

Chronic Rhinosinusitis in Children

Austin S. Rose, MD*, Brian D. Thorp, MD, Adam M. Zanation, MD,
Charles S. Ebert Jr, MD, MPH

KEYWORDS

• Pediatric sinusitis • Chronic rhinosinusitis • Treatment • Management • Surgery

KEY POINTS

- Chronic rhinosinusitis (CRS) represents a heterogeneous spectrum of diseases.
- The definition of CRS has largely been accepted as the persistence of characteristic signs and symptoms beyond 12 weeks.
- Few randomized, placebo-controlled trials or systematic reviews of the literature exist with recommendations for treatment of CRS in children.
- The medical management of CRS has traditionally included combinations of antihistamines, decongestants, nasal saline irrigation, topical nasal steroids, and oral antibiotics.
- When prolonged efforts at medical therapy have failed, children with persistent CRS should be referred to an otolaryngologist for further evaluation and possible surgical intervention.

CLASSIFICATION OF CRS

Rhinosinusitis can be considered a spectrum of disease characterized by concurrent inflammatory and infectious processes that affect the nasal passages and the contiguous paranasal sinuses.^{1–3} Diagnosis and management are aided by the classification of this diverse condition into categories based primarily on the duration of symptoms. In addition, pediatric rhinosinusitis, whether acute or chronic, should be considered a unique conditions because of the differences in predisposing factors and the anatomy of the sinuses seen between children and adults.

Because common viral upper respiratory infections (URI) and acute sinusitis can be difficult to distinguish clinically, acute episodes of sinusitis have traditionally been defined as the persistence of signs and symptoms beyond 10 days, or the concomitant occurrence of related complications, such as orbital abscess or meningitis. Other classifications described in the literature include recurrent acute sinusitis, subacute

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Department of Otolaryngology - Head & Neck Surgery, University of North Carolina School of Medicine, CB #7070, Chapel Hill, NC 27599-7070, USA

* Corresponding author.

E-mail address: austin_rose@med.unc.edu

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sinusitis, eosinophilic sinusitis, sinusitis with and without nasal polyps, and relatively distinct disease processes, including invasive and allergic fungal sinusitis.

The definition of CRS has largely been accepted as the persistence of characteristic signs and symptoms beyond 12 weeks. This extended period of chronic symptoms may also be punctuated by episodes of acute exacerbations.

PATHOPHYSIOLOGY

Along with the nasal passages, the paranasal sinuses filter, warm, and humidify inspired air. They are also key in reducing the overall weight of the human skull. Sinuses grow in size and shape throughout childhood, although this progression may be affected by various disease processes, such as cystic fibrosis (CF).⁴ The result is an underdeveloped or hypoplastic sinus. The frontal sinuses are the last to fully develop, and generally reach adult size by puberty.

The mucosa of the paranasal sinuses is composed of a ciliated, pseudostratified, columnar epithelium with goblet cells for mucous production, and is similar to that found in the remainder of the tracheobronchial passages. Normal function of the sinuses depends on patent ostia, including the important common pathway of drainage and aeration known as the *osteomeatal complex* (OMC) (Fig. 1), and on normal mucous secretion and normal ciliary function. The primary common factor in the pathophysiology of sinus disease is thought to be obstruction of the sinus ostium, either through mechanical means or mucosal inflammation and edema, rather than initial bacterial infection. Obstruction leads to retained secretions and blocks the normal exchange of air, resulting in hypoxia of the sinus mucosa. This process leads to a cycle of mucosal dysfunction characterized by impaired cilia, further retention of secretions, and secondary infection.

