# Consensus document

## Consensus document on the aetiology, diagnosis and treatment of sinusitis

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**Key words:**
- Sinusitis
- Rhinosinusitis
- Amoxiciline
- Diagnosis
- Treatment

**Abstract**

The Spanish National Consensus (Spanish Society of Pediatric Infectious Diseases,Spanish Association of Primary Care Pediatrics, Spanish Society of Pediatric Outpatient and Primary Care, Spanish Society of Otorhinolaryngology and Cervical-Facial Pathology) on Sinusitisis presented. Rhinosinusitis is a difficult to diagnose and often unrecognised disease. The document discusses the aetiology, the clinical signs and symptoms, and the diagnostic criteria. Aproposal for treatment is made based on the epidemiological situation in our country. Oral amoxicillin is the treatment of choice (80 mg/kg/day divided every 8 hours). Alternative treatment is proposed in special cases and when amoxicillin is not sufficient. The main complications are reviewed.

### Documento de consenso sobre etiología, diagnóstico y tratamiento de la sinusitis

**Resumen**

Presentamos el Documento de consenso sobre sinusitis de la Sociedad de Infectología Pediátrica (SEIP), la Asociación Española de Pediatría de Atención Primaria (AEPap), la Sociedad Española de Pediatría Extrahospitalaria y de Atención Primaria (SEPEAP) y la Sociedad Española de Otorrinolaringología Pediátrica (SEORL).

La sinusitis es una enfermedad de diagnóstico difícil, a menudo no reconocida. Se analiza la etiología, la clínica y los criterios diagnósticos más aceptados, y se realizan recomendaciones terapéuticas acordes con la situación epidemiológica actual. Se propone la amoxicilina por vía oral como tratamiento antibiótico de elección en dosis de 80 mg/kg/día repartidas cada 8 horas. Se indican tratamientos alternativos en casos especiales y en ausencia de eficacia de la amoxicilina. Se revisan las principales complicaciones de esta entidad.

**Palabras clave:**
- Sinusitis
- Rinosinusitis
- Amoxicilina
- Diagnóstico
- Tratamiento

## INTRODUCTION

Sinusitis is defined as the inflammation of one or more paranasal sinuses that usually occurs as a complication of a viral upper respiratory tract infection. When the symptoms last more than ten days, the presence of a bacterial superinfection is assumed. It is generally diagnosed based on clinical criteria, and although it is usually a self-limiting disease, it is the third leading cause of antibiotic prescription in Primary Care (following otitis and tonsillitis), despite being an underdiagnosed process that is often undocumented.

Areas of debate on sinusitis include its definition and identification, the involvement of viral or bacterial infections and non-infectious factors in its clinical course, its diagnosis based on clinical criteria versus the usefulness of supplemental tests,

and its management with antibiotics and other coadjuvant measures[1].

Consistent with the methodology of other consensus documents, we have included the strength of the recommendation (A: strong evidence, B: moderate evidence, C: weak evidence) and the quality of the scientific evidence (I: randomised controlled trials, II: well-designed studies that are not randomised, III: expert opinions based on clinical experience or descriptive studies) of the proposed measures, following the grading system of the Infectious Disease Society of America.

## DEFINITIONS

The American Academy of Pediatrics defined these processes in 2001 as[2]:

- **Acute bacterial sinusitis:** bacterial infection of the paranasal sinuses lasting less than 30 days whose symptoms resolve completely.

- **Subacute sinusitis:** bacterial infection of the paranasal sinuses lasting between 30 and 90 days. It presents a microbiology similar to that of acute sinusitis.

- **Recurrent acute sinusitis:** episodes of bacterial infection lasting less than 30 days each and separated by intervals of at least 10 asymptomatic days. The patient must present 3 episodes of acute sinusitis in 6 months, or 4 in 12 months.

- **Chronic sinusitis:** episodes of inflammation lasting more than 90 days. Patients have persistent residual respiratory symptoms such as cough, rhinorrea, or nasal obstruction.

- **Acute bacterial sinusitis superimposed on chronic sinusitis:** patients develop new symptoms that resolve with antimicrobial treatment, but the underlying residual symptoms persist.

The latest international clinical practice guidelines have adopted the term "rhinosinusitis" by consensus to refer to the acute, subacute, or chronic inflammation regardless of its aetiology, as the mucosal lining of the nose and sinuses is contiguous and the sinuses are not affected without antecedent or concomitant inflammation of the nasal mucosa. At any rate, at present the old term "sinusitis" is still used interchangeably with the new one to refer to either entity[3].

