DIAGNOSIS AND TREATMENT OF PEDIATRIC CHRONIC SINUSITIS

By

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Although chronic sinusitis triggers billions of dollars of health care expenditures each year, surprisingly little is known about its epidemiology, pathophysiology, and management. The immune theories of chronic sinusitis serve as a theoretical framework and conceptual model for this paper. To accomplish this, the initial sections of this paper are devoted to a general discussion of basic immunology to lay a strong foundation for understanding the complex immune aspects of the disease. The pathophysiology and management of pediatric chronic sinusitis is presented in this manuscript. Factors thought to contribute to pediatric chronic sinusitis, including inflammation, microbial invasion, allergic rhinitis, non-infectious-non-allergic rhinitis, anatomic obstruction, cystic fibrosis, immunodeficiency, frequent upper respiratory infections, asthma, and gastroesophageal reflux are examined. Drug treatment options including: antibiotics, nasal steroids, decongestants, mucolytics, antihistamines, and nasal irrigation will be evaluated for their efficacy and value. Also, the risks and benefits of surgical intervention are discussed. The use of Computed Tomography (CT) scans in the diagnostic treatment will be discussed. Antibiotic treatment based on recent sinus nasal aspirate culture and sensitivity studies will be reviewed and evaluated for their efficacy.
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INTRODUCTION

The direct medical cost of chronic sinusitis exceeds 2 billion dollars per year (Kaliner et. al, 1997; Chan et. al, 1999; American Academy of Otolaryngology-Head and Neck Surgery web site, 2001). Upward of 5 to 13% of children may experience acute and/or chronic sinusitis, but precise incidence data are not available because many imaging techniques currently available are inappropriate procedures for potential pediatric survey (Fireman, 1992). Chronic sinusitis in children and adolescents has been the source of great controversy and discussion in recent years because it is a diagnosis that has frequently been overlooked (Baroody, 2001).

Pediatric chronic sinusitis is a diagnosis that is often excluded by family physicians, pediatric physicians and mid-level primary care providers (Nurse Practitioners and Physician Assistants) for the following two reasons, they expect to see children for upper respiratory infections, such as pharyngitis and otitis media simply because children frequently get them, and many believe that the sinuses are not well developed and thus can not harbor disease. In actuality, acute sinusitis is frequently overlooked, and when it is properly diagnosed, chronic sinusitis is rarely considered. Chronic sinusitis, especially, can be frustrating and difficult to treat, and medical failures commonly become surgical patients (Hamilos, 2000).

Chronic sinusitis in children is associated with alterations in immune function. The normal physiology of the immune system provides a conceptual framework for understanding the predisposing factors and pathophysiologic mechanisms of this disorder. Normal immune physiology will be summarized to establish a conceptual framework that will be interwoven throughout the literature review. The ultimate goal of
this review is to clarify and update pediatricians, family physicians, physicians assistants, and nurse practitioners on what is known about the pediatric chronic sinusitis, what is not known, and suggest ways in which to diagnose and treat chronic sinusitis in children.

**Immune Physiology**

Leukocytes or white blood cells (WBCs) are composed of six different types of cells, neutrophils, eosinophils, basophils, monocytes, T-lymphocytes, and B-lymphocytes. "All of the leukocytes are a part of the nonspecific defense system except lymphocytes, which are part of the adaptive or specific defense system" (Peterson, Symes, & Springer, 2000, p. 176). Table 1 describes in detail their role in inflammation.

Innate immunity is related to genetically inherited patterns in genes programmed for immune system functions. Neutrophils, eosinophils, and macrophages (monocytes that reside in tissue) are leukocytes with phagocytic characteristics. They move towards an area of damage by chemotaxis, adhere to foreign substances and dispose of them by engulfing and then digesting them. Eosinophils and basophils protect the body against parasitic infection and are often elevated in allergic responses.

B-cells are part of the antibody-mediated or humoral immunity. B-cells become plasma cells, which produce different subclasses of antibodies (ie. IgE, IgA, IgM, and IgG) when a foreign antigen triggers the immune response. Antibodies recognize foreign antigens and mark them for destruction (The Immune System, 1998). Different antibodies have different purposes, some coat foreign invaders to make them more attractive to circulating scavenger cells (phagocytes), that will engulf the microbe, others combine with antigens and activate a cascade of proteins known as complement. Complement combines with the antibodies to help destroy invaders.
Regulatory T-cells orchestrate the response of different types of immune cells. Helper T-cells (CD4) are considered regulatory cells, for example, they alert B cells to make antibodies, activate other T-cells and scavenger cells (macrophages), and trigger which type of antibody will be produced (The Immune System, 1998). Helper T-cells differentiate further into Th1 and Th2 cells. Th1 cells produce lymphokines (cytokines) that act on macrophages. Th2 cells stimulate B-cells to make antibodies. Cytotoxic T-cells, CD8 cells, function as effector cells and can directly lyse and kill infected host cells (Banasik, 2000).

Leukocytes accomplish their roles through the production of cytokines. A cytokine functions as an immune hormone, causing increases or decreases in cellular reaction and reproduction. Cytokines are also called monokines, lymphokines, and interleukins, depending on their cell of origin (Banasik, 2000, p. 196). For example, cytokines produced by lymphocytes are called lymphokines and interleukins are produced by a variety of WBC types. Table 2 describes the details of the role of interleukins in chronic inflammation. “Cytokines produced by innate immunity also partly determine subsequent T-cell differentiation” (Flavell, 1999). Cytokines are signaling molecules that affect the functions of other immune cells by activating surface receptors (Banasik, 2000).

Acute inflammation is a second line defense. It is a nonspecific defense that occurs due to injury. Chemical mediators are released by activated granulocytes, lymphocytes, and macrophages and include histamine, prostaglandins, leukotrienes, cytokines, oxygen radicals, and enzymes (Banasik, 2000). If an antigen invades the mucosa, the antigen stimulates B-cells, which then release IgE. The IgE binds to mast cells and the antigen binds to IgE. This causes mast cell degranulation, releasing
histamine and other chemicals that dilate vessels and increase permeability, causing blood to leak out of the vessels, and thus promoting edema. IgE exists in the bloodstream and is usually found bound to the surface of either a mast cell or a basophil (Banasik, 2000). Inflammatory exudate is fluid that leaks out of porous, edematous vessels that contains neutrophils and debris from phagocytosis. Serous exudate is watery and is associated with mild inflammation (Banasik, 2000). With greater injury, more fibrinous exudate is produced and is sticky and thick. Purulent exudate (pus) is composed of leukocytes, proteins, and tissue (Banasik, 2000).

