HHS Public Access

Author manuscript

Curr Treat Options Allergy. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

Curr Treat Options Allergy. 2016 September ; 3(3): 268–281. doi:10.1007/s40521-016-0096-y.

Pediatric Rhinosinusitis

Dana T. Badr, MD[1], **Jonathan M. Gaffin, MD, MMSc**[2,3], and **Wanda Phipatanakul, MD, MS**[3,4]

[1]Department Of Pediatric and Adolescent medicine, American University of Beirut Medical Center, Lebanon

[2]Division of Respiratory Medicine, American University of Beirut Medical Center, Lebanon

[3]Boston Children's Hospital, Harvard Medical School, American University of Beirut Medical Center, Lebanon

[4]Division of Allergy and Immunology, American University of Beirut Medical Center, Lebanon.

Opinion statement

Rhinosinusitis, is defined as an inflammation of the paranasal and nasal sinus mucosae. Chronic rhinosinusitis (CRS)is a common problem in the pediatric age group and the diagnosis and treatment are challenging due to the chronicity and similarity of symptoms with allergic rhinitis and adenoid hypertrophy.

Although it is less common than acute rhinosinusitis, CRS is becoming more frequent and significantly affects the quality of life in children and can substantially impair daily function. CRS is characterized by sinus symptoms lasting more than 3 months despite medical therapy. Many factors are involved in the pathogenesis of this disease and include a primary insult with a virus followed bybacterial infection and mucosal inflammation, along with predisposition to allergies.

The standard treatment of pediatricacute bacterial rhinosinusitis (ABRS) is nasal irrigation and antibiotic use. Medical treatment of pediatric CRS includes avoidance of allergens in allergic patients (environmental or food) and therapy with nasal irrigation, nasal corticosteroids sprays, nasal decongestants, and antibiotics directed at the most common sinonasalorganisms (Haemophilusinfluenzae, Streptococcus pneumoniae, and Moraxella catarrhalis). Surgical therapy is rarely needed after appropriate medical therapy. Referral to an otolaryngologist and allergy specialist is recommended in case of failure of medical treatment.

Keywords

Rhinosinusitis; Bacterial; Allergic rhinitis; pediatric rhinosinusitis; CRS; ABRS

Corresponding Author: Wanda Phipatanakul, MD, MS, 300 Longwood Ave, Boston, MA 02115, 617-355-6117, wanda.phipatanakul@childrens.harvard.edu.

Compliance with Ethics Guidelines

Conflict of Interest

Dr. Dana T. Badr, Dr. Jonathan M. Gaffin, and Dr. Wanda Phipatanakul declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

Introduction

Rhinosinusitis is an inflammation of the paranasal and nasal sinus mucosae. It is a more accurate term than “sinusitis” since it is almost always preceded by or associated with symptoms of rhinitis. It is classified according to the duration of signs:acute (up to one month), subacute(one to three months) or chronic (more than three months).Acute bacterial rhinosinusitis is diagnosed in a child based on several criteria:persistent upper respiratory tract symptoms more than 10 days (cough or nasal discharge or both); or recurrence of symptoms after initial improvement: fever, worsening cough, or worsening or new purulent rhinorrhea ; or severe onset of symptoms like fever or purulent nasal discharge lasting more than three consecutive days associated with facial tenderness or headache[1**]. Common pathogens involved in ABRS are Streptococcus pneumonia, Haemophilus influenza, and Moraxellacatarrhalis.Up to 5-10 % of viral upper respiratory tract infections in children progress to ABRS[2**, 3], with a number of them developing into chronic rhinosinusitis. The presentation of viral rhinosinusitis is similar to ABRS and it is difficult to differentiate between them since they both have the same clinical and radiological findings.

Compared to ABRS, CRS typically has a complex pathophysiology resulting from multiple environmental and genetic factors. If left untreated, it can significantly affects the quality of life, more than any chronic respiratory or arthritic disease [4].

The management of CRS in children consists primarily of medical treatment to eradicate bacterial infection and reduce underlying sinonasal inflammation. Surgical interventions, such as sinus puncture and lavage, adenoidectomy,balloon sinuplasty, endoscopic sinus surgery, open surgical approaches and turbinate reduction are reserved for patients who fail medical management[5].Such procedures are designed to both eradicate potential bacterial reservoirs and enhance sinonasal aeration and drainage [6].Appropriate management of CRS requires a comprehension of the latent causes of sinonasal inflammation on a patient-by-patient basis due to the heterogeneous nature of CRS. Clinical evaluation is required to diagnose and treat the underlying etiology and associated comorbidities, in addition to the specific interventions necessary to eradicate the sinus disease.

Anatomy and Pathophysiology

Understanding the embryologic development of the paranasal sinuses is crucial for the diagnosis and treatment of pediatric rhinosinusitis. For example, treatment of CRS in children below twelve years is different than children between 13 and 18 yearsdue to differences insinus growth. The ethmoid and maxillary sinuses develop in the 3rd month of gestation and are usually present at birth and displayearly growth, and reach adult size by the age of ten. The sphenoid sinuses are generallyappreciable on imaging before 3 years of age, become aerated at age 5 years, and expand in size into the second or third decade of life, typically becoming fully developed by age 12–14.The frontal sinuses develop from an anterior ethmoidal air cell and are pneumatized by age 5 or 6 years. The majority of all sinuses will reach adult size by the age of 15 yearswith the frontal sinus, the last to develop, reaching adult size by19 years[7**].

The outflow tract of the maxillary sinus is situated at the most superior portion of the medial wall which makes gravitational drainage difficult.

There are six anatomic drainage pathways from the sinuses -- three for each side.The frontal sinus drains via the nasofrontal duct into the anterior superior nasal cavity.The maxillary and anterior ethmoid sinuses drain via a common area, the ostiomeatal unit.The sphenoid and the posterior ethmoid sinuses drain via the sphenoethmoidal recess.Obstruction of any one pathway leads to sinusitis in the respective sinus areas.