## EPIDEMIOLOGY

According to United States statistics[3], acute rhinosinusitis affects approximately 31 million patients (adults and children) a year, impacting the quality of life and the use of healthcare resources, and is the cause of a high volume of drug prescriptions. It is estimated that every year 1% of all children are bound to have sinusitis, which will result in a significant cost both in healthcare and in antibiotic consumption. Since some sinuses are pneumatised at birth, sinusitis can develop in infants, yet paediatricians often do not take into consideration this diagnosis in children younger than one year[4].

In Spain we do not have available actual statistics on the incidence of rhinosinusitis, but if we infer that the situation is similar to that of other developed countries, and keeping in mind that children will have about 3 to 8 respiratory infections a year, we can predict that its impact in healthcare and drug prescriptions will not be insignificant[5].

## PATHOPHYSIOLOGY

We must consider a series of aspects, such as: a) the anatomy and development of the paranasal sinuses in children, b) the role of the nasal mucosa in viral or bacterial infections, and c) predisposing or exacerbating factors.

### The paranasal sinuses in children

The paranasal sinuses are divided in 5 groups according to their location and drainage sites: the anterior and posterior ethmoidal sinuses, which drain in the middle and superior meatus, respec-

tively; the two maxillary sinuses, which drain in the medium meatus, and the frontal sinuses[6]:

- The **ethmoidal sinuses** can be seen at birth, develop rapidly up to 7 years of age, and complete their development by 15-16 years of age.

- The **maxillary sinuses** are pneumatised at birth, reaching a volume of 2 ml by 2 years of age, and of around 10 ml by 9 years. They stop developing by 15 years of age.

- The **frontal sinuses** are indistinguishable from the anterior ethmoidal cells and grow so slowly that they cannot be identified anatomically until a year after birth. After the fourth year of life, they become larger and at six years they can be identified radiographically in 20 to 30% of children. They continue to develop during adolescence and at 12 years of age pneumatisation of these sinuses can be seen in computer tomography (CT) scans in 85% of children.

- The **sphenoidal sinus** is a very small evagination of the sphenoethmoidal recess. By seven years of age it has extended posteriorly to the level of the sella turcica, and by 8 years of age it appears pneumatised in CT scans in 85% of patients. Its growth is complete by 15 years of age[1].

### The sinonasal mucosa

The sinonasal mucosa has specific functions, such as filtering and warming up aspirated air, and the immune response to allergies, environmental irritants, and other particles to protect the delicate structure of the lower respiratory tract. It has been demonstrated that the sinusal mucosa is involved in the viral infection of the upper respiratory tract, which resolves spontaneously in most cases (acute viral rhinosinusitis), although in some cases an obstruction of the ostium occurs where air in the cavity is drawn in by the negative pressure facilitating the aspiration of nasopharyingeal mucus rich in bacteria (acute postviral rhinosinusitis) that contaminates the paranasal sinuses (which are sterile under normal conditions). This in turn can lead to bacterial propagation if the mucociliary apparatus

does clear the mucus, and to the development of a bacterial infection of the sinuses (acute bacterial rhinosinusitis), which happens in 6-10% of cases[1,7,8].

### Predisposing or exacerbating factors

The inflammation of the sinonasal mucosa results from the interaction between the insulting agent (infectious or non-infectious), the local defence factors, and the host system, and there are some predisposing factors[1,9,10] (**Table 1**).

## AETIOLOGY

The factors that influence the development of bacterial rhinosinusitis are, among others, the nasopharyngeal microbiota, immunisation status, and previous treatment with antibiotics.

### Normal nasopharyngeal flora

The nose is colonised by a polymicrobial flora, which studies with children have shown to include the species *Streptococcus pneumoniae (S. pneumoniae)* (50-60%), nontypeable *Haemophilus influenzae (H. influenzae)* (40-68%), *Moraxella catarrhalis (M. catarrhalis)* (34-50%) and, to a lesser degree, *Streptococcus viridans, Streptococcus pyogenes (S. pyogenes)* and *Neisseria* spp.[11]. The percentages are higher in children who have undergone a tonsillectomy[12]. The presence of this microbiota in asymptomatic children reinforces the low reliability of meatal cultures for the purpose of aetiological diagnosis.

### Bacteria involved in acute rhinosinusitis

Most sinus infections are viral, and only a small proportion of cases develop a secondary bacterial infection[5]. Rhinovirus, influenza, and parainfluenza are the most common causes of acute rhinosinusitis. The paranasal sinuses are sterile under physiological conditions[9], so the culture of paranasal sinus puncture samples would be the most suitable test for aetiological diagnosis.

