



Paediatric rhinitis:

Position paper of the European Academy of Allergy and Clinical Immunology

Rhinitis is a common problem in childhood and adolescence. The burden associated with rhinitis is often ignored as it is frequently seen as just a common cold or just as trivial as a cold. In reality, patients experience disruptive sneezing, itching, watery rhinorrhoea and nasal blockage. Other children and adolescents may present atypically with cough or snoring. The direct effect of symptoms, indirect effect of sleep disturbance with consequent daily fatigue and the use of antihistamines all result in impaired school performance.

Definition and classification

Rhinitis is defined as an inflammation of the nasal epithelium and is characterized by at least two nasal symptoms: rhinorrhoea, blockage, sneezing or itching. There are a number of different clinical presentations of rhinitis which overlap. The commonest form is 'allergic rhinitis' (AR) (Box 1) signifying symptoms caused by exposure to an allergen to which a patient is sensitized, in other words, allergen driven. Traditionally, this group would be classified as having AR on the basis of rhinitis symptoms in the presence of sensitization. Typical allergens include house dust mite, grass pollen, tree pollen, weed pollens, cat, dog and moulds. In adults, there is evidence to suggest that this form of rhinitis may exist despite a lack of apparent specific sensitization due to local immunoglobulin E (IgE) production in the nose, otherwise known as entopy. It is unclear whether or not

this is also seen in children. Allergic rhinitis can be seasonal or perennial. The distinction between seasonal and perennial is not globally applicable, and therefore, it has been revised by the Allergic Rhinitis and its Impact on Asthma (ARIA) group. Based on duration of symptoms. ARIA subdivides AR into intermittent or persistent. Both approaches have their value, seasonal-perennial is useful for describing specific seasonal relationships with allergen exposure, whilst the ARIA approach is useful both for describing how the rhinitis manifests in terms of symptoms, its effects on quality of life suggests the treatment approach. Allergic Rhinitis and its Impact on Asthma also usefully divides AR severity into mild, moderate and severe according to its impact on quality of life.

The second form of rhinitis is infectious rhinitis, usually secondary to a viral infection. There is some overlap between allergic and infectious rhinitis in that atopic children with or without allergic rhinitis can also present with an infectious rhinitis. Such atopic individuals may have an exaggerated response to viral upper respiratory tract infections; however, only indirect data support this.

Finally, there is a nonallergic, noninfectious group of other disorders that may present with rhinitis including those associated with exposure to irritants, hormonal dysfunction and specific medications (Box 1).

Prevalence and epidemiology

The International Study of Asthma and Allergies in Childhood (ISAAC) phase three studies (1999–2004) revealed an average prevalence of rhinitis of 8.5% (range 1.8–20.4%) in 6-to7-year-old children and 14.6% (1.4–33.3%) for 13-to14-year-old children. A worldwide increase in reported rhinitis prevalence was observed since the identical phase one studies (1991–8) but with large variations between centres. International Study of Asthma and Allergies in Childhood defines current rhinitis on the basis of a positive answer by parents to 'In the past 12 months, have you (has your child) had a problem with sneezing or a runny or blocked nose, when you (he or she) DID NOT have a cold or "the flu"?'. This question assumes that the respondent can correctly identify a cold or 'flu', for example, some children may only have

Box 1: Classification of rhinitis causation in children					
	Pre-school	School	Adolescent		
Allergic rhinitis	associ	ated with exposure	nitis symptoms that are to an allergen to which he patient is sensitized.		
Infectious rhinitis	Secondary to infection				
Non-allergic, non- infectious rhinitis	Irritant exposure (eg extreflux and in older pregnancy), drug induction NSAID), neurogenic or variable.	children, hormo ced (eg beta-bloo	nal (hypothyroidism, ckers, contraceptives,		
Different pathophysiologies may co-exist, particularly allergic rhinitis and infectious rhinitis. See Box 4 for conditions that may mimic rhinitis.					

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significant symptoms with a combination of both allergic inflammation and a coexisting viral infection. This is a particularly issue in the preschool age. Furthermore, ISAAC uses the presence of coexisting itchy eyes to identify allergic rhinitis although this is probably more relevant for pollen-induced rather than rhinitis driven by perennial allergens such as house dust mite. The ISAAC questions have not been well validated in a paediatric population. There was a male predominance of allergic rhinitis and female predominance of nonallergic rhinitis during adolescence.