Traditionally, normal sinuses, unlike other areas of the upper aerodigestive tract, have been thought to be sterile and without a normal and possibly protective microbial

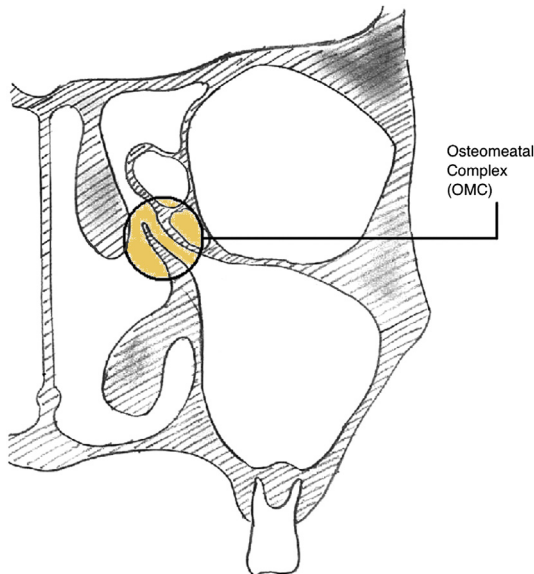


Fig. 1. Diagram of the OMC.

population, although some recent studies suggest otherwise. Abreu and colleagues⁵ describe a reduced diversity of sinus microbes in patients with CRS compared with healthy controls. They also used a murine model of CRS to demonstrate the possible protective effects of one organism in particular: *Lactobacillus sakei*. Although many questions remain, these findings may support a new paradigm in which the disturbance of normal sinus microbial populations proves to be an important factor in the pathogenesis of CRS in children. Given their overuse in routine URIs, antibiotics are certainly one factor that might be expected to disrupt normal sinus flora and therefore could potentially be more causative than curative in CRS.

A host of other innate and environmental factors also contribute to the common pathophysiologic pathways in CRS (Table 1). Local or anatomic factors include direct sinus obstruction caused by anatomic abnormalities, such as the presence of concha bullosa, septal deviation, nasal polyposis, trauma, and foreign bodies. Conditions contributing to mucosal inflammation and secondary obstruction include URI, bacterial infection, allergy, and gastroesophageal reflux disease (GERD). GERD in particular is known to be prevalent in children with CRS⁶ and, in a retrospective study, Bothwell and colleagues⁷ demonstrated a significant decrease in the need for sinus surgery among children on antireflux therapy. In addition to allergens, environmental irritants such as air pollutants or tobacco smoke may occasionally play a role in chronic mucosal inflammation.

Bacterial infection has long been considered a key component of CRS, and the pathogens found in children are generally similar to those in adults. The common isolates associated with CRS include those found in acute sinusitis (*Streptococcus pneumoniae*, *Moraxella catarrhalis*, and nontypeable *Haemophilus influenzae*) and *Staphylococcus aureus*, *Pseudomonas*, and anaerobes. The possible role of relatively ubiquitous fungi in the CRS inflammatory response has also been proposed, although this remains controversial.⁸

Recent evidence has also supported the role of bacterial exotoxins and biofilm formation in the pathogenesis of CRS. Exotoxins are released by bacteria and may contribute to a symptomatic immune response. In particular, Wang and colleagues⁹ demonstrated the presence of staphylococcal exotoxin and its effect on T cells in patients with CRS with nasal polyps. Biofilms form when bacteria aggregate on surfaces within an external matrix of polysaccharides, nucleic acids, and proteins. In CRS, biofilm formation may decrease the efficacy of antimicrobials by as much as 100 fold, allowing bacteria to thrive for a prolonged period within the nose and sinus cavities. In 2005, Sanclement and colleagues¹⁰ used electron microscopy to demonstrate the presence of biofilms in sinus biopsies from 80% of patients undergoing functional endoscopic sinus surgery (FESS) for CRS, whereas none were seen in healthy controls. Other studies have reported the presence of biofilms in adenoid tissue from patients with chronic infectious disease of the upper airways, including

Table 1
Contributing factors in CRS

Local	Inflammatory	Systemic
Sinus obstruction	URI	CF
Septal deviation	Bacterial infection	Primary ciliary dyskinesia
Nasal polyps	Allergy	Immune deficiencies
Trauma	Gastroesophageal reflux disease	
Foreign body	Tobacco smoke	

CRS.¹¹ The literature suggests that both exotoxins and biofilms may be important factors in the role of bacterial infection in CRS.

When evaluating a child with symptoms of CRS, one should always consider the possibility of underlying disease as a contributing factor. Diseases impacting normal sinonasal function include CF, primary ciliary dyskinesia (PCD), and a variety of immune deficiencies, including the still-developing immature immunity of normal young children.