Chronic inflammation is characterized by a slower onset and more protracted course, and by a larger preponderance of lymphocytes, macrophages, and plasma cells (Pasternack, 1996). It also involves fibroblast proliferation and fibrosis (deposition of connective tissue). Chronic inflammation has a broad spectrum of immunologic processes, including antibody formation, antibody-dependent cell-mediated cytotoxicity, and cell-mediated immunity (Pasternack, 1996). Cytokines elaborated by macrophages and lymphocytes (as mentioned previously) are mediators which orchestrate the highly variable manifestations of chronic inflammation. Chronic inflammation may follow acute inflammation when whatever is aggravating the immune system (ie. antigen) is persistent, or when acute inflammation occurs in the same area frequently (Pasternack, 1996). Some agents, such as mycobacteria and viruses tend to lead to direct chronic inflammation by bypassing the usual stage of acute inflammation (Pasternack, 1996). Because there is variability in chronic inflammatory lesions, there is no all-encompassing type of reaction or time course.
Sinus Anatomy and Pathophysiology

The sinuses are air-filled cavities lined with pseudostratified ciliated columnar epithelium interspersed with goblet cells (Spector, 1998). Cilia sweep mucus in the direction of the ostial opening. The paranasal sinuses are composed of paired frontal sinuses along the forehead region, several anterior and posterior ethmoid sinuses (located approximately between the orbits), paired maxillary sinuses below the orbits, and paired sphenoid sinuses behind the eyes at the skull base (see figures 1-7). The purpose of the sinuses is poorly understood, although many believe sinuses exist to warm and humidify air before it enters the lungs. In children, the ethmoid and maxillary sinuses are present at birth. They are fully developed by 3 years of age and are the most commonly affected. The sphenoid sinuses are present at 3 years of age and fully developed by 12 years of age. The frontal sinuses are generally present by 8 years of age and fully developed by 12 years of age (Dunham, 1994).

The hiatus semilunaris, a crescent-shaped groove located lateral to the anterior third of the middle turbinate is a crucial area because it is where the frontal, maxillary, and the anterior ethmoid sinuses drain. Pus usually emanates from this area, when there is infection (Osguthorpe, 2001). Edema in the nose leads to obstruction of the sinus ostium, preventing proper ventilation. The vascular sinus membrane absorbs the trapped gases within the sinus, and a negative pressure develops preventing drainage of sinus secretions. Finally, the negative pressure within the sinus and poor ciliary function allow nasal flora to be virtually sucked into the sinus cavity, resulting in an excellent growth environment for bacteria, especially anaerobic bacteria due to the low partial pressure of oxygen in the blocked sinus(es) (Bothwell, 1999, p. 256). Delayed recovery of
mucociliary function from mucostasis, hypoxia, microbial products, and inflammation, most likely are the contributing factors in chronic sinusitis (Hamilos, 2000).

Sinusitis is thought to originate from a local or systemic insult that causes sinus ostial obstruction and infection (Hamilos, 2000). Anatomical or inflammatory factors can both lead to sinus ostial narrowing. "The primary cause of sinusitis is not bacteria, but rather anything that leads to sinonasal edema" (Bothwell et al., 1999, p. 256). Bacterial growth is secondary and is usually the result of migration of nasal flora into the sinus cavity. Disturbances in mucociliary transport and immune deficiency are common contributing etiologies, however, ostial narrowing is generally thought to be caused by viral infections or chronic allergic inflammation (Hamilos, 2000).

Sinus health depends on mucous secretion, normal viscosity, volume, composition, and mucociliary flow (Hamilos, 2000). An ostial blockage can cause mucous stasis creating a medium for bacterial growth and proliferation beyond what is considered "normal flora" in the sinuses. The anterior ethmoid and maxillary sinuses are most commonly affected by an ostial blockage, because of their location.

**Chronic Sinusitis Defined**

Sinusitis is frequently classified as either acute, recurrent, subacute, or chronic. The definition of chronic sinusitis is variable, depending on the opinion or background of the researcher, but has the same general implications. Kaliner et al., (1997) define chronic sinusitis as signs and symptoms of inflammation of the sinuses for more than 8 to 12 weeks. Fireman, (1992) defines it as persistant sinus infection that occurs longer than 3 months with radiographic evidence of mucosal hyperplasia or opacification of the paranasal sinuses after medical therapy for recurrent symptoms of sinusitis.
Chan et al., (1999) define chronic sinusitis as an illness with 1 or more persistent symptoms for at least 3 months after medical treatment that is corroborated with a positive Computed Tomography (CT) scan. Prior treatment was defined as at least 2 courses of antibiotics during the previous 3 months, at least 1 of which was a second-line agent (eg., second-or third-generation cephalosporin (Ceftin-Cefuroxime, Suprax-Cefixime, or Cedax-Ceftibuten), second-generation macrolide (Biaxin-Clarithromycin or Cleocin-Clindamycin), or a broad spectrum antibiotic with a Beta lactamase inhibitor ([Augmentin]Amoxicillin/Clavulanate) (Chan et al., 1999). In their study, a positive CT scan was described as at least 4 mm of mucosal thickening of any of the sinuses, bubbles, or air-fluid levels. “Plain film radiographs (Waters Views) of the sinuses are rarely indicated. Although such studies can disclose sinus opacification or reveal an air fluid level associated with maxillary, frontal or sphenoid disease, the commonly affected area is the anterior ethmoid region, which is poorly visualized on plain film radiographs” (Osguthorpe, 2001, p.70).

A computed tomographic (CT) scan, performed in a coronal plane is considered the gold standard radiographic delineation of sinus disease, and the costs are only slightly higher than plain films. However, a study done by Cotter, et al. (1999) found that this mucoperiosteal thickening was present in 60% of symptomatic children, and 46% of random CT scans, implying that the diagnosis of chronic sinusitis based on CT scans alone is inappropriate. Puhakka et. al (1998) found that by day 7 of a viral upper respiratory infection, 39% of the subjects had sinusitis, and they concluded that sinusitis occurs frequently during the early days of the common cold, and yet it remains self-limiting. It is essential to understand that abnormal images of the sinuses cannot stand alone as evidence of disease, clinical criteria is just as important, if not more important.
The American Academy of Pediatrics recommends that CT scans of the paranasal sinuses should be reserved for patients in whom surgery is being considered (National Guidelines Clearinghouse, 2000). Hence, a coronal CT scan is appropriate for a patient, already diagnosed with chronic sinusitis based on clinical criteria, if a practitioner is suspicious of an obstruction or extensive mucosal thickening.

**Symptoms and Associations**

Rhinorrhea, postnasal drip and cough are the major complaints associated with pediatric chronic sinusitis (Shapiro, 1992). Parsons, (1993) emphasizes the 7 cardinal symptoms of chronic sinusitis. They include chronic nasal obstruction, purulent nasal discharge, postnasal drainage, chronic cough, halitosis, headaches or head pain, and behavior changes. “A nighttime cough is a common complaint and is usually more prevalent than a daytime cough” (Lippincott & Brown, 2000, p. 470). Headaches may be present, but they may be difficult to appreciate in a younger pediatric patient, who may instead have behavioral changes and irritability (Lippincott & Brown, 2000). In a 3-year study done to establish an outcome-based clinical guideline for the management of chronic sinusitis in children, Chan et al., (1999) found that the top 5 symptoms were purulent nasal discharge (59%), headache (33%), nasal congestion (30%), cough (19%), and wheezing (19%).

