10 Ancillary Medical Approaches to the Treatment of Sinusitis

Christopher Chang, MD, PHD
and Stanley Naguwa, MD

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INTRODUCTION

Acute bacterial sinusitis and chronic bacterial sinusitis are often difficult to treat, especially in the patient with associated allergic disease. In addition to the infective inflammation caused by the bacteria in the sinuses, the presence of allergic rhinitis produces further inflammation both in the sinus mucosa and in the nasal pharynx, which is further complicated by a deficiency in mucociliary clearance, increased nasal secretion, and decreased drainage. Thus, the treatment of sinusitis often requires additional measures other than antibiotics, measures that may also ameliorate the need for surgical intervention *(1)*.

These ancillary measures require an understanding of the features of sinusitis. Sinusitis may be acute, chronic, or subacute. The onset of sinusitis may be heralded by a pre-existing viral infection and exacerbated by a variety of host features *(2)*. These features are listed in Table 1. Several of these host features may be present simultaneously. The sinuses should be considered closed structures, since inflammation in the sinus can inhibit optimal drainage. Therefore, although antibiotic therapy is crucial, it alone will not suffice to eradicate a nondraining sinus, which is essentially an abscess. Other measures must be taken and are of equal importance *(3)*. These measures take into consideration improving mucociliary clearance and changing the consistency of mucus, or enlarging the outflow tract to facilitate drainage. Eosinophilic and basophilic reactions in the sinuses often further complicate bacterial sinusitis, and structural defects are known to inhibit drainage of cellular exudates and pus, and therefore delay the effectiveness of antibiotics. Inherent defects in mucociliary clearance are thought to be important pathologic entities that must be corrected to facilitate antibiotic therapy of sinusitis. Optimization of treatment requires that we improve conditions for the host to eradicate the disease. This includes treatment of all pre-existing conditions, such as allergic rhinitis, polyps, immunodeficiency disorders, and if possible, even viral upper respiratory infections (URIs).

M. E. Gershwin et al. (eds.), *Diseases of the Sinuses*

Table 1
Host Features Involved in Sinusitis

- Allergic causes
  - Allergic rhinitis
  - NARES
- Immune deficiency
  - Antibody deficiency
    - Bruton's agammaglobulinemia
    - Common variable immune deficiency
    - Wiskott Aldrich Syndrome
    - Selective IgG subclass deficiency
    - Ataxia telangectasia
    - AIDS
    - Selective IgA deficiency
    - SCIDS
  - Complement abnormalities
    - C3b inactivator deficiency
    - C3 deficiencies
  - Leukocyte abnormalities
    - Chronic granulomatous disease
    - Hyper IgE syndrome
    - Chediak-Higashi Syndrome
- Structural defects
  - Cleft palate
  - Ciliary defects
  - Osteopetrosis
  - Foreign bodies
- Other
  - Cystic fibrosis
  - Asthma
  - Nasal polyposis
  - Allergic fungal sinusitis
  - Aspirin sensitivity

ANCILLARY MANAGEMENT OF SINUSITIS—PREVENTION

Viral URIs

It is a common practice for primary care physicians to treat runny noses, cough, congestion, and other signs of a simple viral URI with antibiotics. Although this may not be intellectually sound, it may not be as ludicrous as first believed. The number of viral infections that have an associated sinusitis component of either bacterial or viral origin varies between studies, from an average of about 5% *(4)* to a high of about 21% *(5)* in a recent study using computerized tomography (CT) scanning in otherwise healthy adults. Although some of these subjects recovered spontaneously without antibiotics, suggesting a viral origin, there is certainly the subset of these patients who do develop chronic bacterial sinusitis as a result of a viral URI. Early treatment may be a way of preventing a full-blown sinusitis. On the other hand, there are those who would argue that empirical antibiotic therapy would only serve to produce sinusitis caused by bacteria that are even more resistant to treatment.