A key concept in understanding the pathogenesis of acute bacterial sinusitis is that the nasal and nasopharyngeal mucosae are continuous with the paranasal sinus mucosa. Any process that affects the nasal mucosa may also affect the sinus mucosa; moreover, the nasal mucosa is heavily colonized with bacteria and investigations of the sinus microbiome have shown diverse colonization of healthy paranasal sinuses by Firmicutes, Proteobacteria, and Actinobacteria in all subjects, Bacteroides spp. in 83 % of subjects and S. aureus in 68 % of subjects[8, 7, 9, 10*] .

The mucosa consists of mucus secreting goblet cells and pseudo-stratified ciliated columnar epithelium. The role of the mucus covering the mucosa is to catch the dust , stimulating particles and microorganisms. The drainage of mucus isby activemucociliarytransport, and not by gravity. Nasal secretions originate fromgoblet cells, epithelial cells,epithelial cell proteins, vascular transudation and lacrimal fluid. The essential protein parts of these secretions are mucin glycoproteins composed of oligosaccharide side chains and a peptide core structure. Those glycoproteins affect the composition of the mucus and facilitatethe interaction between microorganismsand host. Mucin binds surface adhesins on microorganisms therefore inhibiting their ability to colonize the epithelium. Mucociliary movement transports mucus from the paranasal sinuses to the nasal cavity and pharynx where it is swallowed. The largenasal mucosal surface consists of a mucus layer that moistens the air flowing over it and filters the air particles. In the nasal submucosa, vascular plexi swell and produce nasal congestionafter exposure to certain stimulisuch as noxious or allergic triggers, and temperature changes.A number of local and systemic factors predispose to the development of sinusitis. Any local condition that interferes with normal sinus drainage predisposes to the development of infection.Obstruction of the sinus outflow tract may be due to mucosal swelling (i.e.: allergic rhinitis, viral URI) or mechanical obstruction (i.e.: nasal polyp, foreign body, tumor, anatomic abnormality) (*table 1)* . The obstruction will decrease oxygen supply to the sinus that in turn will result in 1) vasodilation of local vasculature, 2) ciliarydysfunction, and 3) mucus gland dysfunction. These events conspire to cause transudation and stagnation of the viscid fluid thus leading to acute rhinosinusitis with retained thick secretions. Instrumentation (with nasotracheal, nasogastric, orotracheal, or orogastric tubes) is an essentialrisk factor for ABRS. In fact, in a study of pediatric intensive care unit (PICU) patients, Moore *et al* found that almost 50% of PICU patients who underwent imaging for reasons other than assessmentfor sinus abnormality had evidence of sinusitis. This finding raised the concern that sinusitis in PICU patients is frequentand should be considered in the differential diagnosis of fever in PICU patients[11*].

Microbiology

Acute bacterial rhinosinusitis complicatesbetween 5 to 10% of viral URIs in children[7, 3]. A recent cohort published in *Pediatric Infectious Disease Journal*[12]found that viruses were found in 63% during the initial upper respiratory tract infection visit and rhinovirus detection was highly associatedwithABRS risk (p=0.01). 99% of samples obtained at the initial upper respiratory tract infection visit were positive for bacterial cultures with (56%) polymicrobial , (20%) Moraxella catarrhalis and(10%) Streptococcus pneumoniae most commonly cultured. Less commonly isolated organisms included group A streptococcus,groupC Streptococcus, Peptostreptococcusspp, Eikenellacorrodens, and Moraxella spp. [7, 12].

In contrast, chronicrhinosinusitis is a heterogeneous multifactorial disease with a complex pathophysiology compared to acute rhinosinusitis.Astudy by Brook et al published in Arch Otolaryngol Head Neck Surgery 2006demonstrated that the microorganisms isolated from patients with acute exacerbations of CRS were mainlyanaerobic and were similar to those usually recovered in patients with chronic rhinosinusitis. However, aerobic organisms that are generally found in acute infections (e.g., Haemophilusinfluenzae, Moraxella catarrhalis, and S pneumoniae) can also appearin some episodes of acute exacerbations of CRS [13].A multicenter study by Ivanchenko et al published in Rhinology 2015 focused on the identification of the microorganisms inhabiting the maxillary sinus and middle nasal meatus in chronic rhinosinusitis. A total of 244 strains of microorganisms representing more than 50 families were identified .These included 154 (63.0%) strains of aerobic bacteria from 32 species and 90 (37.0%) strains of anaerobic bacteria from 23 species. Aerobes were more common than anaerobes in both the nasal cavity (78.7% vs. 21.3%) and in the maxillary sinus (55.2% vs. 44.8%). Species of Streptococci (28.8%) and Prevotella (17.8%) were the most common findings in the maxillary sinus aspirates. S. pneumonia, H. influenza, and S. aureus were relatively rare, and found in only 6.7%, 5.4%, and 8.9% of the samples, respectively.Hence, the microbiome of inflamed sinonasal mucosa is extremely diverse and involves exotic species of bacteria that, to date, have not been considered as potential inhabitants of the paranasal sinuses[14].This study was done in adults, similar investigations have not yet been performed in pediatrics. Moreover , the inconsistencyof the results from previous studies in CRS may be due to previous antibiotic use , difficulty in distinguishing bacterial flora from pathogenic agents, and the use of different collection techniques. In a cross sectional study, 62 adult patients underwent functional endoscopic sinus surgery for treatment of CRS; cultures from maxillary sinuses were obtained. 33 had no growth(53.2%); 29 counts of aerobic bacteria(45.2%); one case of fungus growth(1.6%); no anaerobic bacteria found. Pseudomonas aeruginosa was the most frequently found :(27.6%) eight samples ,Staphylococcus epidermidis and Staphylococcus aureus in four samples each; Streptococcus pneumonia in three samples (10.4%); other Gram negative agents in seventeen samples (31%).Pseudomonas aeruginosa, staphylococcus spp. and other Gram negativebacteria were the representatives of the bacterial flora in the paranasalsinusesof adult patients with CRS[15].

