

# International Consensus On (ICON) Pediatric Asthma

**Allergy 2012;67(8):976–997**

N. G. Papadopoulos, H. Arakawa, K.-H. Carlsen, A. Custovic, J. Gern, R. Lemanske, P. Le Souef, M. Mäkelä, G. Roberts, G. Wong, H. Zar, C. A. Akdis, L. B. Bacharier, E. Baraldi, H. P. van Bever, J. de Blic, A. Boner, W. Burks, T. B. Casale, J. A. Castro-Rodriguez, Y. Z. Chen, Y. M. El-Gamal, M. L. Everard, T. Frischer, M. Geller, J. Gereda, D. Y. Goh, T. W. Guilbert, G. Hedlin, P. W. Heymann, S. J. Hong, E. M. Hossny, J. L. Huang, D. J. Jackson, J. C. de Jongste, O. Kalayci, N. Ait-Khaled, S. Kling, P. Kuna, S. Lau, D. K. Ledford, S. I. Lee, A. H. Liu, R. F. Lockey, K. Lødrup-Carlsen, J. Lötvall, A. Morikawa, A. Nieto, H. Paramesh, R. Pawankar, P. Pohunek, J. Pongracic, D. Price, C. Robertson, N. Rosario, L. J. Rossenwasser, P. D. Sly, R. Stein, S. Stick, S. Szefler, L. M. Taussig, E. Valovirta, P. Vichyanond, D. Wallace, E. Weinberg, G. Wennergren, J. Wildhaber, R. S. Zeiger.

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## PREFACE

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Asthma is the most common pediatric chronic lower respiratory disease worldwide. In children, asthma often presents unique challenges, because of the maturing respiratory and immune systems, natural evolution of the disease, lack of good evidence, difficulty in establishing its diagnosis and delivery of medications, and a diverse and frequently unpredictable response to treatment.

Guidelines and consensus statements are available to support medical decisions on pediatric asthma; however, implementation of these recommendations is still a major challenge.

The **International Collaboration in Asthma, Allergy and Immunology** (iCAALL), formed in 2012 by **EAACI, AAAAI, ACAAI, and WAO**, addresses this unmet need in this **International Consensus on (ICON) Pediatric Asthma** document. The purpose of this document is to:

- highlight the key messages common to the many existing guidelines
- critically review and comment on differences, thus providing a concise reference

## ASTHMA DEFINITION

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Asthma is a chronic inflammatory disorder associated with variable airflow obstruction and bronchial hyperresponsiveness. It presents with recurrent episodes of wheeze, cough, shortness of breath, and chest tightness.

# CLASSIFICATIONS

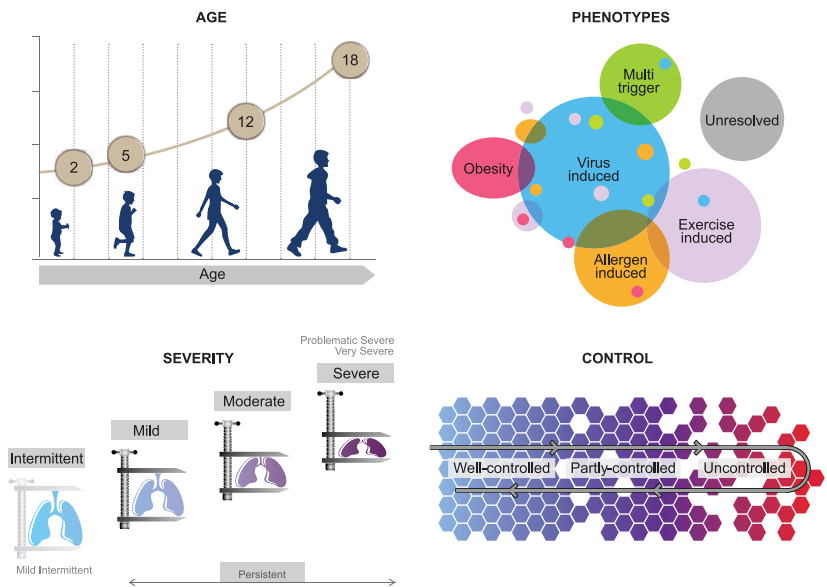
Classifying asthma is useful in its management.

