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Monitoring asthma in childhood: management-related issues

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ABSTRACT Management-related issues are an important aspect of monitoring asthma in children in clinical practice. This review summarises the literature on practical aspects of monitoring including adherence to treatment, inhalation technique, ongoing exposure to allergens and irritants, comorbid conditions and side-effects of treatment, as agreed by the European Respiratory Society Task Force on Monitoring Asthma in Childhood.

The evidence indicates that it is important to discuss adherence to treatment in a non-confrontational way at every clinic visit, and take into account a patient's illness and medication beliefs. All task force members teach inhalation techniques at least twice when introducing a new inhalation device and then at least annually. Exposure to second-hand tobacco smoke, combustion-derived air pollutants, house dust mites, fungal spores, pollens and pet dander deserve regular attention during follow-up according to most task force members. In addition, allergic rhinitis should be considered as a cause for poor asthma control. Task force members do not screen for gastro-oesophageal reflux and food allergy. Height and weight are generally measured at least annually to identify individuals who are susceptible to adrenal suppression and to calculate body mass index, even though causality between obesity and asthma has not been established.

In cases of poor asthma control, before stepping up treatment the above aspects of monitoring deserve closer attention.



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ERS review summarising and discussing the management-related issues regarding the monitoring of asthma in childhood <http://ow.ly/JfjGs>

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Introduction

Monitoring is essential to reach the ultimate goal of asthma treatment: obtaining clinical control and reducing future risks to a child with asthma.

Recently, a European Respiratory Society Task Force on Monitoring Asthma in Childhood was published [1]. In the present review we aim to discuss aspects of monitoring related to the management of children with asthma in more detail. Monitoring adherence to treatment, inhalation technique and side-effects of management are issues that should be routinely checked. In the case of poorly controlled asthma other factors might be considered, such as persistent exposure to tobacco smoke or allergens. This review also covers conditions that may aggravate asthma (e.g. allergic rhinitis, environmental irritant exposure and obesity) or that may become apparent during follow-up. Three other articles in this issue of the *European Respiratory Review* will address general considerations on monitoring asthma in children, monitoring symptoms, exacerbations and quality of life, and monitoring lung function, bronchial responsiveness and inflammation [2–4]. As no formal grading of the evidence was conducted, this statement does not contain recommendations for clinical practice.

Adherence to treatment

According to the World Health Organization, adherence to treatment is defined as the extent to which a person's behaviour (taking medication, following a diet and/or executing lifestyle changes) corresponds with agreed recommendations from a healthcare provider. Although concordance has more recently been used to express the collaborative relationship between care takers and care providers on the basis of equality, adherence is more commonly used and is, therefore, used in this review.

Poor adherence to medication is common in chronic conditions, and patients' and parents' illness and medication beliefs are by far the most consistent and strongest predictors of adherence to inhaled corticosteroids (ICS), the mainstay of treatment for children with persistent asthma [5–8].

Scheduled close follow-up of children with asthma, providing repeated tailored education, agreement on treatment goals and methods, and addressing patients' and parents' beliefs and concerns, helps to improve asthma control [6, 9, 10]. As adherence to ICS is strongly associated with asthma control, improving adherence, compared to any improvement in specific medical treatment, may be the most cost-effective way to improve asthma control [11, 12]. In children with problematic asthma, medication issues and issues on prevention of exposures contributed to poor asthma control in nearly half of the children [13].

Taken together, the evidence indicates that adherence to maintenance treatment is a matter that warrants attention at each appointment with a healthcare provider, in particular in children with poorly controlled asthma.

How to measure adherence

There is no gold standard to measure adherence to treatment. Interviews and self-reporting by patients and/or parents tend to overestimate adherence. Face-to-face interviews have been demonstrated to be more effective than computer-assisted or written interviews in reporting adherence, but still overestimates adherence to treatment [14]. Pharmacy refill rates seem to be as equally unreliable as self-reported adherence [15]. Electronic data recording may be the most reliable way to assess adherence, however, this should be balanced against extra costs [14]. In a recent study in 2–6-year-old children, electronically recorded adherence demonstrated a relatively high median adherence rate of 92% (interquartile range 76–97%) over a 3-month period [16]. Importantly, parents who believed that ICS maintenance therapy was needed for their child's health, those who viewed ICS administration as convenient and those who expected little harm from medication had higher adherence rates to ICS. This evidence suggests that all these are important issues for follow-up visits of children with asthma.