In children, chronic or acute ethmoid sinusitis may cause orbital abscess, which can present with a limited range of motion of the affected eye and swelling of the upper/lower eyelid and orbit. The swelling usually starts between the eye and nose. Any suspicion of an orbital abscess requires immediate referral to an Otolaryngologist (Ear Nose, and Throat (ENT) specialist). Swelling of the upper/lower eyelid without
limitation of eye motion would be indicative of periorbital cellulitis, which is less
dangerous, but requires intravenous antibiotics.

Factors Thought to Contribute to Sinusitis

When either acute or chronic sinusitis is present in children, associated co-
morbidities must be considered. Brook, Yocum, & Shah, (2000) found in their literature
review that otitis media with effusion was the presenting symptom of chronic sinusitis in
23% of patients. Other factors associated with pediatric chronic sinusitis include asthma,
viral upper respiratory infections, cystic fibrosis, immune deficiency, exposure to
cigarette smoke, chlorine, air pollution, polyps, Downs syndrome, nasal obstruction,
barotrauma, immotile cilia syndrome, swimming, choanal atresia, septal deviation, and
aspirin sensitivity (Gungor et al., 1997). Viral infections and allergic inflammation
appear to be the most common etiologies associated with mucosal changes, which often
lead to bacterial sinusitis (Dunham, 1994).

Inflammatory Factors

Inflammation is a key factor in sinusitis (Hamilos, 2000). Both infectious and
noninfectious stimuli contribute, but the exact role of inflammation remains unclear.
“The pathologic features seen in chronic sinusitis mucosa are likely the result of an
overlap of infectious and noninfectious inflammatory stimuli (Hamilos, 2000, p. 217).
Current theory suggests that most cases of pediatric chronic sinusitis begin with a viral
upper respiratory infection, which can cause viral sinusitis (Puhakka et. al, 1998),
promoting an inflammatory response, leading to secondary bacterial sinusitis. It is
controversial on whether the inflammation is caused by a dysfunctional inflammatory
response or sinus dysfunction.
“Recent progress in basic immunologic studies revealed an intricate immune defense network mounted by innate and adaptive immunity” (Jyonouchi, Sun, Le, & Rimell, 2001, p.1488). Jyonouchi et al., (2001) believe that chronic sinusitis is a result of dysregulated cytokines. Jynouchi et al., (2001) believe there could be an excessive inflammatory response by certain individuals, resulting from their innate (i.e., their genetic make-up) immunity that could be causing sinus inflammation and resulting sinus disease.

Marked tissue eosinophilia is the “hallmark” of chronic inflammation (Harlin et al., 1998). Eosinophilia is a prominent feature in both allergic and nonallergic patients, suggesting that a nonallergic mechanism maybe present for eosinophilia in chronic sinusitis (Kaliner et al., 1997). However, the driving force for eosinophilia in chronic sinusitis is poorly understood. Several authors (Bhattacharyya, Vyas, & Fechner, 2001, & Song, Chopra, Yao-shi, & Calcaterra, 1995) have identified hypereosinophilia in the mucosa of sinuses in chronic rhinosinusitis and correlated this finding with the production of inflammatory mediators and subsequent tissue damage within the respiratory mucosa. Despite the evidence that eosinophils may have a significant role in chronic sinusitis, conflicting data have emerged in the literature regarding its impact on the disease (Bhattacharyya et al., 2001). It is apparent that researchers are still trying to find an accurate and reproducible method for quantifying tissue eosinophilia, and this would explain the seemingly contradictory information present in the literature. In general allergic patients have an increase in tissue eosinophils, mast cells, and lymphocytes (Mabry, 1994), and different expressions of cytokines and chemokines.
Helper T-Cells and Their Role in Chronic Sinusitis

As mentioned previously CD4+ lymphocytes differentiate into Type 1 and Type 2 T-Helper cells, which give rise to most of the cytokines that contribute to chronic inflammation. Type 1 T-cells (TH 1) induce phagocytic cell-mediated immune responses by producing T1 cytokines (IFN-gamma, interleukin 12, and tumor necrosis factor alpha). Type 2 T-cells (TH 2) induce eosinophil-mediated inflammatory responses by producing T2 cytokines (IL-4, IL-5, and IL-13) (Swain, 1999). The combined production of IL-4 and IL-5 by TH 2 cells stimulates IgE and IgA production by B-cells, as well as mast cell and eosinophil activation (Feghal & Wright, 1997). Type 1 T-cells and Type 2 T-cells produce cytokines that can counter-regulate each other. An imbalance in this system is thought to occur in many disorders (Swain, 1999). Allergic patients also show high numbers of inflammatory cells believed to be regulated by TH 2 cytokines (IL-4, IL-5, and IL 13). Nonallergic patients tend not to have increased levels of IL-4 (thought to induce B-cells to make IgE) and IL-5, but have an increased level of IL-13 and IFN-gamma (Hamilos, 2000).

Microbial Invasion

The best characterized aspect of pediatric chronic sinusitis is its bacteriology (Slack, Dahn, Abzug, Kenny, & Chan, 2001). Interestingly, in adult chronic sinusitis, the role of bacterial infection is less certain. Children average 8 colds per year, particularly in their early years, with higher frequencies associated with attendance at day care. Pediatric chronic sinusitis appears to represent bacterial invasion following a viral upper respiratory infection. Indigenous bacterial flora of the nose vary depending on the area sampled (Gwaltney, 1996). The more posterior sites of the nares, close to the middle meatus contain bacterial flora, that more commonly cause acute and chronic sinusitis,
serving as a sort of reservoir. Sneezing, coughing, and nose blowing create pressure differentials that deposit these bacteria into the sinuses (Gwaltney et al., 2000). However, the pediatric patient often has other contributing factors that complicate the situation (Lippincott & Brown, 2000).

Culture of the bacterial culprit is frequently necessary in patients with compromised immune systems or sinusitis refractory to standard antibiotic regimens (Axelsson & Brorson, 1973). Cultures are most sensitive and specific when obtained via direct maxillary aspiration (an invasive procedure) or via swab of the maxillary ostium. Unfortunately, cultures obtained by simple intranasal swabs are generally not indicative of the causitive bacteria in sinusitis (Axelsson & Brorson, 1973). However, the 2000 Respiratory Surveillance Program (RESP) involved over 16,213 nasal swabs, and the characteristics of the nasal swab cultures were quite similar to those reported in sinus puncture and rhinoscopic culture studies (Sokol, 2001).

Allergic Rhinitis

The second most common predisposing factor for chronic sinusitis is allergic rhinitis, occurring in 10-15% of children over 9 years of age (Gungor & Corey, 1997). Allergic responses occur when the immune system is hypersensitive to an antigen. In type I hypersensitvity reactions, IgE is produced in response to exposure to the antigen/allergen (Banasik, 2000). Type I sensitivity occurs rapidly (minutes) and is generally associated with seasonal allergic rhinitis. “Eosinophilia with the resultant increase in major basic protein is toxic to mucosa and disrupts mucociliary clearance. This promotes stagnant secretions, increased bacterial counts, increased mucosal inflammation, and further disruption of ciliary function” (Lipincott & Brown, 2000, p. 472). When allergic rhinitis is considered to be the initial insult leading to sinusitis,
environmental factors such as, secondary smoke exposure, primary smoking, recreational drugs, inhaled irritants, pets, foods, and seasonal sensitivities to grasses and pollens should be considered.

