# 6. Rhinitis

## 6.1 Rhinitis

The term "rhinitis" defines an inflammatory process affecting the nasal mucosa that is characterized by the following clinical symptoms: anterior or posterior rhinorrhea, sneezing, blocked nose or nasal congestion and/or pruritis/ itching of the nose. These symptoms must be present for two or more days in a row and for more than an hour on most days [263].

С

D

Sinusitis is always accompanied by rhinitis, which is why inflammation of the paranasal sinuses is known as "rhinosinusitis", and it is characterized by the presence of two or more of the following symptoms: blocked nose/congestion/ obstruction, anterior or posterior rhinorrhea, facial pain/ pressure and/or impairment/loss of sense of smell; the presence of one of the first two symptoms is required [264].

Table 6.1. Classification of rhinitis

#### **Infectious Rhinitis**

- Viral
- Bacterial
- Other Infectious Agents

#### Allergic, depending on:

- The allergen responsible: perennial, seasonal, work-related
- Duration: intermittent, persistent
- Severity: mild, moderate-severe

#### Occupational

- Duration: intermittent, persistent
- Severity: mild, moderate-severe

### Drug-induced

- Aspirin
- Other medications

#### Hormonal

#### Other causes:

- NARES (non-allergenic rhinitis with eosinophilia syndrome)
- Caused by irritants syndrome
- Food-related
- Emotional
- Atrophic

### Idiopathic

Classification of Rhinitis adapted from the ARIA Document (Bousquet [266]).

In the report from the nomenclature review committee of the World Allergy Organization (WAO), allergic rhinitis (AR) was defined as "clinical signs and symptoms of a hypersensitivity reaction which is immunologically mediated (IgE) and affects the nose" [265].

## 6.2 Classification

There are numerous classifications of rhinitis, which have been made by various groups and panels of experts. Many of these classifications are of little use in clinical practice, as they mix pathogenic and aetiological criteria. A clinical classification of rhinitis, supported by a broad international consensus, has been proposed in the recently reviewed ARIA (Allergic Rhinitis and its Impact on Asthma) document [266] (Table 6.1).

Infectious rhinitis is the most common form and it is classified as the common cold or acute viral rhinosinusitis (symptoms last less than ten days), acute non-viral

Table 6.2. Classification of Allergic Rhinitis (AR)

#### According to duration

- INTERMITTENT means that symptoms
- are present:
- 4 days a week
- or during  $\leq$  4 consecutive weeks
- PERSISTENT means that symptoms are present:
- $\ge 4$  days a week - and > 4 consecutive weeks

# According to severity

- MILD means that none of the following items are present:
  - Sleep disturbances
  - Daily, leisure and/or sports activities
  - are affected
  - School or work activities are affected
  - The symptoms cause discomfort

MODERATE means that one, two or three of the above items are present

SEVERE means that the four items are present

Classification of AR according to the ARIA document (modified by Valero [270]).

D

D

D

С

С

rhinosinusitis (the symptoms get worse after the first five days or are maintained longer than ten days) or chronic rhinosinusitis with or without polyps (symptoms last longer than 12 weeks) [264].

AR is the most common form of non-infectious rhinitis [266] and the most closely related to asthma. The classification of AR changed after the publication of the ARIA document [267] because the classical classification into seasonal, perennial and occupational asthma did not reflect the clinical reality of patients [268]. The current classification proposed by ARIA has been validated [269], although criteria to differentiate moderate and severe rhinitis have been proposed [270] (Table 6.2).

# 6.3 Epidemiology

D

С

С

The most common form of rhinitis is infectious rhinitis. Its incidence in adults is from 2 to 5 episodes of the common cold a year and in children is from 7 to 10 episodes a year [264].

The prevalence of AR in the general Spanish population has been estimated to be about 21.5% (average age 31.3 years), of which 21-64% of cases are persistent, 36-79%

intermittent, 48.5-63% perennial and 37-51.5% seasonal [271,272]. 82% of intermittent cases are mild (18% moderate/ severe) and 44% of persistent cases are mild (56% moderate/ severe).

A study conducted in Spain found that rhinitis was the most common reason for consultations at Allergology departments (55.5% of total visits). Of all of these consultations an allergic aetiology was confirmed in 72% of patients. 51.9% were sensitized to pollen and 40.2% to mites, and polysensitization was frequent (31.2%). 37.3% of the rhinitis patients were diagnosed with asthma [273].

In the ISAAC study, a prevalence of rhinoconjunctivitis symptoms of 7.9% was recently confirmed in Spanish children aged 6-7 years (an annual increase of 0.33%) and a prevalence of 15% in children aged 13-14 years (an annual increase of 0.10%) [274].

