Consensus on asthma treatment in Paediatrics

R.M. Busquets Monge[a], A. Escribano Montaner[a], M. Fernández Benítez[b], L. García-Marcos (coord.)[a,b], J. Garde Garde[b], M. Ibero Iborra[b], L. Pardos Rocamora[a], J. Sánchez Jiménez[a], E. Sánchez Sánchez[a], J Sanz Ortega[b] and J.R. Villa Asensi[a*]

[a]Spanish Society of Paediatric Pneumology (SENP). [b]Spanish Society of Immunology and Paediatric Allergy (SEICAP). Spain.

FOREWORD

When the Spanish Society of Clinical Immunology and Paediatric Allergy and the Spanish Society of Paediatric Pneumology agreed to organise a joint meeting in May 2004, they set up a commission to draw up a document that would review the basic features of children's asthma treatment and would unify criteria that had been apparently diverse up to then.

The first meeting of this Commission was held in June 2003 and laid down the guiding principles for this document. Special attention would be paid to those periods of life in which asthma is more complicated for both diagnosis and treatment. The prediction of the asthma phenotype, as a variable to be borne in mind in certain therapy decisions, was included for the first time in a guide of this kind.

The document was not conceived as an exhaustive guide. Consequently, such basic questions as education and self-care were not dealt with because there is general consensus on them.

The most important aspect of the document is the bringing together of two hitherto disparate visions of children's asthma. Both societies assume full responsibility for the document, in which every sentence has been checked carefully. The basic aim is to offer clear, uniform criteria for asthma treatment in Paediatrics.

Both Societies hope that this is not the end of our joint work, but that it will continue on a regular basis with other initiatives, including the updating of this document in the future.

INTRODUCTION

Epidemiology

The epidemiology of asthma in Spain is well-known in children over 6, but no studies on younger children exist. Unlike the Anglo-Saxon countries, asthma prevalence in Spain is relatively low: about 9% of 13-14 year olds report symptoms during the preceding twelve months; and 10% of parents of 6-7 year-old children report that their children suffered wheezing in the same period. This prevalence was the same in older children in 2002 as in 1994, whereas it increased markedly in 6-7 year olds (from 7% to 10%). Grave wheezing is much less common in both age groups (around 2%). This also increased in the 6-7 year-old group, whereas it remained steady among 13-14 year olds[1]. At these ages there appears to be greater prevalence and gravity of asthma in the coastal areas than on the central plain[2,3].

Definition

For the purpose of this document, which refers to children, with particular emphasis on the first years of life, and as the physiopathology of asthma is largely unknown, the consensus paediatric definition[4,5] is the best one to use: "Recurrent wheezing and/or persistent coughing in a situation in which asthma is likely and other less frequent illnesses have been ruled out". From the age of 3, asthma becomes steadily more definitive; and from the age of 6-7, the stricter physio-pathological definitions of general consensus criteria can be used (GINA[6], NHLBI[7], GEMA[8], etc.).

ASTHMA PHENOTYPES

Although the physiopathology of asthma is little understood, there are various clinical phenotypes of it that have been characterised in various cohorts in several countries[9-19] and can be consulted in a number of publications. Though cautiously, we think that these phenotypes can be applied to Spain. This document aims to establish the best line of treatment for each pheno-

*Working party for Consensus on Treatment of Asthma in Children Spanish Society of Paediatric Pneumology and Spanish Society of Immunology and Paediatric Allergy.

Correspondence: FALTA????????

E-mail: lgmarcos@um.es

type, based on the scientific evidence available. Therefore, accurate definitions of these phenotypes are fundamental:

Transient asthma

1. This starts before 3 and tends to disappear between the ages of 6 and 8. It accounts for between 40% and 50% of all cases of asthma.

2. It is not atopic: total IgE normal and/or negative skin tests and/or Phadiatop, along with absence of stigmata – atopic dermatitis (eczema), for example – and of family background of allergy.

