

Review article

Allergic rhinitis management pocket reference 2008*

Allergic rhinitis is a major chronic respiratory disease because of its prevalence, impacts on quality of life and work/school performance, economic burden, and links with asthma. Family doctors (also known as 'primary care physicians' or 'general practitioners') play a major role in the management of allergic rhinitis as they make the diagnosis, start the treatment, give the relevant information, and monitor most of the patients. Disease management that follows evidence-based practice guidelines yields better patient results, but such guidelines are often complicated and may recommend the use of resources not available in the family practice setting. A joint expert panel of the World Organization of Family Doctors (Wonca), the International Primary Care Airways Group (IPAG) and the International Primary Care Respiratory Group (IPCRG), offers support to family doctors worldwide by distilling the globally accepted, evidence-based recommendations from the Allergic Rhinitis and its Impact on Asthma (ARIA) initiative into this brief reference guide. This guide provides tools intended to supplement a thorough history taking and the clinician's professional judgment in order to provide the best possible care for patients with allergic rhinitis. A diagnostic Questionnaire specifically focuses the physician's attention on key symptoms and markers of the disease. When questionnaire responses suggest a diagnosis of allergic rhinitis, a Diagnosis Guide and a simple flowchart then lead the clinician through a series of investigations commonly available in primary care to support the diagnosis. In addition, key aspects of differential diagnosis are illuminated. According to ARIA, allergic rhinitis may be classified as Intermittent or Persistent, and as Mild or Moderate/Severe. The classification of rhinitis determines the treatment necessary, as set out in an ARIA flowchart included in this guide. The guide also includes information about the strength of evidence for efficacy of certain rhinitis treatments, a brief discussion of pediatric aspects, and a glossary of allergic rhinitis medications to assist the clinician in making medication choices for each individual patient. Finally, many patients with allergic rhinitis also have concomitant asthma, and this must be checked. The World Organization of Family Doctors has been delegated by WHO as the group that will be taking primary responsibility for education about chronic respiratory diseases among primary care physicians globally. This document will be a major resource in this educational program.

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Allergic Rhinitis and its Impact on Asthma (ARIA)
Based on the ARIA 2008 and the IPAG handbook, in collaboration with WHO, GA²LEN** and AllerGen.

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The purpose of this guide

This document was prepared by the Wonca Expert Panel, including Bousquet J, Reid J, van Weel C, Baena Cagnani C, Canonica GW, Demoly P, Denburg J, Fokkens WJ, Grouse L, Loh A, Mullol K, Ohta K, Schermer T, Valovirta E, Zhong N and Zuberbier T. It was edited by Dmitry Nonikov. This material is based on the IPAG Handbook and the ARIA Workshop Report, in collaboration with the World Health Organization, GA²LEN (Global Allergy and Asthma European Network), Allergen, International Primary Care Respiratory Group (IPCRG) and European Federation of Allergy and Airways Diseases Patients Associations (EFA). Management that follows evidence-based practice guidelines yields better patient results. However, global evidence-based practice guidelines are often complicated and recommend the use of resources often not available in the primary care setting worldwide. The joint Wonca expert panel offers support to primary care physicians worldwide by distilling the existing evidence based recommendations into this brief reference guide. The guide lists diagnostic and therapeutic measures that can be carried out worldwide in the primary care environment and in this way provide the best possible care for patients with allergic rhinitis. The material presented in sections 1-5 will assist you in diagnosing and treating allergic rhinitis.

Primary care challenge

Allergic rhinitis is a growing primary care challenge as most patients consult primary care physicians. General practitioners play a major role in the management of allergic rhinitis as they make the diagnosis, start the treatment, give the relevant information, and monitor most of the patients. In some countries, general practitioners perform skin prick tests. Studies in Holland and the UK found that common nasal allergies can be diagnosed with a high certainty using simple diagnostic criteria. Nurses may also play an important role in the identification of allergic diseases including allergic rhinitis

in the primary care of developing countries and in schools. In addition, many patients with allergic rhinitis have concomitant asthma and this must be checked.