## 6.4 Diagnosis

The diagnosis of rhinitis is essentially clinical.

A family history of allergy, seasonal variation of symptoms, the fact that ocular and nasal symptoms coincide and a link to exposure to epithelia, pollen and dust are clinical data that





Figure 6.1 Differential diagnosis algorithm for rhinitis (modified by Bousquet) [266].

C

C are diagnostically highly predictive when AR is suspected [275]. In the aetiological diagnosis of allergic rhinitis the most cost-effective analyses are prick and/or in vitro specific serum IgE tests [276]. In cases with any doubt, the specific nasal challenge test must be performed using the suspected allergen [277]. However, positive prick or specific IgE test results to certain allergens may be irrelevant from a clinical point of view. Other complementary tests include the objective evaluation of nasal obstruction (acoustic rhinometry, active anterior rhinomanometry, measurement of peak nasal inspiratory flow) and the assessment of the sense of smell by olfactometry (Fig. 6.1).

## 6.5 Rhinitis and Asthma

Numerous epidemiological, physiopathological and therapeutic studies have demonstrated a link between rhinitis and asthma [266,278].

In asthma patients the prevalence of rhinitis is very high, much higher than in the general population [279]. In this country two recent studies showed a prevalence of rhinitis in asthma patients of 71% [280,281]. In a study conducted in Spain and Portugal, 49% of the AR patients had asthma [272]. A parallel increase in the prevalence of asthma and rhinitis has also been demonstrated in Spain [282]. There is a temporal link between AR and asthma onset, and AR usually precedes the development of asthma [283]. It has been demonstrated that AR and non-allergic rhinitis are risk factors for developing [279,284]. Rhinitis also aggravates asthma and increases the consumption of healthcare resources [285-287].

Inflammatory changes have been demonstrated in the bronchial mucosa of non-asthmatic patients with AR [288], as occurs with eosinophilic nasal inflammation in asthma patients with no clinical nasal symptoms [289].

The treatment of AR can improve some aspects of asthma (Table 6.3); nevertheless, a systematic review failed to confirm that this improvement was statistically significant [290].

Table 6.3. Studies on the effects of treating concomitant rhinitis on asthma

Study Authors	Location	N	Туре	Variable	Comments
Adams, 2002	USA	13844	Retrospective cohort	RR 0.7 (ED visists)	Patients receiving nasal glucocorticoids
Crystal-Peters, 2002	USA	4944	Retrospective cohort	RR 0.5 (visits hospitalizations)	
Corren, 2004	USA		Cases/controls	RR 0.56 (hospitalisations)	Patients receiving nasal glucocorticoids
Moller, 2002	Europe	205	RCT	RR 0.40 (of developing asthma)	IT 3 years
Grembiale, 2000	United Kingdom	44	RCT	BHR ↓ MCT	IT 2 years
Polosa, 2003 <sup>b</sup>	Italy	30	RCT	BHR ↓ AMP but not for MIT	IT 3 years
Dahl, 2005 <sup>b</sup>	Europe	262	RCT	Tendency to improve not statistically significant	Nasal fluticasone
Lombardi, 2001	Italy	51	Non- randomised CT	BHR ↓ MCT	IT 3 years
Taramarcaz, 2003	Multiple (Cochrane review)	425	Systematic RCT review	Tendency to improve not statistically significant	11 RCTs which evaluate the efficacy of nasal glucocorticoids

Abbreviations: RR: relative risk; BHR: bronchial hyperresponse; MIT: methacholine inhalation test; RCT: randomized clinical trial; CT: clinical trial; IT immunotherapy; N: population.

# 6.6 Treatment

The therapeutic strategy for AR includes: patient education, avoidance of allergens and pollutants, and pharmacotherapy and allergen-specific immunotherapy [266,291,292]. When choosing pharmacological treatment, the efficacy, safety and cost-effectiveness of drugs, patients preferences, disease severity and the presence of comorbidities must be assessed. The pharmacological treatment of AR must include clear recommendations graded into different stages, depending on the level of severity (Table 6.4); (Fig. 6.2).

A

In both adults and children **oral H1 antihistamines** improve rhinitis symptoms [293], including rhinorrhea, sneezing, nasal and eye symptoms [294,295], although they are less effective against nasal obstruction [296]. Second-generation H1 antihistamines have fewer side effects (cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, mequitazine, mizolastine and rupatadine) [297] and mild anti-inflammatory effects [298]. Topical H<sub>1</sub> antihistamines (azelastine, emedastine, ketotifen, levocabastine and olopatadine) have also shown themselves to be effective in cases of rhinitis and allergic conjunctivitis [299]. **Glucocorticoids** (beclomethasone, budesonide, fluticasone, mometasone, triamcinolone) are the most potent and effective antiinflammatory drugs for treating AR and non-allergic rhinitis [300,301], in both adults and children. The topical application of glucocorticoids delivers a high drug concentration to the nasal mucosa with a minimal risk of systemic side effects. Their efficacy in improving the symptoms of AR, including nasal obstruction and ocular symptoms, has been well documented. They constitute the first line of treatment for persistent moderate-severe AR.