Prevention

Prevention of viral infections therefore does provide benefit both from a clinical standpoint and from a medically cost-effective standpoint, since measures that prevent viral infections are usually less expensive than the treatment of an ensuing bacterial sinusitis. Simple principles that would help to prevent viral infections are reducing the intensity and frequency of exposure by general hygienic measures or vaccinations, or by simple avoidance, especially in children. The latter has been rendered more difficult to achieve because of the increase in families with two working parents and the increased utilization of day-care facilities with high numbers of infants and toddlers. The time of virus shedding by children with respiratory syncytial virus (RSV) is commonly 3–8 d, except in younger children, where it may be as long as 3–4 wk *(6)*.

General Hygiene. Frequent hand washing by personnel who are in contact with small children, especially those who are sick, will help in reducing exposure to viral infections. Hand washing is applicable to children and adult patients as well. Avoidance of contact of nasal or ocular mucosa by unwashed hands is also helpful. Antiviral measures may be implemented by the use of cleansing agents on work or play surfaces both in the home and work environments. The life-span of RSV, for example, on inanimate objects is probably many hours, and inoculation can be accomplished by contact with contaminated infant secretions long after the infant has been removed from the area *(6)*. RSV can be killed using solvents, such as CIDEX *(7)*. RSV is most common in the winter and early spring, and eventually will infect all children during the first 3 yr of life *(8)*. Bronchiolitis is the most common manifestation of RSV in young children, but in older children and adults, the illness usually presents as an upper respiratory tract illness or bronchitis *(9,10)*. This may thus be a trigger for the onset of sinusitis in the latter population. Although RSV is the most common viral pathogen in young children, other viruses, such as picornavirus,

parainfluenza virus, or coronavirus, may be more predominate pathogens of viral URIs in older children or adults. Influenza virus, common in the winter months, results in a viral syndrome consisting of malaise, congestion, and cough, and may be also be a trigger for sinus infection.

Vaccinations. Prevention of influenza virus illness in individuals with chronic respiratory diseases, such as asthma, has been conducted for several years during the fall/winter season in the US. This strategy to prevent viral URIs in large numbers of individuals during the winter months has been recommended for all individuals with chronic rhinosinusitic or pulmonary disease (perennial allergic rhinoconjunctivitis, asthma, cystic fibrosis), as well as immune deficiency syndromes, immunosuppressive therapy, sickle-cell anemia and other hemoglobinopathies, significant cardiac disease, diabetes mellitus, chronic renal disease, chronic metabolic diseases, AIDS, and long-term aspirin therapy *(11)*. Household contacts of the above-mentioned individuals, day-care providers, and hospital personnel in contact with pediatric patients should also receive influenza vaccine. The split virus vaccine is recommended for children under 12 yr of age, with a second dose given to children under 8 yr of age. Side effects of the vaccine are uncommon, the most frequent being local reactions in older children and adults.

Treatment

Treatment of viral URIs includes the use of antiviral medications, measures that may be toxic to viral replication, as well as a pharmacopoeia of over-the-counter (OTC) medications. Since many of the OTC medications are also utilized by patients with already existing sinusitis, each individual class of these medications will be discussed in a later section. Currently, antiviral medications are not routinely indicated for the chemoprophylaxis or treatment of URIs in older children or adults. Aerosolized Ribavirin is presently being used to treat severe bronchiolitis in hospitalized children *(12,13)*. Amantadine and rimantadine are approved by the Food and Drug Administration (FDA) for use in children and adults for prophylaxis against influenza A infection. There are specific indications for the use of these agents in treatment of influenza because of their potential side effects, including renal toxicity. In addition, these agents are only beneficial in specific strains of influenza virus infection. Although prevention of influenza in some patients may stall the development of sinusitis, amantadine and rimantadine are not currently recommended in the treatment of routine "viral illnesses," and therefore do not play a role in the treatment of sinusitis in otherwise healthy individuals.

It is a popular notion by both the public and the health care sector that milk causes increased production and viscosity of mucus. Although this association is probably no more than a subjective belief that has not been substantiated in two studies in patients with rhinovirus-2 induced infection and asthmatics *(14,15)*, milk avoidance is practiced by patients who have URIs or chronic respiratory diseases.