**Age:** Differences during infancy, preschool age, school age and adolescence exist in the pathophysiology and clinical presentation and are reflected in the management of asthma.

**Phenotypes:** Different underlying pathophysiologies (endotypes) may be responsible for different phenotypes. However, there is considerable overlap and possible changes over time. Phenotypes should be considered in the management of children with asthma, because of differences in response to various treatment modalities.

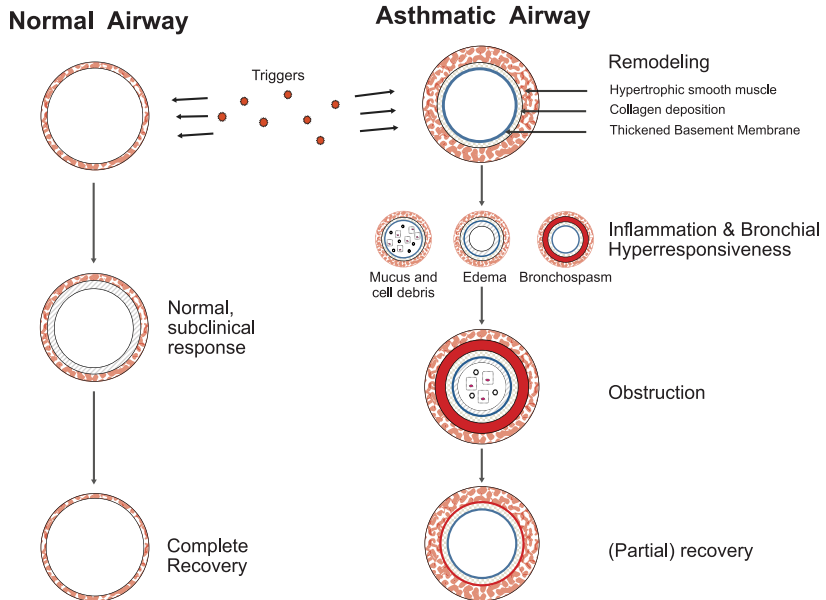
**Severity:** ranges from intermittent to severe; a stepwise approach can guide treatment at the initial evaluation. Acute exacerbations can be life-threatening.

**Control** of current symptoms and future risk is the clinical objective for optimal asthma management.



## PATHOPHYSIOLOGY

Asthma is a chronic inflammatory syndrome. In children, as in adults, pathological changes ('airway remodelling') are present in the airways. Airway narrowing can be triggered by allergens, viruses and irritants and is caused by edema, cellular infiltration, mucus hypersecretion, smooth muscle contraction, and epithelial desquamation. These changes are largely reversible; however, with disease progression, airway narrowing may be progressive and irreversible.



## NATURAL HISTORY

Many children who wheeze early in life 'outgrow' their disease. However, infants with recurrent wheezing have a higher risk to develop persistent asthma, and atopic children are more likely to continue wheezing and develop persistent asthma. Moreover, decrements in lung function occur by the age of six years, particularly in those children whose asthma symptoms started before three years of age. The severity/frequency of asthma symptoms during the first years of life and atopy are strongly related to later prognosis. The Asthma Predictive Index may help as a tool for prognosis.

## DIAGNOSIS

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*To diagnose asthma, confirm the presence of recurrent symptoms of reversible airflow obstruction, and exclude other conditions.*

### I. Medical history

**Symptoms:** cough, wheeze, difficulty in breathing, chest tightness.

**Pattern:** recurrent episodes ( $\geq 3$ ) or persistent symptoms, triggered by irritants (cold air, tobacco smoke), allergens (pets, pollens, etc.), respiratory infections, exercise and crying or laughter. These symptoms occur mostly during the night or early morning.

Also ask: personal history of atopy, e.g. eczema, allergic rhinitis, food allergy and family history of asthma.

### II. Physical examination

Helpful during symptomatic periods, to confirm wheezing. Signs of other atopic diseases are supportive.

### III. Evaluation of lung function

Important for both diagnosis and monitoring. Nevertheless, normal lung function tests do not exclude a diagnosis of asthma in children.