Presentation and associated comorbidities

Classic symptoms and signs

Classic symptoms and signs of allergic rhinitis are intermittent or persistent nasal obstruction, rhinorrhoea (anterior or posterior), pruritus and sneezing. All these impact negatively on quality of life. Symptoms occur generally within minutes after allergen exposure and may last for hours after an isolated exposure. 'Allergic shiners' (darkened lower eyelid due to chronic congestion) are also often present, and their darkness correlates with disease chronicity and severity. AR can present less clearly, particularly in young children. Recommendations for the recognition of rhinitis are presented in Box 2.

Infectious rhinitis can be acute, commonly precipitated by a viral infection, or chronic, caused more often by bacteria and occasionally fungi. Children can typically have up to 11 upper respiratory tract infection episodes per year in infancy, eight episodes at preschool age and four at school age, and 0.2–2% of these develop into clinically important bacterial sinus infection. A chronic mucopurulent discharge

suggests a rhinosinusitis of infective origin. This may be secondary to other pathologies, such as adenoidal hypertrophy, anatomical abnormalities, primary immunodeficiency, primary ciliary dyskinesia or cystic fibrosis.

Nonallergic, noninfectious rhinitis is typically a chronic presentation that does not fit into an allergic rhinitis or infectious rhinitis pattern of symptoms. This should prompt the search for other causes (Box 1).

Presentations associated with rhinitis comorbidities In childhood, the presentation of rhinitis can frequently relate to its associated comorbidities (Box 3). The nose is anatomically and functionally linked to the eyes, paranasal sinuses, nasopharynx, middle ear, larynx and lower airway, and so, presenting features may be conjunctivitis, chronic cough, mouth breathing, nasal speech and snoring with or without obstructive sleep apnoea.

Allergic conjunctivitis is reported as the commonest comorbidity associated with AR. It is characterized by intense eye itching, conjunctival hyperaemia, watering eyes and occasional peri-orbital oedema.

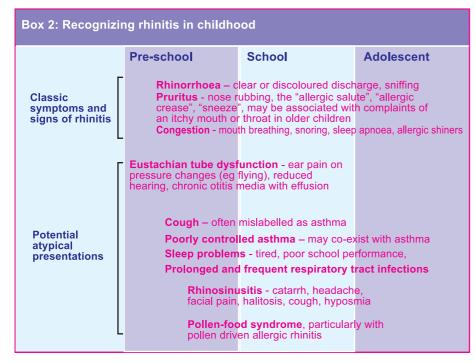
Chronic allergic inflammation of the upper airways can cause lymphoid hypertrophy leading to prominence of the adenoidal and tonsillar tissue. In a case—control study of 600 children aged 4—9 years, more adenoidal hypertrophy was seen in those with rhinitis, and it was suggested that this was driven by localized nasal inflammation. In a case series of 93 children aged 2—10 years referred to a sleep laboratory for polysomnography, sleep apnoea—hypopnoea syndrome was strongly associated with the clinical history of nasal obstruction and AR. Chronic middle ear effusion and eustachian tube

dysfunction, potentially causing hearing impairment, are associated with rhinitis.

Other comorbidities

Asthma

Asthma frequently coexists with AR being seen in half to three quarter of children and teenagers with asthma in a range of studies. Asthma is similarly associated with nonallergic rhinitis. Allergic rhinitis is one of the risk factors for the development of asthma, and its signs and symptoms often precede those of asthma, Allergic rhinitis also increases the risk of asthma hospitalization. Viral upper respiratory tract infection together with allergic sensitization and allergen exposure has been demonstrated to synergistically increase the risk of emergency care with asthma. The presence of a cough in association with rhinitis and postnasal drip may falsely suggest a diagnosis of asthma.



Eczema

Eczema and rhinitis frequently coexist in all age groups.

Pollen-food syndrome

Allergic rhinitis can be associated with pollen-food syndrome (PFS). Symptoms of oral pruritus and swelling occur due to cross-reactivity between aeroallergens, such as birch pollen, and fruits and vegetables such as apple.

Diagnosis

Clinical history, including type, duration and frequency of symptoms and exacerbating factors (see Box 1), is the cornerstone for diagnosing and characterizing rhinitis in children. Specific findings such as unilateral symptoms, nasal obstruction without other symptoms, mucopurulent discharge, pain or recurrent epistaxis may suggest other diagnoses (see differential diagnosis section below).

