Pediatric Rhinitis: position paper of the European Academy of Allergology and Clinical Immunology

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ABSTRACT (191 words)

Rhinitis is a common problem in childhood and adolescence and impacts negatively on physical, social and psychological well-being. This position paper, prepared by the EAACI Taskforce on Rhinitis in Children, aims to provide evidence-based recommendations for the diagnosis and therapy of pediatric rhinitis. Rhinitis is defined as at least two nasal symptoms: rhinorrhea, blockage, sneezing and itching. It is classified as allergic, infectious or non-allergic, non-infectious. Similar symptoms may occur with other conditions such as adenoidal hypertrophy, septal deviation and nasal polyps. Examination by anterior rhinoscopy and allergy tests may help to substantiate a diagnosis of allergic rhinitis. Avoidance of relevant allergens where possible should be the first intervention for allergic rhinitis (AR). Oral and intranasal antihistamines and nasal corticosteroids are both appropriate for first-line AR treatment although the latter are most effective. Potentially useful add-on therapies include oral leukotriene receptor antagonists, short bursts of nasal decongestants, saline douches and nasal anticholinergics. Finally, allergen specific immunotherapy can be helpful in IgE-mediated AR in patients over the age of five years. There are still a number of areas that need to be clarified in the management of rhinitis in children and adolescents.
INTRODUCTION

Rhinitis is a common problem in childhood and adolescence[1;2]. The burden associated with rhinitis is often ignored as it is frequently seen as just a common cold. In reality patients experience disruptive sneezing, itching, watery rhinorrhoea and nasal blockage. Other children and adolescents may present atypically with cough or snoring. Rhinitis impacts negatively on physical, social and psychological well-being[3;4]. The direct effect of symptoms, indirect effect of sleep disturbance with consequent daily fatigue and the use of sedative antihistamines[5] all result in impaired school performance[6]. The impact extends to the rest of the family[7].

This position paper has been prepared by the EAACI Taskforce on Rhinitis in Children. The Taskforce was initiated as at present, there are no guidelines specifically for pediatric rhinitis despite the huge burden of rhinitis in childhood and adolescence as well as the differences from adult rhinitis. The paper uses the terms children and childhood to cover patients up to 18 years of age unless specific age groups are mentioned. The position paper aims to provide evidence-based recommendations for diagnosis and therapy. The breadth of rhinitis is encompassed although, for brevity, the therapy section focuses on allergic rhinitis. A systematic extensive literature search was undertaken using Medline and EMBASE (search terms: rhinitis, prevalence, diagnosis and differential diagnosis, comorbidity, education, pathophysiology, presentation, quality of life and treatment; restricted to children) and Cochrane Library in September 2010 for the previous 5 years. The literature search returned 4955 references that were reviewed to remove case reports and non-systematic reviews to give 589 that were reviewed as part of the Taskforce. Members were also free to add other papers from before 2005. An updated search was undertaken in June 2012, it returned another 2913 reference of which 63 were reviewed in detail. Although a systematic review of the evidence was
undertaken, only the highest available evidence for each issue is presented here.
The recommendations in this document are labelled to indicate the grade of recommendation[8].

Definition and classification
Rhinitis is defined as an inflammation of the nasal epithelium and is characterized by at least two nasal symptoms: rhinorrhea, blockage, sneezing or itching. There are a number of different clinical presentations of rhinitis which overlap. The commonest chronic 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[9]. Typical allergens include house dust mite, grass pollen, tree pollen, weed pollens, cat, dog and moulds[10]. In adults there is evidence to suggest that this form of rhinitis may exist despite a lack of apparent specific sensitization due to local IgE production in the nose, otherwise known as entopy[11]. This may also be seen in children[12]. Allergic rhinitis can be seasonal or perennial, according to the relevant allergen. 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[9]. Based on duration of symptoms, ARIA subdivides AR into intermittent or persistent, and into mild or moderate/severe depending on the impact of the disease[9]. 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 and suggests the treatment approach. The second presentation 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[13]. Finally there is a non-allergic, non-infectious group of other disorders that may present with rhinitis including those associated with hormonal dysfunction and specific medications (Box 1).

**BOX 1. CLASSIFICATION OF RHINITIS CAUSATION IN CHILDREN**

1. **Allergic rhinitis** – rhinitis symptoms that are associated with exposure to an allergen to which the patient is sensitized.
2. **Infectious rhinitis** - secondary to infection.
3. **Non-allergic, non-infectious** – hormonal (hypothyroidism, pregnancy), drug-induced (eg beta-blockers, contraceptives, NSAID), neurogenic, gastroesophageal reflux, idiopathic.