Hyperthermia

Hyperthermia may exert physical changes on the consistency of mucus, but its beneficial effects may not end there. Rhinoviral replication has been shown to be inhibited at temperatures at or around 43°C *(16)*. To what degree this in vitro observation can be extrapolated to the clinical setting has yet to be confirmed *(17–21)*. Studies have been inconclusive, although this has not prohibited the manufacture, patent, and selling of devices, such as the Rhinotherm or Virotherm, both of which deliver heated air to the nasal mucosa by various devices *(17,18,20,21)*. The success of the Rhinotherm has been demonstrated in one study, where three 22- or 30-min treatments were able to improve nasal symptoms by 73–81% within 24 h *(22,23)*. These reports have not been confirmed by subsequent studies. Similarly, although the Virotherm has been found to improve symptoms of a treatment group significantly over a group given 30°C air *(17)*, there were enough problems with the design and methodology of the study that the results are still equivocal. One must be careful not to use heated air indiscriminately, since the in vitro effects of air between 40 and 55°C on ciliary beat frequency is one of beat cessation. This has not been proven to be so in vivo, suggesting that the nasal mucosa regulates nasal temperature enough that all this discussion of nasal air temperatures may be academic.

Using Hot Drinks (Tea, Water, or Chicken Soup)—Does It Work (24,25)? On the other hand, it has been common among old wives' tales of various cultures to recommended hot liquids to treat

a cold. In China, hot tea has been a remedy for the common cold for many centuries, and in the Western world, chicken soup has been passed down from generation to generation as a mode of treatment for the "flu." The longevity of these beliefs would lead one to conclude that there is indeed some benefit from the administration of hot liquids. More recently, attempts to study this phenomenon have revealed that hot liquids have improved mucociliary clearance without having much effect on nasal airway resistance *(26)*.

Allergies and Environmental Exposure

Allergic Rhinitis

Allergen-induced inflammation of the nasal mucosa is known to lead to decreased sinus clearance and drainage owing to the swelling around the nasal osteomeatal complex *(27)*. Skin testing or radioallergosorbent (RAST) assay may improve identification of specific environmental or food triggers in allergy-prone individuals. This would subsequently allow for the avoidance of such triggers, if possible, and if not, by desensitization. Immunotherapy and sinusitis are discussed further below.

Barotrauma

Swimming, diving, working in tunnels, and playing wind or brass instruments all increase intranasal, intrasinus, and intrapharyngeal pressures *(28)*. There are no studies to confirm that these activities will cause sinusitis, but to the extent that such activities may reduce clearance of secretions, they do have the potential to exacerbate already existing problems with sinus drainage, such as in those people with allergic rhinitis, polyps, and so forth.

Cigaret Smoke, Pollution, and Other Irritants

Passive smoking is known to increase the incidence of upper and lower respiratory infections in children and adults *(29–32)*. Exposure to other irritants, such as air pollution *(33)*, as well as odors and perfumes in susceptible individuals can cause edema of the nasal, conjunctival, and airway mucosa, and thus increase the risk for developing sinusitis. Passive cigaret smoking, in particular, causes an increased incidence of nasal congestion and irritation in both atopic and nonatopic children, but also increases the incidence of middle ear effusions, tympanostomy tubes, and tonsillectomy and adenoidectomies. There are no studies attempting to relate passive smoking with sinusitis, but considering the similarities in pathogenesis between otitis media and sinusitis *(34)*, it is reasonable to postulate that a connection does exist.

Anatomic Obstruction

Septal deviation, nasal polyps, sinus polyps, sinus mucous retention cysts, tumors, and foreign bodies are all fixed conditions that inhibit sinus drainage. CT scan imaging *(35)* and rhinoscopy *(36)* have been invaluable in making the diagnosis of underlying structural abnormalities that may decrease sinus ostia diameter and subsequently decrease drainage. In addition, it has been shown that a sinus ostia diameter of <2.5 mm leads to a decrease in sinus paO_2, which is associated in turn with an increased incidence of sinusitis *(37)*. The use of corticosteroids to reduce the size of such obstructions will be discussed later.