However, unlike other chronic respiratory diseases, a study by Pandak*et al* on 60 patients with CRS showed that the sinus aspirates of patients with CRS didn't grow any of the

atypical organisms (Mycoplasma pneumonia and Chlamydia pneumonia) that are frequently found in the chronic respiratory conditions (i.e.: COPD , asthma) [16].

Odontogenic sinusitis is defined as sinusitis due to a dental lesion. Brook et al examined the causative organisms of chronic and acute sinusitis associated with odontogenic infection in a cohortof48 patients. 66 isolates were recovered from 20 cases of acute sinusitis, 16 were aerobic and facultative organisms, and 50 anaerobic. The predominant aerobes were Staphylococcus aureus,alpha-hemolytic streptococci andmicroaerophilic streptococci. The predominant anaerobes were Peptostreptococcus, Fusobacterium spp. and anaerobic gram-negative bacilli .98 isolates were recovered from 28 cases of chronic sinusitis: 77 anaerobic and 21 aerobic and facultatives. The predominant aerobes were staphylococcus aureus ,microaerophilic streptococci and alpha-hemolytic streptococci. The predominant anaerobes werefusobacterium spp,peptostreptococcus, and Gram-negative bacilli. No association was found between the microbiological findings and the predisposing odontogenic conditions. These data demonstrate the similar microbiology of chronic and acute maxillary sinusitis associated with odontogenic origin where anaerobic organisms predominate in both types of infections[17].

Chronic rhinosinusitis is frequently associated with underlying conditions that affect the structure and/or function of the upper airway.

Below, we discuss common predisposing and comorbid conditions.

Genetic

Familial association studies have demonstrated strong heritability of CRS within immediate and secondary family members. According to a recent study by Orb, Q.*et al* on 496 patients with CRS, a strong genetic predisposition was involved in CRS pathogenesis,where relativesof patients with CRS had a 57.5 times higher risk of having CRS. First cousins had 9times increased risk and second cousins had a 2.9times increased risk of pediatric CRS[18**]. Another study has suggested that thisgenetic predispositionmay be related to the genes encoding potassium channels on the airway epithelium.Theseapical potassium channels mediate mucociliary clearance, air surface liquid hydration and control ion transport in epithelial cells[19*]. Other genetic diseases, like primary immunodeficiencies, primary ciliary dyskinesia (Kartagener's syndrome),and cystic fibrosis are highly associated with CRS, but their contribution to the overall prevalence is low[20].

Allergy

Allergic rhinitis is an important contributing factor and a comorbid condition with pediatric CRS [18, 6]. A retrospective review of 4044 children with an average age of 8.9 years concluded that AR is more prevalent than the other comorbidities (cystic fibrosis, primary ciliary dyskinesia, and immunologic disorder) combined in children with CRS.However, the prevalence of AR in CRS patients was not different from the prevalence of AR in the general pediatric population. In the evaluation of CRS in pediatric patients, it is essential to test for aeroallergen sensitization. Knowledge of the aeroallergen sensitivities in children with CRS and allergic rhinitis will enhance treatment strategies by avoiding exposure to known allergens and promoting allergy therapies to minimize nasal mucosal inflammation.

Pediatric patients with allergic rhinitis and CRS had the same aeroallergen sensitivity profile when compared to the general pediatric population with allergic rhinitis[21].

In a recent retrospective cohort study Sedaghat and colleagues found that indoor aeroallergen sensitivity (63–100%) was more common than outdoor aeroallergen sensitivity (44–50%)in all three cohorts of children with CRS (1- CRS with immune deficiency, 2- CRS with cystic fibrosisand 3- uncomplicated CRSDust mites werethe most common indoor aeroallergen (50 to 75% sensitivity) and tree pollens the most common outdoor aeroallergen detected(44 to 50% sensitivity)[21].

Inflammation in CRS—Moreover, inflammation of the sinuses can be evaluated by histopathological examination and detection of molecular components of the immune system as well as expression of pro and anti-inflammatory cytokines in the sinus and adenoid tissues, in nasal tissues obtained by nasal scraping, and in rhinonasal lavage.

Earlier studies of sinus inflammation in CRS showed lymphocytic predominance in children and eosinophilic predominance in adults[22]. In an immunohistopathological study, Coffinet et al. defined the cellular characteristics in maxillary mucosal biopsies from children and adults. The authors showed that when compared to adults with CRS, children had significantly increased CD8+ T lymphocytes (cytotoxic T lymphocytes), MPO (myeloperoxidase; neutrophils), and CD68+cells (monocytes/macrophages) anda trend toward more CD3+ lymphocytes (total T lymphocytes) and CD4+ T lymphocytes (helper T lymphocytes) cells in the epithelium. They also showed significantly more CD20+ lymphocytes (B lymphocytes), lambda+and kappa+ (plasma cells), MPO+, and CD68+ cells and a trend toward more CD4+ cells in the submucosa [23].

A recently reported study about inflammatory cytokines in pediatric CRS with and without allergies and with and without asthma demonstrated that TNF-a levels were higher in the sinus tissues, and epidermal growth factor, eotaxin, fibroblast growth factor-2, growth-related oncogene, and plateletderived growth factor-AA were higher in adenoid tissues in all children with CRS (without allergy and asthma) compared with the controls[24**] .