3. Lung function reduced from birth, but normal by 11 years old.

Early-onset persistent asthma

1. This starts before 3 and lasts beyond the age of 6-8. It accounts for 28% to 30% of all asthma cases.

2. Normal lung function at 12 months and reduced at 6 years.

Two sub-phenotypes of this can be distinguished:

Atopic

1. Total IgE high and/or skin tests positive, generally with stigmata and family background of allergy.

2. Positive bronchial hyper-responsiveness.

3. Usually still persists at the age of 13.

4. The first crisis usually appears after 12 months.

5. Predominantly in boys.

Not atopic

1. Total IgE normal and skin tests negative, without stigmata or family background of allergy.

2. Increase in bronchial hyper-responsiveness, which diminishes over the years.

3. Usually disappears at the age of 13.

4. The first crisis is usually before 12 months and related to Bronchiolitis due to respiratory syncytial virus.

5. Affects both sexes equally.

Late-onset asthma

1. Starts between 3 and 6 years old. It accounts for 20%-30% of all cases of asthma.

2. Normal lung function at 6 years of age, which deteriorates subsequently.

3. Often atopic (history in mother, Rhinitis in early years and positive cutaneous tests by the age of 6).

4. Mainly in boys.

5. It is atopic persistent asthma, but with a late onset.

Prediction of asthma phenotype

For practical reasons, it is important to try and establish the phenotype of a particular child in his/her first crises. A child with early wheezing and a major or two minor risk factors from the lists below will be highly likely to suffer persistent atopic asthma. However, it must not be forgotten that these criteria provide low sensitivity (39.3%, i.e. they include a lot of false negatives), but quite high specificity (82.1%, i.e. they exclude almost all the false positives)[20].

Major risk factors

1. A parent with medical diagnosis of asthma.

2. Medical diagnosis of atopic dermatitis.

Minor risk factors

1. Medical diagnosis of Rhinitis.

2. Wheezing unrelated to colds.

3. Eosinophilia $\geq$ 4%.

The development of specific IgE antibodies to egg during the first year of life is a predictive indicator of risk of atopic illness. It is the main and earliest serological marker of subsequent sensitisation to inhaled allergens and the development of respiratory allergic pathology[21,22]. In addition, when allergy to egg is linked to atopic dermatitis, there is 80% probability of respiratory allergic pathology presenting at 4 years of age[23].

Diagnosis of asthma in children

Clinical assessment

The taking of the clinical history must aim to clarify the most important asthma-related points, especially those relating to the differential diagnosis. The symptoms, signs and characteristics of crises must be recorded; the inter-crisis periods have to be assessed; and any precipitating and aggravating factors need to be identified (see the diagnosis algorithm in figure 1).

Function assessment

The examination of respiratory function serves to confirm the diagnosis of asthma, measure the seriousness of the illness, control its evolution and clarify the response to treatment. In collaborative children, Forced Spirometry can be used, as its simplicity and cost make it the main test for measuring bronchial obstruction. Other tests can be used for non-collaborative children, such as body plethismography, impulse oscillometry, resistance after occlusion or thorax-abdomen compression.

The reversibility of this bronchial obstruction and/or the degree of hyper-responsiveness of the bronchii need to be studied. For this, bronchodynamic tests, such as the bronchodilation test and tests of non-specific bronchial hyper-responsiveness (metacholine, exercise etc.), are used.

Bronchodilator test

This consists of a basal forced spirometry, repeated 15 minutes after administering a β_2-adrenergic agonist inhaled for a short time (400 μg salbutamol = 4 pulses, or equivalent of terbutalin). This should be a normal examination in every child with suspected asthma, including when the FEV_1 is normal. The use of portable machines to measure peak espiratory flow (PEF) for functional diagnosis of asthma is not recommended.

There are various methods or indexes to express bronchodilatory response and the most common of them is the percentage change from the initial value in FEV1, i.e. $\Delta\% = [(FEV_1 \text{ post} - FEV_1 \text{ pre})/FEV_1 \text{ pre}] \times 100$. Increase in FEV_1 of 12 % over the base figure or 9 % over the theoretical figure[8] (Proof C) is considered positive. Normal lung function with negative bronchodilatory test does not rule out a diagnosis of asthma.

Bronchial Hyper-responsiveness

Bronchial provocation tests demonstrate the presence or absence of non-specific and/or specific (due to allergens) bronchial hyper-responsiveness. Normally, these are not needed for the diagnosis and monitoring of asthmatic children, but may be very useful for a differential diagnosis.