Clear nasal discharge with boggy, pale inferior turbinates are common findings. Patients often complain of nighttime cough, itchy eyes, frequent sneezing, and morning headaches (Lippincott & Brown, 2000). The presence of allergic shiners (dark, almost bluish circles under the eyes), or the presence of an "allergic salute" (slightly upturned nostrils from constantly wiping the nose), should alert the practitioner to an allergic etiology.

The majority of allergic patients will have positive skin tests (if older than 4) and elevated serum IgE. If the history suggests an allergic origin of sinus obstruction, an in vitro IgE screen will identify 94% of patients in whom antiallergy therapy and further testing may be needed (Fergusen & Mabry, 1997). "Measurement of total IgE is not indicated in evaluation of allergic rhinitis, because 20% of nonallergic patients have an elevated level. However, a multiallergen radioallergosorbent test (RAST) is a reasonable screening test for allergies" (Graft, 1996, p.2). The results are not specific for a given allergen. Skin tests are faster, more sensitive, and more cost-effective. RASTs are good for those who need to be tested for only a few allergens and are helpful for the pediatric population (Graft, 1996). It is important for the practitioner to realize that extensive allergy testing is both costly and time consuming, and consideration to whether controlling the symptoms with medications such as nasal steroids and antihistamines is satisfactory to the patient and parents, or whether extensive testing to identify the allergen is necessary.
Non-Infectious-NonAllergic Rhinosinusitis

Rhinosinusitis is a chronic disease of unknown etiology (Mygund, 1996). In the majority of cases, it characterized by eosinophil-dominated inflammation in the mucous membranes of the paranasal sinuses.

Patients with nonallergic rhinitis can be differentiated further on the basis of nasal cytology, with approximately 66% of nonallergic patients have an absence of eosinophils on nasal smear. Patients with nonallergic rhinitis are often hyperreactive to irritant exposure, have watery rhinorrhea, and respond poorly to antihistamines, decongestants, and topical corticosteroids (Mullarkey, 1988). The symptoms of chronic rhinitis and nasal eosinophilia in the absence of allergies (ie. absence of perennial rhinitis and skin reactivity to allergy tests) is labeled nonallergic rhinitis with eosinophilia syndrome (NARES) (Davidson et. al, 1992). Davidson et. al, 1992 studied 56 non-atopic patients, 12 of which had NARES. Using the saccharine challenge to evaluate the speed at which a patient was able to clear mucous from the sinuses via mucociliary transport, they found that patients with NARES had prolonged mucociliary clearance times. Vasomotor rhinitis (bright lights, exercise), perennial nonallergic rhinitis, cold air-induced or hot soup-induced rhinorrhea, gustatory rhinitis, endocrine abnormalities (hypothyroidism), and medications (antihypertensives and oral contraceptives) are all potential causes of nonallergic noninfectious rhinitis (Zeiger, 1992; Graft, 1996).

Anatomic Obstruction

Enlarged adenoids are a primary cause of chronic sinusitis in children. Adenoid tissue sits at the back of the nose in the nasopharynx. The tissue is similar to tonsil tissue and generally shrinks and becomes insignificant by the late teens. However, problems
can arise, if the tissue remains enlarged and becomes chronically infected, causing bilateral nasal obstruction (Rosin, 1998).

Nasal polyps are grape-like inflammatory swellings of the nasal and sinus linings caused by hyperplastic mucosal production that are benign in origin. They are caused by irritation of the mucosa and are linked to asthma but no clear evidence shows a link with allergies (Lund, Flood, Sykes, & Richards, 1998). Nasal polyps frequently block the ostia and contribute to sinus infections (Rosin, 1998). This may present clinically, as chronic rhinorrhea.

Other common anatomic obstructions in the pediatric population include deviated nasal septum, obstructing concha bulla (air cell inside the normally bony middle turbinate), and nasal foreign body (Bothwell et al., 1999). An intranasal foreign body will often present as unilateral, with often foul-smelling rhinorrhea, and can usually be diagnosed with simple anterior rhinoscopy using a bright light and nasal speculum, or even using an otoscope to look in the nostrils. If anatomic abnormalities are suspected a coronal CT should be ordered.

Cystic Fibrosis

In any child with chronic sinusitis, cystic fibrosis should be part of the differential. Nearly all patients with cystic fibrosis will have problems with sinusitis and chronic sinusitis. Typical pathogens include Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, Aspergillus fumigatus, in addition to more common polysaccharide-encapsulated organisms (Spector et al., 1998). Chronic Pseudomonas infections and nasal polyps (which are uncommon in children) are clues to possible cystic fibrosis (Spector et al., 1998). The Gibson-Cooke sweat test is the gold standard for
identifying patients with cystic fibrosis, with chloride values greater than 60Eq/L in children.

**Immunodeficiency**

Immunodeficiency is present in 0.5% of the population, which is 16 to 40 times less than the incidence of respiratory allergy. The undiagnosed immunodeficient child frequently develops bacterial infections following upper respiratory infections and becomes ill shortly after discontinuing antibiotics. The most common types are common variable immunodeficiency (reduced levels of two or more immunoglobulin classes), IgG subclass deficiency, and selective antibody deficiencies (Shapiro et al., 1991). Most immunodeficient patients that have major sinusitis problems have a humoral immunodeficiency (Polmar, 1992). As many as, one third of cases of refractory rhinosinusitis may involve immune deficiencies (Lipincott & Brown, 2000). If congenital or acquired immunodeficiency is suspected quantitative immunoglobulins, antibody tests, serum IgE, and complement component tests may be useful (Spector, 1998). Monitoring the patient’s response to tetanus toxoid or pneumococcal vaccine may be useful as children with immunodeficiency may have unexpectedly low titers after immunization (Lippincott & Brown, 2000).

IgG3 subclass deficiency was the most common immunoglobulin abnormality in a study done by Shaprio et. al (1991) on 61 children with chronic sinusitis referred for allergy evaluation. Interestingly, 7 of the 9 patients with low IgG3 levels had impressive allergic characteristics, either elevated IgE levels, positive prick tests, or both.

**Gastroesophageal Reflux**

Clinicians are becoming more aware of gastroesophageal reflux as the cause for chronic cough, hoarseness, and asthma symptoms in the pediatric population (Lipincott &
Gastro-nasal reflux is thought to induce inflammation of the eustachian tube orifices or sinus ostia because of mucosal irritation (Barbero, 1996). The gold standard in evaluating the esophageal manifestations of reflux is the pH probe (Bothwell et al., 1999). Some professionals have recently become suspicious that gastric acid reflux affects nasal mucosa because of incidences where children's symptoms were not relieved by functional endoscopic surgery. Bothwell et al., (1999) conducted a study of 30 children with chronic sinusitis that had recent gastroenterology referrals and pH probe testing. All were appropriate candidates for Functional Endoscopic Surgery (FESS). Ranitidine (Zantac) and Cisapride were used initially, and Omeprazole and Cisapride were reserved for more severe cases. The mean duration of the study was 8.2 months. Overall, 68% of chronic sinusitis symptoms (including nasal obstruction, chronic cough, purulent discharge, postnasal drainage, halitosis, headaches, head pain or behavioral changes) resolved. Twenty-five of the thirty children were able to avoid surgery. Bothwell et al., (1999) suggest that children who have received the maximal traditional medical therapy of antibiotics for 1 month, should undergo at least a trial of anti-reflux therapy, if not a gastroenterology reflux workup before considering sinus surgery.