Box 3: Recognizing comorbidities of rhinitis in childhood

Conjunctivitis

Ask about a history of red, itchy, watery eyes, eye rubbing
Eye examination looking for signs of conjunctivitis

Ask about any history of cough, wheeze, shortness of breath, exercise-induced bronchospasm

Examine the chest – wheeze, hyperexpansion

Assess peak expiratory flows, spirometry in older children preferably with reversibility testing with beta-2 agonists If in doubt, undertake an exercise, mannitol or methacholine challenge test

Impaired hearing

Ask about any speech and language delay, increasing volume of TV, shouting, poor concentration, failing performance at school, frustration, irritability

Examine the ears – pneumatic otoscopy if possible, Weber and Rinne tests

Tympanoscopy for evaluation of tympanic membrane and middle ear

Tympanometry

Whisper test for screening of otitis media with effusion and hearing loss

Audiometry in older children – pure tones, speech

Rhinosinusitis

Ask about a history of nasal obstruction or discharge (purulent) with or without hyposmia, headache, facial pain or cough.

Undertake nasendoscopy in older children

CT scan/sinus X-rays not recommended unless there are complications or failed therapy, unilateral symptoms or severe disease unresponsive to medical therapy

Sleep problems

Enquire about any history of disturbed sleep, snoring, apnoea, tiredness, irritability

Assess nasal airway – spatula misting, nasal inspiratory peak flow, visual examination of nostrils and nasendoscopy in older children to view nasal airway and adenoids Consider sleep study

Pollen–food syndrome

Ask about any oral pruritus with symptoms with (not cooked or frozen) foods such as apples

Skin prick tests – seldom necessary to perform skin prick tests, and if so, it should be by prick-prick test with fresh foods and only with the incriminated fruit as nonclinically relevant positivity could be elicited

Examination of the nose is essential and should always be carried out, principally to rule out alternatives such as nasal polyps. In daily practice, diagnosis is usually based on a suggestive clinical history supported by examination by anterior rhinoscopy demonstrating swollen mucosa and a small number of IgE sensitization tests (SPT or specific IgE), in accordance with the history, population and region, which can suggest an allergic origin of the symptoms. Where the diagnosis is in doubt, nasal provocation testing can be utilized although this has not been standardized.

Defining the presence of allergy

Allergic sensitization can be defined as a positive skin test or allergen-specific serum IgE. Measurement of total serum IgE has little value in assessing allergic aetiology of rhinitis in childhood. The presence of sensitization is a major risk factor for AR in children. Outdoor allergens constitute a risk of seasonal rhinitis, whereas indoor allergens are associated with perennial rhinitis. The information on absence of sensitization can be clinically very valuable potentially ruling out a diagnosis of AR. The negative predictive value may be as high as 95% in a clinic population, and false negatives are associated with local specific IgE production, particularly in young children who have recently become symptomatic. Additionally, a proportion of children with positive tests have no symptoms and many children with symptoms of rhinitis are sensitized to allergens that do not give rise to the symptoms. So, a positive allergen-specific IgE test alone does not confirm the allergic origin of the symptoms, and results must be interpreted in the context of the clinical history. Quantification of specific IgE antibodies or the size of wheal following skin testing can improve the specificity of these tests in the assessment of airway diseases in childhood, and in practical terms, quantification of sensitization offers more information to the clinician than simple presence or absence of atopy.

Other investigations

Further investigations may be required to evaluate other possible diagnoses, especially in cases of treatment failure. Measurement of nasal mucociliary clearance and nasal nitric oxide may be useful in diagnosing primary ciliary dyskinesia. Nasal endoscopy may be useful for visualizing polyps. Acoustic rhinometry can reveal a reduction in the cross-sectional diameter of the nasal cavity at the level of the nasopharynx. Lateral radiographs can be used to evaluate the nasopharyngeal airway, and computer tomography may be helpful in the diagnosis of chronic rhinosinusitis. It may be necessary to utilize other tests to evaluate potential coexisting medical problems such as asthma (Box 3).

Differential diagnosis

The differential diagnosis of rhinitis (Box 4) in children can best be approached using a symptom-based and agerelated differential diagnosis.