ANCILLARY MANAGEMENT OF SINUSITIS—TREATMENT

Ancillary treatment of sinusitis begins at home, where most people will employ a variety of medical and nonmedical measures to relieve the symptoms of sinusitis. These modes of therapy are possible because of the wide variety of medications and nonmedical equipment available to the public without a prescription. Decongestants, antihistamines, expectorants, mucolytics, and combinations of these make up the major revenue generated business for pharmaceutical manufacturers. Clearly, not all of the above are safe or even medically indicated for the treatment of sinusitis. In addition, vaporizers, humidifiers, air filters, special vacuum devices and so on, are examples of the equipment that may be purchased in any general merchandise store.

Nonmedical Approaches to the Treatment of Sinusitis

Humidification

The rationale behind the use of humidification of surrounding air is that moisture tends to facilitate mucociliary clearance, partly by changing the consistency of the mucus. There are many techniques available to accomplish this, ranging from simple saline nose drops *(38,39)* to the use of (relatively) expensive equipment *(40)* to increase the

humidity in the nasal passages. In patients with chronic sinusitis, nasal saline irrigation has resulted in clinical improvement in 11 of 13 patients, primarily as a result of removal of the obstructing media. Nasal saline nose drops are available in any drugstore. They may also be prepared at home by mixing 1/4 teaspoon of salt with one small cup of warm water, and agitating until all the saline is dissolved. The saline can then be administered with a standard medicine dropper or by irrigation of the sinuses with a bulb syringe. Although this mode of therapy appears safe and there are no documented cases of sinusitis caused by the use of saline made from tap water, one must realize that tap water may contain contaminants, as evidenced by Acanthamoebic eye infections in contact lens wearers who have prepared their saline in the above fashion *(41)*.

The use of warm, humidified air delivered via controlled delivery devices, such as the Rhinotherm and Virotherm, has been extensively studied in the treatment of allergic rhinitis and viral URIs, as described above. Whether these devices have any role in treatment of sinusitis has yet to be determined.

Improving the humidity of environmental air also has been proposed to have an effect on mucociliary clearance. The use of either vaporizers or humidifiers has been recommended by various specialists, including allergists, pediatricians, and otolaryngologists. Occasionally, patients may achieve symptomatic relief from a hot washcloth placed over the face.

Exercise and Sinusitis

Exercise has been beneficial in reversing ostial obstruction in patients with allergies *(42)*. The reason for this may be the stimulation of systemic catecholamine release or by an increase in sympathetic release at the local level *(43)*. This effect appears to be transient and does not occur in patients with concurrent sinus disease *(44)*. Since the effect is not persistent after cessation of physical exertion, the use of exercise in the treatment of sinusitis or even to treat allergic rhinitis in an attempt to circumvent sinusitis is not recommended at this time.

Ancillary Medications Used in Sinusitis

Decongestants

α-Adrenergic decongestants are commonly found in OTC medications for colds, sinuses, and other ailments. They are frequently used for symptomatic relief and make up much of the revenue generated by the pharmaceutical industry. The rationale behind the use of these agents is that they decrease edema in the nasal mucosa, and thereby maintain or widen ostea patency via their vasoconstrictive effects. There are both nasal (topical) and oral (systemic) decongestants.

Table 2
Nonantibiotics Used in Sinusitis—Oral Decongestants

Pseudoephedrine
Onset of action 15–30 min
Duration of action—variable
Typical dosage—120 mg a day in divided doses
Side effect: raises blood pressure
Phenylpropanolamine
Onset of action 15–30 min
Duration of action—variable
Typical dosage—100 mg qid in divided doses
Side effect: raises blood pressure

Nasal Decongestants. Nasal decongestants are widely sold in drugstores, supermarkets, and large discount stores. Both α_1- and α_2-adrenergic agents are available (Table 2). The advantage of the α_1-adrenergic topical decongestants is that they have less action on nasal resistance vessels and thus cause less compromise of mucosal blood flow. In general, however, the use of nasal decongestants is not recommended because of its potential for overuse or abuse, its addictive nature, and a condition known as rhinitis medicamentosa. In addition to rhinitis medicamentosa, prolonged use of nasal decongestants (especially the α_2 class) results in atrophy of the nasal mucosa owing to vasoconstriction. Vasoconstriction may theoretically lead to decreased delivery of antibiotics to the sinuses and thereby compromise antibiotic therapy. Rhinitis medicamentosa appears to occur predominately in patients with pre-existing chronic nasal disease. In these patients, tolerance to the topical agent develops and increased use of the drug ensues. A rebound interstitial edema results, leading to a rebound congestion, whereupon most patients who use this type of medication enter into a viscous cycle, with progressive edema complicated by continued overuse of topical α-adrenergic decongestants. In a controlled trial in patients with uncomplicated vasomotor rhinitis, the prolonged (3 wk) use of topical xylometazoline resulted in decreased effectiveness of the medication, but did not cause tolerance in any of the subjects *(45)*.