DIAGNOSIS

Careful history and physical examination is clearly important in the evaluation of this heterogeneous and multifactorial disease. The symptoms of CRS in children are different than in adult patients and include persistent cough, and prolonged anterior and posterior nasal drainage, congestion, low-grade fever, irritability, and behavioral difficulties (**Box 1**). Headache, especially in the frontal area, is a less common complaint among children than adults. Parents may report a history of frequent URI or recurrent acute episodes of sinusitis requiring treatment. Additional history should focus on identification of any potential underlying diseases or contributing environmental factors. The diagnosis of CRS is rarely made in isolation, and commonly associated findings include allergy, asthma, dental disease, CF, PCD, and immunodeficiency syndromes. A nasal foreign body should be considered in children with a history of prolonged unilateral rhinorrhea and a foul odor reported by parents.

Physical examination includes a complete head and neck evaluation with careful attention to the middle ear, because otitis media with effusion (OME) is another common comorbidity. Anterior rhinoscopy (**Fig. 2**) should be performed with a nasal speculum or otoscope using a large ear speculum. Characteristic findings are summarized in **Table 2** and include mucosal erythema and irritation, thickened nasal mucous, polyps, and frank purulent drainage. Periorbital allergic shiners or a pronounced nasal crease may indicate adenoid enlargement or disease. Otolaryngologists will usually include fiberoptic sinonasal endoscopy as part of their examination when possible, allowing improved visualization of the middle meatus, a common site of polyps or purulent drainage from the maxillary and ethmoid sinuses. Endoscopy is also useful for visualizing the posterior nasal cavity, nasopharynx, and adenoid tissue.

The radiologic evaluation of children with suspected CRS is generally reserved for those with disease refractory to medical management. Plain films, computed tomography (CT), and magnetic resonance imaging have all been used in the evaluation of chronic sinusitis; however, CT scanning is generally considered the preferred study

Box 1 CRS symptoms
Nasal congestion
Purulent rhinorrhea
Chronic cough
Postnasal drainage
Low-grade fevers
Irritability
Behavioral issues

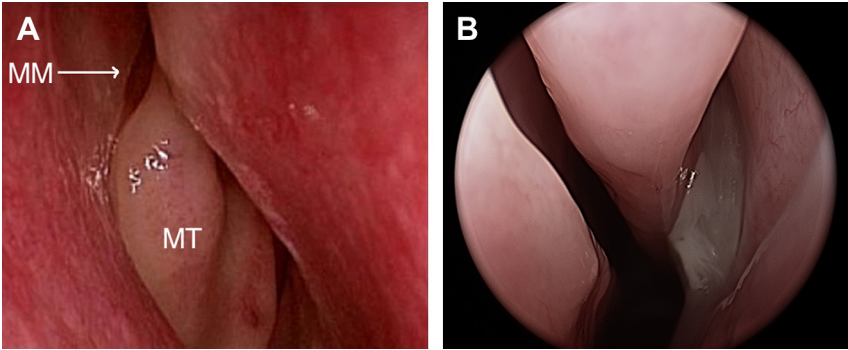


Fig. 2. (A) Normal anterior rhinoscopy with view of the middle turbinate (MT) and middle meatus (MM). (B) Anterior rhinoscopy demonstrating purulent drainage from the middle meatus.

(Fig. 3). CT provides a much higher resolution of bone and soft tissue without the interference of overlying structures compared with plain radiography.¹²

Recent literature has supported restraint in the use of CT scanning in children because of concerns of excess radiation exposure.¹³ In evaluating CRS, most otolaryngologists advocate CT scans of the sinuses only when deciding on surgical intervention. In most cases, these scans can also be used intraoperatively, without additional radiation exposure, for image guidance to help reduce the risk of complications during sinus surgery. In a 2012, clinical consensus statement for the American Academy of Otolaryngology-Head and Neck Surgery Foundation, Setzen and colleagues¹⁴ reported a strong consensus (>75% of the panel) for the statement “CT imaging is indicated in pediatric patients for chronic sinusitis when medical management and/or adenoidectomy have failed to control symptoms.”