Allergolological assessment

The aim of this evaluation is to determine whether there is/are a relevant allergen or allergens involved in the pathology of the child with asthma. Then, proper measures of prevention can be adopted.

The fundamental techniques in this evaluation are the cutaneous tests: the prick (simple, rapid and safe) or intradermoreaction test. However, on occasions, we may find false positives or negatives, and the cutaneous test has to be complemented by other diagnostic tests such as the determination of antigen-specific IgE in serum (RAST or CAP system). On occasions, the specific bronchial provocation test may be necessary, to detect the trigger allergen involved.

The positive result of cutaneous tests or the determination of specific IgE only indicates allergic sensitisation.

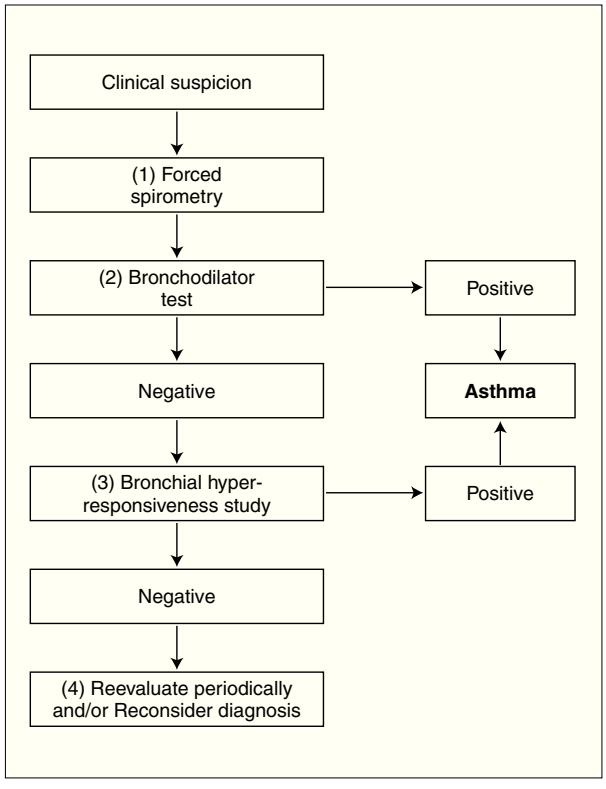

Figure 1. *Algorithm for diagnosing asthma (modification of ref.[51]).*

Treatment of acute episodes in Paediatrics

General considerations

1. Therapeutic management of acute asthma crises will depend on their gravity.

2. As there are few protocols on the acute episode in the nursing child, use of medication is based on clinical experience and extrapolation from data obtained from older children.

3. It is recommended that Health Centres have a Pulsoxymeter available to improve evaluation of asthma crises.

4. On treating an acute episode, the following must be borne in mind:

a) The evolution time of the acute period.
b) The medication administered previously.
c) The maintenance treatment that the patient may be receiving.
d) The existence of associated illnesses.

5. Mild and moderate crises can be treated in Primary Care.

6. The child must be referred to Hospital Emergencies when there is:

a) A grave crisis.
b) Suspected complications.
c) A history of high-risk crises.
d) Impossibility of proper follow-up.
e) Lack of response to treatment.

7. Drug dosage and administration times have to be modified in relation to the gravity of the crisis and the response to treatment.

TABLE 1. **Seriousness of the acute episode of asthma***

	Mild	Moderate	Grave	Imminent respiratory failure
Dyspnoea	Walking Can lie down	On talking In feeding child, the cries more soft and brief; difficulty in feeding Prefers to sit	At rest Breast-feeding child stops eating Arched forward	
Talk	Long sentences	Short sentences	Words	
Awareness	Possible agitation	Agitation	Agitation	Confusion
Breathing frequency	Increased	Increased	Much increased	
		Respiratory frequencies in awake children < 2 months < 60/min 2-12 months < 50/min 1-5 years < 40/min 6-8 years < 30/min		
Accessory muscles and suprasternal retractions	Not usually	Usually	Usually	Paradoxical thoracic-abdominal movement
Wheezing	Moderate, at the end of expiration	Audible	Generally audible	Absence of wheezing
Pulse beats/min	Normal	Increased	Much increased	Bradycardia
		Normal pulse rates in children Breast-feeding 2-12 months < 160/min Pre-school 1-2 years < 120/min School-children 2-8 years < 110/min		
PEF (Peak Expiratory Flow) after bronchodilator % envisaged or % of the best	> 80 %	60-80 %	< 60 %	
PaO_2 (environmental air) and/or $PaCO_2$	Normal Test not needed < 45 mmHg	> 60 mmHg < 45 mmHg	< 60 mmHg Possible cyanosis > 45 mmHg	
SaO_2% (environmental air)	> 95 %	91-95 %	< 90 %	

