6. Rhinitis and nasal polyposis

6.1 Definitions

The term rhinitis defines the inflammatory process of the nasal mucosa, which is characterized by the following clinical symptoms: anterior or posterior rhinorrhea, sneezing, block of nasal passages or congestion and/or nasal pruritus/itching. These symptoms should be present for two or more consecutive days and for more than one hour on most of the days. Rhinosinusitis (RS) occurs when inflammation also affects paranasal sinuses. The exclusive involvement of sinuses, with nasal mucosa being unaffected, is rare. RS is defined as the inflammation of the nasal and paranasal sinus mucosa and is characterized by two or more of the following symptoms, one of which should be nasal obstruction/congestion and/or anterior/posterior rhinorrhea, with or without facial pain/tenderness and/or reduction or loss of smell, as shown by endoscopic signs or changes on computerized tomography.

Allergic rhinitis (AR) is defined as a group of immunologically-mediated inflammatory type symptoms occurring after allergen exposure and including nasal itching, sneezing, nasal obstruction/congestion and posterior rhinorrhea/discharge, which may resolve either spontaneously or with medication.

6.2 Classification

Multiple classifications of rhinitis are currently available. Their clinical usefulness in daily practice, however, is limited as they combine pathogenic and etiologic criteria. A clinical classification of rhinitis, supported by a broad worldwide consensus, is that proposed in the document Allergic Rhinitis and its impact on Asthma (ARIA) (table 6.1).

Since the publication of the ARIA document, classification of AR has changed to the groups of intermittent and persistent, because the former classification comprising seasonal, perennial and occupational types did not reflect the clinical status of real-world patients. The categorization based on duration and severity of AR proposed in the ARIA document has now been validated. Based on the ARIA items concerning classification of severity, a number of clinical criteria have been defined to enable discrimination between three severity stages: mild, moderate and severe. These criteria have been validated for the adult and pediatric populations, as well as for treated and untreated adults (table 6.2).

A local AR characterized by a positive response to the specific nasal challenge in patients with negative intraepidermal tests and a negative specific serum IgG has recently been described.

Table 6.1. Clinical classification of rhinitis

<table>
<thead>
<tr>
<th>Infectious</th>
<th>Drug-induced</th>
<th>Hormonal</th>
<th>Other causes</th>
<th>Idiopathic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Viral</td>
<td>• Acetylsalicylic acid and non-steroidal anti-inflammatory drugs</td>
<td>• Responsible allergen: perennial, seasonal, work-related</td>
<td>• NARES (non-allergic rhinitis with eosinophilia syndrome)</td>
<td></td>
</tr>
<tr>
<td>• Bacterial</td>
<td>• Other medicines</td>
<td>• Duration: intermittent, persistent</td>
<td>• Due to irritants</td>
<td></td>
</tr>
<tr>
<td>• Other infectious agents</td>
<td></td>
<td>• Severity: mild, moderate and severe</td>
<td>• Due to food</td>
<td></td>
</tr>
<tr>
<td><strong>Allergic, according to</strong></td>
<td></td>
<td><strong>Other causes</strong></td>
<td>• Emotional</td>
<td></td>
</tr>
<tr>
<td>• Responsible allergen: perennial, seasonal, work-related</td>
<td></td>
<td><strong>Other causes</strong></td>
<td>• Atrophic</td>
<td></td>
</tr>
<tr>
<td>• Duration: intermittent, persistent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Severity: mild, moderate and severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Classification of rhinitis adapted from the document Allergic Rhinitis and its Impact on Asthma (ARIA)
Table 6.2. Classification of allergic rhinitis

<table>
<thead>
<tr>
<th>According to duration</th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms are present for ≤ 4 days a week or for ≤ 4 consecutive weeks</td>
<td>Symptoms are present for &gt; 4 days a week and for &gt; 4 consecutive weeks.</td>
<td></td>
</tr>
</tbody>
</table>

According to severity

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>None of the following items is present:</td>
<td>- One</td>
<td>The four items are present</td>
</tr>
<tr>
<td>- Sleep disturbances</td>
<td>- Two</td>
<td></td>
</tr>
<tr>
<td>- Impairment of daily, leisure and/or sports activities</td>
<td>- Or three of the aforementioned items</td>
<td></td>
</tr>
<tr>
<td>- Impairment of school and work tasks</td>
<td>are present</td>
<td></td>
</tr>
<tr>
<td>- Symptoms are bothersome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