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Nasal obstruction

Nasal obstruction in children may be the result of mucosal pathology and/or anatomical abnormalities. Nasal obstruction is often the presenting symptom of rhinitis in preschool children, with open mouth breathing, snoring and nasal secretions. However, adenoidal hypertrophy is a common disorder inducing similar symptoms. Severe septal deviations may occur in children and induce impaired nasal breathing, often unilateral in nature. Two thirds of children with cleft lip complain of nasal obstruction due to nasal septal deviation and the frequently associated stenosis of the nasal vestibulum.

Rare conditions like choanal atresia or stenosis of the piriform aperture should not be overlooked in nasal obstruction in children. Nasal polyps in children impairing nasal breathing are rare, warranting investigations for cystic fibrosis and/or primary ciliary dyskinesia or an encephalocoele if unilateral polyp. Rarely, nasal obstruction may be due to a malignancy.

Colour of nasal secretions

CSF leakage

Coagulopathy

Septal deviation

The colour of nasal secretions provides a first diagnostic clue to the nature of the underlying pathology. Transparent secretions are seen initially in viral common colds, in AR and in the rare condition of leakage of cerebrospinal fluid (CSF). Thickened and often discoloured mucus is found in the nasal cavity of patients with adenoidal hypertrophy, recurrent adenoiditis and/or rhinosinusitis and in the later stages of the common cold which is a viral rhinosinusitis. Sinusitis in children is always associated with inflammation of the nasal cavity; hence, the term 'rhinosinusitis' is

preferred. Chronic severe rhinosinusitis may also be associated with primary ciliary dyskinesia, cystic fibrosis and humoral and/or cellular immune dysfunction. These conditions should be screened for in children with persistent and severe sinonasal symptoms. Children with unilateral discoloured secretions should be evaluated for foreign bodies.

Smell dysfunction

Smell dysfunction represents a typical feature of rhinosinusitis and has not been well studied in children. It is, however, known that children with severe rhinosinusitis and nasal polyps, as in primary ciliary dyskinesia or cystic fibrosis, may experience hyposmia or anosmia, often without major subjective impairment. The rare Kallmann syndrome is characterized by anosmia due to hypoplasia of the olfactory bulb.

Headache

Headache in children is a manifestation of rhinosinusitis rather than rhinitis.

Epistaxis

Minor epistaxis in children is common in AR or in children with congestion of the vessels at the locus Kiesselbach. Excessive nasal bleedings warrant a nasal endoscopy excluding a nasopharyngeal angiofibroma and coagulopathies.

Cough

Cough is an important manifestation of rhinitis due to postnasal drip and stimulation of cough receptors in nasal

cavity, pharynx and larynx. Other diagnoses should be considered when there are no other features of rhinitis or where it fails to respond to therapy. Examples are recurrent upper airway infections, pertussis, habit cough, aspiration bronchiectasis, foreign body or tuberculosis; asthma is unlikely without other symptoms of bronchospasm.

Box 4: Differential diagnosis of rhinitis in children

Diagnosis	Pre-school	School	
Choanal atresia or stenosis	Obstruction without other features of allergic rhinitis		
Immunodeficiency	Persisting mucopurlen	t discharge	
Encephalocoele	Unilateral nasal "polyp	"	
Adenoidal hypertrophy	Mouth breathing, disco secretions, snoring in t features of allergic rhir	he absence of other	
Foreign body	Unilateral discoloured nasal secretions, foul smell		
Rhinosinusitis		Discoloured nasal sec facial pain, poor smel	
Cystic fibrosis	Bilateral nasal polyps, malabsorption, failure t	poor smell, chest sympto o thrive	oms, symptoms of

Primary ciliary dyskinesia

Persisting mucopurlent discharge without respite between "colds", bilateral stasis of mucus and secretions at the nasal floor, symptoms

Colourless nasal discharge often with a history of trauma

Recurrent epistaxis with minimal trauma

Obstruction in the absence of other features of allergic rhinitis

Therapy

Apart from antibiotics in bacterial infectious rhinitis, we currently have no effective therapy for infectious rhinitis, and so, in this section, we will focus on AR.

Allergen avoidance

Outdoor allergens, such as pollen, cannot be completely avoided. For indoor allergens, avoidance should be more possible.

Pharmacological treatment

Oral and intranasal antihistamines

Both oral and intranasal second-generation antihistamines are equally effective for AR. Oral ones may be better tolerated, whilst intranasal antihistamines have a more rapid onset of action. First-generation antihistamines should no longer be used, given their unfavourable therapeutic index. In a minority of children, second-generation ones may also cause sedation with perhaps the exception of fexofenadine.