In clinical trials where electronic monitoring was applied, adherence was ~70% for all diseases that needed twice daily dosing of medication [17].

In general, an increasing number of daily doses leads to decreased adherence, even in clinical trials, although the effect is small [17]. In real life, adherence can therefore often be expected to be lower. Additional risk factors for poor adherence are growing up in single parent families, replacement of the caregiver, lower education of the mother and prescribing more than two inhalations a day [18, 19]. In most studies a link between education level and adherence was not shown.

Motivational interviewing is a patient-centred approach to discuss behaviour change by helping children or their parents to say why and how they might change [20]. A systematic review that included 72 studies (no paediatric studies) found that motivational interviewing outperformed traditional advice given in 80% of studies [21]. The evidence suggests that adherence can be improved by applying specific communicative consultation skills [22].

All task force members discuss adherence to treatment at every patient visit and a non-confrontational way of interviewing may be preferred, which may be sufficient in children with mild-to-moderate disease. However, in children with severe, uncontrolled asthma, assessing adherence by electronic measurement or directly observed therapies is more reliable and might be considered. If these are unavailable, prescription records or refill rates could provide useful information. In some cases home visits may be useful. Educational interventions alone are insufficient to enhance medication adherence in children and adolescents [23].

Inhaler technique

After adequate adherence to treatment, correct inhaler technique is a prerequisite of successful asthma treatment. Correct inhaler technique involves using an age appropriate device, handling the device correctly and performing an (age dependent) adequate breathing manoeuvre [24]. Healthcare professionals should demonstrate any asthma inhaler device that a child needs to use to the child and their family and then have the child or parent demonstrate how they would use the device [25]. Less than one-third of asthmatic children receiving treatment with a dry powder inhaler performed all essential steps correctly compared with 67% of children using a pressurised metered dose inhaler (pMDI)/spacer combination [26]. Repeated instruction led to improved performance compared to a single instruction given by a general practitioner [26].

In younger children it may be necessary to demonstrate to the parents how to hold a child securely to aid treatment administration, particularly with a spacer and facemask. Furthermore, patients should be actively encouraged to ask questions regarding asthma medication devices [25]. In adults, there is evidence that a patient is more likely to correctly use an inhaler that they like [27]. Although in general it is logical to provide both anti-inflammatory and rescue medication in one type of inhaler, concurrent use of pMDIs and dry powder inhalers (DPIs) by children did not adversely affect spacer/inhalation technique in an observational study [28].

It has been well documented that children learn through play and utilising some simple play strategies can improve inhaler technique. Placing stickers on spacers, distracting children with nursery rhymes or videos and trying to make the whole experience fun rather than a stressful intervention can help with the acceptance of inhaler devices. Although appealing, this is not supported by strong evidence; for example, an attractive spacer device like the “funhaler” did not improve adherence or asthma control [29, 30].

In order to achieve and maintain a correct inhalation technique, the procedure has to be taught and checked and taught again; the number of newly referred patients demonstrating a correct inhalation technique improved from 57.4 to 97.9% after three comprehensive instruction sessions [31]. Telepharmacy counselling *via* interactive compressed video (which allows real-time video and audio interaction between individuals in different physical locations) was superior to education provided *via* written instructions on an inhaler package insert in adolescents with asthma [32]. Instruction of inhaler technique by telephone resulted in an improvement in inhaler technique both for pMDIs and for DPIs in adults [33]. Also, repeated instruction by a respiratory therapist led to a relevant improvement in inhaler technique [34].

Although it might be anticipated that combination inhalers improve adherence compared with the use of separate inhalers, this was not demonstrated in a randomised controlled trial [35].

The evidence indicates that inhaler technique is improved if taught, repeated back and checked at least twice when new drugs or devices are prescribed, with deteriorating asthma control or at least annually. The European Respiratory Society/International Society for Aerosols in Medicine consensus paper provides detailed recommendations on checking inhalation technique and states that this should be performed regularly and that adherence should be reviewed at every visit. Furthermore, this paper recommends not switching to a new device without the patient's involvement or without follow-up education on how to use the device properly [24].