Asthma—Similar to AR, asthma is frequently associated with CRS. The epidemiologic link between CRS and asthma has been suggested by pathophysiologic and therapeutic observations. Histologic studies have shown mast cells and eosinophils both in the nasal mucosa of individuals with allergic rhinitis and in the bronchial mucosa of asthmatics[24], and the exposure of patients with rhinitis to specific allergens triggers eosinophilic infiltration into both nasal and bronchial mucosa. Furthermore, several studies have shown that medical management of CRS improves asthma symptoms and lung function, and that surgical management improves asthma symptoms and reduces emergency visits in children with both conditions.When compared to non-asthmatic children with CRS, Anfuso et al found that the sinus tissue of asthmatic children with CRS showed increased levels for 27 of the 40 inflammatory cytokines tested , but the increase was statistically significant only for TNF-β($p=0.009$). All cytokines that were significantly high in the CRS-only group compared to the control group were also high in the asthmatic CRS group compared to the non-asthmatic CRS group. These inflammatory patterns can inform the future use of specific

cytokines as biomarkers to better understand inflammation in children with CRS. CRS subjects exhibit a decreased percentage of peripheral blood Tregulatory cells compared with normal controls. Peripheral blood mononuclear cells from CRS subjects shows a more proinflammatory and lessregulatory phenotype[25].

Diagnosis

The IDSA guidelines suggest that ABRS can be diagnosed with each of the following clinical scenarios:

- **i.** URI symptoms lasting more than 10 days without any improvement;
- **ii.** Severe onset of signs and symptoms lasting more than 3-4 consecutive days,like high grade fever (>39°C),facial pain or purulent nasal discharge;
- **iii.** Worsening of signs and symptoms following a typical viral URI that lasted 5-6 days and were initially improving, like new onset of fever, headache, or increase in nasaldischarge“double-sickening”.

Confirmation is by nasal exam and by documenting purulent discharge beyond the nasal vestibule by rhinoscopy or endoscopy; or posterior pharyngeal drainage. CT scan is not recommended for routine management, but may be helpful in complex cases or if complications are suspected. Other clinical symptoms associated with ABRS includetenderness overlying the sinuses, nasal erythema, increased posterior pharyngeal secretions, periorbital edema ,halitosis, eustachian tube dysfunction on ear exam.The clinical presentation of pain in ABRS may provide the clinician with clues as to which sinus is infected*(table 2)*

A recent studypublished by G. Leo *et al*. concludedthat early recognition of children with a high probability of CRS via initial symptoms assessment reduces the need for imaging and nasal endoscopy.[26*] . The symptoms considered were nasal discharge and obstruction, facial pain, halitosis and cough. The multivariate logistic regression for CRS symptoms indicated rhinorrhea as the strongest predictor of CRS. With any three of the following symptoms:halitosis, cough, facial pain or nasal obstruction;the probability of having CRS was from 60% to 75% without rhinorrhea and increased to 77-91% in the presence of rhinorrhea.With all four symptoms present (cough, halitosis, facial pain, and nasal obstruction) the probability was over 93%, and with the four symptoms in addition to rhinorrhea, the probability was almost 100%[26].

Imaging

Plain radiographic studies are not sufficiently sensitive or specific to detect sinusitis and are essentially not recommended for either diagnosis or follow up of acute or chronic rhinosinusitis. Computerized tomography (CT) is the imaging of choice and both coronal and axial images are obtained. The limited coronal sinus CT scan allows assessment of osteomeatal unit patency and the anatomy of the sinuses.Use of contrast with the CT scan is usually reserved for cases where abscess formation is suspected in either the orbit or the brain. Rim enhancement allows the improved detection of possible abscesses and facilitates the decision for surgical intervention if necessary. Three radiographic findings indicate

sinusitis:air-fluid level, opacification (partial or complete), and 4 - 6 mm thickening of the mucus membrane .Although imaging is not routinely recommended in the diagnosis of sinusitis, a negative CT effectively eliminates the diagnosis. Addition of magnetic resonance imaging maybe useful when complications of sinusitis are suspected.In this situation, fluid collections that require surgical drainage may be identified[7].

Flexible or rigid nasal endoscopy is adequatein visualization of purulent discharge, adenoid hyperplasia or infection, nasal polyps, mucosal edema, and septal deviation [2].

Sinus aspiration

Indicationsfor sinus aspiration include sinusitis unresponsive to multiplecourses of antibiotics,severe facial pain, and suspected sinusitis in animmunocompromised child in whom unusual pathogenssuch as fungi may be present. It can be performed on an outpatient basis but is usually poorly tolerated in children without anesthesia[7].

Additional testing to complete the workup for refractory CRS may include:

1. Testing for a primary immunodeficiency, i.e.: quantitative immunoglobulins, immune profile, vaccine titers. There is a high prevalence of CRS in individuals with CVID and selective IgG3 subclass deficiency weakens host defense against Moraxella catarrhalis and the M component of Streptococcus pyogenic[27].
2. Testing for allergies: skin prick testing or specific allergens IgE levels.
3. Sweat chloride test and genetic testing for cystic fibrosis.
4. Nasal and preferably bronchial biopsy and genetic testing for primary ciliary dyskinesia.

Complications

Complications of sinusitis may be divided into those involving theorbit (optic neuritis, orbital and periorbital cellulitis, orbital and subperiostealabscess), the central nervous system (meningitis, subdural and epidural empyema, brain abscess andvenous sinus thrombosis), or the bone (maxillaryosteitis, frontal osteitis (Pott puffy tumor)).

The frontal and ethmoid sinuses are the mostcommon sinuses from which complications arise. Thedelicate and thin walls of the ethmoid sinuses, can allow for spread of infection into the orbit.