Intranasal corticosteroids

Corticosteroids address the inflammatory component of AR, and results from a large number of well-designed studies would recommend their use in children and adolescents from 2 years. Several studies have shown that the effects of mometasone, fluticasone and ciclesonide commence within a day of starting therapy. Intranasal corticosteroids probably also improve coexisting asthma, and fluticasone furoate and mometasone may be effective for conjunctivitis.

In general, nasal corticosteroids are well tolerated. Newer, once-daily products (e.g. fluticasone propionate, mometasone, fluticasone furoate nasal spray) are preferred as these have been shown, unlike beclomethasone, not impair growth velocity albeit only after a year of therapy. This is probably due to the much lower systemic bioavailability of the newer products. Nasal perforation and epistaxis have been described as risks of nasal corticosteroids but there are no systematically collected data on these adverse effects in the literature.

Systemic corticosteroids

been performed in adults. In adults, a daily 7.5 mg prednisolone dose was marginally effective, whereas a 30 mg dose was effective but also associated with systemic side-effects. Depot corticosteroid injections are associated with local atrophy of the skin and muscles, reduced bone mineralization and impaired growth. If systemic corticosteroid treatment is necessary in children, a short course with 10–15 mg oral prednisolone a day for 3–7 days for school-age children may be sufficient.

A few studies on systemic corticosteroid therapy have

Montelukast monotherapy is effective in both seasonal and perennial AR in two well-designed, but small, paediatric studies as well as in two meta-analyses dominated by adult studies.

Nasal anticholinergics

Anticholinergics have been reported to be effective in controlling watery nasal discharge in the elderly but not for itching, sneezing or obstruction. It is rarely prescribed in children.

Nasal decongestants

Topical decongestants can be used for a few days for severe nasal obstruction but should only be used for a few days as prolonged use may lead to rebound swelling of the nasal mucosa.

Nasal sodium cromoglicate

Intranasal sodium cromoglicate is an effective AR therapy albeit the trials are relatively old, and repeated use several times a day renders concordance difficult.

Other therapies

Saline douches are inexpensive and have been shown to be effective for rhinitis. In patients with poorly controlled, moderate-to-severe allergic asthma and AR, omalizumab has been found to be effective for both rhinitis and asthma. There is no convincing evidence for the efficacy of alternative medication for AR.

Relative effectiveness of different pharmacological approaches in allergic rhinitis

Assessing the relative efficacies of therapies and the potential benefit of combining them is compromised by the lack of studies in the preadolescent age group. Nasal corticosteroids are more effective at controlling AR than either antihistamines or montelukast. All are more effective than nasal cromoglicate. Symptoms of congestion are only effectively controlled by nasal corticosteroids. In children, there are insufficient comparative data to determine whether antihistamines or montelukast is more effective. studies indicate although some antihistamines are more effective for itching. Antihistamines and montelukast may provide some additional benefit when used as add-on

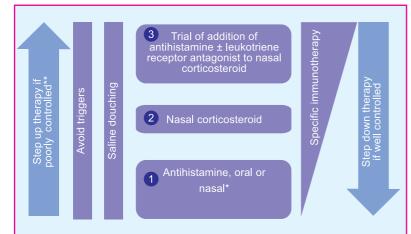


Figure 2 Approach to therapy for paediatric allergic rhinitis (1), (2), (3) and are potential entry points into therapeutic approach depending on the severity of the rhinitis symptoms. For seasonal disease, regular therapy should be commenced 2 weeks before the anticipated start of symptoms. *Oral antihistamines may be better tolerated, whilst intranasal antihistamines have a more rapid onset of action. **Reconsider diagnosis if not controlled within 1-2 weeks. If less than 2 years of age and do not re spond to antihistamine within a week, reconsider diagnosis before stepping up therapy. If poorly controlled, consider a short rescue course of a decongestant or low-dose oral prednisolone to gain symptom control; topical ipratropium may be useful for rhinorrhoea.

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therapy with nasal corticosteroids. Given these data, we propose the approach to pharmacological management described in Fig. 2. We would suggest that topical nasal corticosteroids are the appropriate first-line therapy in moderate-to-severe AR, especially when congestion is the predominant complaint, but antihistamines may be preferred in mild AR to minimize the exposure to corticosteroid in children.