6.3 Epidemiology

The most common clinical presentation of rhinitis is common cold, with an incidence of 2 to 5 episodes/year in adults and 7 to 10 episodes/year in children. AR is the most frequent type among non-infectious rhinitis and is often associated with conjunctivitis and asthma. It represents an overall health problem affecting 10-20% of the population. The prevalence in the general population has been estimated to be around 21.5% (mean age 31.3 years), among which 21-64% of cases are persistent, 36-79% intermittent, 48.5-63% perennial and 37-51% seasonal. Eighty-two percent of intermittent AR are mild (18% moderate/severe) and 44% of persistent AR are mild (56% moderate/severe). A study carried out in Spain showed that rhinitis was the most common presenting complaint in Allergy outpatient clinics (55.5% of total). Allergic etiology was demonstrated in 72% of cases, 51.9% of patients were sensitized to pollens and 40.2% to dust mites, with polysensitization being very frequent (31.2%). Asthma was diagnosed in 37.3% of patients with rhinitis. The ISAAC study reported that the prevalence rate of rhinoconjunctivitis was 7.9% among Spanish children aged 6-7 years (with an annual increase of 0.33) and 15% among those aged 13-14 years (annual increase of 0.10).

6.4 Diagnosis

By definition, AR diagnosis is mainly clinical, although symptoms do not enable to establish either the cause or type of rhinitis. Therefore, clinical examination and diagnostic tests may be necessary for a complete disease characterization. Family history of allergy, seasonal distribution of symptoms, concomitant ocular and nasal symptoms and an association with exposure to animal dander, pollens and dust, are clinical data with a high predictive value for the diagnosis of suspected AR (figure 6.1). The most cost-effective tests for the etiologic diagnosis of AR are intraepidermal puncture or skin prick testing and/or in vitro tests for determination of specific serum IgE.

It should be borne in mind that positivity of skin tests and specific IgE against different allergenic sources may be irrelevant from a clinical point of view. A high percentage of individuals with positive skin tests do not have the disease. It has been shown that specific IgE assay techniques enabling the molecular diagnosis of the different allergens found in various allergenic sources, improve the allergologic diagnosis in polysensitized patients and are, therefore, more specific for the indication of immunotherapy with allergens.

The reference test for diagnosing AR is the specific nasal challenge (or the nasal provocation test). When there is diagnostic doubt, this test can be performed with the suspected allergen. The Committee on Rhinoconjunctivitis of the Spanish Society of Allergology and Clinical Immunology has recently published a consensus document on the indications and methodology of the specific nasal challenge with allergens.

Other diagnostic studies that may be useful for evaluating nasal function include the objective assessment of obstruction (acoustic rhinometry, active anterior rhinomanometry, measurement of the maximum inspiratory nasal flow) the assessment of nasal inflammation (nasal cytology, biopsy) and the evaluation of smell by olfactometry.

6.5 Rhinitis and asthma

Multiple epidemiological, pathophysiological and therapeutic studies have demonstrated the association between rhinitis and asthma. The prevalence of asthma in patients with allergic rhinitis is much higher than in the general population (<2%). In different studies carried out in Spain and Portugal, approximately half of patients with AR patients suffer from asthma. Factors determining why some patients with AR will develop asthma are unclear. The prevalence of rhinitis in asthma patients is very high, much higher than in the general population.

In our country, two recent studies have shown a prevalence of rhinitis in patients with asthma of 71% and 89.5%. A parallel increase in the prevalence of asthma and rhinitis has been also reported in Spain.
A greater severity and duration of AR may increase the probability of suffering from asthma.417,418 There is a temporal relationship between the onset of allergic rhinitis and asthma, with rhinitis usually preceding the development of asthma.423 AR and non-allergic rhinitis have been shown to be risks factors for asthma.423 Also, rhinitis aggravates asthma,424 worsens asthma control,425,426 and asthmatic symptoms.427, and increases the use of healthcare resources.428

Inflammatory changes in the bronchial mucosa of non-asthmatic patients with AR have been observed, as has been the case with nasal eosinophilic inflammation in asthma patients without nasal symptoms.429

Treatment of AR with intranasal glucocorticoids may improve some aspects of asthma, such as pulmonary function, symptom score, quality of life or the use of reliever or rescue medication.433

6.6 Treatment

The treatment strategy of allergic rhinitis includes: patient education, avoidance of allergens and contaminants, pharmacotherapy and specific allergen immunotherapy.114,423 At the time of selecting the pharmacological treatment, efficacy, safety, cost-effectiveness relationship, patients’ preferences, severity of disease and the presence of comorbidities should be evaluated. Pharmacological treatment of allergic rhinitis should include clear-cut recommendations that will have to be implemented in a stepwise fashion according to severity (figure 6.2).