Side-effects of drug treatment

During long-term use of low-to-moderate doses of ICS (beclometasone 200–400 $\mu\text{g}\cdot\text{day}^{-1}$ or equivalent), the risk of systemic side-effects is very low [36, 37]. Height growth may be reduced by approximately 0.5–2 cm during the first 1–2 years of treatment [38]; whether or not this persists over time a matter of debate [39, 40]. Even if the effect is persistent, the advantages of ICS maintenance therapy outweigh its risks [37]. Although more serious systemic side-effects, such as adrenal suppression, are almost exclusively seen during treatment with high-dose ICS, they may occur in children on low-dose ICS [41]. Children using high doses of ICS warrant monitoring for possible adrenal suppression. More research is needed to define which adrenal suppression tests are useful and in which children. Most members of the task force would consider nasal and topical corticosteroids when assessing total corticosteroid dose.

Local side-effects, such as thrush and hoarseness, are rare and easily manageable by teeth brushing or mouth rinsing after administration of ICS [42]. Apart from monitoring height growth, which is mandatory for all paediatric chronic conditions, there is no need to monitor children with asthma with respect to potential side-effects of ICS maintenance therapy. Height and weight should be measured at least annually but preferably at every routine visit [43]. It may be important to discuss the fear of side-effects with parents during the clinic visits.

Monitoring diseases that may aggravate asthma

Food allergy, obesity and gastro-oesophageal reflux are conditions that may present simultaneously with asthma, may aggravate asthma or may mimic asthma. Their potential role has recently been reviewed and therefore is only discussed briefly here [44]. It may be necessary to identify these comorbidities and treat them accordingly, particularly in those with poor asthma control.

Asthmatic children with rhinitis, compared with those without, have been reported to have poorer asthma control, reduced quality of life, increased risk for emergency visits or hospitalisations and higher healthcare costs [45–48]. Signs and symptoms suggestive of rhinitis and rhinosinusitis are described in table 1. Most physicians ask about these symptoms and look for them at least annually. Although treatment for rhinitis has not been proven to improve asthma control, it is considered good practice to ensure that rhinitis symptoms are managed appropriately in a child with asthma.

Food allergy is commonly considered to be a risk factor for poor asthma control based on its association with severe and even fatal asthma exacerbations [49, 50]. However, it should be realised that the diagnosis of food allergy was not based on the gold standard for food allergy, the double-blind, placebo-controlled food challenge, in any of these studies. As up to 80% of children sensitised to a certain food do not show clinical allergy following oral ingestion of the food [51, 52], most studies assessed sensitisation for foods and not allergy as a risk factor. Most patients with sensitisation to foods are also sensitised to aeroallergens, which is associated with a distinct, clinically more severe, atopic phenotype [53]. Therefore, it is not the food allergy *per se* but sensitisation to multiple foods and aeroallergens that may be a risk factor for poor asthma control or severe exacerbations. In children with asthma, without any history of adverse reactions to foods, the members of the task force do not screen for food allergy. Children with asthma with confirmed food allergy and anaphylaxis might receive an adrenalin auto injector after appropriate training in its use [54].

Gastro-oesophageal reflux can trigger cough in children, whether they are asthmatic or not [55, 56]. Based on largely descriptive small studies, gastro-oesophageal reflux has been suggested to cause impaired asthma control in children but there is limited data to support this. Usually these studies do not include an adequate control group and a causal link between gastro-oesophageal reflux and asthma symptoms

TABLE 1 Symptoms and signs of rhinitis/rhinosinusitis

Typical symptoms and signs of (allergic) rhinitis

- Runny nose
- Congestion
- Sneezing
- Nasal itching (check for allergic salute, allergic crease and shiners)

Atypical manifestations of (allergic) rhinitis

- Cough (check for post-nasal drip)
- Eustachian tube dysfunction
 - Secretory otitis media and effusion/ask if otitis media occurs frequently
 - Decreased hearing (speech and language delay, child speaks loudly, child increases TV sound)
- Poor school performance/poor concentration
- Consider hearing test/audiometry
- Sleep problems
 - Disturbed sleep (ask about fatigue/irritability, poor concentration and school performance)
 - Snoring
 - Apnoea (check for hypertrophy of adenoids or of tonsils and consider a sleep study)