Different pathophysiologies may co-exist, particularly allergic rhinitis and infectious rhinitis. See Box 4 for conditions that may mimic rhinitis.
PREVALENCE AND EPIDEMIOLOGY

Rhinitis is highly prevalent worldwide in childhood. The International Study of Asthma and Allergies in Childhood (ISAAC) phase three studies (1999-2004) revealed an average prevalence of 8.5% (range 1.8-20.4%) in 6-7 year old children and 14.6% (1.4-33.3%) for 13-14 year old children[14]. A worldwide increase in rhinoconjunctivitis prevalence was observed since the identical phase one studies (1991-8) but with large variations between centres[15].

ISAAC defines current rhinitis on the basis of a positive answer 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”?“[16]. This question assumes that the respondent can correctly identify a cold or “flu”; for example some children may only have significant symptoms with a combination of both allergic inflammation and a coexisting viral infection. Additionally, ISAAC uses the presence of coexisting itchy eyes to identify allergic rhinitis though this is probably more relevant for pollen-induced rhinitis. The ISAAC questions have not been well validated in a pediatric population[16].

There are a few studies looking at the natural history of rhinitis in childhood. The 1989 Isle of Wight birth cohort of 1456 children had prevalences of 2.8 and 11.8% at 4 and 18 years for rhinitis in non-sensitized individuals with figures of 3.4 and 27.3% for those who were sensitised[17]. There was a male predominance of allergic rhinitis and female predominance of non-allergic rhinitis during adolescence. The MAS study followed up 467 children until 13 years and showed similar rates of rhinitis[18]. Allergic rhinitis, but not non-allergic rhinitis, in early childhood is a risk factor for developing asthma in later childhood[19] and adulthood[20].
PRESENTATION AND ASSOCIATED CO-MORBIDITIES

Classic symptoms and signs
Classic symptoms and signs of allergic rhinitis are intermittent or persistent nasal obstruction, rhinorrhoea (anterior or posterior), pruritus and sneezing[21]. All these impact negatively on quality of life[22]. 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[23]. 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 infection episodes per year in infancy, 8 episodes at preschool age, and 4 at school age[24] and 0.2-2% of these develop into clinically important bacterial sinus infection[25]. A chronic mucopurulent discharge suggests a rhinosinusitis of infective origin(Fokkens, 2012 889 /id). This may be secondary to other pathologies, such as primary immunodeficiency, primary ciliary dyskinesia (PCD) or cystic fibrosis (CF)[25].

Presentations associated with rhinitis co-morbidities
In childhood, the presentation of rhinitis can frequently relate to its associated co-morbidities (Box 2). 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 co-morbidity associated with AR[15;26]. It is characterized by intense eye itching, conjunctiva 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 localised nasal inflammation[28]. There is a significant increase in adenoidal size during the pollen season in children with pollen-driven rhinitis[29]. In a case series of 93 2-10 year children referred to a sleep laboratory for polysomnography, sleep apnoea-hypopnoea syndrome was strongly associated with the clinical history of nasal obstruction and AR[30]. Chronic middle ear effusion and eustachian tube dysfunction, potentially causing hearing impairment, are associated with rhinitis[31-33]. Significantly higher levels of eosinophils, T lymphocytes and Th2 cytokines have been detected in the middle ear effusion of atopic children when compared with non-atopic patients[34]. Local production of non-specific and specific IgE against both environmental allergens and staphylococcal enterotoxin antigens maybe involved in ongoing allergic inflammation observed in the adenoidal lymphatic tissue from atopic children[11;35].

Other co-morbidities

Asthma
Rhinitis and asthma frequently co-exist, with AR being seen in half to three-quarter of children and teenagers with asthma in a range of studies[36-39]. Asthma is similarly associated with non-allergic rhinitis as demonstrated by the COPSAC birth
cohort[40]. AR is one of the risk factors for the development of asthma and its signs and symptoms often precede those of asthma. In an international survey involving 8 countries in Europe and Asia, 76% of children had pre-existing symptoms of AR when asthma was first diagnosed[41]. AR also increases the risk of asthma hospitalization, in a cross-sectional study involving 126 asthmatic children and adolescents, the prevalence of AR was high and in combination with asthma severity constituted the major risk factor for emergency care attendance[42]. 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[43]. The presence of a cough in association with rhinitis and postnasal drip may falsely suggest a diagnosis of asthma[44].

