



Update on Chronic Rhinosinusitis in Children

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Introduction

Chronic rhinosinusitis (CRS) in the pediatric population is a complex disease with considerable impact upon the economy of the United States. Most otolaryngologists agree that the cornerstone of treating CRS is a prolonged course of a broad-spectrum, beta-lactamase stable oral antibiotic. Although the direct cost of pediatric chronic sinusitis is unknown, it is estimated that more than \$2 billion is spent annually on the purchase of over-the-counter medications for the treatment of CRS. When combined with the cost of antibiotic therapy, the public health impact is enormous. Rhino/sinus infection is a very common disease in childhood, causes large numbers of visits to pediatricians and ENTs and, depending on the severity and presence of complications, visits are included with those to other specialists such as in infectious diseases, ophthalmology, immunology, pneumology, genetics and allergology.

In this chapter we are going to discuss traditional and new horizons in this pathology. There is new linguistic terminology on the immune aspect of rhinological and sinus processes that cause medical concern due to lack of understanding of medical explanations of the mechanisms, reactions, receptors, mediators and analysis. But every day ENTs learn more about immunology, and immunologists learn more about otorhinolaryngology. The idea is to speak the same language in order to understand the best approach for our patients.

Definition, signs and symptoms

Chronic rhinosinusitis is a disease caused by dysfunction of the immune system in combating the environment, where we will have a modified inflammatory response. In acute sinus infection, symptoms are severe and can last up to four weeks, affecting only the mucosa. Chronic sinusitis is an infectious process of the paranasal sinuses lasting for longer than three months. The concepts derive from the EPO's 2007 - European Position Paper on Rhinosinusitis. There is no ideal definition. In EPO's 2007 guidelines the terms "sub-acute" and "persistent intermittent" were removed, and only "acute" and "chronic" are accepted.

Nasal discharge is most often purulent, but may be minimal or absent, in CRS. Throat-clearing may be more prominent. Cough may be present in the daytime and worsen at night. The child may suffer from sleep impairment, poor appetite, and poor performance in school. Osteitis can be present in a chronic infection of bones in the sinus.

Anatomy

To remember the development of paranasal sinuses in children: the ethmoidal sinuses have been present since the baby was born (**Figure 1**), maxillary sinuses will be pneumatized at three to four years of age, frontal sinuses will be pneumatized at ten to 12 years of age, and sphenoid sinuses will be pneumatized from 12 years of age up. All events may occur from mild symptoms to symptomatic, severe symptoms of short or long duration. Both acute and chronic sinus infection can be recurrent. In acute sinus infections the symptoms disappear completely and the mucosa becomes normal, while in CRS, despite not too many symptoms being present, the mucosa maintains minimal persistent inflammation leading to irreversible changes such as remodeling of respiratory mucosa of the nose and sinuses.

Figure 1. Anatomy of sinuses in infants



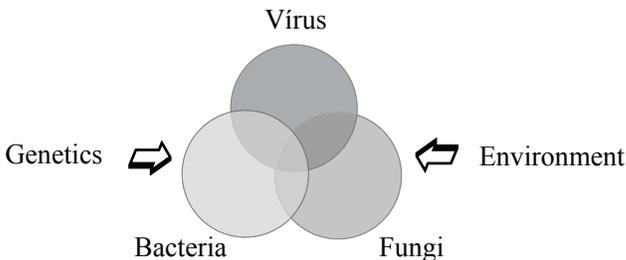
Physiology

Sometimes the physiology of the nasal cycle may appear completely normal in one side of the nose/sinus, with effective mucociliary transport and a permeable middle meatus, but the opposite side may have CRS with mucosal inflammation, with abundant production and secretion of mucus, ciliary disruption and meatal obstruction. This can also be seen in an imaging scan (CT), on endoscopic examination, and in surgery.

Etiology

Etiologic factors (**Figure 2**) are referred to as acute or CRS. Inflammation is where we find viruses, bacteria, and fungi that are widely influenced by **genetics** and **environment**.

Figure 2. Etiological Choreographies Virus, Gram+ bacteria, Gram-bacteria, Fungi, Biofilms