*The presence of several parameters, though not necessarily all, indicates the general classification of exacerbation.

Assessment of gravity

Table 1 establishes a system for evaluating the seriousness of the acute asthma episode, modified from the GINA guidelines[6].

Medication

Short-term β_2 adrenergic agonists: These are the first line of treatment. Their benefits in treating crises have been sufficiently contrasted[24-33] (Proof B). Inhalation is the pathway of choice, as it gives greater effectiveness with fewer side-effects.

The pressurised inhaler system with spacer chamber is as effective, if not more so, than nebulisers in the Emergency Department and is the treatment of choice for mild or moderate episodes of asthma[31,34,35] (Proof B).

Ipratropium Bromide: Some studies thought this useful, when linked to short-acting β_2 agonists in moderate or grave crises[36-38], although evidence on its use in nursing infants is limited and contradictory[39-41]. The nebulised dose is 250 μg/4-6 hours in children under 30 kg and 500 μg/4-6 hours in those over 30 kg. It should not replace β_2 adrenergic agonists.

Glucocorticoids: They have shown their use when used early[42,43] (Proof B) and the oral, rather than parenteral, is the pathway of choice[44,45]. There is not sufficient evidence to justify use of inhaled corticoids in acute crises[46-48] (Proof B). Recommended dose is 1-2 mg/kg/day of Prednisone (maximum 60 mg) or equivalent. When the doctor decides to withdraw medication before the tenth day, there is no need for steady reduction of the dose.