| Table 1. Predisposing and associated factors in sinusitis development | |
|---|---|
| **Factor** | **Contribution** |
| Viral infections | Impaired mucociliary function |
| Bacterial pathogens | Bacterial superinfection of the respiratory flora |
| Allergy | Obstruction and inflammation |
| Adenoid hypertrophy | Bacterial reservoir |
| Pollution and tobacco smoke | Irritants |
| Structural abnormalities: deviated septum, nasal wall abnormalities, maxillary sinus hypoplasia, choanal atresia | Impaired mucosal function and aeration, obstruction |
| Gastroesophageal reflux | Nasopharyngeal reflux |
| Immunological factors | IgA and/or IgG subclass deficiencies |
| Chronic diseases: ciliary dyskinesia, Kartagener syndrome, cystic fibrosis, diabetes | Impaired mucociliary function and decreased mucus quality |

In the few studies that evaluated the application of this technique on children, *S. pneumoniae* was isolated in 35-42% of cultures, *H. influenzae,* in 21-28%, *M. catarrhalis,* in 21-28%, *S. pyogenes,* in 3-7%, and anaerobic microorganisms (in chronic and odontogenic processes), in 3-7%[13-16]. There is also the possibility of bacterial coinfection and that different bacterial distributions are involved in infections that involve multiple sinuses[17].

### Impact of immunisation against pneumococcus

Some studies have assessed the impact of the alterations in the microbiome brought upon by the introduction of pneumococcal conjugate vaccines in the aetiology of respiratory infections:

- Children show a decrease in nasal and oropharyngeal colonisation by *S. pneumoniae* with a relative increase in the presence of nontypeable *H. influenzae*[18].

- The herd immunity resulting from immunisation is manifested in the aetiology of sinusitis in adults, with a 10% decrease in the recovery of *S. pneumoniae,* and a change in its identified serotypes, along with a 6% increase in *H. influenzae*[19].

Studies assessing the impact of the introduction of the 13-valent conjugated pneumococcal vaccine on rhinosinusitis need to be done, as the published studies refer to the heptavalent vaccine.

### Antibiotic resistance

The prevalence of penicillin resistance in *S. pneumoniae* ranges from 10 to 30%, and the prevalence of macrolide resistance is around 25%, with geographical variations and changes caused by the introduction of routine immunisations, as there has been a decrease in penicillin resistance following the introduction of the 13-valent conjugated pneumococcal vaccine (this vaccine is not included in the unified immunisation schedule presented by the Ministry of Health, but it is included in the recommendations of, CAV-AEP (Advisory Committee on Vaccines of the Spanish Association of Paediatrics)[20-25]. Macrolide resistance has been decreasing, from 26.4 to 20%, while resistance to levofloxacin has increased from 0.1 to 1.3% (2007), both in relation to the use of these antibiotics (greater and lesser, respectively). The production of beta-lactamases by *H. influenzae* has decreased in a sustained manner from 33 to 17.4% in recent years[26] with the occasional appearance of ampicillin resistance in some strains that is not beta-lactamase-dependent [27], while 90 to 100% of *M. catarrhalis* strains still produce beta-lactamases[28].

## CLINICAL PRESENTATION

The most frequent symptoms of bacterial rhinosinusitis are nasal congestion, usually bilateral, nasal discharge of any type, consistency, and colour, and persistent cough, which may get worse at night. There may be vomiting caused by postnasal drip[29]. Other symptoms may include facial pain or pressure, which may be felt in the teeth, upper jaw, eyes, forehead, or one side of the face, and get worse when bending forward (pain is generally less prevalent in children)[30]. There may also be hyposmia or anosmia, and periocular swelling. Younger children may show less specific symptoms, such as irritability or poor appetite[31]. Preschool children may present with halitosis, otalgia and odynophagia, as well as wheezing. A headache could be the only symptom in some patients (sphenoiditis), but headache and facial pain in isolation of other symptoms are not specific signs of sinusitis.

Symptoms that suggest the development of complications include periorbital oedema, ocular motility abnormalities, recurring fever, severe headache, vomiting, mental state alterations, convulsions, focal neurological signs, and signs of increased intracranial pressure[29,32].

## DIAGNOSIS

The gold standard diagnostic for bacterial rhinosinusitis is the isolation of $\geq 10^4$ colony-forming units from the culture of a sinus puncture aspirate[33], but this procedure is not performed routinely—nor should it be—in clinical practise.

Bacterial sinusitis must be diagnosed based on clinical criteria, and supplemental testing must be reserved in case of suspected complications, poor response to treatment, recurrence of the disease, or special clinical situations such as immunodeficiency or severe underlying disease.

Three types of presentation are defined for the diagnosis of sinusitis[34]:

- Persistent catarrhal symptoms: congestion or nasal discharge, cough, or both, lasting for more than 10 days and less than 30 with no improvement (IIB). Nasal discharge could be watery, unusually mucoid, or purulent, while the cough could be either dry or productive and get worse at night. This is the most frequent presentation of acute bacterial sinusitis.

- Sudden onset of severe symptoms, essentially a high fever (≥39 °C) lasting more than 3-4 days, and purulent nasal discharge (IIB).