Treatment Options

Antibiotic Treatment

Antibiotic therapy should be tried with all pediatric chronic sinusitis, because of the high prevalence of microbial involvement. One month of treatment is recommended. For chronic sinusitis not responding to repeated medical therapy, sinus aspiration for culture and susceptibility testing and targeted antibiotic treatment should be considered (Slack et al., 2001, p.250).
The aerobic and anaerobic pathogens of pediatric chronic sinusitis appears to be polymicrobial. Slack et al., (2001) studied the prevalence of bacterial resistance among aerobic isolates from 240 children with chronic sinusitis.

The most frequent organisms found were Haemophilus Influenza (24%), Streptococcus pneumoniae (19%), Moraxella catarrhalis (17%), coagulase-negative Staphylococcus (6%), alpha-streptococci (6%) diphtheroids (5%), and Neisseria spp.(3%). Rates of nonsusceptibility of S. pneumoniae were 64% for Penicillin, 40% for cefotaxime, 18% for clindamycin and 0% for vancomycin. Thirty-nine percent of H. Influenza isolates and 100% of M. catarrhalis isolates were beta-lactamase-positive. (Slack et al, 2001, p. 248).

The researchers demonstrated that many of the aerobic bacteria found in pediatric chronic sinusitis are the same as those found in acute sinusitis. The authors point out that because maxillary sinus specimens can never be obtained in a sterile manner, the results may not represent pathogens, but rather commensals (ie. bacterial co-habitation without harm to the host). Maxillary sinus puncture and aspiration is one of the better techniques in acquiring specimens, but is technically difficult, not without complications, and poorly accepted by patients (Sokol, 2001). Rhinoscopically guided middle meatal culture is another effective technique used to obtain cultures, but require special equipment. These procedures are generally outside the scope of a primary care provider.

Brook, Frazier, & Foote, (1996) studied the transition from acute to chronic sinusitis. They demonstrated an initial presence of aerobic bacteria typical of acute sinusitis to a gradual emergence of Staphylococcus and anaerobes due to past exposure to antibiotic therapy. S. pneumoniae, H. influenzae, non-type b and M. catarrhalis were predominant. Subsequent aspirates showed a mixture of these plus anaerobes, including
Fusobacterium, Prevotella, Porphyromonas, and Peptostreptococcus. The aerobic organisms found were increasingly resistant to antibiotics.

One of the greatest limitations in the treatment of chronic sinusitis is the difficulty in getting useful microbial cultures. The Respiratory Surveillance Program (RESP) was done in an effort to elucidate trends in bacterial pathogen occurrence and antimicrobial resistance in the community office-based environment involving acute sinusitis. Many of the surveillance data available have focused attention on specimens that were collected from hospital-based laboratories or patients hospitalized with more severe infections that are most likely not representative of pathogens encountered in the community (Pfaller et al., 2001). The RESP study was done over a 10-month period. A total of 16,213 nasal swab samples were taken by primary care physicians in outpatient settings. The samples were sent to a central lab where pathogens were identified and antibiotic susceptibilities were done (Sokol, 2001). Physicians did nasal swabs based on their clinical impression of acute sinusitis. A pathogen was isolated in 34% of the samples. Haemophilus influenza was the most frequently identified pathogen followed by Streptococcus pneumoniae (11.3%), Moraxella catarrhalis (28.9%), and Staphylococcus aureus (17.9%) (Pfaller et al., 2001). H. influenzae isolates were more susceptible to azithromycin (Zithromax) (99.4%) than to clarithromycin (Biaxin) (64%), but were 100% susceptible to gatifloxacin (Tequin) and levofloxacin (Levaquin). Unfortunately in the pediatric population quinolones are generally avoided due to controversy related to joint arthropyathy. Strep pneumoniae had a 64% susceptibility to penicillin; 65% susceptibility to macrolides. Ninety-five percent of Strep pneumoniae isolates were susceptible to amoxicillin/clavulanate (Augmentin) and a 99.8% susceptibility to gatifloxacin (Tequin) and levofloxacin (table 3). Previous antibiotic use and susceptibility of organisms was
also studied and it was found that the use of antibiotics within the 3 months prior to the current clinic visit was associated with higher resistance of S. pneumoniae isolates to antibiotics (table 4). These results included the average of all 9 divided regions in the U.S.

As mentioned previously, otitis media is often associated with both acute and chronic sinusitis. Brook, Yocum, & Shad, (2000) studied the association of the occurrence of otitis media and chronic sinusitis in children. Interestingly, the sinus aspirates were mostly common aerobic isolates including Haemophilus influenza, Streptococcus pneumoniae, and Staphylococcus aureus (similar to the RESP study). Prevotella species, Peptostreptococcus species, and Fusobacterium nucleatum were the most common anaerobic bacteria recovered.

There is no single antibiotic that is effective in all cases of chronic sinusitis. Choices need to be made based on recent antibiotic treatment history (Slack et al., 2001). Augmentin (Penicillin and clavalanic acid), Ceftin (Cerfuroxime), Cefzil (Cefprozil), Clindamycin (Cleocin) (especially for S. pneumoniae), and Biaxin (Clarithromycin) are good choices for the treatment of chronic sinusitis. There is some question as to whether Azithromycin is able to penetrate the nasal sinus mucosa effectively. There are several studies that found that a 3-day course of Azithromycin, is as effective as a 10-day course of amoxicillin/clavulanate (Augmentin) in the treatment of sinusitis (Klapan, et. al, 1999; Ng et. al, 2000), but all the studies have been done with a small sample size and lack of a double-blind method.

The most common side effects of Augmentin are gastrointestinal upset and diarrhea. Macrolides (Biaxin, Clindamycin, and Cleocin), generally, cause nausea. The cephalosporins (Cefzil and Ceftin) can cause elevations in liver enzymes. Quinolones
can cause central nervous system aggravation and can raise caffeine and theophylline levels. Reports of bone arthropathies in young animals treated with quinolones has led to hesitancy to prescribe quinolones to children, however recent literature suggests the drug is safe to administer to children (Burkhardt, Walterspiel, & Schaad, 1997). It is important to realize that 90% of the quinolone drug is rendered ineffective, if given with magnesium, aluminum hydroxide, zinc, iron, or calcium, and parents should be advised not to give the drug concomitantly with antacids, vitamins, or milk products.

**Nasal Steroids**

Corticosteroids are potent anti-inflammatory agents that exert their effects by binding to a cytoplasmic steroid receptor. This complex formed within a pro-inflammatory cell, such as eosinophils, macrophages, and lymphocytes, causing inhibition of the cytokine/mediator that tends to be released causing an inflammatory response (Parikh et al., 2001).