- **Spirometry:** recommended for children able to perform it properly (from 5-7 years of age and above). Current decision points are extrapolated from adults ( $FEV_1$ : 80% of predicted, reversible after bronchodilation by 12%, 200 ml, or 10% of predicted).
- **Peak Expiratory Flow (PEF) measurements:** the normal range for PEF is wide, making it more suitable for monitoring than diagnosis. Reversibility and variability can be more useful.
- Lung function tests requiring less cooperation, such as **oscillometry or specific airway resistance**, can be used in children  $< 5$  years; however, these may not be universally available.

### IV. Evaluation of atopy

Identification of specific allergic sensitizations can support the diagnosis of asthma, can help identify avoidable triggers and has prognostic value for disease persistence. Both *in vivo* (skin prick) and *in vitro* (specific IgE antibody) tests can be used.

### V. Evaluation of airway hyperresponsiveness (AHR)

AHR evaluation has a supportive role in asthma diagnosis

- Provocation tests with methacholine, histamine, mannitol, hypertonic saline, and cold air are used in adults to help confirm the diagnosis of asthma. In children, these methods are generally supported with reservation due to technical/standardization challenges, including difficulty in lung function measurements. In addition, AHR can be used for prognosis.
- Exercise can also be used to assess AHR, but standards for this purpose are difficult to establish in children of different ages.

## VI. Evaluation of airway inflammation

- Exhaled Nitric Oxide (FENO) is useful to detect eosinophilic airway inflammation, helping confirm the diagnosis of asthma, determining the likelihood of corticosteroid responsiveness, and monitoring and unmasking of non-adherence to treatment. However, this test may not be widely available and easy to interpret correctly.
- Sputum eosinophils are not currently recommended to diagnose or monitor childhood asthma.

## VII. Differential diagnosis

Asthma-like symptoms may occur in a variety of, mostly infrequent, conditions. Differential diagnosis should always be considered, particularly in atypical or non-responsive cases

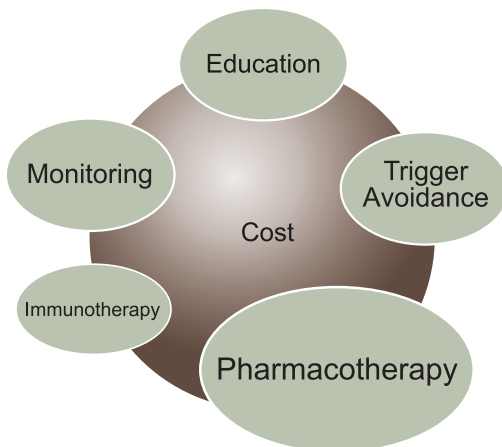
Infectious & Immunological Disorders	Mechanical Obstruction
Allergic bronchopulmonary aspergillosis	Congenital malformations
Anaphylaxis	Enlarged lymph nodes or tumor
Bronchiolitis	Foreign body aspiration
Immune deficiency	Laryngomalacia/tracheomalacia
Recurrent respiratory infections	Vascular rings or laryngeal webs
Rhinitis	Vocal cord dysfunction
Sinusitis	
Sarcoidosis	Other Systems
Tuberculosis	Congenital heart disease
	Gastroesophageal reflux disease
<b>Bronchial Pathologies</b>	Neuromuscular disorder (leading to aspiration)
Bronchiectasis	Psychogenic cough
Bronchopulmonary dysplasia	
Cystic fibrosis	
Primary ciliary dyskinesia	

### VIII. Special considerations

- ***Asthma diagnosis in infants:*** Diagnosing asthma in children younger than 2–3 years is difficult due to the lack of objective measurements, suboptimal responses to medications and a variable natural history, which make diagnosis in this age group, at best, provisional.
- ***Therapeutic trial:*** In cases of uncertainty in the diagnosis, particularly in preschool age children, a short therapeutic trial period (e.g. 1–3 months) with inhaled corticosteroids is suggested. Considerable improvement during the trial and deterioration when it is discontinued supports the diagnosis of asthma, although a negative response does not preclude this diagnosis.
- Although the diversity of childhood asthma is generally recognized, there is still little detail or agreement on diagnostic criteria for particular phenotypes, with the exception of exercise-induced asthma/bronchoconstriction.