FURTHER EVALUATION

Beyond history-taking and physical examination, the further workup and evaluation of children with suspected chronic sinusitis should include steps to identify or eliminate associated or causative factors (**Box 2**).

- Allergy testing, including total IgE and either serum radioallergosorbent testing or skin end point titration testing can be used to identify children with underlying allergies. Ultimately, immunotherapy may prove beneficial in appropriate patients.
- Bacterial cultures can evaluate for specific pathogens and help guide antimicrobial treatment. Sinus aspirates for culture-directed treatment can be obtained via sinus trephination or intraoperatively. Cultures from the middle meatus are

Table 2 CRS physical findings	
Nasal Examination	Head & Neck Examination
Nasal congestion	OME
Purulent drainage	Allergic shiners
Mucosal erythema	Nasal crease
Increased mucous	Sinus tenderness
Nasal polyps	Reduced transillumination

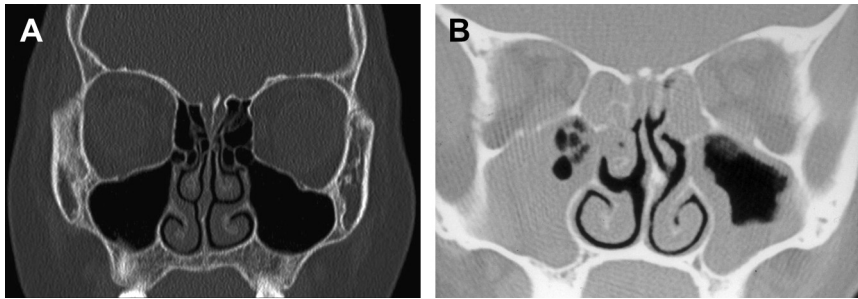


Fig. 3. (A) A normal coronal CT scan of the sinuses. (B) A coronal CT scan of the sinuses demonstrating bilateral ethmoid sinus opacification, maxillary sinusitis on the right and mucosal thickening within the maxillary sinus on the left.

generally easier to obtain in most cases, and have a high predictive value in the diagnosis of bacterial sinusitis.¹⁵

- Immunologic testing can diagnose immunodeficiencies and usually includes levels of IgG with subclasses, IgA, and postvaccination titers.
- Sweat chloride or CF genetic testing can be used to rule out CF.
- A nasal or tracheobronchial ciliary biopsy can be obtained to evaluate ciliary function and rule out PCD. Usually, both light microscopy and electron microscopy are performed.
- An otolaryngology referral is recommended for children with suspected CRS refractory to medical management and can facilitate further evaluation and treatment, including fiberoptic nasal endoscopy and surgical intervention, such as adenoidectomy and, if necessary, endoscopic sinus surgery.
- Other consultations that may be of significant help in a multidisciplinary approach to CRS include pediatric allergy and immunology and pediatric pulmonary medicine.

MEDICAL TREATMENT

Evidence suggests that CRS can resolve spontaneously in children and that complications are rare.¹⁶ Still, the various contributing factors in the pathogenesis of CRS

Box 2

CRS workup and evaluation

Allergy testing

Sinus aspirate or middle meatus cultures

Immunologic testing

Sweat chloride or genetic testing for CF

Ciliary biopsy to rule out PCD

Possible consultations:

Pediatric allergy and immunology

Pediatric pulmonary medicine

Otolaryngology

afford several potential targets in treatment when necessary for persistent disease. However, few randomized controlled trials or systematic reviews of the literature exist with recommendations for treatment of this complex disease in children. Much of what is known, therefore, about the efficacy of therapies for CRS is based on findings in adult populations or studies of acute sinusitis. For example, a recent review of the Cochrane and PubMed databases by Makary and Ramadan¹⁷ revealed no randomized controlled studies comparing medical treatment with FESS, or other surgical procedures, for CRS in children.