Eczema

Eczema and rhinitis frequently coexist in all age groups[45].

Oral Allergy Syndrome

AR can be associated with oral allergy syndrome. Symptoms of oral pruritis and swelling occur due to cross-reactivity between aeroallergens, such as birch pollen, and fruits and vegetables such as peach[46]. There are limited paediatric data focusing on this link although one study suggests that a quarter of 8 year olds with AR are affected[47].
BOX 2: RECOGNISING RHINITIS IN CHILDHOOD (D)

Classic symptoms and signs of rhinitis in children and teenagers:
Rhinorrhoea - sniffing
Pruritus - nose rubbing, the “allergic salute”, “allergic crease”, paroxysmal sneeze,”
Conjunctivitis - red, itchy, watery eyes
Congestion - mouth breathing, snoring, sleep apnoea, allergic shiners
Habitual open mouth breathing

Consider the following as potential atypical presentations:
Cough
Poorly controlled asthma
Eustachian tube dysfunction - ear pain on pressure changes, eg flying, reduced hearing, chronic otitis media with effusion
Sleep problems - tired, poor school performance, irritability
Rhinosinusitis - catarrh, headache, facial pain, halitosis, cough, hyposmia
Prolonged and frequent respiratory tract infections
Oral allergy syndrome
### BOX 3: RECOGNISING CO-MORBIDITIES OF CHILDHOOD RHINITIS (D)

**Conjunctivitis**

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

**Asthma**

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  
Undertake an exercise, mannitol or methacholine challenge test

**Hearing problems**

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

**Sinusitis**

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

**Oral allergy syndrome**

Ask about any oral pruritus with symptoms with (not cooked or frozen) foods such as pears and 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 non-clinically relevant positivity could be elicited.
**DIAGNOSTIC TESTS**

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[48](D). Specific finding such as unilateral symptoms, nasal obstruction without other symptoms, mucopurulent discharge, pain or recurrent epistaxis will suggest other diagnoses (see differential diagnosis section below). Examination of nose is essential, and should always been carried out, principally to rule out alternatives such as nasal polyps[48](D). In daily practice, diagnosis is usually based on a suggestive clinical history supported by examination by anterior rhinoscopy and a small number of tests (including SPT or specific IgE), which can suggest an allergic origin of the symptoms.

**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[49] although non-symptomatic sensitization is common. Outdoor allergens constitute a risk for seasonal rhinitis whereas indoor allergens are associated with perennial rhinitis[49]. The information on absence of sensitization can be clinically very valuable potentially ruling out a diagnosis of AR. Negative predictive value may be as high as 95%, false negatives are associated with local specific IgE production, particularly in young children who have recently become symptomatic[11]. Additionally, a proportion of children with positive tests have no symptoms[50] and many children with symptoms of rhinitis are sensitization to allergens that do not give rise to the symptoms[10]. So a positive allergen-specific IgE test alone does not confirm the allergic origin of symptoms and results must be interpreted in the context of the clinical history (C). 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[51-53] and in practical terms, quantification of sensitization offers more information to the clinician than simple presence or absence of atopy (C). Recent studies employing a molecular diagnostic approach suggest that measurement of IgE response to specific allergenic components may be more useful in determining genuine sensitization to a specific pollen[54] and in predicting food allergy than currently used skin or blood tests based on whole extracts[55;56]; this approach may provide new tools for the assessment of children with symptoms suggestive of AR.

Other investigations

Further investigations may be required to evaluate other possible diagnoses, especially in cases of treatment failure[48](D). Measurement of nasal mucociliary clearance and nasal nitric oxide may be useful in diagnosing PCD[57](C). Nasal endoscopy may be useful for visualizing polyps (D). Acoustic rhinometry can reveal a reduction of the cross-sectional diameter of the nasal cavity at the level of the nasopharynx[48](C). Lateral radiographs can be used to evaluate the nasopharyngeal airway and computer tomography to diagnose chronic rhinosinusitis[48](D). It may be necessary to utilize other tests to evaluate potential co-existing medical problems such as asthma.
DIFFERENTIAL DIAGNOSIS

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

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 pre-school 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[25], warranting investigations for CF and/or PCD or an encephalocele if unilateral polyp (D). Rarely, nasal obstruction may be due to a malignancy.