Figure 6.1. Diagnostic algorithm of allergic rhinitis.397

Oral H1-antihistamines improve symptoms of rhinitis in both adults and children, including rhinorrhea, sneezing, nasal itching and ocular symptoms, although they are less effective in relieving nasal obstruction.436, Second generation H1-antihistamines (non-sedating) (bilastine, cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, mequitazine, mizolastine, rupatadine) have fewer side effects and should be preferred over the first generation (sedating) antihistamines, in terms of efficacy and particularly safety.438,439

Topical H1-antihistamines (azelastine, emedastine, epinastine, levocabastine, olopatadine) have also shown to be effective in allergic rhinitis and conjunctivitis.433,434,435

Intranasal glucocorticoids (budesonide, ciclesonide, fluticasone, mometasone, triamcinolone) are highly potent and effective anti-inflammatory drugs for the treatment of allergic and non-allergic rhinitis, in both adults and children. The application of intranasal glucocorticoids results in high drug concentrations being achieved within the nasal mucosa, with a minimum risk of systemic adverse effects. Their efficacy on the symptoms of allergic rhinitis, including nasal obstruction and ocular symptoms, is well documented, and they represent a very effective first-line treatment of moderate-severe allergic rhinitis.433-436,438

Intranasal glucocorticoids are more effective than antihistamines and antileukotrienes.437

The combination of a glucocorticoid and an antihistamine (fluticasone propionate and azelastine) administered through the intranasal route has been shown to be more effective than the individual administration of each drug, and it is currently considered one of the first-line treatment options for moderate-severe allergic rhinitis.439-440

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Investigate the presence of asthma especially in patient with severe and/or persistent rhinitis

**Diagnosis of allergic rhinitis**

**Intermittent symptoms**

**Persistent symptoms**

**Mild**
- oral or intranasal antihistamine
- and/or decongestant
- or LTRA

**Moderate-severe**
- oral or intranasal antihistamine
- and/or decongestant - or intranasal GC
- or intranasal combination of fluticasone + azelastine
- or LTRA - (or chromone)

In persistent rhinitis, the patient should be evaluated at 2-4 weeks

In failure: increase one step
If improvement: continue with treatment for 1 month

**Moderate-severe**

In order of preference
1st option: fluticasone + azelastine in intranasal combination or 2nd option: intranasal GC with or without oral antihistamine or LTRA

The patient should be evaluated at 2-4 weeks

Improvement
No Improvement

Step-down and continue treatment for < 1 month
Check diagnosis
Check adherence
Ask for infections or other causes

Add or increase the dose of intranasal GC
Rhinorhea
Add ipratropium

Blockage: add nasal decongestant or oral GC (short course)

If failure: refer to the specialist

**Avoidance of allergens or irritant may be beneficial**

If conjunctivitis:
Add:
oral antihistamine
or intraocular antihistamine
or intraocular chromone (or saline)

**Consider specific: immunotherapy**

GC: Glucocorticoids; LTRA: leukotriene receptor antagonist.

Figure 6.2. Treatment algorithm for allergic rhinitis

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Short courses of oral glucocorticoids (prednisone, methylprednisolone, deflazacort) can be used in case of severe rhinitis failing to respond to other treatments. Intramuscular glucocorticoids should not be prescribed for the treatment of AR because of the potential appearance of serious adverse effects433.

**Intranasal decongestants** (phenylephrine, naphazoline, oxymetazoline, tramazoline, xylometazoline) may be used over a short period of time in patients with clinically relevant nasal blockage. The use of intranasal decongestants in children is not recommended433. The prolonged use of topical nasal decongestants (> 5 days) may cause rhinitis medicamentosa441.