Orbital complications are the most common. Signs of orbital infection include eyelid swelling, proptosis, and impairment of extraocular muscle movement. This complication may result from spread of infection through the natural dehiscencesof the lamina papyracea,the bone that comprises the medial wall of the orbit, or from transmission by venous thrombophlebitis across the same route. This leads to the development of a subperiostealabscess of the orbit. The prevalence of orbital complications of ARS in children is higher in children than adults and has a more favorable prognosis [28]. Orbital complications are classified according to Chandler's

Classification

I – Preseptal cellulitis, II – Orbital cellulitis,III – Subperiostealabscess, IV – Orbital abscess,V – Cavernous sinus thrombosis[29]. The mainstay of treatment starts with broad spectrum intravenous antibiotics. If the infection is not controlled, or there are any signs of decreased vision or compromise of the orbit, surgical drainage is recommended.

The frontal sinuses share venous drainage with intracranial structures, allowing for infection to develop within the brain and surrounding structures. Although they are less common than orbital complications, intracranial infections are more serious with higher morbidity and mortality.They may present with severe headache, photophobia, seizures, focal neurologic signs, or meningeal signs and can include brain abcess ,subdural and epidural empyema.

The bony complication of acute frontal sinusitis is Pott puffy tumor, which is a subperiosteal abscess of the frontal bone.Severe intracranial complications and neurologic deficits are associated with streptococcus angina subgroup more than any other bacteria . The growth of this pathogen alerts for a low threshold for neurosurgical intervention. [30].

Treatment

Acute rhinosinusitis

High-dose amoxicillin (90 mg per kg per day) should be considered as a first-line agent for the treatment of sinusitis because of its activity against sinus pathogens. Because the proportion of cases caused by Haemophilus influenza is likely increasing and the rate of B-lactamase production by this organism is also increasing ,the addition of clavulanic acid to amoxicillin provides an advantage over amoxicillin alone. Using (90mg/kg/day) of the amoxicillin component provides better coverage for penicillin nonsusceptible S.pneumoniae[3]. Cephalosporins, such as cefpodoxime, cefdinir, or cefuroxime, are alternative antibiotics,although they are less active against S pneumonia than amoxicillin-clavulanate. For those children in whom amoxicillin-clavulanate or second or third generation cephalosporins fail, a combinationofcefixime (or cefdinir) and linezolid may be used as an alternative to the use of parenteral antimicrobialagents. For patients in whom beta-lactam antibiotics are contraindicated, respiratory fluoroquinolones (levofloxacin or moxifloxacin) or doxycycline may be used. Referenceto local antibiotic susceptibility patterns may aid in choosing appropriate therapy.

Response to therapy is rapid in children who have sinusitisand are adherent to therapy with an appropriate antimicrobialagent. Symptoms typically improve within 48 hours (i.e. fever, cough, discharge.). If symptoms worsen within 72 hours or are not improved within 3-5 days, then clinical reassessment is warranted[1]. If the diagnosis remains unchanged, a second line antimicrobial shouldbe prescribed. Alternatively, sinus aspiration may be consideredfor precise identification of the causative organism.

The appropriate duration of antimicrobial therapy hasnot been studied thoroughly. For children who havea rapid response to the initiation of antimicrobial, ten daysof therapy usually is appropriate. For those who respond ata slower rate, treating until the patient has no more symptoms plus an additional 7 days is reasonable[7].

While antibiotics remain the standard of care for ABRS, their role has been debated. Several randomized trials of antimicrobial therapy vs placebo in the treatment of sinusitis in children have conflicting results[31]. Ragab A. *et al*In a blind placebo-controlled prospective randomized trial conducted on 62 pediatric patients, compared the use of nasal 0.9% saline irrigation and placebo with amoxicillin.After 14 days of treatment, it was found that the use ofnasal saline irrigation alone had the same clinical, bacteriological and cytological cellular changes when compared to amoxicillin. Moreover, nasal saline irrigation with placebo had a higher safety profile than nasal saline irrigation with amoxicillin with less adverse events (P value = 0.005).83.9% clinical cure was observed in the amoxicillin group in comparison to 71% in nasal saline irrigation without antibiotics groupwith an insignificant p value (= 0.22). No differences were found between groups in the reported nasal symptom scores and total symptoms scores improvements at day 7 and day 14, respectively[32].

Furthermore, in a study by Tugrul et al, in 91 pediatric patients with ABRS about the combination use of fluticasone propionate and large volume of low pressure nasal saline,found that this combination therapy can be used as a new line of treatment for pediatric acute rhinosinusitis since it is highly effective. It can be used alone or with standard therapy[33].Moreover, comparison study of amoxicillin + clavulanic acid with or without intranasal fluticasone for the treatment of pediatric acute rhinosinusitis recently foundno significant differences between treatement with co-amoxiclav with or without intranasal steroids. However, if there is comorbid allergic rhinitis, the efficacy of co-amoxiclav with intranasal steroids is higher than in children treated with co-amoxiclav alone[34].

Chronic rhinosinusitis

In pediatric CRS associated with allergic rhinitis, allergen avoidance,anti-histamines, and nasal steroids will help in ameliorating the symptoms. Moreover, allergen immunotherapy may be an underused option that could benefit patients with persistent allergic rhinitis and can change the natural course of the disease by reducing the symptoms and medications use[35]. Whereas data supports the efficacy of immunotherapy for the treatment of allergic rhinitis, there is no evidence for this treatment modality in patients with CRS.

In the latest concensus statement in pediatric CRS published by Brietzke et al, an agreement was reached that dailytopical nasal steroid spray with nasal irrigationsare favorable adjunctive medical therapies for PCRS[2]. Hong and colleagues studied 77 children with an age average 8.3 years with refractory CRS andfollowed them up after 6.2 months (2-32 months)use of daily nasal saline irrigation and found that nasal irrigationwas relatively well tolerated (63.6%) and effective. Nasal saline irrigation should be considered as a primary treatment in pediatric CRS[36]. In another cohort of144 pediatric patients with CRS, investigatorsfoundthat long term use of nasal saline irrigation reduced the need for functional endoscopic sinus surgery and CT imaging [37][38]. Concerning the use of antibiotics, consensus was reached that antibiotic use for 20 consecutive days had a superior clinical response in pediatric CRS when compared to 10 days . Moreover, culture-directed antibiotic therapy improves outcomes for pediatric CRS patients who have not responded to empiric antibiotic therapy [2].