Colour of nasal secretions

The colour of *nasal secretions* provides a first diagnostic clue on the nature of the underlying pathology (D). 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 PCD, CF, and
humoral and/or cellular immune dysfunction. These conditions should be screened for in children with persistent and severe sino-nasal symptoms (D). Children with unilateral discoloured secretions should be evaluated for foreign bodies (D).

**Smell dysfunction**

*Smell dysfunction* represents a typical feature of sinus pathology[25] but has not been well studied in children. It is however known that children with severe rhinosinusitis and nasal polyps, as in PCD or CF, may experience hyposmia or anosmia. The rare Kallman syndrome is characterized by anosmia due to hypoplasia of the olfactory bulb[58].

**Headache**

*Headache* in children is a manifestation of rhinosinusitis rather than rhinitis[48].

**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[59](D).

**Cough**

Cough is an important manifestation of rhinitis due to postnasal drip. Other diagnoses should be considered when there are no other features of rhinitis or where it fails to respond to therapy[Shields, 2008 919 /id]. Examples are pertussis, habit cough, aspiration bronchiectatis, foreign body or tuberculosis; asthma is unlikely without other symptoms of bronchospasm.
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Suggestive features</th>
</tr>
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<tbody>
<tr>
<td>Adenoidal hypertrophy</td>
<td>Mouth breathing, discoloured nasal secretions, snoring in the absence of other feature of allergic rhinitis</td>
</tr>
<tr>
<td>Septal deviation, choanal atresia or stenosis</td>
<td>Obstruction in the absence of other feature of allergic rhinitis</td>
</tr>
<tr>
<td>Foreign body</td>
<td>Unilateral discoloured nasal secretions</td>
</tr>
<tr>
<td>Rhinosinusitis</td>
<td>Discoloured nasal secretions, headache, facial pain, poor smell, halitosis, cough</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Bilateral nasal polyps, poor smell, chest symptoms, symptoms of malabsorption, failure to thrive</td>
</tr>
<tr>
<td>Primary ciliary dyskinesia</td>
<td>Persisting mucopurulent discharge without rest bite between “colds”, bilateral stasis of mucus and secretions at the nasal floor, symptoms from birth</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>Unilateral nasal “polyp”</td>
</tr>
<tr>
<td>CSF leakage</td>
<td>Colourless nasal discharge often with a history of trauma</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Recurrent epistaxis with minimal trauma</td>
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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. The management of AR includes avoidance of relevant allergens, symptomatic treatment and specific immunotherapy.

Allergen avoidance

Outdoor allergens, such as pollen, cannot be completely avoided. For indoor allergens, avoidance ought to be more possible. Few studies have investigated the effect of effective house dust mite avoidance in paediatric AR. In general, they have failed to demonstrate a benefit but cannot be described as conclusive due to their small size and design[60](D). There is insufficient evidence on pet allergen avoidance in AR to make any recommendations[61].

Pharmacological treatment

Oral and intranasal antihistamines

Both oral and intranasal second generation antihistamines are equally effective for AR[62-70](A). Oral ones may be better tolerated while intranasal antihistamines have a more rapid onset of action[Simons, 2011 814 /id]. First-generation antihistamines should no longer be used, given their unfavourable therapeutic index[22;71;72](B). Second generation ones may also cause sedation when given orally[73] with the exception of fexofenadine [ref].

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[74-88](A). The recent Cochrane review[89] failed to find evidence supporting the effectiveness of intranasal nasal corticosteroids but it excluded all the recent high quality randomised controlled trials as they allowed rescue medication. Several studies have shown that the effect of mometasone, fluticasone and ciclesonide commence within a day of starting therapy[90]. Intranasal corticosteroids may also improve co-existing asthma[92;93](B) and fluticasone furoate and mometasone may be effective for conjunctivitis[74;79;91](B).

In general, nasal corticosteroids are well tolerated. Newer, once daily products (eg fluticasone propionate[94], mometasone[95-97], fluticasone furoate nasal spray[79]) are preferred as these have been shown, unlike older products (eg beclomethasone, budesonide), to not impair growth velocity albeit only after a year of therapy [98;99](A). Nasal perforation and epistaxis are described as risks of nasal corticosteroids but there are no systematically collected data on these adverse effects in the literature.