## PRINCIPLES OF MANAGEMENT



Asthma management includes all elements necessary to achieve control: 1) patient and parent **education**, 2) identification and avoidance of **triggers**, 3) use of appropriate **medication** with a well-formulated plan (including allergen immunotherapy in selected cases), and 4) regular **monitoring**. Cost should also be taken into account.

## CONTROL

The goal of asthma treatment is to achieve control using the least number of medications. It is a long-term process.

Domain	Component	Level of Control			
		Complete	Good	Partial	None
Impairment	Symptoms – Daytime	None	≤twice/week	≤twice/week	Continuous
	Symptoms–Nighttime awakenings	None	≤once/month	≤once/month	Weekly
	Need for rescue medication	None	≤twice/week	≤twice/week	Daily
	Limitation of activities	None	None	Some	Extreme
	Lung function – FEV <sub>1</sub> , PEF (predicted or personal best)	>80%	≥80%	60%-80%	<60%
Risk	Exacerbations (per year)	0	1	2	>2
	Medication side effects	none	Variable		

## EDUCATION

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- Asthma education is a key element of asthma management and is a continuous, progressive process to be repeated at each consultation. It includes essential information about the chronic nature of the disease, the need for long-term therapy, the types of medications and how to use the devices.
- The use of a written, **personalised asthma management plan** is recommended, including the daily medication regimen and specific instructions for early identification and management of exacerbations or loss of control.
- **School-based programs** may have increased penetration and acceptance in large numbers of asthmatic children. Patients and their families may also be provided focused educational courses during hospitalisations. Computer, audio-visual and internet-based educational methods are also useful, especially for adolescents.

## TRIGGER AVOIDANCE

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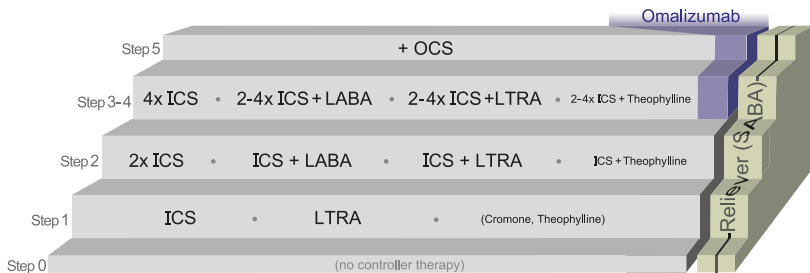
Identification and avoidance of non-specific (e.g. tobacco smoke) and specific (i.e. allergens) triggers, can be beneficial.

- Allergy testing is needed before any specific environmental intervention
- Single interventions have limited efficacy
- An intensive, multifaceted approach can be effective for indoor allergens, such as dust mites
- Irritants are major triggers particularly in developing countries:
  - ▷ Vigorous measures to avoid tobacco smoke exposure should be taken
  - ▷ Avoidance of other indoor and outdoor pollutants should be attempted

## PHARMACOTHERAPY

Pharmacotherapy is the cornerstone of treatment; it is long-term and should be distinguished from the treatment of acute asthma attacks.

- Treatment decisions are based on the level of **disease control**
- **Severity** can also be used during the initial assessment
- **A stepwise approach** is proposed:
  - ▷ Stepping up should be considered if control is not achieved after 1–3 months, after reviewing device use, compliance, trigger avoidance, treatment for comorbid rhinitis, and, possibly, the diagnosis
  - ▷ Stepping down can be considered (based on expert opinion) when control has been achieved for at least three months
- **Age** is an important consideration. In infants, the evidence base for treatment is small, and responses are inconsistent and frequently suboptimal. In adolescents, issues that may affect asthma management are frequently related to lack of compliance.



An easy way to memorize this stepwise approach is that the number of each step suggests the number of medications, or inhaled corticosteroid (ICS) level, to be used.