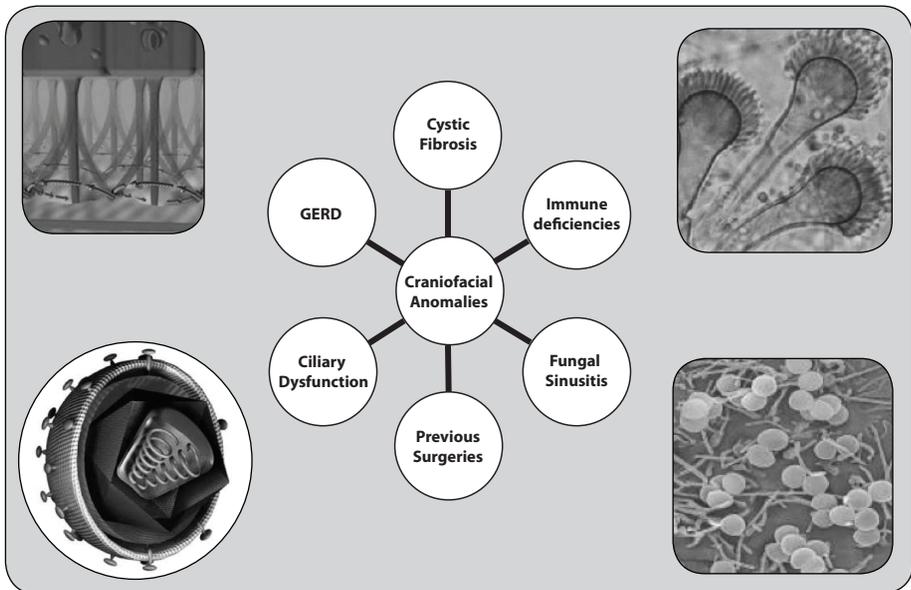


Genetic and Environmental Factors

During the Rhinology World 2009 Congress in Philadelphia (April 2009), in a panel's discussion, it was said that the **genetic factor predominates over the environmental** where immunity or genetics plays a role in chronic rhino/sinus infection. Susceptibility to CRS is genetically determined: there are ten to 12 genes, especially the S100 gene responsible for the repair of innate defenses, as well as many more genes associated. Everything has a place in the nasal respiratory epithelium, a most important element of the immune system. So, environmental origins may have 40% and genetics 60% of influence on CRS.

We also know that CRS has multifactorial origins. It is found in cystic fibrosis, immunodeficiency, ciliary dysfunction, craniofacial abnormalities, and gastroesophageal reflux disease (GERD) (**Figure 3**) with **genetic** influences. On the other hand **environmental causes of CRS** include viruses, bacteria, and fungi harboured in the nose and sinuses in an allergic process, anatomical alterations, inadequate use of medicine, surgical trauma, dental infections, or manipulations.

Figure 3. Multifactorial etiology of CRS



Virus and Bacteria

Bacteria in acute sinus infections are *Streptococcus pneumoniae* in 43%, *Haemophilus influenzae* in 35%, *Moraxella catarrhalis* in 10%, anaerobes in 9% and *Staphylococcus aureus* in 8%. The pathogens observed in CRS are not exactly the same well defined set of organisms which cause acute sinusitis. Overall, bacteriology is difficult to ascertain in CRS as many organisms are recovered in low densities. As a causative agent in CRS we can also have the same bacteria as for an acute sinus infection plus other microorganisms like viruses, gram+

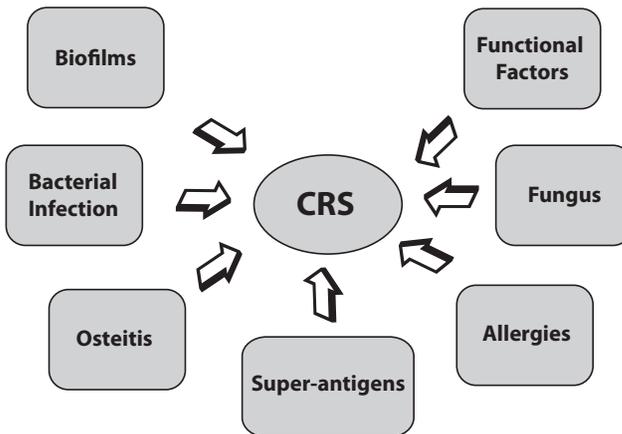
bacteria, gram - bacteria, fungi and biofilms. In CRS we also find anaerobes like *Fusobacterium sp*, *Prevotella sp*, *Propionibacterium sp* and *Peptoestreptococcus sp*. Sometimes there is even *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and coagulase-negative Staphylococci. In CRS the organisms are more resistant to antimicrobials and can even produce super-antigens.

Fungi and Biofilms

Bacterial products cause as much damage in respiratory epithelium as the eosinophil, with all its enzymes, injures epithelial cells and cilia. There is therefore an important relationship between the respiratory cycle and nasal infection. **Fungi** can colonize nasal/sinus areas in immune-suppressed patients receiving treatments for leukemia or malignant tumors, and they may be present in metabolic disorders, reinforcing multi-resistant bacteria (**Figure 4**).

Biofilms are bacterial communities in a matrix of polysaccharides. The process of formation of a biofilm occurs when individual cells adhere and coalesce to various surfaces. Exopolysaccharides (EPS) are produced, resulting in an EPS matrix which forms much of the volume of a biofilm community. Microchannels form through the hydrated EPS matrix, resulting in connections between microbes and periodic shedding of planktonic cells. Individual planktonic cells may then multiply, disperse, and infect the host. Biofilms themselves have been shown to result in a state of chronic inflammation causing collateral damage to tissue not involved in the microbial infection. Biofilms can be detected by scanning electron microscopy (SEM) and right now, as was presented at the Rhinology World 2009 Congress, an electronic nose can identify *Pseudomonas aeruginosa* biofilms.