The role of empiric anti-reflux medication, topical antibiotics, and antral irrigation are not supported for the treatment of pediatric CRS[2].

However, special populations may benefit from antibiotic rinses. A double-blind controlled study on 27 patients with cystic fibrosis found that the combination treatment with hyaluronateand tobramycin was more effective than hyaluronate alone in the treatment of bacterial rhinosinusitis in cystic fibrosis [39]. Adjunctive therapy, such as antihistamines and decongestants, have not been found consistently to provide benefit in children with sinusitis and may be associatedwith toxic effects[7].

Surgery

Surgical intervention is not the mainstay of treatment ofCRS and is only used in the presence of complications, in failure of medical treatment and in patients with suspected anatomic abnormalities.[40, 3]

Adenoidal tissue acts as a bacterial reservoir in children with CRS regardless of their size and removing them improves outcomes[41, 24]. Adenoidectomy is highly effective as an initial surgical therapy in children aged up to 6 years, it has been found that the efficiency of this treatment decreases between the age of 6 and 12. However for older pediatric patients the panel could not reach an agreement[2].Tonsillectomy (without adenoidectomy) is ineffective treatment for PCRS [2].

Surgeries such as adenoidectomy, balloon sinuplasty ,sinus puncture and lavage, endoscopic sinus surgery, turbinectomy, and open surgical approachesare reserved for patients who fail medical management.

Endoscopic sinus surgeryin PCRS is performed in case of failure of medical management and/or adenoidectomy in controlling the symptoms of PCRS. CT scan of the sinuses is indicated before endoscopic sinus surgeryin order to assess the anatomy of the sinuses and the severity of sinus disease [2, 42].

In a series of eighty-six patients with acute complicated sinusitis, nine patients required atleast one surgery following resolution of acute complicatedsinusitis. A majority of these patients presented within one yearof their initial hospitalization and required secondary surgery forpersistent rhinosinusitis[40]. Consequently, otolaryngologists should consider following patients with a complication of acute sinusitisfor up to one year. However, the incidence of surgical interventionfollowing resolution of acute complicated rhinosinusitis was quitelow and subsequent intervention is best guided by clinicaljudgment.

Conclusion

Pediatric rhinosinusitisis divided into acute and chronic according to the duration of symptoms. They are diagnosed and treated differently. CRS is highly associated with allergic diseases and other comorbidities and it is essential to treat the underlying conditions as part of the medical and, if necessary, surgical approach.

Acknowledgements/Funding NIH

K24 AI 106822, K23AI106945

Abbreviations

ARS	acute Rhinosinusitis
ABRS	acute bacterial rhinosinusitis
CRS	chronic rhinosinusitis

REFERENCES

Papers of particular interest, published recently, have been highlighted as:

• Of importance

•• Of major importance

1••. Chow AW, Benninger MS, Brook I, Brozek JL, Goldstein EJ, Hicks LA, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2012; 54(8):e72–e112. doi:10.1093/cid/cir1043. [PubMed: 22438350] [Large evidence based guidelines and recommendations for acute bacterial rhinosinusitis.]

2••. Brietzke SE, Shin JJ, Choi S, Lee JT, Parikh SR, Pena M, et al. Clinical consensus statement: pediatric chronic rhinosinusitis. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2014; 151(4):542–53. doi: 10.1177/0194599814549302. [PubMed: 25274375] [This consensus report presents the recent updates concerning the diagnosis and management of CRS]

3. Wald ER, Applegate KE, Bordley C, Darrow DH, Glode MP, Marcy SM, et al. Clinical practice guideline for the diagnosis and management of acute bacterial sinusitis in children aged 1 to 18 years. Pediatrics. 2013; 132(1):e262–80. doi:10.1542/peds.2013-1071. [PubMed: 23796742]

4. Cunningham MJ, Chiu EJ, Landgraf JM, Gliklich RE. The health impact of chronic recurrent rhinosinusitis in children. Archives of otolaryngology--head & neck surgery. 2000; 126(11):1363–8. [PubMed: 11074834]

5. Isaacson G. Surgical treatment of pediatric rhinosinusitis. Minerva pediatrica. 2015; 67(4):357–68. [PubMed: 25369207]

6. Sedaghat AR, Phipatanakul W, Cunningham MJ. Prevalence of and associations with allergic rhinitis in children with chronic rhinosinusitis. International journal of pediatric otorhinolaryngology. 2014; 78(2):343–7. doi:10.1016/j.ijporl.2013.12.006. [PubMed: 24388318]

7••. DeMuri G, Wald ER. Acute bacterial sinusitis in children. Pediatrics in review / American Academy of Pediatrics. 2013; 34(10):429–37. quiz 37. doi:10.1542/pir.34-10-429. [Excellent review of the diagnosis and management ofacute bacterial rhinosinusitis]

8. Abou-Hamad W, Matar N, Elias M, Nasr M, Sarkis-Karam D, Hokayem N, et al. Bacterial flora in normal adult maxillary sinuses. American journal of rhinology & allergy. 2009; 23(3):261–3. doi: 10.2500/ajra.2009.23.3317. [PubMed: 19490798]

9. Wilson MT, Hamilos DL. The nasal and sinus microbiome in health and disease. Current allergy and asthma reports. 2014; 14(12):485. doi:10.1007/s11882-014-0485-x. [PubMed: 25342392]

10•. Ramakrishnan VR, Feazel LM, Gitomer SA, Ir D, Robertson CE, Frank DN. The microbiome of the middle meatus in healthy adults. PloS one. 2013; 8(12):e85507. doi:10.1371/journal.pone.0085507. [PubMed: 24386477] [In this study they examined the microbiome of the middle meatus in healthy adults using middle meatus swabs, quantitative PCR and 16S rRNA pyrosequencing thereby establishing a baseline for understanding how the sinonasal microbiome may impact diseases.]