The medical management of CRS has traditionally included combinations of antihistamines, decongestants, nasal saline irrigation, topical nasal steroids, and oral antibiotics. In a survey of pediatric otolaryngologists in 2005, Sobol and colleagues¹⁸ reported that 95% of respondents used antibiotics in the treatment of CRS, whereas 90% prescribed topical steroids and 68% recommended nasal saline spray. Antihistamines and decongestants are commonly used in suspected sinusitis because of their role in reducing mucosal edema, and to treat any component of underlying allergy. However, in a recent Cochrane systematic review of acute sinusitis, no significant evidence was found to support the use of antihistamines or decongestants.¹⁹

Nasal saline sprays, or irrigations when tolerated, are also used in the treatment of CRS, and are thought to help primarily in the clearance of sinonasal secretions, pathogens, and debris. Although the Cochrane review could not support any recommendations regarding nasal saline irrigation either, several studies have shown some degree of efficacy in CRS. In a prospective study of 40 children, Wei and colleagues²⁰ showed a significant improvement in both quality of life and CT scan Lund-Mackay scores after 6 weeks of once-daily nasal saline irrigation. Other reviews of the literature also support a clinical benefit from the use of topical nasal saline.²¹ For the most part, the use of regular nasal saline sprays or irrigation is well tolerated in children, with minimal side effects.

Topical nasal steroids suppress mucosal inflammation and are also therefore widely used in the treatment of CRS in children. Examples include fluticasone propionate, which is widely available in generic form, and mometasone furoate, which is indicated for use in nasal congestion because of allergic rhinitis for children 2 years of age and older. Evidence is limited but supports the use of both intranasal and systemic corticosteroids in the treatment of sinusitis, either alone or in combination with antibiotic therapy.^{22,23} The use of topical nasal steroids is generally preferred for children with CRS because of their low systemic bioavailability. Systemic side effects are therefore rare, with minor epistaxis the most commonly reported complication.²⁴ The duration of treatment generally coincides with the longer courses of antibiotics used in CRS, typically 3 to 6 weeks, although long-term prophylactic use seems safe and may help suppress chronic symptoms and recurrent disease. Although controversial, nasal steroids may also have a role in combination with surgery as part of a postoperative and preventive medical regimen along with nasal saline. Although Dijkstra and colleagues²⁵ found no effect on the recurrence of CRS symptoms or nasal polyps after FESS, others have shown a decreased need for revision surgery in patients with CRS treated with topical nasal steroids postoperatively.²⁶

The use of antibiotics in treating acute sinusitis is generally accepted. In choosing a particular agent, however, one should consider the likely offending pathogens and any information on local patterns of antibiotic resistance. Recent guidelines from the Infectious Diseases Society of America include prompt treatment for children with suspected acute bacterial sinusitis.²⁷ Amoxicillin/clavulanate, or levofloxacin for children with type I hypersensitivity reactions to penicillin, for 10 to 14 days was recommended as first-line treatment.

In CRS, available evidence suggests that longer courses of antibiotic treatment (3–12 weeks) are necessary to achieve any significant benefit.²⁸ In the absence of culture data, amoxicillin/clavulanate remains a good choice for first-line treatment, although antibiotic choices should also reflect the differences in possible pathogens in CRS, including *S aureus*, *Pseudomonas*, and anaerobes. Long-term macrolide treatment (12 weeks) may also be of benefit in patients with CRS with low IgE levels.²⁹

Although oral and sometimes intravenous are the most frequently used routes of antibiotic administration in CRS, the potential for topical antibiotic therapy has also gained recent attention.⁸ The theory is that topical treatment, via spray, nebulizer or irrigation, should serve to deliver a high concentration of antibiotic directly to the sino-nasal mucosa while minimizing systemic side effects. Although recent reviews have not supported the use of topical antibiotics for CRS, several studies have reported symptomatic improvement.^{30,31} Uren and colleagues³² treated 16 patients with surgically recalcitrant CRS and endoscopic cultures positive for *S aureus*. After 3 weeks of twice-daily topical mupirocin, 12 patients were improved symptomatically, with 15 demonstrating an improvement in endoscopic findings and negative cultures.

So far little evidence has shown that topical antibiotics are effective in reducing biofilm formation, although, perhaps surprisingly, regression of biofilms has been reported in patients with CRS after 8 weeks of treatment with oral clarithromycin.³³ Although topical antibiotic treatment is not currently recommended in most cases of CRS, initial findings do seem to warrant further study. Questions regarding dosage, length of therapy, optimal method of delivery, and the potential for combination with other treatments remain to be answered. In summary, topical nasal steroids, nasal saline, and systemic antibiotics when necessary remain the preferred medical treatments for CRS in children based on the best evidence to date.