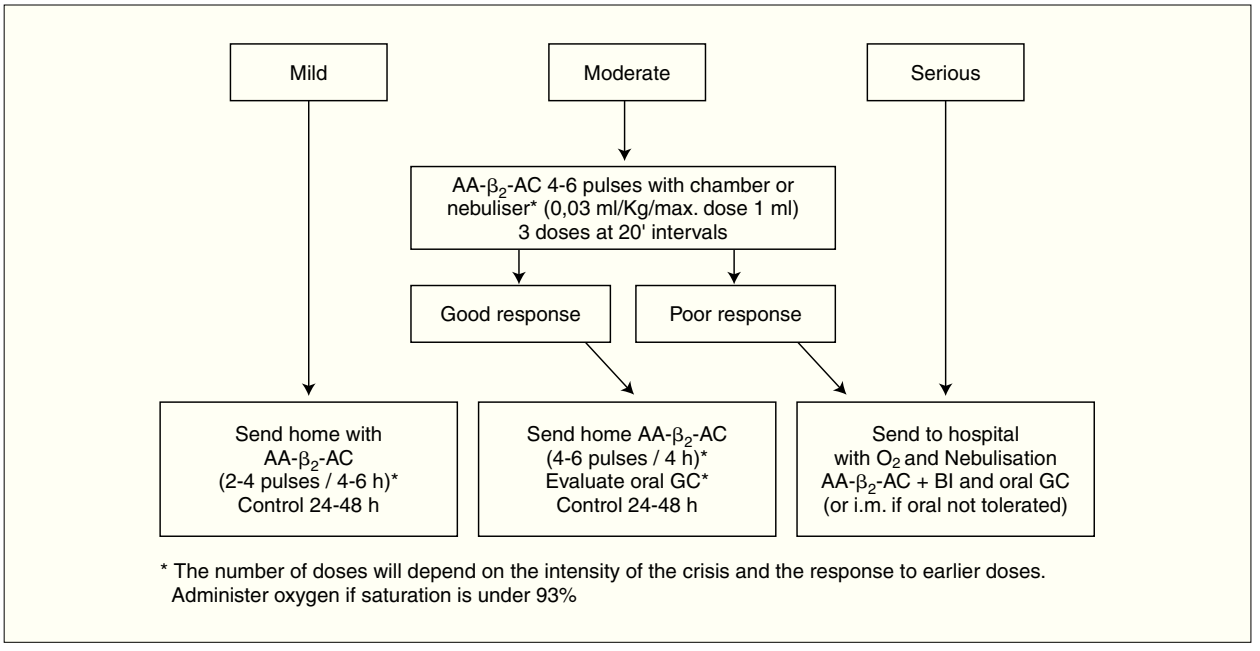

Figure 2. *Treatment of acute episodes of asthma in Primary Care. AA-β_2-AC: short-term β_2 adrenergic agonist; IB: Ipratropium bromide; GC: Glucocorticoid; oral: Oral pathway; i.m.: intra-muscular pathway.*

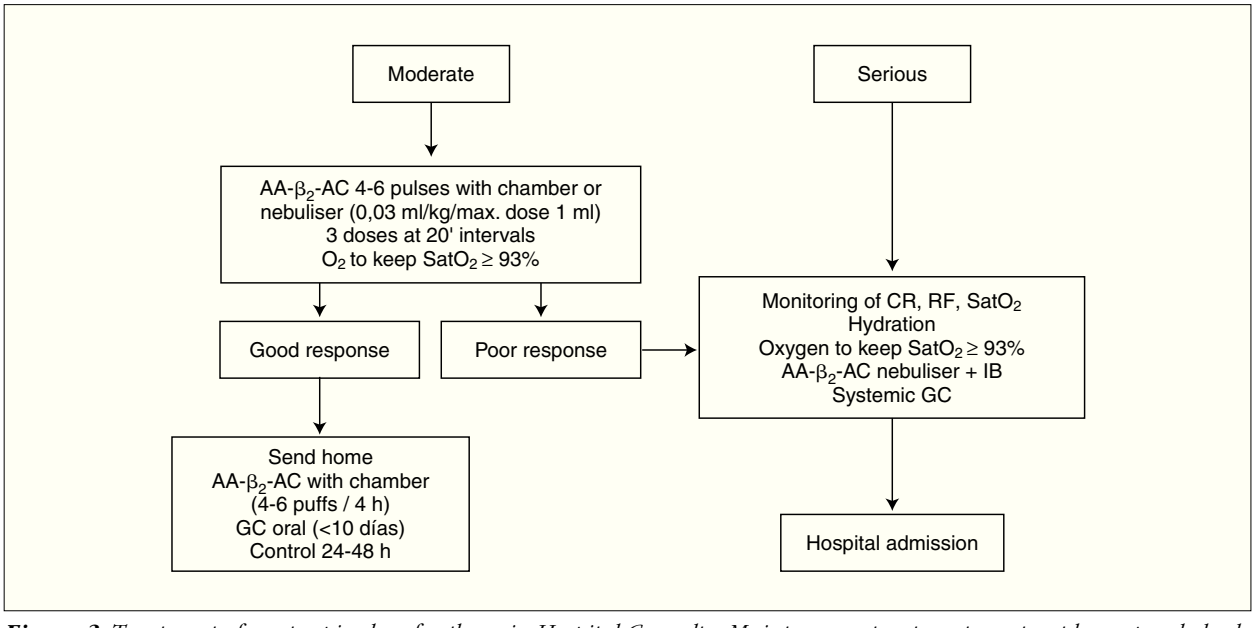

Figure 3. *Treatment of acute episodes of asthma in Hospital Casualty. Maintenance treatment must not be suspended, although the dose can be adjusted. AA-β_2-AC: short-term β_2 adrenergic agonist, IB: Ipratropium bromide, CR: Cardiac Rate, RF: Respiratory Frequency, GC: Glucocorticoid, $SatO_2$: Oxygen saturation, oral: Oral pathway.*

Antibiotics: Since most of these episodes are due to viral infections, administration of antibiotics must be exceptional.

Treatment in Primary Care

The algorithm of the treatment of the acute episode of asthma in Primary Care is shown in figure 2.

Treatment in Casualty

Figure 3 indicates the algorithm of treatment of acute episodes of asthma in Hospital Casualty.