Allergic rhinitis recommendations

- 1- Allergic rhinitis is a major chronic respiratory disease due to its:
 - Prevalence
 - Impact on quality-of-life
 - Impact on work/school performance and productivity
 - Economic burden
 - Links with asthma
- 2- In addition, allergic rhinitis is associated with comorbidities such as conjunctivitis.
- 3- Allergic rhinitis should be considered as a risk factor for asthma along with other known risk factors.
- 4- A new subdivision of allergic rhinitis has been proposed:
 - Intermittent (IAR)
 - Persistent (PER)
- 5- The severity of allergic rhinitis has been classified as "mild" or "moderate/severe" depending on the severity of symptoms and quality-of-life outcomes.
- 6- Depending on the subdivision and severity of allergic rhinitis, a stepwise therapeutic approach has been proposed.
- 7- The treatment of allergic rhinitis combines:
 - Pharmacotherapy
 - Immunotherapy
 - Education
- 8- Patients with persistent allergic rhinitis should be evaluated for asthma by means of a medical history, chest examination, and, if possible and when necessary, the assessment of airflow obstruction before and after bronchodilator.
- 9- Patients with asthma should be appropriately evaluated (history and physical examination) for rhinitis.
- 10- Ideally, a combined strategy should be used to treat the upper and lower airway diseases to optimize efficacy and safety.

Recognize allergic rhinitis – allergic rhinitis questionnaire (1)

Allergic Rhinitis Questionnaire	
Question	Response Choices
1. Do you have any of the following symptoms?	
• Symptoms on only one side of your nose	Yes No
• Thick, green or yellow discharge from your nose (see NOTE)	Yes No
• Postnasal drip (down the back of your throat) with thick mucus and/or runny nose (see NOTE)	Yes No
• Facial pain (see NOTE)	Yes No
• Recurrent nosebleeds	Yes No
• Loss of smell (see NOTE)	Yes No
2. Do you have any of the following symptoms for at least one hour on most days (or on most days during the season if your symptoms are seasonal)?	
• Watery runny nose	Yes No
• Sneezing, especially violent and in bouts	Yes No
• Nasal obstruction	Yes No
• Nasal itching	Yes No
• Conjunctivitis (red, itchy eyes)	Yes No

Instructions: To evaluate the possibility of allergic rhinitis, start by posing the questions below to patients with nasal symptoms. This questionnaire contains the questions related to allergic rhinitis symptoms that have been identified in peer-reviewed literature as having the greatest diagnostic value. It will not produce a definitive diagnosis, but may enable you to determine whether a diagnosis of allergic rhinitis should be further investigated or is unlikely.

Evaluation:

- The symptoms described in Question 1 are usually NOT found in allergic rhinitis. The presence of ANY ONE of them suggests that alternative diagnoses should be investigated. Consider alternative diagnoses and/or referral to a specialist.
- NOTE: Purulent discharge, postnasal drip, facial pain, and loss of smell are common symptoms of sinusitis. Because most patients with sinusitis also have rhinitis (though not always allergic in origin), in this situation, the clinician should also evaluate the possibility of allergic rhinitis.
- The presence of watery runny nose with ONE OR MORE of the other symptoms listed in Question 2 suggests allergic rhinitis, and indicates that the patient should undergo further diagnostic assessment.
- The presence of watery runny nose ALONE suggests that the patient MAY have allergic rhinitis. (Additionally, some patients with allergic rhinitis have only nasal obstruction as a cardinal symptom.)

- If the patient has sneezing, nasal itching, and/or conjunctivitis, but NOT watery runny nose, consider alternative diagnoses and/or referral to a specialist.
- In adults with late-onset rhinitis, consider and query occupational causes. Occupational rhinitis frequently precedes or accompanies the development of occupational asthma. Patients in whom an occupational association is suspected should be referred to a specialist for further objective testing and assessment.