**Systemic corticosteroids**

A few studies on systemic corticosteroid therapy have been performed but only in adults. In adults, a daily 7.5mg dose was marginally effectiveness whereas a 30mg dose was effective but also associated with systemic side effects[100]. Depot corticosteroid injections are associated with local atrophy of the skin and muscles, reduced bone mineralisation and impaired growth [101]. If systemic corticosteroid treatment is necessary in children, a short course with 10-15mg oral prednisolone a day for 3-7 days for school age children may be sufficient (D).

**Oral leukotriene receptor antagonist**
Montelukast is effective in both seasonal and perennial AR in two well designed, but small, paediatric studies[102;103] as well as in two meta-analyses dominated by adult studies[104;105](A).

**Nasal anticholinergics**

Anticholinergics have been reported to be effective in controlling watery nasal discharge (C) but not for itching, sneezing or obstruction [106].

**Nasal decongestants**

Topical decongestants can be used for a few days for severe nasal obstruction but prolonged use may lead to rebound swelling of the nasal mucosa[107](C).

**Nasal sodium cromoglicate**

Intranasal sodium cromoglicate is an effective AR therapy albeit the trials are relatively old[108](A) and repeated use several times a day renders concordance difficult.

**Other therapies**

Hypertonic or normal saline douches is inexpensive and has been shown to be effective for rhinitis[109-111](A). In patients with poorly controlled, moderate-to-severe allergic asthma and AR, omalizumab has been found to be effective for both rhinitis and asthma[112]. There is no convincing evidence for the efficacy of alternative medication for AR[113].

**Relative effectiveness of different pharmacological approaches in rhinitis**

Assessing the relative efficacies of therapies and the potential benefit of combining them is compromised by the lack of studies in the pre-adolescent age group. Nasal corticosteroids are more effective at controlling AR than either antihistamines or
montelukast[70;114-116](B). All are more effective than nasal cromoglicate[70](B). Symptoms of congestion are only effectively controlled by nasal corticosteroids[116](B). In children, there are insufficient comparative data to determine whether antihistamines or montelukast are more effective, although some studies indicate that antihistamines are more effective for itching[117;118]. Antihistamine and montelukast may provide some additional benefit when used as add-on therapy with nasal corticosteroids[Simons, 2011 814 /id][70;114;116](B).

Given these data, we propose the approach to pharmacological management described in Figure 1. We would suggest that topical nasal corticosteroids are the appropriate first line therapy in moderate to severe AR, especially when congestion is the predominate complaint, but antihistamines may be preferred in mild AR to minimized the exposure to corticosteroid in children.

Immunotherapy

Allergen specific immunotherapy (SIT) is the specific treatment of IgE-mediated allergic diseases in patients over the age of five years[119]. This may utilize the subcutaneous or sublingual route.

Indications and contraindications

There should be a clear history of AR with evidence of a small number of clinical relevant sensitizations, in other words allergen-driven AR[120;121](D). SIT should be performed with a standardized allergen extract or preparation registered or approved by the authorities (D). Therapy should be initiated by a physician with training in the diagnostic procedures, treatment and follow-up of allergic and asthmatic children[122](D). Significant concurrent disease, fixed airway obstruction and severe asthma are contra-indications[120](D).
Subcutaneous injection immunotherapy (SCIT)

The 2007 Cochrane systematic review of SCIT[123] in AR demonstrates that it is effective although there were no accepted studies which were conducted exclusively in children. There are though more recent data demonstrating the effectiveness of SCIT in children with pollens and house dusts mite[124-126](A). SCIT has been associated with systemic reactions but it is generally well tolerated in children[123;127]. There are also some unblinded data to suggest that SCIT may alter the natural history of allergic disease in childhood[128]; these studies are now being repeated with a SLIT product using a placebo controlled design[129]. Factors associated with severe adverse effects are unstable asthma, elevated allergen exposure during therapy, concomitant diseases such as severe infections and inexperienced healthcare staff. There is some evidence to suggest that antihistamine premedication may reduce the rate of adverse effects[130](B). Also, pre-treatment with anti-IgE has been used to successfully minimize the rate of adverse reactions associated updosing with SCIT[131](A).