Pharmacotherapy for nonallergic, noninfectious rhinitis There are no high-quality data to formulate treatment recommendations in children with nonallergic, noninfectious rhinitis. Management should be directed by the underlying cause (Box 1). Where this is not obvious, saline douches and/or topical corticosteroids should be tried first. If symptoms continue, further investigation should be undertaken to exclude possible differential obstruction, diagnoses. For persistent antihistamine then short-term topical decongestants may be considered. For watery rhinorrhoea, ipratropium may help. There are adult controlled study data to suggest that capsaicin may reduce symptoms.

Immunotherapy

Allergen-specific immunotherapy (SIT) is the specific treatment for IgE-mediated allergic disease in patients, and this may utilize the subcutaneous or sublingual routes.

Indications and contraindications

There should be a clear history of AR with evidence of a small number of clinically relevant sensitizations, in other words allergen-driven AR; this may limit its use in the preschool children. The need for injections also effectively limits the use of subcutaneous immunotherapy to schoolage children. Specific immunotherapy should be performed with a standardized allergen extract or preparation registered or approved by the authorities. Therapy should be initiated by a physician with training in the diagnostic procedures, treatment and follow-up of allergic and asthmatic children. Significant concurrent disease, impaired lung function and severe asthma are contraindications.

Subcutaneous injection immunotherapy (SCIT)

The 2007 Cochrane systematic review of SCIT in AR demonstrates that it is effective although there were no accepted studies that were conducted exclusively in children. Subcutaneous injection immunotherapy has been associated with systemic reactions but it is generally well tolerated in children. There are also some nonblinded data to suggest that SCIT may alter the natural history of allergic disease in childhood. Factors associated with severe adverse effects are unstable asthma, elevated allergen exposure during therapy, concomitant diseases such as severe infections and inexperienced healthcare staff.

Sublingual immunotherapy (SLIT)

The effectiveness of SLIT for AR has been evaluated in a number of systematic reviews. The 2011 review demonstrates its effectiveness for pollen and house dust mite-driven rhinitis. This review highlights the considerable heterogeneity between studies, not all preparations seem to be effective. Local oral reactions are experienced in up to three quarter of the patients but are mild to moderate, self-resolve after a few minutes and usually disappear after a few weeks therapy. Severe adverse reactions have been seen but are very rare.

Compliance with therapy

The compliance of children with rhinitis therapy has not been well studied. Adherence to the use of nasal sprays may be suboptimal due to discomfort, particularly in young children. Further work is required in this area. Even when patients use their medication, it is critical that they know how to do so correctly, especially nasal medications and education are essential. Reassurance of the patient and caregivers about the safety of nasal corticosteroids is almost certainly necessary, together with information about the nature of rhinitis, its comorbidities and complications and the benefits of effective therapy.

Summary and conclusions

Rhinitis is a prevalent yet underappreciated paediatric problem. These are the first paediatric specific recommendations. Many children present with typical nasal symptoms, such as rhinorrhoea, blockage, sneezing or itching. Atypical presentations usually relate to associated comorbidities such as asthma, eczema, pollen - food syndrome, sleep disorders and hearing problems. The commonest presentations are allergic rhinitis and infectious rhinitis. Other children have a nonallergic, noninfectious rhinitis usually associated with exposure to irritants, gastro-oesophageal reflux, hormonal dysfunction, specific medications or simply idiopathic. A detailed comprehensive clinical history supported by a thorough examination of the nose is important to aid accurate diagnosis. A limited number of allergy tests are useful to confirm or refute allergic origins of symptoms. In case of treatment failure, further investigations are required to exclude other possible diagnoses. A successful therapeutic approach to paediatric AR should involve a holistic approach to all the manifestations with avoidance of relevant allergens where possible, pharmacotherapy with or without specific immunotherapy. Both oral and intranasal antihistamines are appropriate for first-line treatment for AR, whilst intranasal corticosteroids are considered the most effective therapeutic option for children with AR and nonallergic rhinitis with congestion. Add-on therapies are oral montelukast, intranasal anticholinergics for nasal discharge and decongestants for severe nasal obstruction.

Ref: Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology. Allergy 2013; 68: 1102–1116.

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Dear Doctor

We are happy to present you the "Allergy News Letter" Vol. 03 No. 01. In this issue, we have concentrated on "Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology". We hope you will enjoy reading the publication.

We appreciate your comments and queries.

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