Allergic rhinitis diagnosis guide

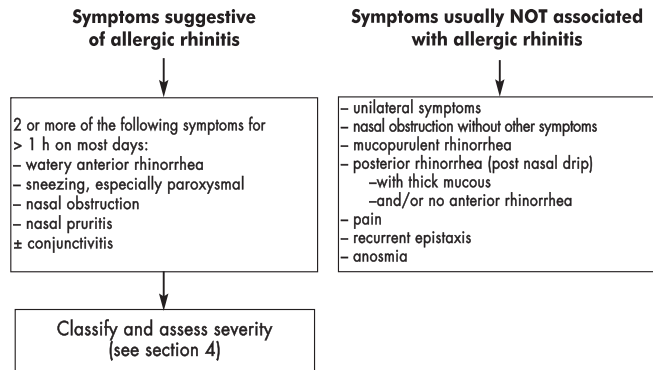
Allergic Rhinitis Diagnosis Guide	
Diagnostic Tool	Findings that Support Diagnosis
Physical examination	Transverse crease of nose, allergic shiners, allergic salute.
In persistent rhinitis: • anterior rhinoscopy using speculum and mirror gives limited but often valuable information • nasal endoscopy (usually performed by specialist) may be needed to exclude other causes of rhinitis, nasal polyps, and anatomic abnormalities	Exclusion of other causes.
Trial of therapy	Improvement with antihistamines or intranasal glucocorticosteroid.
Allergy skin testing or measurement of allergen-specific IgE in serum (if symptoms are persistent and/or moderate/severe, or if quality of life is affected)	• Confirm presence of atopy. • Specific triggers identified.
Nasal challenge tests (if occupational rhinitis suspected)	Confirm sensitivity to specific triggers.

¹International Primary Care Airways Group (IPAG) Handbook available at <http://www.globalfamilydoctor.com>.

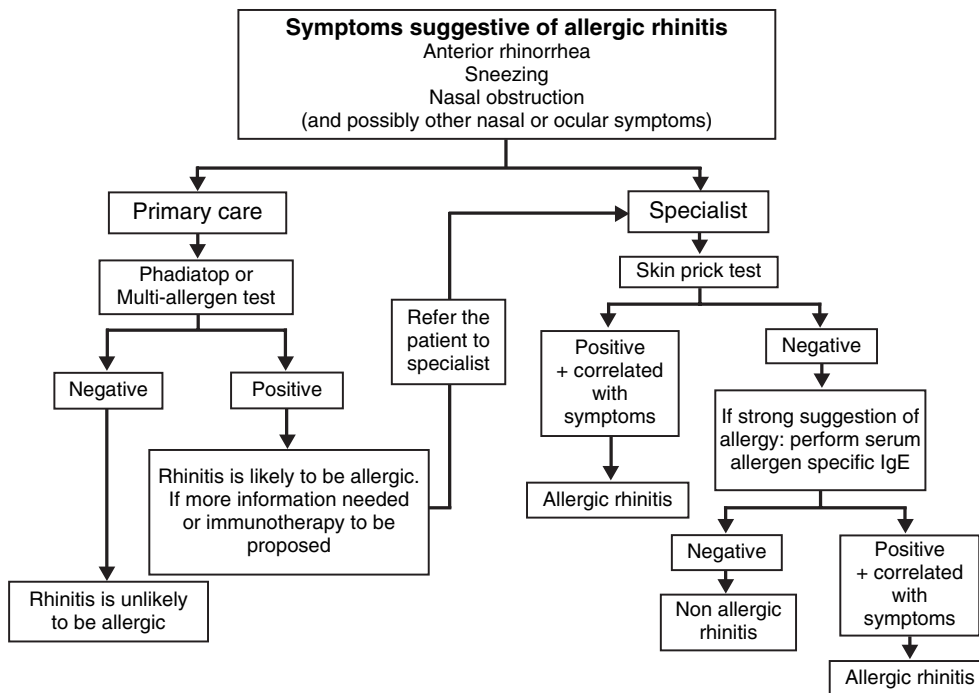
Instructions: In patients of all ages with lower nasal symptoms only, whose responses to the Allergic Rhinitis Questionnaire suggest that this diagnosis should be investigated, use this guide to help you evaluate the possibility of allergic rhinitis. All of the diagnostic investigations presented in this guide may not be available in all areas; in most cases, the combination