SURGICAL TREATMENT

When prolonged efforts at medical therapy have failed, children with persistent CRS should be referred to an otolaryngologist for further evaluation and possible surgical intervention. Adenoidectomy is the first line of surgical treatment and is often performed even before radiologic imaging with CT. Large adenoids may physically disrupt the normal mucociliary clearance of the nasal cavity and sinuses, although adenoid tissue of any size is thought to act as a reservoir for bacteria. Evidence also suggests frequent biofilm formation on adenoid tissue in children with CRS.³⁴ A 2008 meta-analysis of adenoidectomy in children with rhinosinusitis found an overall rate of clinical improvement of approximately 70%, consistent with prior studies.³⁵ In teenage children, adenoid tissue may tend to recede and become less clinically relevant. For this age group, endoscopic sinus surgery, either with or without treatment of adenoid tissue, may be considered more frequently as an acceptable initial surgical procedure.³⁶

The goal of sinus surgery beyond adenoidectomy is generally to enlarge the natural opening of the sinuses, while preserving normal sinus mucosa, in an effort to reestablish sinus aeration and normal mucociliary function. Surgical intervention may also include the removal of any obstructive or diseased tissue, such as nasal polyps. A CT scan is often obtained at this point to demonstrate persistent sinus disease despite maximal medical therapy, and for a careful review of sinonasal anatomy for preoperative planning.

In recent years, the refinement of fiberoptic endoscopes has allowed for most sinus surgery to be performed endoscopically. In children, the most common procedure is limited FESS and involves widening of the natural ostium of the maxillary sinus along

with a limited or anterior ethmoidectomy. Some surgeons, however, recommend a complete removal of the anterior and posterior ethmoid cells, resulting in a larger, better-aerated, and well-mucosalized ethmoid cavity. More recently, balloon dilation of sinus ostia known as *balloon catheter sinuplasty* (BCS) has been reported as an alternative to conventional FESS. In children, this is primarily used for treatment of the maxillary sinus and has been described both alone and in combination with other procedures, such as adenoidectomy and ethmoidectomy.

Although surgery is clearly indicated for complications of acute sinusitis or underlying disease such as allergic fungal sinusitis, its role in CRS is less clear. Sinus surgery in CRS is probably best thought of as an adjuvant treatment to medical therapy, with the goal of improving sinus function. Parents should be counseled about reasonable expectations for symptomatic improvement, because children will remain prone to URIs, allergies, and other underlying factors. A reduction in the frequency and severity of symptoms is a reasonable goal, and many children will benefit from continued medical management, including topical nasal steroids and saline postoperatively. In fact, the enlargement of sinus ostia achieved through sinus surgery may also improve the delivery and efficacy of topical treatments such as nasal steroid sprays and saline irrigations.

In terms of the efficacy of FESS in children, most studies are retrospective, although they demonstrate significant clinical improvement for CRS refractory to medical treatment and adenoidectomy. In 2009, Siedek and colleagues³⁷ reported a 76% rate of improvement in both CRS symptoms and overall quality of life. In a review of 11 studies, Makary and Ramadan¹⁷ found a success rate for pediatric FESS ranging from 82% to 100%. In a study of adults aged 18 years and older, a recent prospective trial found a greater improvement for patients with CRS treated with FESS compared with those managed medically. After 12 months of follow-up, the surgical patients also reported significantly less use of oral antibiotics and steroids and fewer missed days of work or school.³⁸ Results also seem to be lasting, with one study showing the symptomatic benefits of FESS over medical therapy as far out as 10 years.³⁹

Although BCS is appealing as a potentially less invasive technique, its role in children with CRS seems limited to treatment of the maxillary sinuses (**Fig. 4**). Most children lack full development of the frontal sinuses, and dilation is not a particularly effective method for ethmoidectomy. Still, Ramadan and colleagues⁴⁰ showed safety of the procedure and an improvement in symptoms for children undergoing BCS, both by itself and with concurrent adenoidectomy. A subsequent prospective