Symptoms and signs of rhinosinusitis

- Cough
- Purulent discharge (examine nose in older children)
- Headache
- Facial pain
- Halitosis
- Hyposmia

could not be proven. The results from two controlled studies do not support wide-spread use of oesophageal pH testing in children with asthma who have symptoms despite being on controller medication [57, 58]. Treatment with lansoprazole in children with poorly controlled asthma, without symptoms of gastro-oesophageal reflux, did not improve symptoms or lung function. Therefore, diagnostic testing for gastro-oesophageal reflux has no role in monitoring asthma in children.

The relationship between obesity and asthma is complex and not yet fully understood. Being overweight *per se* is known to induce respiratory symptoms such as dyspnoea and wheezing which can mimic asthma [59, 60]. Furthermore, obesity can have metabolic effects that contribute to airway inflammation [61, 62]. Comorbidity, including gastro-oesophageal reflux and obstructive sleep apnoea, may present symptoms that mimic asthma. More studies are needed to establish whether poorly controlled asthma leads to a more sedentary lifestyle and increasing obesity or whether obesity in itself decreases asthma control and, if so, whether it is just symptoms or also objective measures of control [63]. In obese patients with uncontrolled asthma it is probably not sufficient to rely on symptoms alone. Exercise testing and/or measurement of markers of airway inflammation may be useful. Therefore, the task force members monitor weight and height in children with asthma in order to record body mass index.

Environmental factors

Multiple environmental agents are known to worsen asthma symptoms; in this section only the most common indoor and outdoor environmental factors will be discussed, such as tobacco smoke, combustion-derived air pollutants, house dust mites, fungal spores, pollens and pet dander.

Tobacco smoke

There is good evidence that second-hand tobacco smoke exposure causes asthma, more severe asthma symptoms, bronchial hyperresponsiveness, airways inflammation and adverse effects on respiratory health in children and adolescents [64–67]. Studies in emergency departments have identified that children presenting with wheeze are more likely to be exposed to second-hand tobacco smoke compared with those presenting with other conditions and that second-hand tobacco smoke exposure is weakly associated with more severe acute asthma [66, 68]. Due to ethical considerations, no study has deliberately exposed children to second-hand tobacco smoke in a randomised controlled trial, but intervention studies have sought to reduce second-hand tobacco smoke exposure in children with asthma with mixed success. In a study where asthma education included awareness of second-hand tobacco smoke exposure, exposure was reduced in only 17% of households but children living in these households experienced a 50% decrease in the number of hospital admissions over the following year [69]. A second study in children with asthma, of whom 50% were exposed to second-hand tobacco smoke, aimed at reducing second-hand tobacco smoke exposure by educating the parents, in combination with a high efficiency particulate air filter in the child's bedroom and allergen reduction interventions [70]. Children who received the intervention had reduced symptoms and exacerbations during the 1-year trial plus the subsequent year but the intervention was not associated with a reduction in the number of households with smokers. A third study recruited young children with asthma whose parents smoked and studied an educational intervention, which included feedback on the child's urinary cotinine; the intervention was associated with reduced exacerbations but a nonsignificant reduction in urinary cotinine [71]. A better understanding of how to motivate parents of children with asthma to change their smoking habits is required and once this has been achieved the impact of such an intervention on asthma exacerbations and control should be evaluated [72, 73].

Self-reported exposure to second-hand tobacco smoke by parents and older children is generally unreliable [74]. There are several methods (measurements of cotinine, hair or nail nicotine, exhaled carbon monoxide and airborne nicotine) to objectively measure children's exposure to second-hand tobacco smoke but no gold standard. Currently there is no single recommended method for monitoring second-hand tobacco smoke exposure in children with asthma.