There are specific instances in which topical adrenergic agents may be indicated. They may be used just prior to the use of anti-inflammatory nasal sprays to improve delivery during administration of the latter, or they may be used for short-term therapy of acute viral and bacterial sinusitis. In addition, they may be beneficial in improving mucociliary clearance. However, in any event, we do not recommend topical α-adrenergic agents for long-term therapy under any circumstances.

Oral Decongestants. Unlike nasal decongestants, several studies have not clearly shown untoward effects of oral decongestants on nasal mucosa and turbinate edema. In contrast, oral decongestants have clearly been shown to be able to decrease nasal airway resistance. The two oral decongestants used are pseudoephedrine, in doses of 60–120 mg, and phenylpropanolamine, dosage 30–100 mg. Clinically, these agents are effective in reducing symptoms of congestion, and multiple studies have demonstrated a significant increase in the ostial openings from the sinuses in patients who are treated with oral decongestants. The effects of oral decongestants generally have their onset within 30 min and last anywhere from 4–12 h, depending on the manufacturing methodology. The nonregulated use of these medications alone or in combination speaks for its low adverse effect rate. However, oral decongestants do have potential to cause hypertension at fairly low dosages, and safety issues with regard to the frequent use by patients are yet to be fully resolved. There is some evidence that high-dose oral decongestants may be of additional benefit in the treatment of sinusitis.

Antihistamines

First-Generation Antihistamines. Although use of antihistamines is generally not recommended for the treatment of sinusitis alone, they are beneficial when the sinusitis occurs in atopic individuals *(39)*. Most of the earlier antihistamines had significant anticholinergic effects, and this may play a role in drying out secretions, which generally makes them more difficult to clear.

Second-Generation Antihistamines. Currently, there are three nonsedating antihistamines available. All are prescription medications. These are astemizole, terfenadine, and loratadine. Two of the three, terfenadine and loratadine, have recently been combined with an α-adrenergic decongestant.

Table 3
Nonantibiotics Used in Sinusitis—Mucoactive Agents

Mucolytics
Expectorants
Mucokinetics
Mucoregulators
Mucorrheics
Ciliary stimulants
Detergents

Antihistamine use should be reserved for those patients with allergic rhinoconjunctivitis.

Combination Products

There are numerous combination products on the market. These products attempt to combine the beneficial effects of decongestants, antihistamines, and expectorants. Often an agent with cough-suppressant activity or an analgesic is added. Most of these products are OTC. Most manufacturers provide a variety of combinations for the public to choose from. Unfortunately, this strategy of treating sinusitis is scientifically unsound and essentially adheres to the "shotgun" approach to medicine. Most people who purchase these medications from their local supermarket have little knowledge of the actions of each of the ingredients. Much of the beneficial effects are psychological in nature. Clearly, should there be tighter restrictions on the use of these medications, a decrease in unwarranted medical costs would be seen.

Mucoactive Agents

Mucoactive agents may include expectorants, mucolytics, mucorrheics, mucokinetic agents, and other mucoregulatory agents *(46)* (Table 3). In addition, there are also detergents and ciliary stimulants available. Many products have multiple activities. The most commonly used mucolytic agent is *N*-acetylcysteine *(47–49)*, which is not available in the United States for treatment of upper respiratory conditions. However, its experience in Europe and Asia both in nebulized and oral liquid form has shown that it is an effective agent in decreasing sputum viscosity in chronic bronchitis. Other activities of *N*-acetylcysteine include normalization of mucoprotein secretion, stimulation of gastropulmonary vagal reflexes, and stimulation of mucosal secretions. In addition, *N*-acetylcysteine also acts as a chelator and an antioxidant.