Oral glucocorticoid regimens lasting for short periods of time are used in cases of severe rhinitis that fails to respond to other treatments [266].

**Intranasal decongestants** (oxymetazoline and xylometazoline) can be used for a short period of time in patients with substantial nasal obstruction [302]. Prolonged use can trigger drug-induced rhinitis. Although they are effective, oral decongestants (phenylephrine and pseudoephedrine), used alone or in association with oral antihistamines, are not exempt from systemic side effects.

**Leukotriene receptor antagonists** (montelukast and zafirlukast) are effective in the treatment of allergic rhinitis

Table 6.4. Levels of recommendation for the drugs used in the treatment of allergic rhinitis (partly based on Bousquet) [266]

	Seasonal Rhinitis Adults	Seasonal Rhinitis Children	Perennial Rhinitis Adults	Perennial Rhinitis Children	Persistent Rhinitis
Oral H <sub>1</sub> antihistamines	R1	R1	R1	R1	R1
Nasal H <sub>1</sub> antihistamines	R1	R1	R1	R1	No data
Nasal glucocorticoids	R1	R1	R1	R1	No data
Oral glucocorticoids	R1	R1	R1	R1	No data
Antileukotrienes	R1	R1 (> 6 years)	-	-	No data
Nasal chromones	R1	R1	R1	R1	No data
Nasal descongestants	R2	R2	R2	R2	No data
Nasal anticholinergics	_	_	R1	R1	No data
Subcutaneous immunotherapy	R1	R1	R1	R1	No data
Sublingual immunotherapy	R1	R1	R1	R1	No data
Anti-IgE	R1	R1 (> 12 years)	R1	R1 (> 12 years)	No data
Allergenic avoidance	R2	R2	R2	R2	No data

D

Α

40

Δ



GC: glucocorticoids.

Α

A

Figure 6.2. Algorithm for treating allergic rhinitis in accordance with ARIA International Guidelines [266].

and conjunctivitis in both adults and children. These drugs have shown themselves to be as effective as antihistamines, but less than topical nasal glucocorticoids [303].

**Topical anticholinergics** (ipratropium bromide) are effective and are recommended for the treatment of rhinorrea that is refractory to other treatments, and for AR and non-allergic rhinitis [304].

**Topical chromones** (sodium cromoglycate) have demonstrated moderate efficacy in the treatment of rhinitis and allergic conjunctivitis [305].

Omalizumab (anti-IgE) has proved effective in the treatment of AR in adults and children over 12 years of age [306]. However, in Spain its use has not been approved for this purpose.

D

D

**Specific allergen immunotherapy**, using either subcutaneous or oral (sublingual) administration, is effective for treating AR caused by pollen and mites in adults and children. A correct allergological diagnosis is required for its indication. It can alter the natural course of allergic respiratory disease, reducing the frequency of asthma episodes and preventing new sensitizations [165,307,308].

Measures designed to ensure avoidance of indoor

**allergens** (mites) have demonstrated a reduction in exposure levels, but no improvement in the symptoms or progression of the disease [309].

The principles which underlie the treatment of rhinitis in children are the same as in adults, but special care needs to be taken with adverse effects. The right doses must be used and in some cases the age of the patient needs to be taken into consideration when prescribing certain drugs [266].

## RECOMMENDATIONS

Α

D

<ul> <li>The classification of allergic rhinitis will depend on: duration, the disease being classified as intermittent or persistent, and severity, which is considered mild, moderate or severe</li> </ul>	R2
- It is recommended that the diagnosis of rhinitis should be based on clinical criteria (symptoms).	<b>R2</b>
<ul> <li>To confirm a diagnosis of allergic rhinitis it is advisable to perform prick tests and/or the determine of specific serum IgE.</li> </ul>	<b>R2</b>
<ul> <li>When asthma has been confirmed, it is advisable to investigate the presence or not of rhinitis in order to devise a combined diagnostic and treatment strategy.</li> </ul>	R2
_ The use of oral and topical nasal antihistamines, together with topical nasal glucocorticoids, is recommended for the <b>pharmacological treatment of allergic rhinitis</b> .	<b>R1</b>
- In appropriately selected allergic patients (adults and children) allergen-specific immunotherapy is recommended.	<b>R1</b>