### **Step 0: No controller medication is needed**

### **Step 1: Use one controller medication**

- An ICS at low dose, as a preferred option, or a leukotriene receptor antagonist (LTRA) can be used. Cromones and theophylline are included in older texts, but have lost support from experts and literature

### **Step 2: Use two medications, or double (medium) dose of ICS**

### **Step 3-4: Maximize conventional treatment (high ICS dose, alone or in combination with additional medications)**

- This step may include two distinct steps: in the first, long-acting beta agonists (LABA) or LTRA are added to the medium-dose ICS, and in the second, the ICS is increased. Omalizumab can also be considered

### **Step 5: Oral glucocorticosteroids are added as the final resort**

Medications in each step are not identical, either in efficacy or safety, and preferred choices can be described, especially for different age groups and/or phenotypes. However, there is considerable variation in individual responses to each medication, suggesting the need for flexibility in choice and the option of trying a different strategy if the first is not successful.

## **DELIVERY DEVICES**

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### **0 to ~5 years:**

Pressurized meter-dose inhaler (pMDI) with static-treated spacer and mask (or mouthpiece as soon as the child can use it)

### **>~5 years:**

Choice of pMDI as above, dry powder inhaler (DPI) (rinse or gargle after inhaling ICS), breath-actuated pMDI (depending on ability to use and preference)

**Nebulizer:** can be used as a second choice at any age

## ALLERGEN-SPECIFIC IMMUNOTHERAPY (AIT) \_\_\_\_\_

AIT should be considered for children whose symptoms are clearly linked to a relevant allergen.

- **Subcutaneous immunotherapy (SCIT)** is effective in allergic asthma, when standardised allergen extracts of house dust mites, animal dander, grass, weed, or tree pollen are administered. In clinical practice, SCIT is typically administered for 3–5 years.
  - ▷ SCIT should be administered only by clinicians experienced in its use and appropriately trained to identify and treat potential anaphylactic reactions.
  - ▷ SCIT is not recommended in severe asthma, because of the possible risk of severe reactions.
- **Sublingual immunotherapy (SLIT)** is painless, child-friendly and has an excellent safety profile. Most guidelines recommend additional evidence of efficacy before recommending it; however efficacy has been confirmed in recent meta-analyses.

## MONITORING \_\_\_\_\_

- Once the diagnosis is confirmed and treatment initiated, ongoing monitoring is essential.
- A 3-month interval is suggested, depending on severity and disease activity; shorter time periods after an exacerbation and when stepping down or pausing controller therapy are indicated.
- Parameters to be monitored include: control, lung function (spirometry, PEF), treatment adherence, inhaler technique.
  - ▷ Additional outcomes may include quality of life and adverse events, particularly growth rate.
  - ▷ Monitoring inflammation with FENO can also be useful
- Control is defined by the most severe level of impairment or risk. Validated questionnaires to assess asthma control in children (such as the ACT, TRACK and more) are available.

## ASTHMA EXACERBATIONS (ATTACKS, EPISODES) \_\_\_\_\_

An exacerbation of asthma is an acute or subacute episode of progressive increase in asthma symptoms, associated with airflow obstruction

The management of asthma exacerbations has remained unchanged for the last several years. It consists of bronchodilation, humidified oxygen supplementation and systemic corticosteroids

- **Bronchodilation:** inhaled salbutamol, 2-10 puffs, or nebulized 2.5-5mg, every 20' for the first hour, according to response thereafter. Ipratropium, 2-8 puffs, or nebulized 0.25-0.5mg, can be added. Upon no improvement, the child should be referred to a hospital
- **Oxygen supplementation:** aim at SaO<sub>2</sub> > 95%
- **Systemic corticosteroids:** oral prednisolone 1-2mg/kg/24h (up to 20mg in children <2 years and up to 60mg in older children), usually for 3-5 days
  - ▷ Very high-dose ICS may also be effective either during the exacerbation or to prevent it developing after a common cold; however, they are not generally recommended to substitute systemic corticosteroids. There is also some evidence for a modest preemptive effect of montelukast, however, this is not currently recommended.
- **At the hospital or ICU,** if necessary, consider: IV beta-2 agonists, IV aminophylline, IV magnesium sulfate, helium-oxygen mixture