**Oral decongestants** (phenylephrine, pseudoephedrine) either alone or associated with oral antihistamines (pseudoephedrine and cetirizine; pseudoephedrine and ebastine; pseudoephedrine and loratadine) are not devoid of systemic side effects, although they have shown to be effective. Their use should be reserved for patients in whom the occurrence of these side effects would be highly unlikely433.

**Leukotriene receptor antagonists** (montelukast) are effective for the treatment of allergic rhinitis and conjunctivitis, in both adults and children, although their efficacy is lower than that of intranasal glucocorticoids or oral antihistamines433, thereby representing a second-line treatment. Since these compounds are also effective in treating asthma, they are indicated in patients with both disorders432,443.

**Topical anticholinergics** (ipratropium bromide) may be used to improve treatment-resistant rhinorrhea in children and adults with perennial rhinitis434, as well as in common cold434.

**Topical chromones** (sodium nedocromil, disodium cromoglycate) have shown moderate efficacy in the treatment of allergic rhinitis and conjunctivitis433.

The anti-IgE monoclonal antibody, *omalizumab*, has been shown to be effective in treating AR symptoms, particularly in patients with suboptimal relief of symptoms despite being correctly treated following current recommendations466. In Spain, however, AR is not included as an indication for the use of omalizumab in the technical specifications of the product.

**Allergen immunotherapy** is effective and cost-effective for the treatment of adult and pediatric AR caused by pollens or dust mites when administered both subcutaneously and orally (sublingual route)434,447,448. For this therapy to be prescribed a correct assessment of the allergic nature of the rhinitis is necessary. It may alter the natural course of the respiratory allergic disease, decreasing the development of asthma and preventing new sensitizations449.

Allergen immunotherapy is effective for symptom improvement in patients with concomitant asthma and rhinitis433,450,451.

**Avoidance measures** for indoor (mites, molds), pet and occupational allergens have led to a decrease in exposure levels, but only to a slight improvement on symptoms and the course of disease433,452.

Principles for the treatment of rhinitis in children are the same as those for adults, although special care must be taken with adverse effects. Adequate doses should be prescribed and, for some drugs, the patient’s age should be considered437,453,454.

### 6.7 Sinonasal polyposis and asthma

Sinonasal polyposis (SP) is a distinct subtype of chronic RS (CRS) characterized by chronic mucosal inflammation of the nasal cavities and the paranasal sinuses that leads to the formation of edematous and fibrous polypoid masses in the nasal fossae445. The prevalence of SP is high, approximately 2.4 % of the population456,457.

Among patients with CRS a 3.48 times higher risk of asthma has been reported458. Half of the patients with SP suffer from asthma459. The presence of SP relates to a worse control460 and a greater severity of asthma461.

A phenotype has been identified that is associated with a greater severity and a worse prognosis of the disease. This phenotype links SP, severe asthma (occasionally difficult to control) and intolerance to non-steroidal anti-inflammatory drugs (NSAIDs), known as aspirin-exacerbated respiratory disease (AERD)462 (see section 9.4).

Treatment of SP improves both clinical and functional parameters of asthma463.

The diagnosis of SP should be established by visualization of polyp masses occupying the nasal cavities bilaterally, ideally through nasal endoscopy, given that only smell impairment is sufficiently specific to diagnose SP among other nasal symptoms (nasal obstruction, anterior or posterior rhinorrhea and/or headache)459.

Severity and degree of involvement can be evaluated using a visual analogue scale, assessing the size of polyps and/or using validated questionnaires to assess the impact on quality of life455.

Radioimaging studies does not increase the value of endoscopic diagnosis464 and should be reserved for surgical planning, diagnosis of complications (computerized tomography) and differential diagnosis with other tumors of the nasal cavities (magnetic resonance)465.

Treatment of SP includes the use of topical application of intranasal glucocorticoids (budesonide, mometasone, fluticasone) at high doses and during a prolonged period of time, given the tendency of the disease to relapse466.

Surgery has not been found to be superior to medical treatment in patients with CRS467. Functional endoscopic sinus surgery offers advantages in terms of safety and efficacy as compared to other techniques used in patients with a more severe disease and who fail to respond to other treatment modalities468.

Medical treatment with intranasal glucocorticoids should be prescribed postoperatively in order to prevent recurrences and improve the outcome of surgery466.

Endoscopic sinus surgery may improve clinical asthma parameters, except pulmonary function469.