of those diagnostic investigations that are available and the individual health care professional's clinical judgement will lead to a robust clinical diagnosis. This guide is intended to supplement, not replace, a complete physical examination and thorough medical history.

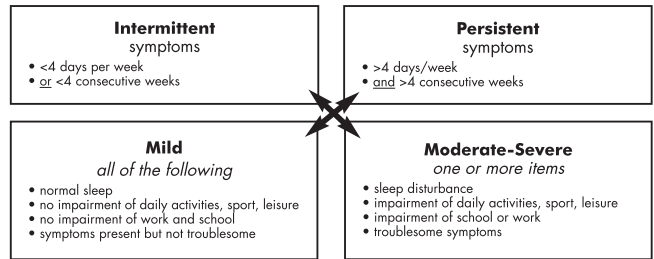
Differential diagnosis of allergic rhinitis (2)



Make the diagnosis of allergic rhinitis (2)



Classify allergic rhinitis (2)



Treat allergic rhinitis

Treatment goals

Goals for the treatment of rhinitis assume accurate diagnosis and assessment of severity as well as any link with asthma in an individual patient. Goals include:

- Unimpaired sleep
- Ability to undertake normal daily activities, including work and school attendance, without limitation or impairment, and the ability to participate fully in sport and leisure activities
- No troublesome symptoms
- No or minimal side-effects of rhinitis treatment

Strength of evidence for efficacy of rhinitis treatment (2)

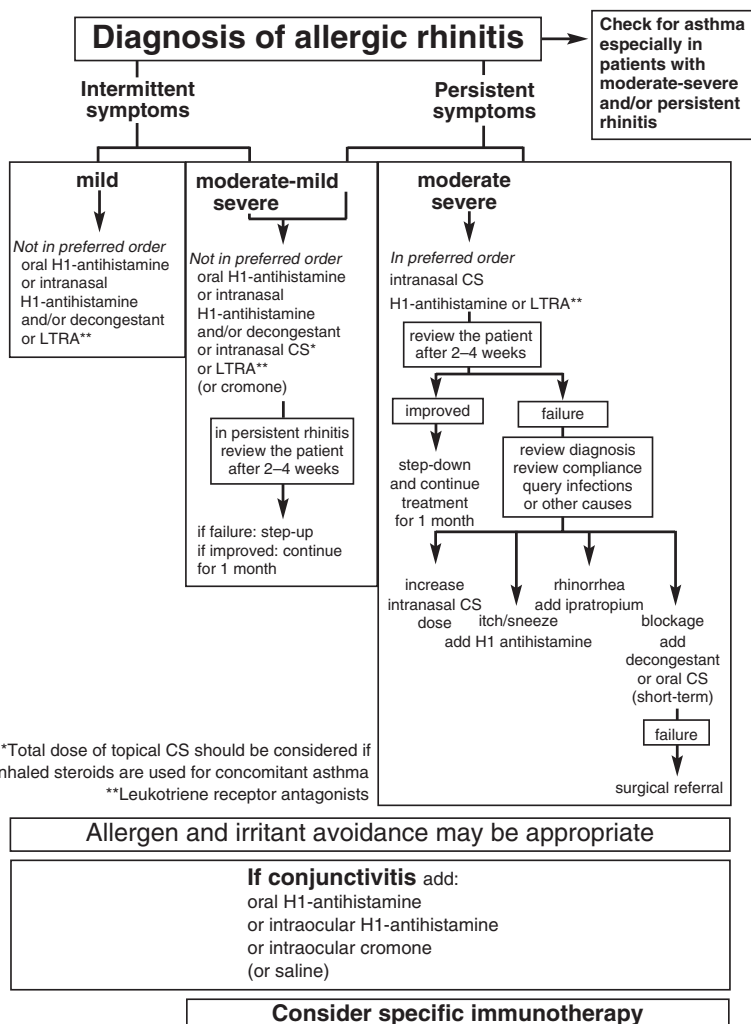
ARIA 2007					
Intervention	SAR		PAR		PER
	adults	children	adults	children	
Oral H1 Antihistamine	A	A	A	A	A
Intranasal H1 Antihistamine	A	A	A	A	A**
Intranasal CS	A	A	A	A	A**
Intranasal cromone	A	A	A	A	
LTRAs	A	A (>6 yrs)	A		A**
Subcutaneous SIT	A	A	A	A	A**
Sublingual / nasal SIT	A	A	A	B	A**
Allergen avoidance	D	D	A*	B*	