- Worsening of symptoms in the course of a common cold, with an increase in nasal discharge, daytime cough, or the development or recurrence of fever, especially if symptoms worsen starting at 6-7 days from the initial onset (IIB).

In 70% of school-children who develop a cold, some symptoms persist after 10 days, but they have improved[35]. The latest guidelines (American and European) agree that the persistence, severity, and worsening of symptoms are the key diagnostic criteria for the disease. However, they warn of the impossibility of differentiating viral from bacterial sinusitis accurately based solely on clinical signs and symptoms, which makes it difficult to select patients who could be given antibiotic therapy and assessed for its results, a difficulty that stems mostly from the lack of well-defined inclusion criteria for patient selection in research studies[1,34].

## PHYSICAL EXAMINATION

It does not usually help make the diagnosis, as possible findings may be absent, have low specificity, and do not differentiate between a viral and a bacterial aetiology[36]. The nasal mucosa may have an erythemathous or pale appearance, there may be nasal discharge in the nasal fossae, mucus in the posterior wall of the pharynx, and pharyngeal and tympanic membrane erythema. There may be a soft and painless periorbital swelling. Palpation of the frontal and maxillary sinuses may cause pain, but facial pain is a low-sensitivity and low-

specificity finding. The presence of halitosis in the absence of pharyngitis, of a foreign body, or poor dental hygiene may lead to suspecting sinusitis.

## SUPPLEMENTAL TESTING

Routine supplemental testing is not recommended in case of presumed acute rhinosinusitis without complications.

### Imaging tests

- Plain **radiography** of the sinuses has been used traditionally as a diagnostic test, but this is a sensitive but low-specificity test in the paediatric population. The signs found most frequently, sinus opacification and mucosal hypertrophy greater than 4 mm, are of little predictive value for a positive diagnosis, as they are found regularly in children who are healthy or have a common cold, viral rhinosinusitis, or allergic rhinitis[37]. Also, 35-50% of healthy children one to nine years of age and up to 97% of patients with a current or recent cold get false positives[38]. Hydroaerial levels, which have a higher specificity, are an infrequent finding[37,38]. Radiography should only be considered in cases of therapeutic failure or severe symptoms with suspected intracranial complications.

- **CT** is more reliable, but it can also give abnormal results in children with mild cold symptoms without clinical evidence for sinusitis, it often requires sedation, and it involves a greater exposure to radiation than plain radiography. Still, if an imaging test is required, this technique offers the best diagnostic performance[39]. A CT scan must be done on an urgent basis in case of proptosis, ocular motility or vision abnormalities, severe headache, repeated vomiting, convulsions, or sensory abnormalities.

- **Magnetic resonance imaging** (MRI) is very costly, and often requires sedation. It is worse than CT at demonstrating the bony structure of the osteomeatal complex, and it also shows abnor-

malities in patients with a common cold[40], although it is more sensitive in the early detection of intracranial complications, in the differentiation between inflammation and tumours, and in cases of chronic fungal sinusitis, which is very rare in children[41].

We may conclude that routine imaging is not recommended for evaluating acute bacterial sinusitis without complications in the paediatric population, and that it should be reserved for evaluating persistent, recurrent, or chronic sinusitis, or in case of suspected complications.

### Other supplemental tests

- **Endoscopic sinus examination** has been shown to correlate adequately with CT findings, but cannot be performed on a routine basis[42].

- **Transillumination or diaphanoscopy** is of little value in the paediatric population, as the sinuses are small and the findings are difficult to evaluate and apply only to the maxillary sinuses[43].

- Portable ultrasound imaging of the paranasal sinuses is much more promising, but it is still relatively unknown and not widely practised. It is a quick, simple and non-invasive test. The procedure is painless, can be repeated as many times as needed, and does not require exposure to radiation. When performed expertly, this technique has shown much higher sensitivity (>86%) and specificity (>96%) than radiography in detecting the presence of secretions in the maxillary sinuses. However, it also has its limitations: it cannot be used for diagnosing ethmoidal or sphenoidal sinusitis, and the elevated cost of the machine poses a challenge to its systematic addition to the paediatrician's office[44-46].

## DIFFERENTIAL DIAGNOSIS

The following conditions are considered in differential diagnosis:

- Common cold and acute rhinitis: usually, there is no fever or a short-lived low-grade fever, and the cough and nasal discharge start improving by the fifth or sixth day from onset. In sinusitis, these symptoms do not improve, there may be general malaise, and the fever (should it be present) and other symptoms are more severe and persistent. It may be difficult to differentiate sinusitis from recurrent colds, which are quite frequent in children, although asymptomatic intervals must occur in case of recurrent colds[1,29].