Table 4
Nonantibiotics Used in Sinusitis—Nasal Steroids

Medication	*Made by*	*Topical potency relative to hydrocortisone*	*Systemic potency*	*μg/spray*	*Adult dosage*	*μg/d/relative daily topical potency*	*Delivery method*
Flunisolide (Nasalide)		3000	12.8	25	2 sp bid	100/300,000	Freon
Beclomethasone dipropionate (Beconase AQ, Vancenase AQ)		5000	3.5	42	2 sp bid	168/840,000	Freon or aqueous
Triamcinolone (Nasacort)	Rhone Poulenc Rorer	1000	5.3	55	2 sp qid	110/110,000	Freon
Budesonide (Rhinocort)		10,000	1.0	50	2 sp bid	200/2,000,000	Freon
Fluticasone propionate		20,000		50	1 sp bid	100/2,000,000	Aqueous

Its use as an antidote for acetaminophen poisoning is based on its antioxidant properties. Similar derivatives of L-cysteine include *S*-carboxymethyl cysteine (SCMC), which has also been shown to be effective in the treatment of bronchitis when given in oral dosages of 3 or 2.25 g daily over placebo *(50)*. Improvement in sputum volume and viscosity, forced expiratory volume in 1 s, and overall clinical symptomatology were noted. Both *N*-acetylcysteine and SCMC have been extensively studied, and their safety has been clearly demonstrated. However, like other OTC medications available in the US, their use in chronic sinusitis has not been clearly demonstrated, although one study with SCMC did show an improvement in mucociliary clearance *(51)*. Serratio peptidase and L-cysteine ethyl ester also improved the viscoelastic properties of mucus. Improvement in symptoms was also noted in patients with chronic bronchitis *(52)*.

A double-blind, placebo-controlled study was done to investigate the effectiveness of the mucolytic iodoglycerol in relieving symptoms of chronic bronchitis in adults *(53)*. Iodoglycerol is a potent mucolytic with a long history of widespread use for upper respiratory disease. It is also a significant ciliary excitatory agent. Iodoglycerol in 60 mg qid dosaging resulted in subjective clinical improvement in cough frequency and productivity, chest pain, and number of days of illness. There are, however, no controlled studies on the use of iodoglycerol in chronic sinusitis, and it has been taken off the market by the FDA.

Guaifenesin has an even longer history, and is a common component of cold and cough formulations. It is reputed to have significant expectorant effects, owing to its ability to change sputum adhesiveness, although it has no effect on the amount of secretions and their viscosity *(54)*. However, its clinical efficacy in the treatment of sinusitis is not scientifically proven, and, like other OTC medications, is of dubious value for this indication.

Other mucoregulatory agents include bromhexine, 2 mercaptoethane sulfonic acid, and ambroxol. Most of the medications have been studied for chronic bronchitis, and any benefit in chronic sinusitis is speculative at the present time. However, there are similarities between the two diseases, and there is preliminary evidence that decrease in mucoviscosity with improvement in mucociliary clearance may result from SCMC, L-cysteine ethyl ester, and *N*-acetylcysteine (NAC) use.

Anti-Inflammatory Agents

Steroids: Topical. Nasal steroids are now the mainstay of therapy for allergic rhinitis (Table 4). The effectiveness of nasal steroids in treating sinusitis is less clear. The rationale behind the use of nasal steroids in sinusitis is based on the observation that sinusitis, whether infectious or not, involves a significant inflammatory process. Patients with seasonal allergic rhinitis demonstrate an increase in sinus mucosa activity during allergy seasons, as shown by single-photon emission CT scanning. Pathologic findings in patients with allergic rhinitis-related sinus disease include increased levels of nasal eosinophils, as well as sinus mucosa damage similar to the inflammation seen in asthma. Neutrophilic and basophilic cell

Table 5
Nonantibiotics Used in Sinusitis—Nasal Decongestants

Sympathomimetic agents
Phenylephrine
Neosynephrine, NS, Dristan
Imidazoline derivatives
Naphazoline
Tetrahydozoline
Oxymetazoline
Xylometazoline

infiltrates are also seen. Increased levels of eosinophilic cellular secretions are found in patients with allergy-related sinusitis. Eosinophilic cationic protein and major basic protein exert opposite effects on respiratory glycoconjugate and lactoferrin release from respiratory epithelium.