SAR - Seasonal Allergic Rhinitis
 PAR - Perennial Allergic Rhinitis
 PER - Persistent Allergic Rhinitis
 CS - Corticosteroids
 LTRAs - Anti-Leukotrienes
 SIT - Specific Immunotherapy

*not effective in the general population
 **extrapolated from studies in SAR/PAR

²Allergic Rhinitis and its impact on Asthma (ARIA) 2007. Full text ARIA documents and resources: <http://www.whiar.org>.

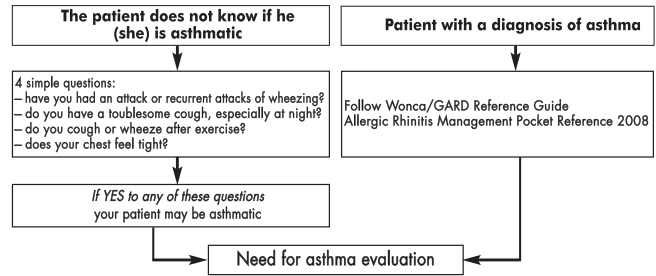
Diagnosis and severity assessment of allergic rhinitis (2)



Pediatric aspects

Allergic rhinitis is part of the “allergic march” during childhood but intermittent allergic rhinitis is unusual before two years of age. Allergic rhinitis is most prevalent during school age years. In preschool children, the diagnosis of AR is difficult. In school children and adolescents, the principles of treatment are the same as for adults, but doses may be adapted, and special care should be taken to avoid the side effects of treatments typical in this age group.

Assess possibility of asthma (2)



Glossary of rhinitis medications (1)