Air pollution

Outdoor air pollution is a mixture of multiple toxic chemicals and gases, with varying composition depending on the source and meteorological conditions. Children appear to be more vulnerable to health effects of air pollution than adults due to a higher minute ventilation, higher levels of physical activity outdoors and that fact that their lungs are still developing [75–78]. A recent review, which included 20 studies in children investigating evidence of air pollution causing exacerbations of respiratory symptoms, found a high consistency of positive association [79]. This conclusion was similar to an earlier extensive review conducted by the World Health Organization [80]. In a more recent study of 40 children living near roads, SPIRA-COHEN *et al.* [81] showed that the relative risk for shortness of breath, wheeze and total symptoms was associated with personal elemental carbon exposure. In Greece, mean daily concentrations

of particles with a 50% cut-off aerodynamic diameter of 10 µm were significantly related to asthma admissions over a 4-year period in 3600 children [82].

There is also a positive association between exposure to traffic-related air pollution and reduced growth in lung function [83]. The measurement of outdoor pollutants is mainly carried out for regulatory purposes and is currently not used in clinical settings to monitor children with asthma.

The most common source of indoor pollutants is incomplete combustion of biomass and solid fuels (e.g. dung, wood, agricultural residues, charcoal and coal) [84], kerosene, candles and incense [85, 86], and mosquito coils [87]. Exposure to mosquito coil smoke is common among working class populations in warm climates [88]. Chronic exposure is associated with bronchial irritation, increased sputum production and persistent wheeze in children [88–90]. A recent study from Taiwan, in which 3764 school children (mean age 12 years) were evaluated, demonstrated that the frequency of incense burning at home was associated with an increased risk of current asthma, medication use and exercise-induced wheeze [87]. Indoor dampness is another important factor that is associated with a higher risk of asthma [91, 92].

Environmental allergen load

Common aeroallergens include house dust mites, pollens, pet allergens and fungal spores. In a recent review it was concluded that chemical and physical measures aimed at reducing house dust mite exposure could not be recommended; however, the meta-analysis was considered flawed for various reasons [93, 94]. In a large study of 937 inner city children with asthma, individualised environmental intervention programmes reduced exposure to indoor allergens and resulted in decreased asthma morbidity [70].

Most task force members ask specific questions, tailored to the local environment, about exposures likely to increase the risk of asthma or to trigger asthma exacerbations and these questions should be included in the assessment of all asthmatic children (table 2). Regional pollen counts are freely available on TV or the internet, and these may guide patients and parents in strategies to manage a potential increase in symptoms. Environmental manipulation within the home should be multifaceted, and may incur the family a great deal of time and expense with the possibility that the benefits may be limited. Most task force members do not take single measures to reduce allergen load as they are likely to be of little benefit.

The evidence for routine home visits to children with asthma to assess the environmental allergen load is limited, but such visits may be part of the work-up of children with persistent severe asthma before any changes or increase in treatment regimens are considered [95].

Socioeconomic circumstances

Low education of parents is associated with under treatment of children with asthma and risk of exacerbations [7]. Socially disadvantaged children with asthma have elevated asthma morbidity including more emergency room visits. Less access to quality healthcare and medications, more environmental exposures (including allergens, pollution and environmental tobacco smoke), psychosocial stress, exposure to violence and belonging to a minority group may all account for this [96]. It may be speculated that improving social and educational factors may improve asthma management in these children.

Conclusion

Monitoring of asthma in children includes an evaluation of adherence on every check-up. Current practice by task force members is to teach inhalation technique at least twice when new drugs or devices are prescribed, and then at least annually or with deteriorating asthma control.

TABLE 2 Possible pollutants/exposures for discussion with parents and children in the clinic/ during a home visit

Second-hand tobacco smoke
Traffic density near home/school
Industries near home/school
Cooking: use of wood/gas
Type of heating: any use of biomass
Pets: dogs/cats
House dust
Mould
Chemicals used at home for cleaning
Use of incense sticks/candles

Apart from the generally accepted monitoring of height gain, there is no need to monitor children with asthma with respect to potential side-effects of ICS therapy. Particularly in children with poor asthma control, it is practice to screen for allergic or nonallergic rhinitis/rhinosinusitis and treat accordingly.

There is no evidence to use oesophageal pH testing in asthmatic children who have symptoms despite use of controller medication. Task force members do not screen for food allergy, except in children with a history suggesting food allergy and asthma.

All task force members educate parents about the possible environmental agents (e.g. second-hand tobacco smoke, other air pollutants) triggering asthma exacerbations. Single measures to reduce allergen loads are likely to be of little benefit.

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