A placebo-controlled multicenter study in which flunisolide was evaluated as an adjunct to antibiotics in sinusitis patients revealed that the flunisolide-treated group did better clinically, according to global assessment evaluation. The flunisolide-treated group also showed a significant improvement in the degree of radiologic involvement. Both groups went into remission after 3 wk of antibiotics, but in neither group was the remission long-standing and relapses occurred in 1/4 to 1/3 of patients *(55)*.

In a double-blind study using maxillary sinus irrigation with neomycin alone or in conjunction with the topical steroid tixocortal pivalate, there was a significantly better rate of ostia patency in the steroid-treated group *(56)*. Clinical symptomatology was not studied. In another study, dexamethasone with or without tramazoline was associated with a higher improvement rate of sinus drainage, mucociliary clearance, and nasal airway resistance over placebo. There was no significant difference between the two study groups *(57)*.

Topical corticosteroid therapy is considered safe as an ancillary treatment of sinusitis. Human ciliary function and mucociliary clearance is not adversely affected by topical steroid therapy *(58,59)*. The nasal steroids currently commercially available are shown in Table 5. Beclomethasone dipropionate sprays are provided both as an aqueous solution and as a Freon powder, whereas flunisolide, triamcinolone, and budesonide are available only as Freon powder. In contrast, fluticasone propionate is provided only in aqueous solution form. Some patients prefer one delivery mode over the other. In general, topical corticosteroids only need to be administered once or twice a day, so patient compliance is fairly good.

Steroids: Systemic. Systemic steroids can be given orally, intramuscularly, intravenously, or intraturbinate. There are no controlled trials of systemic corticosteroids in sinusitis. However, in a comparative study of 53 adults with nasal polyps, it has been shown that a single dose of oral steroids had at least an equivalent improvement in smell and nasal airway resistance over surgical polypectomy after 1 yr and an even greater short-term improvement *(60)*. Both groups also received intranasal beclomethasone sprays twice daily during the year-long trial. In addition, a single dose of methylprednisolone was shown to be able to decrease nasal obstruction for 4 wk in patients with allergic rhinitis *(61,62)*. Systemic steroids may be indicated in patients in whom nasal obstruction is so severe that nasal sprays are ineffective in penetrating the nasal mucosa. Intraturbinate injections of steroids are an unproven mode of delivery in sinusitis. The safety of intraturbinate injections is also not yet established.

Cromolyn Sodium—Is There a Role? Cromolyn is widely used as an anti-inflammatory in asthmatic patients. It is also used for allergic rhinitis. Cromolyn inhibits immediate- and late-phase allergic reactions. Controlled studies have failed to demonstrate any significant improvement in the clinical symptomatology in patients with URIs and documented maxillary sinusitis *(63)*. Cromolyn has also not been found to be effective for treatment of the so-called nonallergic rhinitis with eosinophilia syndrome (NARES) *(64)*. Cromolyn is therefore not recommended as an ancillary measure for prevention or treatment of sinusitis.

Anticholinergics

Ipratropium bromide (Atrovent) is currently the only anticholinergic agent used topically to treat nonallergic or vasomotor rhinitis. Although its effectiveness in the treatment of nonallergic forms of rhinitis has been clearly demonstrated *(65)*, there are no good studies on its use in chronic sinusitis. However, it may also have some usefulness in sinusitis, because of its ability to reduce methacholine hyperactivity, thereby indirectly modulating secretion volume and edema of the sinus and nasal mucosa. Ipratropium bromide is a derivative