Conflicting results about the efficacy of nasal steroids still abounds in the medical literature (Dolor et al., 2001). “The properties of corticosteroids that make them potentially useful include their ability to reduce mucosal swelling thereby facilitating drainage of the sinuses, reduction in tissue eosinophilia and their proven efficacy of corticosteroids in shrinking nasal polyps” (Kaliner et al., 1997, p. 66). Corticosteroids have proven effective in the treatment of allergic and nonallergic rhinitis (Kaliner et al., 1997).

Dolor et al., (2001), studied whether the addition of intranasal corticosteroids to antibiotic therapy affects the speed and rate of recovery of sinusitis. The study was a double-blind, randomized, placebo-controlled multicenter trial involving 95 adult patients with a history of recurrent sinusitis or chronic rhinitis. The researchers found that the
addition of fluticasone to cefuroxime therapy improved the rate of clinical success over patients receiving placebo (93.5% vs 73.9%; P=.009).

Most of the trials demonstrating the benefits of topical corticosteroid therapy have been focused on patients with nasal polyposis (Chalton et al., 1985; Lindholt et al., 1995; Lund et al., 1998; Parikh et al., 2001). Nasal steroids have been proven to shrink polyps and adenoids to such an extent that chronic sinusitis is often cured along with the associated anatomic blockage. More large-scale studies are needed to validate the efficacy of corticosteroid treatment in chronic sinusitis.

Nasonex (Mometasone furoate) is the only nasal steroid currently marketed and FDA approved for use in children 3 years and older. The approval follows the FDA’s review of clinical trials specifically designed to evaluate the safety and efficacy of Nasonex. The fear with nasal steroids has been the suspicion of possible delayed or inhibited growth in young children due to the corticosteroid suppression of the adrenal gland. Long-term clinical studies were conducted that have shown no statistically significant effect of Nasonex on the growth velocity in children (Doctor’s Guide, 2000).

For long-term treatment of chronic sinusitis, many practitioners advise the patient to use the nasal spray 3 weeks out of the month, stopping the use for 1 week to reduce the chemical irritant potential that can cause such side effects as epistaxis and sneezing (Turkoski, Lance, & Bonfiglio, 2001). Another method is to use the spray everyday for 1 month and then decrease to several times a week for long-term therapy. Practitioners often instruct patients to stop taking the medication during upper respiratory illnesses, as it is presumed that nasal steroids may aggravate or prolong the illness. Contrary to this non-evidence-based theory, Puhakka et al., (1998) have shown that the use of fluticasone
propionate (Flonase) for 6 days at the onset of a cold reduces progression to sinusitis, which is in direct opposition to current advice by many ENT specialists.

**Nasal Atrovent**

Vasomotor rhinitis may be treated topically with a 0.03% ipratropium bromide (Atrovent) nasal inhaler, as needed (Zeiger, 1992).

**Decongestants**

"Decongestants are vasoconstrictor agents that reduce the thickness of nasal mucosa. No controlled studies document the beneficial effects of topical or systemic vasoconstrictors" (Kaliner, 1997, p.67). With phenylpropanolamine having recently been pulled from the market due to a link between it and hemorrhagic strokes in women, pseudoephedrine remains the only effective decongestant on the market. Pseudoephedrine’s side effects include irritability, tremor, increased pulse rate, and insomnia in children and adults (Turkoski, Lance, & Bongiglio, 2001). Topical decongestants such as Afrin (Phenylephrine) are also effective in decreasing mucosal swelling, but if used for more than 3-7 days in-a-row can cause rebound congestion, causing many patients to become dependent on the medication.

**Mucolytics**

Guaiifenesin is a mucolytic agent that was created to thin respiratory secretions, but is being used more and more for sinus related disease. “It is thought to act as an expectorant by irritating the nasal mucosa and stimulating respiratory tract secretions, thereby increasing respiratory fluid volumes and decreasing phlegm viscosity” (Turkoski, Lance, & Bonfiglio, 2001, p.578).
in a double-blind study, Wawrose, Tami, & Amoils, (1992), gave 2400 mg of guaifenesin or placebo to 23 HIV-positive patients with chronic sinusitis. There were statistically significant improvements in nasal congestion and thick secretions in the experimental group compared to control subjects. With only one significant study, guaifenesin is being frequently prescribed to patients, often in combination with Sudafed (pseudoephedrine), but is not recommended for children under six. In order to be effective patients must be well hydrated, and this may be the actual reason for its apparent effectiveness. Common side effects include drowsiness, headache, rash, nausea, and vomiting (Trukoski, Lance & Bonfiglio, 2001).

Antihistamines

Antihistamines are not routinely used to treat chronic sinusitis. However, if there is a definite underlying allergic rhinitis that is the potential cause of the sinusitis, antihistamines may be called for. Antihistamines may dry out the paranasal passage, so much, that it thickens the mucus, inhibiting mucociliary clearance, and thus aggravating sinusitis instead of improving it (Zeiger, 1992). No reasonable rationale exists for the use of antihistamines because histamine does not seem to be involved in this disorder (Zeiger, 1992). More research needs to be conducted on the use of antihistamines.

Nasal Irrigation

Nasal irrigation for the alleviation of sinonasal symptoms is being stressed in clinics and in the literature. In a study done by Heatley, McConnell, Kille, & Leverson, (2001), 70% of subjects had improvement of their chronic sinusitis using daily nasal irrigation. “Saline irrigation of the nose is an inexpensive technique that can be used either alone or in conjunction with other interventions for paranasal sinus disease” (Heatley et al., 2001, p. 44). The physiologic reasons for the apparent effectiveness of
hypertonic nasal irrigation is unknown, but the assumption is that it removes and decreases viscosity of nasal secretions improving mucociliary transport (Ziegler, 1992).

**Adenoidectomy**

It is thought that the adenoids act as a reservoir for bacteria, causing chronic sinusitis. Ramadan, (1999) compared the success rate of endoscopic sinus surgery (ESS) with adenoidectomy. “This tightly controlled study involved patients in whom at least 6 months of medical treatment had failed and who were referred by the pediatric allergy service” (Ramadan, 1999, p. 3). The study revealed that the success rate was 77% for the ESS group and 47% in the adenoidectomy group. If enlarged adenoids that create characteristics symptoms of mouthbreathing and chronic runny nose are not removed, there is a potential to affect the development of the facial bones. If the mouth is kept open throughout the day, the tongue is not placed next to the roof of the mouth and the upper jaw becomes narrow with less room for the permanent teeth. The face becomes long and narrow, and dental surgery may be needed. Severe enlargement of the adenoids is associated with tonsil enlargement and sleep apnea. Other symptoms include voice changes with nasal, muffled quality. In this case, a chronic sinusitis infection is secondary to enlarged adenoids, and an adenoidectomy is needed. A chronic runny nose with bad breath should raise the suspicion for this problem (Pediatric Medicine, world wide web). Nasal steroids in children older than 3 should be considered because of the potential to reduce the size of the adenoids and may enable the patient to bypass surgery altogether.