- Conditions with symptoms that include nasal obstruction, nasal discharge, and persistent cough[1,47,48]. These are detailed in Table 2.

- Conditions with symptoms that include with facial or cranial pain, such as tension headache, toothache, atypical facial pain, and temporomandibular joint dysfunction[49]. Predisposing factors and underlying primary conditions must be ruled out in case of recurrent or atypical clinical courses (Table 1).

## REFERRAL CRITERIA

Referral criteria are noted in Table 3.

## COMPLICATIONS OF SINUSITIS

Complications develop in 3.7-11% of acute bacterial sinusitis cases and can be classified as orbital (60-70%), intracranial (15-20%), and bony (5-10%) (Table 4). Orbital complications develop most often between 3 and 6 years of age, and intracranial complications are more frequent in adolescents[50,51]. The most common complication of acute rhinosinusitis is periorbital cellulitis.

### Orbital complications

Infection may spread easily to the orbit directly through the lamina papyracea, which is very thin and may be dehiscent; it can also spread along venous channels[52]. Chandler *et al.*[53] did the classifi-

| Table 2. Differential diagnosis of sinusitis. Conditions with symptoms that include nasal obstruction, rhinorrhoea, and persistent cough |
|---|
| • Allergic rhinitis: the prevailing symptoms are usually nasal, unless it is associated to asthma, and there is no antecedent infectious disease. |
| • Foreign body in the nose: usually associated to obstruction and unilateral purulent and malodorous nasal discharge. |
| • Unilateral choanal stenosis |
| • Adenoiditis/tonsillitis: its symptoms include obstruction, breathing through the mouth, snorting sounds, nasal voice. It is very hard to distinguish these two entities based on clinical criteria, and comorbidity may occur. |
| • Nasal polyps: when presence, cystic fibrosis and allergic fungal sinusitis must be ruled out, especially if the polyps are bilateral. |
| • Septum abnormalities |
| • Tumours (rare): they usually produce chronic unilateral symptoms, may lead to production of bloody discharge and unilateral facial swelling. |
| • Cough-equivalent asthma. |
| • Bacterial bronchitis caused by *Haemophilus influenzae*, *Streptococcus pneumoniae* o *Moraxella catarrhalis*: characterised by a 2-4 week cough that evolves favourably with antibiotic treatment in two weeks, when there is no alternative diagnosis. |
| • Pertussis. |
| • Other causes of protracted cough, including tuberculosis and gastroesophageal reflux |

| Table 3. Hospital referral criteria | |
|---|---|
| Immediate referral | Suspected complication: toxic appearance, high fever, severe headache, orbital oedema, frontal swelling, abnormal, displacement of the globe, ophthalmoplegia, diplopia, diminished visual acuity, confusion, meningeal signs, focal neurological signs. |
| Urgent referral | Unresponsive to prolonged treatment, immunocompromised patient, underlying primary disease, suspicion of rare or resistant microbial agent |
| Scheduled | Anatomic defects, recurrent episodes, chronic sinusitis |

| Table 4. Complications of acute rhinosinusitis | | | |
|---|---|---|---|
| **ORBITARY COMPLICATIONS** | | | |
| **Stage** | **Diagnosis** | **Clinical signs** | |
| I | Periorbital (preseptal) cellulitis | Upper eyelid oedema with normal vision and extraocular movement | |
| II | Orbital (postseptal) cellulitis | Palpebral and periorbital oedema, proptosis, chemosis, extraocular movement may or may not be limited | |
| III | Subperiosteal abscess | Orbital contents displaced downward and laterally. Limited extraocular movement and decreased visual acuity. | |
| IV | Orbital abscess | Severe proptosis. Complete ophthalmoplegia, decrease in visual acuity that can lead to irreversible blindness | |
| V | Cavernous sinus thrombosis | Orbital pain, ecchymosis, proptosis, sepsis, ophthalmoplegia. It can spread to the other eye. | |
| **OTHER COMPLICATIONS** | | | |
| **Tipo** | **Clínica** | **Diagnóstico** | **Tratamiento** |
| Endocranial: epidural or subdural abscess, brain abscess, meningitis, cerebritis and cavernous sinus thrombosis | High fever, severe headache, signs of intracranial complications (nausea, vomiting, meningeal signs, and alterations of consciousness) In cavernous sinus thrombosis, bilateral ptosis, exophthalmos, ophthalmic nerve neuralgia, retro-ocular headache, complete ophthalmoplegia, papilloedema, cranial nerve pathology (6th, 7th) | Frequently associated to frontoethmoidal or sphenoidal sinusitis Contrast CT scan Angioresonance for cavernous sinus thrombosis | High-dosage IV antibiotic treatment (covering aerobic and anaerobic pathogens) + Neurosurgical drainage and endoscopic drainage of affected paranasal sinuses |
| Bony: maxillary or frontal bone osteomyelitis | Affects older children Painful frontal swelling (Pott's puffy tumour) Fever | CT or MRI | Broad-spectrum IV antibiotic treatment + Surgical drainage and cleaning of affected bones |

**MRI:** magnetic resonance imaging; **CT:** computer tomography.

cation of orbital complications in 1970, a system that organises the typical models of orbital pathology with their expected disease progression (**Table 4**). It is important to be aware that orbital complications may be painless in children.