Sublingual immunotherapy (SLIT)

The effectiveness of SLIT for AR has been evaluated in a number of systemic reviews. The 2011 one[132] demonstrates its effectiveness for pollen and house dust mite-driven rhinitis (A). This review highlights the considerable heterogeneity between studies, not all preparations seem to be effective. Both continuous and co-seasonal protocols have been described, both seem to be effective although the latter may take longer to impact on the symptoms[133]. Two commercial grass extracts have received European market authorization for patients at least 5 years of age[134;135]. 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[127;132;136;137]. Severe adverse reactions have been seen but are very rare[138]. There is concern about compliance with
SLIT with sales data suggesting 44% compliance in the first year, 28% in second year and 13% in the third years[139].

Health economics
Pharmacoeconomic models based on data provided by clinical trials and meta-analyses indicate that SIT is cost-efficient[140]. One of the few real patient cohort studies to investigate cost-effectiveness of SCIT was performed in US children with allergic rhinitis, patients in the SCIT group incurred 33% (1625 USD) lower health care costs [141;142].

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[143]. 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 (D). Reassurance of the relevant carer about the safety of nasal corticosteroids is almost certainly necessary, together with information about the nature of rhinitis, its co-morbidities and complications and the benefits of effective therapy.
Figure 1 Approach to therapy for pediatric allergic rhinitis

1, 2, and 3 are potential entry points into therapeutic approach depending on the severity of the rhinitis symptoms.

* Oral antihistamines may be better tolerated while intranasal antihistamines have a more rapid onset of action.

**Reconsider diagnosis if not controlled. If less than 2 year of age and do not respond to antihistamine, 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.
**Box 5. UNMET RESEARCH NEEDS**

- Randomised double-blind, placebo-controlled studies focusing on potential for SIT to alter the natural history of allergy (eg development of further sensitization and asthma).
- Identification of those in whom rhinitis will progress to asthma
- Generation of paediatric specific data for efficacy of SCIT and cost-effectiveness of SIT
- Evaluation of effective allergen avoidance as a useful therapy for AR.
- Evaluation of the potential value of component resolved diagnosis in the evaluation of children with rhinitis.
- Investigate the potential role of local IgE production in paediatric rhinitis. Identifying patients with poor compliance and developing educational and other strategies to address this.
- Development of effective therapy for the small but important proportion of children with uncontrolled rhinitis despite maximal therapy.
- Role of viral infections in the aetiology of allergic rhinitis and as co-factors in the development of symptoms with allergen exposure.
- Development and validation of improved epidemiological definitions of the different types of childhood rhinitis.
SUMMARY AND CONCLUSIONS

Rhinitis is a prevalent yet underappreciated pediatric problem. These are the first pediatric recommendations. Many children present with typical nasal symptoms, such as rhinorrhea, blockage, sneezing, itching. Atypical presentations usually relate to associated co-morbidities such as asthma, eczema, oral allergy syndrome, sleep disorders and hearing problems. The commonest presentations are allergic rhinitis and infectious rhinitis. Other children have a non-allergic, non-infectious presentation associated with hormonal dysfunction, specific medications, gastroesophageal reflux 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 pediatric AR should involve avoidance of relevant allergens, pharmacotherapy with or without specific immunotherapy. Both oral and intranasal antihistamines are appropriate for first-line treatment of AR while intranasal corticosteroids are considered the most effective therapeutic option for children with AR and non-allergic rhinitis with congestion. Add on therapies are oral montelukast, intranasal anticholinergics for nasal discharge and decongestants for severe nasal obstruction. There are a number of unmet research needs in pediatric rhinitis, including developing new approaches to control effectively the small but important number of children with ongoing symptoms despite the use of current medications.
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APPENDIX [not for publication]

Box 1 Revised grading system for recommendations in evidence based guidelines

Levels of evidence
1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+ Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1- Meta-analyses, systematic reviews or RCTs, or RCTs with a high risk of bias
2++ High quality systematic reviews of case-control or cohort studies or High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal
2+ Well conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal
2- Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal
3 Non-analytic studies, eg case reports, case series
4 Expert opinion

Grades of recommendations
A At least one meta-analysis, systematic review, or RCT rated as 1 ++ and directly applicable to the target population or A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1 + directly applicable to the target population and demonstrating overall consistency of results
B A body of evidence including studies rated as 2 ++ directly applicable to the target population and demonstrating overall consistency of results or Extrapolated evidence from studies rated as 1 ++
or 1 +
C A body of evidence including studies rated as 2 + directly applicable to the target population and demonstrating overall consistency of results or Extrapolated evidence from studies rated as 2 + +
D Evidence level 3 or 4 or Extrapolated evidence from studies rated as 2 +