**Functional Endoscopic Sinus Surgery**

The “basic purposes of endoscopic sinus surgery (ESS) are to remove the diseased ostiomeatal complex including the anterior ethmoid sinus and to reestablish
ventilation and drainage of the dependent larger sinuses" (Ikeda et al., 1997, p. 48). The final goal of ESS requires the restoration of mucociliary function (Ikeda et al., 1997). “Functional endoscopic sinus surgery (FESS) or endoscopic sinus surgery (ESS), has been accepted as a useful treatment for children with chronic sinusitis refractory to medical therapy” (Raz & Tunkel, 1999, p. 369). The word Functional in endoscopic sinus surgery refers to improving mucociliary flow by maintaining physiological function and anatomic structure. The technique frequently involves opening of the Ostial Meatal Complex (Gungor & Corey, 1997).

Raz & Tunkel, (1999) conducted a meta-analysis of articles retrieved from MEDLINE that reported new patient data on outcomes in pediatric FESS. Positive outcome of pediatric FESS in eight publications chosen ranged from 77% to 100%. Complications of FESS in children have raised concern. Surgical treatment in the pediatric population is controversial. Complications such as blindness, severe ear pain, and abnormal facial bone growth have made surgeons more conservative with operating on children. The growth plate areas in the nose are unknown and the fear is that these growth plates will be damaged during surgery, causing abnormal facial growth and deformity. “However, with the help of enhanced illumination and the angled, magnified views of endoscopes, pediatric ESS can be relatively safely preformed” (Rong-San Jiang, & Chen-Yi Hsu, 2000, p. 1113). Long-term effectiveness of surgery is still unknown.

“There has been a significant shift in the past 5 years or so from an initial emphasis on surgical treatment of chronic sinusitis in children and adults to a more recent emphasis on maximizing medical treatment with antibiotics” (Baroody, 2001, p. 2001). The reasons for the shift were due to the realization that opacification alone of the sinuses
was not a reason for surgery, as well as the fear of affecting facial growth as mentioned previously (Baroody, 2001).

CONCLUSION

Pediatric chronic sinusitis is often multi-factorial and poorly understood. Its contributing factors can confuse and frustrate even the most highly skilled practitioners. Despite recent advances in diagnostics tools, clinical judgement based on signs and symptoms still remains the single most important ability in the diagnosis of chronic sinusitis. Figure 8 presents an algorithm developed based on a review of the literature. It is meant to be used as a clinical guideline to help primary care providers in their decision making process in the diagnosis and treatment of chronic sinusitis. There is no definitive route to the diagnosis and treatment for pediatric chronic sinusitis and many aspects are highly controversial or lack extensive research on their efficacy, therefore this algorithm, as with any algorithm, should used with discretion.

It is important that providers stay up-to-date with the research. Using research-based evidence is important, but clinical judgement in the diagnosis and treatment of sinus disease is extremely important, because of the uncertainty that exists among experts in regards to treatment, as well as the underlying cause of the disease. Pediatricians, family physicians, physicians assistants and nurse practitioners need to assume responsibility for initial steps in attempting to resolve symptoms before considering referral. These responsibilities include:

1. Doing a complete history and physical with attention to possible immunodeficiency, seasonal allergies, reflux disease, associated asthma, frequent bronchitis, frequent otitis media infections, and signs of adenoid enlargement and airway obstruction.
2. Ensuring that the patient has been on appropriate antibiotics for an appropriate length of time.

3. Diagnosing chronic sinus disease based on clinical signs and symptoms.

4. Prescribing nasal steroids and/or antibiotics, based on history and physical, and using evidence-based research in prescribing these medications.

5. Making appropriate referrals when necessary.

If a practitioner suspects extensive sinus disease and is planning to refer a patient to an Otolaryngologist, it is appropriate to order a coronal CT scan and have the results sent to him/her. This will save time and money, eliminating an extra return visit to the specialist, because they will inevitably want a CT scan.

   Research that defines the role of antibiotics and other medical therapies (including topical and systemic corticosteroids, decongestants, and mucolytics) needs to be explored with greater scrutiny and detail. Lastly, practitioners should remember that treating the patient, not the symptoms, must be kept in mind. Because of the current “infancy” of a true understanding of the disease process as well as the multiple contributing factors, what works for one patient does not necessarily work for another.
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http://oac.med.jhmi.edu/LectureLinks/LectureNotes/Pathology/ChronicInflamm.Pas ter.HTML

Pediatric Medicine: ENT kids’ center. Retrieved March 2, 2002 from the World Wide Web:


http://www.niaid.nih.gov/final/immun.htm


### Table 1

<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage Present</th>
<th>Role in Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>60-80</td>
<td>First to appear after injury; phagocytosis</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>20-30</td>
<td>Immune response</td>
</tr>
<tr>
<td>Monocytes (Macrophages)</td>
<td>3-8</td>
<td>Phagocytosis</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1-6</td>
<td>Allergic reaction, parasite infection</td>
</tr>
<tr>
<td>Basophils</td>
<td>0-2</td>
<td>Contain histamine; mediate type I allergic reactions, initiate inflammation</td>
</tr>
</tbody>
</table>

(Copstead, 2000, p. 176 & Sacher & McPherson, 2000, p.38)
<table>
<thead>
<tr>
<th>Immune Modulator</th>
<th>Also Known as</th>
<th>Origin</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon-gamma</td>
<td>Immune interferon</td>
<td>Lymphokine secreted By activated T-cells</td>
<td>Inhibits virus replication; promotes antigen expression</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Activates macrophages;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inhibits cell growth</td>
</tr>
<tr>
<td>Tumor necrosis factor</td>
<td>Cachectin</td>
<td>Monokine</td>
<td>Induces leukocytosis, fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Weight loss, inflammation,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Necrosis of some tumors;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Stimulates lymphokine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Synthesis; activates</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Macrophages; toxic to viruses</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>And tumor cells</td>
</tr>
<tr>
<td>Interleukin-4 (IL-4)</td>
<td>B-cell stimulating</td>
<td>Lymphokine</td>
<td>Promotes T-cell/B-cell</td>
</tr>
<tr>
<td>Factor I</td>
<td>Factor</td>
<td></td>
<td>interactions; promotes</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>CD4 cells</td>
<td>Synthesis of IgE by B-cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mast cells, basophils</td>
<td>And T-cell growth; promotes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mast cell and hematopoietic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cell growth.</td>
</tr>
<tr>
<td>Interleukin-5 (IL-5)</td>
<td>T-cell replacing</td>
<td>Lymphokine</td>
<td>Promotes the growth and</td>
</tr>
<tr>
<td>Factor Eosinophil</td>
<td>Factor</td>
<td></td>
<td>differentiation of B-cells</td>
</tr>
<tr>
<td>Differentiation</td>
<td>Factor</td>
<td>secreted by T-cells</td>
<td>to secrete IgA; induces</td>
</tr>
<tr>
<td>Factor</td>
<td></td>
<td>CD4 helper cells</td>
<td>Differentiation of eosinophils.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Natural Killer cells</td>
<td></td>
</tr>
<tr>
<td>Interleukin-13 (IL-13)</td>
<td>none</td>
<td>TH2 lymphocytes</td>
<td>exhibits antiinflammatory</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Activity by inhibiting IL-1B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TNP-alpha, IL-8, and IL-6.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Enhances monocyte and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>B lymphocyte differentiation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>And proliferation; induces</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IgG and IgE class switching</td>
</tr>
<tr>
<td>Interleukin-12</td>
<td>none</td>
<td>TH1 lymphocytes</td>
<td>Mediates chronic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inflammatory processes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Causing cellular inflammation</td>
</tr>
</tbody>
</table>