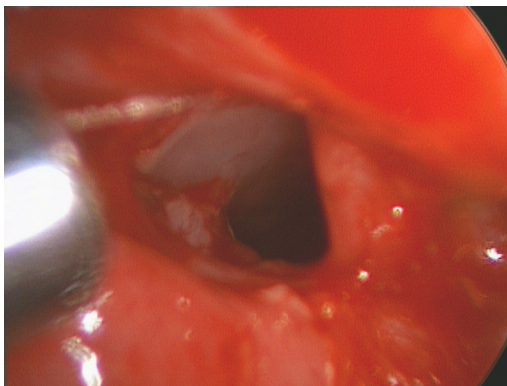


Fig. 4. Dilated maxillary sinus ostium immediately after balloon catheter sinuplasty.

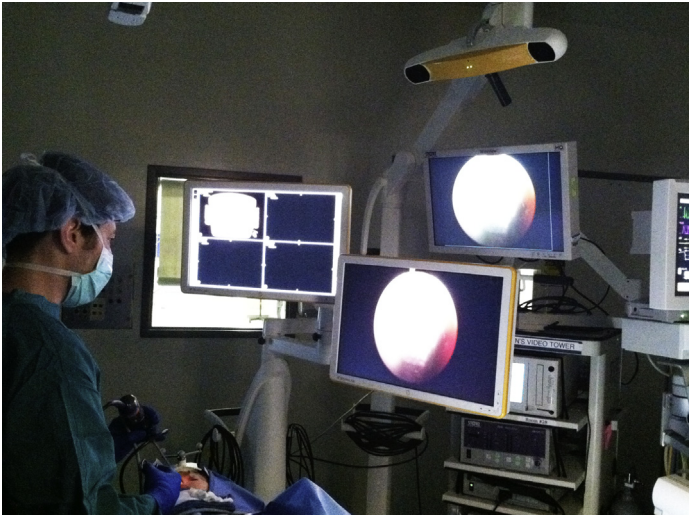


Fig. 5. Endoscopic sinus surgery with use of intraoperative CT image guidance.

review suggested that BCS may be even more effective than adenoidectomy in the treatment of pediatric CRS.⁴¹ In addition, a 2012 review found BCS combined with traditional endoscopic ethmoidectomy comparable to FESS in terms of clinical improvement. The BCS/ethmoidectomy group also required fewer antibiotics post-operatively over 4 months of follow-up.⁴² A recent Cochrane review, however, found insufficient evidence to recommend BCS over FESS for the treatment of chronic sinusitis.⁴³

Although safe, the potential complications of endoscopic sinus surgery include bleeding, infection, recurrent disease, cerebrospinal fluid leak, and orbital injury, including hematoma and loss of vision. Makary and Ramadan¹⁷ estimated an overall complication rate of 1.4%. In this study, no cases of cerebrospinal fluid leak or major orbital injury such as hematoma or blindness were reported, supporting the relative safety of FESS. Further reducing the risk of complications, the intraoperative use of CT image guidance has quickly become a routine part of endoscopic sinus surgery, and may also facilitate more complete removal of diseased tissue (**Fig. 5**).

SUMMARY

CRS in children is a multifactorial disease, and the evidence seems to support combined approaches to treatment, including medical and, when necessary, surgical options (**Table 3**). As the pathogenesis becomes clearer through ongoing basic

Table 3 Evidence-based treatment in CRS	
Medical	Surgical
Watchful waiting	Adenoidectomy
Nasal saline spray/irrigation	Limited FESS
Topical nasal steroids	Balloon catheter sinuplasty
Antibiotics	

science research, the ability to treat CRS effectively and safely in children should continue to improve. The potential roles of protective sinonasal flora and biofilm formation are important areas for further investigation, as are the possible benefits of topical antimicrobial therapy. Regardless of future developments, careful history, physical examination, and workup will remain vital in the diagnosis and management of this disease, as will close communication and cooperation between pediatricians and their colleagues in pediatric allergy and immunology, pediatric pulmonary medicine, and otolaryngology.

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