Name and Also known as	Generic name	Mechanism of action	Side effects	Comments
Oral H₁ antihistamines H₁-blockers	2nd generation Cetirizine Ebastine Fexofenadine Loratadine Mizolastine Acrivastine Azelastine Mequitazine New products Desloratadine Levocetirizine Rupatadine	- blockage of H ₁ receptor - some anti-allergic activity - new generation drugs can be used once daily - no development of tachyphylaxis	2nd generation - no sedation for most drugs - no anti-cholinergic effect - no cardiotoxicity - acrivastine has sedative effects - oral azelastine may induce sedation and a bitter taste	- First-line therapy except in Moderate/ Severe Persistent Allergic Rhinitis - 2nd generation oral H ₁ -blockers are preferred for their favorable efficacy/safety ratio and pharmacokinetics; first generation molecules are no longer recommended because of their unfavorable safety/efficacy ratio - Rapidly effective (less than 1hr) on nasal and ocular symptoms - Moderately effective on nasal congestion * Cardiotoxic drugs (astemizole, terfenadine) are no longer marketed in most countries
Local H₁ antihistamines (intranasal, intraocular)	Azelastine Levocabastine Olopatadine	- blockage of H ₁ receptor - some anti-allergic activity for azelastine	- Minor local side effects - Azelastine: bitter taste in some patients	Rapidly effective (less than 30 min) on nasal or ocular symptoms
Intranasal glucocorticosteroids	Beclomethasone dipropionate Budesonide Ciclesonide Flunisolide Fluticasone propionate Fluticasone furoate Mometasone furoate Triamcinolone acetonide	- potently reduce nasal inflammation - reduce nasal hyperreactivity	- Minor local side effects - Wide margin for systemic side effects - Growth concerns with BDP only - In young children consider the combination of intranasal and inhaled drugs	- The most effective pharmacologic treatment of allergic rhinitis; first-line treatment for Moderate/ Severe Persistent Allergic Rhinitis - Effective on nasal congestion - Effective on smell - Effect observed after 6-12 hrs but maximal effect after a few days - Patients should be advised on the proper method of administering intranasal glucocorticosteroids, including the importance of directing the spray laterally rather than medially (toward the septum) in the nose

¹International Primary Care Airways Group (IPAG) Handbook available at <http://www.globalfamilydoctor.com>.

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Glossary ...*(continued)*

Oral / IM glucocorticosteroids	Dexamethasone Hydrocortisone Methylprednisolone Prednisolone Prednisone Triamcinolone Betamethasone Deflazacort	- Potently reduce nasal inflammation - Reduce nasal hyperreactivity	- Systemic side effects common in particular for IM drugs - Depot injections may cause local tissue atrophy	When possible, intranasal glucocorticosteroids should replace oral or IM drugs However, a short course of oral glucocorticosteroids may be needed if moderate/severe symptoms
Local cromones (intranasal, intraocular)	Cromoglycate Nedocromil Naaga	- mechanism of action poorly known	- Minor local side effects	Intraocular cromones are very effective Intranasal cromones are less effective and their effect is short lasting Overall excellent safety
Oral decongestants	Ephedrine Phenylephrine Phenylpropranolamine Pseudoephedrine Oral H1-antihistamine-decongestant combination	- sympathomimetic drug - relieve symptoms of nasal congestion	- Hypertension - Palpitations - Restlessness - Agitation - Tremor - Insomnia - Headache - Dry mucous membranes - Urinary retention - Exacerbation of glaucoma or thyrotoxicosis	Use oral decongestants with caution in patients with heart disease Oral H1-antihistamine decongestant combination products may be more effective than either product alone but side effects are combined
Intranasal decongestants	Oxymethazoline <i>Others</i>	- sympathomimetic drugs - relieve symptoms of nasal congestion	- Same side effects as oral decongestants but less intense - Rhinitis medicamentosa is a rebound phenomenon occurring with prolonged use (over 10 days)	Act more rapidly and more effectively than oral decongestants Limit duration of treatment to less than 10 days to avoid rhinitis medicamentosa
Intranasal anti-cholinergics	Ipratropium	- anticholinergics block almost exclusively rhinorrhea	- Minor local side effects - Almost no systemic anticholinergic activity	Effective in allergic and nonallergic patients with rhinorrhea
CysLT antagonists Antileukotrienes	Montelukast Pranlukast Zafirlukast	- Block CysLT receptor	- Excellent tolerance	Effective on rhinitis and asthma Effective on all symptoms of rhinitis and on ocular symptoms

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References

1. International Primary Care Airways Group (IPAG). Handbook available at <http://www.globalfamilydoctor.com>.
2. Bousquet J, Khaltar N, Cruz AA, Denburg J, Fokkens WJ, Togias A et al. Allergic rhinitis and its Impact on Asthma 2008 update. *Allergy* 2008;63(suppl. 86):8–160.