11•. Moore BM, Blumberg K, Laguna TA, Liu M, Zielinski EE, Kurachek SC. Incidental sinusitis in a pediatric intensive care unit. Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies. 2012; 13(2):e64–8. doi:10.1097/PCC.0b013e31820ac3f5. [This is the first study demonstrating the association between nasal instrumentation and sinusitis.]

12. Marom T, Alvarez-Fernandez PE, Jennings K, Patel JA, McCormick DP, Chonmaitree T. Acute bacterial sinusitis complicating viral upper respiratory tract infection in young children. The Pediatric infectious disease journal. 2014; 33(8):803–8. doi:10.1097/inf.0000000000000278. [PubMed: 24717966]

13. Brook I. Bacteriology of chronic sinusitis and acute exacerbation of chronic sinusitis. Archives of otolaryngology--head & neck surgery. 2006; 132(10):1099–101. doi:10.1001/archotol.132.10.1099. [PubMed: 17043258]

14. Ivanchenko OA, Karpishchenko SA, Kozlov RS, Krechikova OI, Otvagin IV, Sopko ON, et al. The microbiome of the maxillary sinus and middle nasal meatus in chronic rhinosinusitis. Rhinology. 2016; 54(1):68–74. doi:10.4193/Rhin15.018. [PubMed: 26501135]

15. Mantovani K, Bisanha AA, Demarco RC, Tamashiro E, Martinez R, Anselmo-Lima WT. Maxillary sinuses microbiology from patients with chronic rhinosinusitis. Brazilian journal of otorhinolaryngology. 2010; 76(5):548–51. [PubMed: 20963334]

16. Pandak N, Pajic-Penavic I, Zidovec-Lepej S, Planinic A, Troselj-Vukic B, Peric L. Chlamydophila pneumoniae and Mycoplasma pneumoniae were not identified in sinus mucosa of patients with chronic rhinosinusitis. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2014; 271(6):1553–5. doi:10.1007/s00405-013-2745-0.

17. Brook I. Microbiology of acute and chronic maxillary sinusitis associated with an odontogenic origin. The Laryngoscope. 2005; 115(5):823–5. doi:10.1097/01.mlg.0000157332.17291.fc. [PubMed: 15867647]

18••. Orb Q, Curtin K, Oakley GM, Wong J, Meier J, Orlandi RR, et al. Familial risk of pediatric chronic rhinosinusitis. The Laryngoscope. 2015 doi:10.1002/lary.25469. [The largest population-based study on children with CRS demonstrating a significant familial risk]

19•. Purkey MT, Li J, Mentch F, Grant SF, Desrosiers M, Hakonarson H, et al. Genetic variation in genes encoding airway epithelial potassium channels is associated with chronic rhinosinusitis in a pediatric population. PloS one. 2014; 9(3):e89329. doi:10.1371/journal.pone.0089329. [PubMed: 24595210] [The first study demonstrating variations in two airway potassium channel genes as possible contributing factors in pathogenesis of CRS.]

20. Min JY, Tan BK. Risk factors for chronic rhinosinusitis. Current opinion in allergy and clinical immunology. 2015; 15(1):1–13. doi:10.1097/aci.0000000000000128. [PubMed: 25479315]

21. Sedaghat AR, Phipatanakul W, Cunningham MJ. Characterization of aeroallergen sensitivities in children with allergic rhinitis and chronic rhinosinusitis. Allergy & rhinology (Providence, RI). 2014; 5(3):143–5. doi:10.2500/ar.2014.5.0102.

22. Chan KH, Abzug MJ, Coffinet L, Simoes EA, Cool C, Liu AH. Chronic rhinosinusitis in young children differs from adults: a histopathology study. The Journal of pediatrics. 2004; 144(2):206–12. doi:10.1016/j.jpeds.2003.11.009. [PubMed: 14760263]

23. Coffinet L, Chan KH, Abzug MJ, Simoes EA, Cool C, Liu AH. Immunopathology of chronic rhinosinusitis in young children. The Journal of pediatrics. 2009; 154(5):754–8. doi:10.1016/j.jpeds.2008.11.035. [PubMed: 19159906]

24••. Anfuso A, Ramadan H, Terrell A, Demirdag Y, Walton C, Skoner DP, et al. Sinus and adenoid inflammation in children with chronic rhinosinusitis and asthma. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2015; 114(2):103–10. doi:10.1016/j.anai.2014.10.024. [This is the first study demonstrating the inflammatory patterns both in adenoid and sinus tissues in children with CRS.]

25. Sharma S, Watanabe S, Sivam A, Wang J, Neuwirth SJ, Perez RI, et al. Peripheral blood and tissue T regulatory cells in chronic rhinosinusitis. American journal of rhinology & allergy. 2012; 26(5):371–9. doi:10.2500/ajra.2012.26.3800. [PubMed: 23168151]

26•. Leo G, Incorvaia C, Cazzavillan A, Consonni D. May chronic rhinosinusitis in children be diagnosed by clinical symptoms? International journal of pediatric otorhinolaryngology. 2015; 79(6):825–8. doi:10.1016/j.ijporl.2015.03.011. [PubMed: 25847466] [The first study that defines acombination of symptoms thatconfirms the presence of CRS.]

27. Veskitkul J, Vichyanond P, Pacharn P, Visitsunthorn N, Jirapongsananuruk O. Clinical characteristics of recurrent acute rhinosinusitis in children. Asian Pacific journal of allergy and immunology / launched by the Allergy and Immunology Society of Thailand. 2015; 33(4):276–80. doi:10.12932/ap0591.33.4.2015.