### Periorbital or preseptal cellulitis

It is the swelling of the eyelid and the conjunctiva, which affects the tissue anterior to the orbital septum and can be discerned easily in a CT as a soft-tissue inflammation. It often occurs as a complication of upper respiratory tract infection, dacryocystitis or skin infection, and sinusitis[54]. It presents with palpebral oedema, erythema, and fever. It is not associated to proptosis, and it does not lead to limited ocular motility. It usually responds well to antibiotic therapy, but if it is not treated early on it can spread beyond the orbital septum. In most cases, preseptal cellulitis is a clinical diagnosis that does not require evaluation with a CT scan[55].

### Orbital or postseptal cellulitis

It develops as inflammatory changes affect the orbit, and symptoms include chemosis, proptosis, and limited and painful eye movements[56]. This complication requires intensive treatment with intravenous antibiotic therapy and ruling out the presence of a subperiosteal or orbital abscess by means of CT. If intracranial complications are suspected, the evaluation must also include MRI.

### Subperiosteal and orbital abscess

Subperiosteal abscesses form between the periorbita and the paranasal sinuses in the outermost

part of the extraocular muscles. The clinical signs include swelling, erythema, ecchymosis, and proptosis, with decreased ocular motility (ophthalmoplegia) and diminished visual acuity[57].

Orbital abscesses are intraconal, limited by the recti muscles and their sheaths, and by Tenon's capsule. They usually develop in cases of delayed diagnosis or in immunocompromised patients, and their prevalence ranges between 8 and 13%[58].

Surgical drainage is indicated when there is an abscess confirmed by CT and progressive vision loss or absence of symptom improvement after 48 hours of intravenous therapy[59]. An ophthalmologist must monitor visual acuity, and the patient can be switched to oral antibiotic therapy once fever has been absent for over 48 hours and ophthalmological signs and symptoms have resolved.

The current consensus guidelines recommend that preseptal and orbital cellulitis be treated with antibiotic therapy first, with surgical intervention required for subperiosteal and intraorbital abscesses, usually by endoscopy[57]. However, there are recent studies that show good results with intravenous antibiotics in children with subperiosteal abscesses[60] when the following conditions are met: improvement of symptoms in 24-48 hours, normal visual acuity; small subperiosteal abscess (<0.5 to 1 ml) located medially, absence of systemic disease, and patient age between 2 and 4 years[61].

## MANAGEMENT

### Non-antibiotic treatment

The use of vitamin C, zinc, echinacea, decongestants, systemic antihistamines, or mucolytics is not recommended in the latest reviews due to a lack of efficacy and/or potential toxicity[62,63].

Isotonic or hypertonic saline solutions result in a self-reported improvement of the symptoms and of mucociliary clearance[64-66], improve the elimination of secretions, and prevent crust formation, but the data are still too few to make a recommendation based on strong-enough evidence[67]. Oral

corticosteroids as adjuvant treatment with antibiotic treatment are effective in the short-term alleviation of acute sinusitis symptoms. Still, the data are limited and there are no quality studies justifying their use as a monotherapy or as an adjuvant treatment in antibiotic therapy[68].

Intranasal corticosteroids seem to be somewhat useful in combination with antibiotics, especially in studies done with adults, and could be beneficial in children with underlying allergic rhinitis, but there need to be more studies supporting their usefulness in sinusitis in the paediatric population[69].

### Antibiotic treatment

In 2001, the AAP recommended the use of antibiotics in acute bacterial sinusitis, although its efficacy in symptom control and above all in preventing the development of potential complications of the disease remains the subject of heated controversy[1,34,70-75]. There is a high rate of spontaneous resolution of uncomplicated acute sinusitis (60-80%), so at present the trend is to recommend antibiotic prescription only for persistent or complicated cases. The consensus group also recommends starting antibiotic therapy whenever the diagnostic criteria for bacterial sinusitis are met (see the section on diagnosis), except in children whose symptoms have lasted at least 10 days but are showing improvement. In these cases, the approach would be one of watchful waiting, monitoring the patient closely and treating the symptoms.