Short courses of oral glucocorticoids (prednisone, methylprednisolone, deflazacort) have been beneficial in the short-term and might be used as an alternative to surgery in patients with severe disease470. Other treatment options that have shown some efficacy include montelukast473 or the anti-IgE monoclonal antibody omalizumab473 (figure 6.3).
**Figure 6.3. Treatment algorithm for sinonasal polyposis (SP).**

<table>
<thead>
<tr>
<th>Mild SP (VAS$^1$ &lt; 3)</th>
<th>Moderate SP (VAS$^1$ 3 to 7)</th>
<th>Severe SP (VAS$^1$ &gt; 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intranasal glucocorticoids (doses recommended in the technical specifications) ± nasal irrigations</td>
<td>Short-course of oral glucocorticoids$^2$ + intranasal glucocorticoids (high doses) + nasal irrigations</td>
<td>Short-course of oral glucocorticoids$^2$ + intranasal glucocorticoids (high doses) + nasal irrigations</td>
</tr>
<tr>
<td>Evaluation$^3$</td>
<td>Improvement$^4$</td>
<td>No improvement$^4$</td>
</tr>
<tr>
<td>Maintain treatment long-term (Self-control of doses according symptoms mainly the degree of hyposmia$^3$)</td>
<td>Treat as SP moderate or severe</td>
<td>High doses of intranasal glucocorticoids prolonged treatment (Self-control of doses according symptoms mainly the degree of hyposmia$^3$)</td>
</tr>
<tr>
<td>Evaluation$^3$</td>
<td>Improvement$^4$</td>
<td>No improvement$^4$</td>
</tr>
<tr>
<td>Improvement$^4$</td>
<td>High doses of intranasal glucocorticoids (maintain for a prolonged period) + If asthma or NSAIDs intolerance: Antileukotriene (montelukast) If mucopurulent rhinorrhea or repeated infections: prolonged antimicrobial treatment (macrolides, doxycycline) Maintain nasal irrigations</td>
<td>Proposed surgery (ESS) + Continue with intranasal glucocorticoids (high doses) + Nasal irrigations</td>
</tr>
<tr>
<td>No improvement$^4$</td>
<td>Improvement$^4$</td>
<td>No improvement$^4$</td>
</tr>
</tbody>
</table>

1. For the therapeutic management of SP a stepwise disease severity-based approach is recommended. To assess severity the use of a visual analogue scale (VAS) is suggested.
2. 0.5-1 mg/kg/day of prednisone or equivalent for 7 to 14 days. Dose tapering is not required if dose is lower than 50 mg/day of prednisone or equivalent.
3. Although no scientific evidence is available to suggest a specific review period, initial evaluation is recommended at month 1 of treatment and at 3 months (moderate or severe) or 6 months (mild or controlled) thereafter.
4. Improvement (control or good treatment response) is defined as a one-step decrease in severity of moderate or severe SP or a reduction in VAS score in mild SP.
5. The degree of hyposmia can be measured subjectively (by means of a visual analogue scale) or by olfactometry. Hyposmia is well correlated with the severity of SP, is the most specific symptom of SP and may contribute to disease control, as its worsening or improvement may alert the patient to the need for either increasing or decreasing the dose of the intranasal steroid.
RECOMMENDATIONS

6.1. It is recommended to classify allergic rhinitis as intermittent and persistent, according to its duration, and as mild, moderate and severe, according to its severity.

6.2. It is recommended to establish the diagnosis of rhinitis by clinical criteria.

6.3. To confirm the diagnosis of allergic rhinitis, skin tests (prick test) and/or determination of specific serum IgE should be performed.

6.4. Patients diagnosed with asthma should be assessed for the presence of rhinitis/sinonasal polyposis and vice versa, so as to implement a joint diagnostic and therapeutic strategy for both conditions.

6.5. For the pharmacological treatment of allergic rhinitis, the use of oral and topical nasal antihistamines, intranasal glucocorticoids or the association of these medications in cases of moderate or severe disease is recommended.

6.6. In appropriately selected allergic patients (adults and children), immunotherapy with allergens is recommended for the treatment of allergic rhinitis.

6.7. It is recommended to treat sinonasal polyposis with intranasal topical glucocorticoids at high doses and continuously.

6.8. In patients with concomitant rhinitis/sinonasal polyposis and asthma, it may be considered to add antileukotrienes or immunotherapy with allergens (in case of allergy) to treatment with intranasal glucocorticoids.