Sources: Copstead, 2000, Feghali & Wright, 1997.
<table>
<thead>
<tr>
<th></th>
<th>Streptococcus pneumonia</th>
<th>Haemophilus influenzae</th>
<th>Moraxella catarrhalis</th>
<th>Staphylococcus aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% S/I/R (not tested)</td>
<td>% S/I/R (not tested)</td>
<td>% S/I/R (not tested)</td>
<td>% S/I/R (not tested)</td>
</tr>
<tr>
<td></td>
<td>N=618</td>
<td>N=1,189</td>
<td>N=1,588</td>
<td>N=983</td>
</tr>
<tr>
<td>Penicillin</td>
<td>64/20/16 (2)</td>
<td>Not done</td>
<td>8.5/0/91.5 (1)</td>
<td>10.8/0/89 (6)</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>99.8/0/0 (2)</td>
<td>100/0/0 (3)</td>
<td>100/0/0 (7)</td>
<td>97/1.1/2.0 (6)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>68/0.3/32 (2)</td>
<td>Not done</td>
<td>85/13/2 (7)</td>
<td>39/32/29 (7)</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>64.7/0.6/34.7 (264)</td>
<td>99.4/0/0.6 (3)</td>
<td>100/0/0 (324)</td>
<td>31.2/18.7/50.1 (448)</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>65/0/35 (264)</td>
<td>64/31/5 (3)</td>
<td>100/0/0 (324)</td>
<td>68.8/2.1/29.2 (448)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>99.8/0/0.2 (2)</td>
<td>100/0/0 (3)</td>
<td>100/0/0 (7)</td>
<td>95.1/1.6/3.3 (6)</td>
</tr>
</tbody>
</table>

I= Intermediate susceptibility; R= Resistant ; S= Susceptible

Sokol, 2001, p.21S.
Table 4

Correlation Between *Streptococcus pneumoniae* Antimicrobial Sensitivity and Patient’s Prior Antibiotic Exposure in the Past 3 Months

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>No Prior Antibiotic</th>
<th>Previous B-Lactam</th>
<th>Previous Macrolide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>67% (340/505)</td>
<td>45% (25/55)</td>
<td>48% (14/29)</td>
</tr>
<tr>
<td>I</td>
<td>19% (97/505)</td>
<td>20% (11/55)</td>
<td>31% (9/29)</td>
</tr>
<tr>
<td>R</td>
<td>13% (66/505)</td>
<td>35% (19/55)</td>
<td>21% (6/29)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S</td>
<td>72% (365/505)</td>
<td>49% (27/55)</td>
<td>45% (13/29)</td>
</tr>
<tr>
<td>I</td>
<td>0.4% (2/505)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>R</td>
<td>27% (136/505)</td>
<td>51% (28/55)</td>
<td>55% (16/29)</td>
</tr>
</tbody>
</table>

I= intermediate susceptibility; R= resistant; S= susceptible

*S. pneumoniae* isolated from a nasal/pharyngeal swab during the current sinusitis episode. Prior antibiotic may have been prescribed for any reason, not necessarily previous sinusitis. (Sokol, 2001, p. 228.)
Paranasal Sinuses

- Frontal sinus
- Maxillary sinus
Figure 2

- Left orbit
- Middle nasal concha
- Nasal cavity
- Nasal septum
- Inferior nasal concha
- Molar tooth
- Palate

Paranasal Sinuses
Figure 3
Figure 4
Frontal sinus
Nasofrontal duct opening
Semilunar hiatus
Uncinate process
Maxillary sinus opening

Figure 5
Figure 6

Brain
Nasal cavities
Nasal septum
Middle nasal concha
Middle nasal meatus
Inferior nasal meatus
Maxillary sinus
Inferior nasal concha
Hard palate
Tongue
Figure 7

- Frontal sinus
- Orbital fat
- Ethmoidal cells
- Maxillary sinus opening
- Infraorbital recess of maxillary sinus
- Zygomatic recess of maxillary sinus
- Alveolar recess of maxillary sinus
- Alveolar process of maxilla
Figure 8: Approach for primary providers to the management of chronic sinusitis

**Initial Diagnosis: Acute Sinusitis**
History of recent Upper Respiratory Infection
Or history of allergic rhinitis. With 2 or more of the following symptoms:
Symptoms of:
Pharyngitis, postnasal drip, halitosis, facial pressure, facial pain, fever, lethargy, cough, asthma, purulent secretions, pain with leaning forward, headache.

**Persistent symptoms after 2 weeks:**
1. Second Line Antibiotics give for 4-6 weeks
   a. Amoxicillin-clavulante (Augmentin)
      40mg/kg/24 hr TID.
   Or
   b. Clarithromycin (Biaxin)
      15mg/kg/24 hr BID
   Or
   c. Cefuroxime axetil (Ceftin)
      20-30 mg/kg/24 hr BID

**Diagnosis of Chronic Sinusitis based on clinical Evidence:**
1. 1 or more persistent symptoms for at least 3 months after medical treatment that is corroborated with a positive CT.
   Symptoms can include:
Purulent nasal discharge • headache • nasal congestion • cough • wheezing • post nasal drip • Sore throat • halitosis • allergic shiners • Facial pressure

**Additional Clues to sinus involvement**
Behavioral changes • throat clearing • family of immunodeficiency • HIV infection • history of Cystic fibrosis • frequent otitis media with effusion

**Baseline limited CT scan**
Evaluate for asthma
Evaluate for allergies (skin test)

1. Nasal Steroids (re-evaluate X 1 month, if no improvement refer To an ENT
2. Nasal Irrigation

**Negative for Allergies/asthma**

1. Nasal Steroids
2. Antibiotics X 30 days
3. ENT Referral for +CT of anatomic abnormalities or mucosal thickening > 4mm.

**Initial Treatment:**
1. First line Antibiotics for 2 weeks.
   a. Amoxicillin (40mg-80 mg/Kg/24 hour TID.
   Or
   b. Trimethoprim-sulfameth oxazole (Bactrim sulfa)
      8-40 mg/kg/24 hr BID
   Or
   c. Cefprozil (Cefzil)
      30mg/kg/24 BID

**Symptoms Resolved**

**Resolution of Acute Or Recurrent Sinusitis**

Obtain History and review past medical Records. Do full complete physical exam.

**Suspicion of immune Deficiency (recurrent infection)**
otitis media, pneumonia, bronchitis.

**Evaluate for IgG, IgA, IgM immunodeficiency**
Refer to Immunologist
Sources for Figure 4: (Hamilos, 2000); (Chan et al., 1999); & (Gungor & Corey, 1997).