### First-line treatment

Our first-line treatment is amoxicillin[76-78], which shows good activity against pneumococcus, the pathogen most frequently involved and causing the highest rate of complications. In areas with high rates of immunisation against pneumococcus, we have observed a decrease in nasopharyngeal colonisation by pneumococcus and an increase in nontypeable *H. influenzae* and *M. catarrhalis* isolates. In such instances, amoxicillin-

clavulanic acid can be used as an alternative, as most *M. catarrhalis* isolates and 10-20% of *H. influenzae* isolates produce beta-lactamases. Amoxicillin-clavulanic acid is also recommended in sinusitis with a high risk for complications where all possible conditions need to be covered: children younger than 2 years, frontal or sphenoidal sinusitis, complicated ethmoidal sinusitis, patients with very severe or protracted symptoms (lasting longer than a month), patients with chronic conditions or who are immunocompromised, or patients who did not respond to initial treatment with amoxicillin.

In Spain, the recommended dose of amoxicillin (be it alone or in combination with clavulanic acid) is 80-90 mg/kg/day divided at 8-hour intervals, as the resistance to penicillin rates of pneumococcus are greater than10%.

### Alternative treatment

Various studies have shown that second-generation oral cephalosporins (cefuroxime axetil), and third-generation cephalosporins (cefpodoxime proxetil o ceftibuten) and fluoroquinolones are efficacious, but the results were not better than those achieved with amoxicillin or amoxicillin-clavulanic acid[79,80], so their use should be reserved for patients with a non-severe (not Type I) hypersensitivity to penicillin. Although macrolides are not a good treatment option due to the high percentage of resistance to these drugs (25-30%), in case of immediate or rapid (Type I) hypersensitivity and low-severity disease they can be used while reserving other treatment options. Another option when these patients have mild symptoms is to monitor them carefully and delay initiation of antibiotic therapy. Levofloxacin can be used as a last option for this particular group of children with severe Type I allergy to penicillin and poor response to treatment with macrolides.

### Duration of antibiotic therapy

It is recommended that antibiotic treatment lasts between 7 and 14 days[1,32], with 10 days being the duration recommended most frequently[76,77,81,82].

Some patients respond slowly to treatment and require longer courses, in which case it is recommended to extend antibiotic therapy until 7 days after symptoms resolve. In some cases (children with partial responses to treatment), the therapy can extend to up to 3 weeks[76,81].

### Recommended approach in case of therapeutic failure

With adequate treatment, in 48-72 hours children no longer have a fever and the coughing and rhinorrhoea are gradually subsiding[76,82]. If this is not the case, the diagnosis and treatment must be re-evaluated[76,82]. The main causes of treatment failure, once it is ascertained that the treatment was administered correctly, are: microbial resistance to the antibiotic used, development of complications, non-infectious aetiology (intranasal foreign bodies, structural malformations, and allergy) or, in rare cases, the existence of a chronic condition or an immunodeficiency. If microbial drug resistance is suspected, it is advisable that the empiric antibiotic therapy is modified by adding an antimicrobial that is efficient against beta-lactamase-producing bacteria or pneumococci with high-level penicillin resistance: amoxicillin-clavulanic acid, or even third-generation cephalosporins, respectively (intramuscular ceftriaxone)[76,82].

### Criteria for hospital admission and selection of empiric intravenous antibiotic therapy

Children showing signs of sepsis or deterioration of their general health status, whose treatment with oral drugs has failed, or who have developed complications (to be considered in case of preseptal cellulitis) must be hospitalised and treated parenterally with one of the following antibiotics: amoxicillin-clavulanic acid, cefotaxime or ceftriaxone[76,82]. Imaging is recommended for confirmatory diagnosis and for evaluation by an otorhinolaryngology specialist (ORL). If intracranial complications with the presence of anaerobic bacteria are suspected, cefotaxime must be administered in conjunction with metronidazole. In case of

Type I penicillin allergy, levofloxacin in conjunction with metronidazole may be an option for patients with severe disease.

### Treatment protocol

1. **Non-antibiotic medical treatment:**
   - Pain relief: recommended (IA). Ibuprofen or paracetamol administered orally at regular doses. Ibuprofen shows a better time course of action due to its double analgesic and anti-inflammatory properties.
   - Saline solution washes: recommended therapy (IIB). It is an inexpensive and innocuous treatment that has proven useful in some studies.
   - Intranasal corticosteroid therapy: recommended in children with underlying allergic rhinitis (IIIC); and in children with no underlying allergic condition (IIIC), especially in patients who are being monitored without antibiotic treatment.
   - Mucolytics, decongestants, and antihistamines: not recommended (IA).
   - Monitoring without antibiotic treatment: it is recommended to delay initiating treatment with antibiotics in children whose symptoms have lasted more than ten days but are showing improvement.

