872-8370, Journal Fulfillment, ext. 4351). Prepayment required. Make checks payable to Mosby-Year Book, Inc. (All payments must be in US funds drawn on a US bank.) Price: \$36.50 in the US, \$40.50 in Canada, and \$41.50 international (surface shipping charges included).