Table 6
Nonantibiotics Used in Sinusitis—Intravenous Immunoglobulins

Nonantibiotic	*Distributor*	*Concentration*	*IgG content*	*IgA content, μg/mL*	*Shelf-life, mo*	*Half-life, d*
Polygam	American Red Cross	5% (10%)	>90%	<3.7	24	24
Venoglobulin-I	Alpha	5% (10%)	>97%	24–38	24	29
Venoglobulin-S	Alpha (solution)	5%	>99%	10–27	24	33.5
Gammar-IV	Armour	5% (10%)	>98%	20	36	25
Gammagard S/D	Baxter/Hyland	5% (10%)	>90%	<3.7	27	24
Gamimune N	Cutter/Miles	5%, 10%	>98%	<270	5%: 36, 10%: 27	21–35
Iveegam	Immuno-US	5%	100%	<2	24	23–29
Sandoglobulin	Sandoz	3, 6, 9, 12%	>96%	<970	36	23

of noratropine, and acts to inhibit nasal glandular secretion, but, in contrast to atropine, has no effect of lacrimal gland, goblet cell, or sinus secretions. Atropine, therefore, is not recommended for the treatment of sinusitis, since decreased mucociliary clearance may result from its use.

IV γ-Globulin

Patients who present with recurrent bouts of sinusitis or pneumonia often have an underlying immune deficiency, which usually lies in B-cell function. This usually presents as IgA deficiency or IgG subclass deficiency. Encapsulated organisms like *Haemophilus influenzae* are the most commonly seen pathogens. In these patients, monthly infusions of iv γ-globulin, given to keep the trough level of serum IgG within a normal range, have been effective in preventing further episodes of sinusitis. A typical dose of immunoglobulin may be 200 mg/kg/mo. Several different preparations of immunoglobulin are available, as shown in Table 6.

Immunotherapy and Sinusitis

There are no controlled studies on the use of immunotherapy in sinusitis. Immunotherapy may be beneficial in patients whose sinusitis is secondary to increased mucosal edema and secretions caused by allergic rhinitis.

Pain Management

Control of headache and facial pain in sinusitis must not be de-emphasized, since many patients are often debilitated by a bout of sinusitis. Acetaminophen, aspirin, or ibuprofen is often sufficient to alleviate pain of sinusitis. Since drug sensitivity to aspirin and other nonsteroidal anti-inflammatory medications may occur in patients with asthma, nasal polyps, and sinusitis, acetaminophen is generally safer. Desensitization to aspirin in this small group of patients, who comprise about 3–4% of all asthmatics with sinusitis, may be performed. Sinusitis, along with allergic rhinitis and nasal congestion may play a trigger role in migraine headaches.

Others

Furosemide is beneficial in patients with asthma. However, its efficacy in rhinitis and sinusitis has not been uniformly demonstrated *(66,67)*. Although astringents are frequently recommended, again they have not been subjected to controlled studies *(68)*. Posture has been shown to affect nasal patency, and it is recommended that the patient attempt to lie on the side opposite to a unilateral sinusitis since nasal patency decreases on the "down" side, presumably owing to gravitational shifting of the turbinates *(69)*. As our understanding of the mediators involved in the inflammatory response increases, we anticipate future promising areas of study to include the modulation of the inflammatory response in sinusitis by platelet-activating factor antagonists, leukotriene antagonists, protease inhibitors, and tachykinins. As our understanding of gene regulation and our ability to control bodily functions at a DNA level increases, mucin gene regulation may become one of the mechanisms by which we may control the consistency and volume of secretions during an episode of sinusitis and thereby facilitate treatment.

CONCLUSIONS

Despite exciting advances in medical research, the ancillary treatment of sinusitis is still limited to a few very popular age-old therapies. From the above discussion, we are able to formulate a plan to reduce the incidence of sinusitis and to treat sinusitis that does not involve, or is complementary to the use of antibiotics and surgery. This recommendation takes into account the known causes or exacerbating factors of sinusitis in a wide range of patients.

Avoidance

1. Identify known host factors;
2. Identify environmental factors;
   a. Avoid allergens;
   b. Avoid passive smoking;
   c. Avoid contact with URIs;
3. Immunotherapy.

Treatment

1. Hot liquids (potential indirect benefit);
2. Nasal saline irrigation and hydration;
3. Topical nasal steroids;
4. Oral decongestants (not nasal decongestants);
5. Antihistamines (may help in allergic patients);
6. Mucoactive agents;
7. IV γ-globulin (in patients with immunodeficiency).

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