28. Al-Madani MV, Khatatbeh AE, Rawashdeh RZ, Al-Khtoum NF, Shawagfeh NR. The prevalence of orbital complications among children and adults with acute rhinosinusitis. Brazilian journal of otorhinolaryngology. 2013; 79(6):716–9. doi:10.5935/1808-8694.20130131. [PubMed: 24474483]

29. Healy GB, Chandler, et al. “The pathogenesis of orbital complications in acute sinusitis.” (Laryngoscope 1970;80:1414-1428). The Laryngoscope. 1997; 107(4):441–6. [PubMed: 9111370]

30. Deutschmann MW, Livingstone D, Cho JJ, Vanderkooi OG, Brookes JT. The significance of Streptococcus anginosus group in intracranial complications of pediatric rhinosinusitis. JAMA otolaryngology-- head & neck surgery. 2013; 139(2):157–60. doi:10.1001/jamaoto.2013.1369. [PubMed: 23429946]

31. Cronin MJ, Khan S, Saeed S. The role of antibiotics in the treatment of acute rhinosinusitis in children: a systematic review. Archives of disease in childhood. 2013; 98(4):299–303. doi: 10.1136/archdischild-2012-302983. [PubMed: 23418037]

32. Ragab A, Farahat T, Al-Hendawy G, Samaka R, Ragab S, El-Ghobashy A. Nasal saline irrigation with or without systemic antibiotics in treatment of children with acute rhinosinusitis. International journal of pediatric otorhinolaryngology. 2015; 79(12):2178–86. doi:10.1016/j.ijporl.2015.09.045. [PubMed: 26514931]

33. Tugrul S, Dogan R, Eren SB, Meric A, Ozturan O. The use of large volume low pressure nasal saline with fluticasone propionate for the treatment of pediatric acute rhinosinusitis. International journal of pediatric otorhinolaryngology. 2014; 78(8):1393–9. doi:10.1016/j.ijporl.2014.06.006. [PubMed: 24972936]

34. Wan KS, Wu WF, Chen TC, Wu CS, Hung CW, Chang YS. Comparison of amoxicillin + clavulanate with or without intranasal fluticasone for the treatment of uncomplicated acute rhinosinusitis in children. Minerva pediatrica. 2015; 67(6):489–94. [PubMed: 26530491]

35. Anolik R, Schwartz AM, Sajjan S, Allen-Ramey F. Patient initiation and persistence with allergen immunotherapy. Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology. 2014; 113(1):101–7. doi:10.1016/j.anai.2014.04.008.

36. Hong SD, Kim JH, Kim HY, Jang MS, Dhong HJ, Chung SK. Compliance and efficacy of saline irrigation in pediatric chronic rhinosinusitis. Auris, nasus, larynx. 2014; 41(1):46–9. doi:10.1016/j.anl.2013.07.008. [PubMed: 23932052]

37. Pham V, Sykes K, Wei J. Long-term outcome of once daily nasal irrigation for the treatment of pediatric chronic rhinosinusitis. The Laryngoscope. 2014; 124(4):1000–7. doi:10.1002/lary.24224. [PubMed: 23712296]

38. Wei JL, Sykes KJ, Johnson P, He J, Mayo MS. Safety and efficacy of once-daily nasal irrigation for the treatment of pediatric chronic rhinosinusitis. The Laryngoscope. 2011; 121(9):1989–2000. doi: 10.1002/lary.21923. [PubMed: 22024856]

39. Di Cicco M, Alicandro G, Claut L, Cariani L, Luca N, Defilippi G, et al. Efficacy and tolerability of a new nasal spray formulation containing hyaluronate and tobramycin in cystic fibrosis patients with bacterial rhinosinusitis. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society. 2014; 13(4):455–60. doi:10.1016/j.jcf.2014.02.006. [PubMed: 24656944]

40. Patel RG, Daramola OO, Linn D, Flanary VA, Chun RH. Do you need to operate following recovery from complications of pediatric acute sinusitis? International journal of pediatric otorhinolaryngology. 2014; 78(6):923–5. doi:10.1016/j.ijporl.2014.03.008. [PubMed: 24704319]

41. Neff L, Adil EA. What is the role of the adenoid in pediatric chronic rhinosinusitis? The Laryngoscope. 2015; 125(6):1282–3. doi:10.1002/lary.25090. [PubMed: 25523938]

42. Vlastarakos PV, Fetta M, Segas JV, Maragoudakis P, Nikolopoulos TP. Functional endoscopic sinus surgery improves sinus-related symptoms and quality of life in children with chronic

rhinosinusitis: a systematic analysis and meta-analysis of published interventional studies. Clinical pediatrics. 2013; 52(12):1091–7. doi:10.1177/0009922813506489. [PubMed: 24146231]

Table 1

Predisposing factors for rhinosinusitis

Local predisposing factors	Systemic predisposing factors
• Allergic rhinitis	• Immune deficiency
• URI	– IgA deficiency
• Anatomic abnormality:	– Panhypogammaglobulinemia
– Deviated septum	– IgG subclass deficiency
– Concha bullosa	– HIV
– Enlarged adenoids	• Cystic fibrosis
• Nasal polyps	• Ciliary disorder
• Tumor	• Wegener's granulomatosis
• Foreign body	
• Trauma	
• Barotrauma	
• Diving, swimming	
• Smoke	
• Topical decongestant abuse	
• Nasal intubation, Nasogastric tube[2, 11]	

Table 2

Pain distribution in acute sinusistis.

Maxillary sinus	malar, posterior nasopharynx, pain in the upper teeth, zygoma, temple hyperalgesia
Frontal sinus	Forehead, orbit, zygoma, temple
Ethmoid sinus	Nasal bridge, inner canthus, with eye movement
Sphenoid sinus	Vertex, retro-orbit, between eyes, zygoma, temple