Figure 4. CRS multifactorial agents



Inflammation and Remodeling

When mucus and its transport is not normal, bacterial colonization will be promoted and polymorphonuclear cells (that produce large amounts of inflammatory mediators) will be attracted, causing tissue damage and disrupting normal local defenses. Remodeling of the nasal/sinus mucosa leads to altered

histology with possible fibrosis and local host deficiencies. A nasal mucosal biopsy can detect remodeling even up to the most severe degree of change seen in nasosinusitis polyposis.

Classification

The EPOs 2007 classification divides rhino/sinus infections into four groups.

- 1- Acute bacterial
- 2- Chronic without polyps
- 3- Chronic with polyps
- 4- Fungal allergies.

Diagnosis

Clinical symptoms and the time it takes a disease to evolve are very important. To confirm the organism it is possible, via nasal endoscopy, to collect samples for culture and cytology from the upper half of the middle meatus. Laboratory tests, a CT scan and so on are also used. Laboratory studies can check on immune-status and test for allergies. Studies can evaluate secretion of mucus, ciliary function, ciliary structure and/or mobility, mucociliary transport, and ciliary dyskinesias.

Ideal Medical Treatment

As no concrete subset of organisms exists to target with oral antibiotics, CRS is a difficult disease to treat. Although broad spectrum beta lactamase stable oral antibiotics are often used to target pathogens, CRS typically does not respond to antibiotic therapy with permanent or sustained improvement. Due to the wide variety of both aerobic and anaerobic organisms cultured from paranasal sinuses, there is no current consensus as to length of treatment length, coverage of organisms, or antibiotics that are most effective. It is generally believed that high-dose antibiotics should be given for a minimum of three weeks in the treatment of CRS.

Surgical Treatment

Alternatives to oral antibiotic therapy in CRS include functional endoscopic sinus surgery (FESS) and adenoidectomies. Pediatric FESS is widely used for the treatment of refractory CRS, with rates of success ranging from 80% to 93%. Published reports suggest that adenoidectomies may be beneficial to patients who have a diagnosis of CRS. In a study by Vandenberg and Heatley, 58% of patients demonstrated near or complete resolution of the symptoms of CRS. The adenoidectomy both eliminates obstruction of the nasal airway and removes a nidus for chronic bacterial infection.

As was presented at the Rhinology World 2009 Congress in Philadelphia, surgical criteria for treatment of sinuses should be considered when:

- 1- rhinosinusitis is refractory to medical treatment;
- 2- there are complications;
- 3- there are local injuries;
- 4- there are local malformations;
- 5- there are tumors.

Therefore, there is no indication for surgery on the sinuses in some specific situations such as these cited below:

- 1- recurrent sinusitis;
- 2- hyper-reactive mucosa;
- 3- uncontrolled allergies;
- 4- active or passive smoking;
- 5- allergy to aspirin with polyposis;
- 6- non-controlled systemic disorders;
- 7- chronic headaches.

Just as a reminder, for both conventional and endoscopic surgery on the sinuses the indications are the same:

- 1- rhinosinusitis refractory to medical and surgical treatment. It is important to remember cystic fibrosis;
- 2 - spread of infection, frequently to the orbit;
- 3 - in cases of trauma or injuries, it is important to preserve the integrity of important structures in the area such as the optic nerve, orbit, skull base and great vessels;
- 4- persistent bleeding despite nasal packing. We can go directly to blocking the sphenopalatine artery;
- 5- local malformations and fistulas;
- 6- tumors (endoscopic surgery alone or in combination with conventional techniques), with the collaboration of an ophthalmologist and neurosurgeon whenever it's needed.
- 7- dacryocystostomy
- 8- pediatric local tumors.

Actually there is a new surgical approach to the sinuses, balloon sinusoplasty with very specific indications (**Figure 5 A, B, C**) that quickly resolves the collection of fluid in the sinus cavity. There are also new optical tweezers (**Figure 5 D**) built with excellent flexibility for viewing sharp angles within the sinus cavities.

Figure 5. Balloon sinusoplasty (A, B, C) and optical tweezers (D)

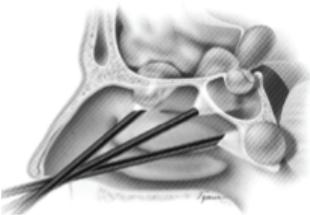


Fig. 5 A

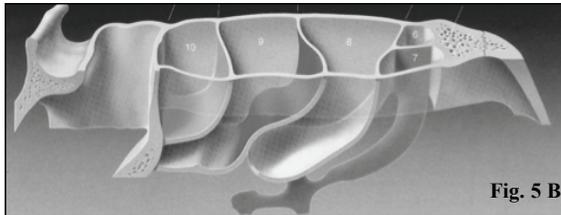


Fig. 5 B

Fig. 5 C

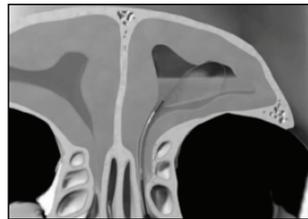


Fig. 5 D

It is important to consider that adequate surgical training in every new technique and newly released tool is a must, because of the close relationship of the sinuses to the orbit and skull base.

Recommended readings

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