2. **Oral antibiotic treatment: recommended in all other patients (IIB):**
   - First-line treatment:
     – Amoxicillin: 80-90 mg/kg/day in divided doses every 8 hours for 10 days (IIB).
   - In children younger than two years with sphenoid or frontal sinusitis, incipient preseptal cellulitis, who are immunocompromised, or have a significant underlying condition, with very severe or protracted symptoms (lasting more than one month), and whenever the patient does not seem to respond to initial treatment with amoxicillin:
     – Amoxicillin-clavulanic acid (8/1): 80-90 mg/kg/day in divided doses every 8 hours for 10 days (IIB).

- In children with delayed hypersensitivity (non-anaphylactic reaction):
  – Cefpodoxime proxetil: 10 mg/kg/day doses in divided doses every 12 hours for 10 days (IIB).
  – Ceftibuten: 9 mg/kg/day doses every 24 hours (maximum of 400 mg/day), for 5-10 days (IIIC).
  – Cefuroxime axetil: 30 mg/kg/day in divided doses every 12 hours for 10 day (IIB).
- In children with immediate or rapid hypersensitivity to penicillin (Type I, anaphylactic reaction):
  – Strongly consider the option of watchful waiting without antibiotic treatment (IIIC).
  – In non-severe cases, clarithromycin 15 mg/kg/day divided in doses every 12 hours (IIIC) or azithromycin 10 mg/kg/day every 24 hours for 3 days, or 10 mg/kg/day the first day and 5 mg/kg/day for four more days.
  – In severe cases or if treatment with macrolides has failed, levofloxacin, 10-20 mg/kg/day in divided doses every 12-24 hours for 10 days (off-label use) (IIIC).
- In children with poor tolerance to the initial oral treatment:
  – Intramuscular ceftriaxone intramuscular in 50 mg/kg/day doses every 24 hours for 1-3 days, followed by one of the treatment courses noted above (depending on clinical history) until completion of 10 days of treatment (IIIC). Ceftriaxone is a hospital-only drug, so the patient must be referred to the hospital to evaluate its administration.

3. **Recommended approach in case of therapeutic failure after 48-72 hours of correct initial antibiotic treatment:**
   - Differential diagnosis:
     – Complications.

- Non-infectious aetiology.
- Immunodeficiencies.
- Consider imaging tests in case of complications (IIIC).
- Change of empiric oral antibiotic determined by the antibiotic used initially (IIB):
  - Amoxicillin-clavulanic acid: 80-90 mg/kg/day divided in doses every 8 hours if treatment started with amoxicillin (IIB).
  - Oral cephalosporins (cefuroxime o ceftibuten) provide benefits beyond those of treatment with amoxicillin-clavulanic acid, so they are not recommended in this consensus in case of initial treatment failure.
  - Levofloxacin in 10 mg/kg doses every 12 hours in children aged 6 months to 5 years, and in 10 mg/kg doses every 24 hours in children older than five years (maximum dose 500 mg/day) (off-label use) in children with Type I penicillin allergies (anaphylaxis) if treatment with macrolides has not been effective (IIIC).
  - Patients who have not improved with the treatments indicated above should be referred to the hospital to receive intramuscular ceftriaxone.

4. **Criteria for hospital referral and treatment:**
   - Criteria for hospital admission:
     - Signs of sepsis.
     - Deterioration of general health status.
     - Persistent failure after two rounds of oral treatment (criterion for evaluation at the hospital with or without admission).
     - Complications (with the possible exception of preseptal cellulitis).
     - High-risk household environment where compliance with treatment is not guaranteed.
   - Recommended radiographic tests (IIB).

- Assessment by ORL and Ophthalmology specialists in case of orbital or periorbital cellulitis (IIIC).
- Intravenous treatment (IIB):
  - Amoxicillin-clavulanic acid: 100 mg/kg/day in divided doses every 6 hours (IIB).
  - Cefotaxime: 150-200 mg/kg/day in divided doses every 6-8 hours (IIB) or ceftriaxone, 50-100 mg/kg/day in divided doses every 12-24 hours (IIIC), if the patient had been treated previously with amoxicillin-clavulanic acid.
  - Levofloxacin in 10 mg/kg doses every 12 hours in children 6 months to 5 years of age, and 10 mg/kg doses every 24 hours in children older than 5 years (maximum dose 500 mg/day) (*off-label* use) (IIIC), in children with a Type I penicillin allergy.
- In case of suspected intracranial complications or possible infection with anaerobes:
  - Add metronidazole to treatment with cefotaxime (or levofloxacin in allergic patients), 30 mg/kg/day in divided doses every 6 hours (IIIC).
- If intravenous antibiotic treatment fails, potential complications must be evaluated in consultation with the ORL specialist and an expert in paediatric infectology.

## CONFLICT OF INTERESTS

## ACRONYMS

**ORL:** Otorhinolaryngology • **MRI:** nuclear magnetic resonance imaging • **CT:** computer tomography.

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