Maintenance treatment in Paediatrics

Maintenance treatment has three sections:

TABLE 2. **Objectives of asthma treatment in infancy (GINA)[6]**

Make chronic symptoms minimal or non-existent
Prevent exacerbation
Maintain lung function as close as possible to normal levels
Maintain normal levels of activity, including exercise
Avoid the adverse side-effects of anti-asthma medication
Anticipate evolution towards irreversible restriction of air flow
Prevent asthma mortality

TABLE 3. **Anti-asthma medication in Paediatrics**

Bronchodilators	Anti-inflammatories
Short-acting β_2 agonists:	Inhaled Corticoids
Salbutamol	Budesonide
Terbutaline	Fluticasone
Long-acting β_2 agonists	Oral Corticoids
Salmeterol	Prednisone
Formoterol	Prednisolone
Cholinergic drugs:	Methylprednisolone
Ipratropium Bromide	Leukotrienes
	Montelukast
	Chromones
	Disodium Chromoglycate
	Nedocromil Sodium

TABLE 4. **Equipotent doses of inhaled corticoids ((μg/day)* (Proof D)**

	Low doses	Medium doses	High doses
Budesonide	≤ 200	200-400	> 400
Fluticasone	≤ 100	100-250	> 250

*In children weighing less than 40 kg.

1. Education of patients and families, along with control of the environment.

2. Pharmacological treatment.

3. Immunotherapy.

This document does not pretend to be exhaustive. Therefore, for general themes of avoiding triggers, of education or of the pharmacology of asthma medication, short guides are recommended, such as the protocols promoted by the Spanish Paediatrics Society (AEP)[49,50], or longer guides such as the SEICAP Asthmatic Child-care Guide[51], Asthma in Paediatrics[52], The Spanish Guidelines for Managing Asthma (GEMA)[8] or the "Global Strategy for Asthma Management and Prevention" of the Global Initiative for Asthma (GINA)[6].

Drug treatment

This section is divided into two, depending on the age of the child to be treated: children under 3 years old and children over 3. Most guides focus on adults, with a section devoted to children. None of them specifies a treatment for nursing infants in line with the asthma phenotype classification.

Classifying a child's asthma has the sole purpose of helping decide the treatment to choose at first. Subsequently, it will have to be the disease's clinical evolution and the achievement of control objectives that dictate modifications in treatment.

Regardless of the classification of the seriousness or clinical situation of asthma, the final objective is to control it properly (table 2).

Anti-asthma drugs divide into two basic groups: bronchodilators (usually used to alleviate symptoms) and anti-inflammatories (to control the disease) (table 3).

The essential asthma-control drugs are inhaled corticoids. The equipotent doses of these drugs are shown in table 4.

The addition of prolonged-action β_2 agonists to inhaled corticoids enables lower doses of the latter to be used. These combined therapies have been extensively tested in adults and in school-age children[53,54].

Inhaled medication must be administered by means of the systems most suited to the age of the patient (see section on inhalation systems).

Children under 3

General considerations

1. Many nursing infants with wheezing during their first months of life will cease to have symptoms (transient wheezing), regardless of the maintenance treatment employed[55].

2. Most of these episodes are side-effects of viral infections[14].

3. The underlying inflammation in these cases is probably different from that in the atopic asthma of schoolchildren or adolescents[56].

4. As there are few studies on which to base with any certainty treatment criteria for this age-group, physicians will often have to start a treatment and then vary or interrupt it if it is not effective[33,57].

5. Therefore, the recommendations that can be made are largely empirical and in line with the following precepts:

a) The nursing child possesses functioning β_2 receptors[29,58].

b) Both systemic and topical anti-inflammatory drugs have the same anti-inflammatory properties at all ages.

c) Side-effects of anti-asthma drugs in nursing children coincide with those that occur at later ages.

6. It must be borne in mind that in nursing children a differential diagnosis with other illnesses is needed, such

as gastro-oesophageal reflux, cystic fibrosis, broncho-pulmonary malformations, immunodeficiency, etc.

Medication

Inhaled Glucocorticoids: In this age group, children with a clinical diagnosis of asthma and risk factors of developing persistent asthma may respond adequately to this treatment[59-65] (Proof B). However, for nursing children with post-Bronchiolitis wheezing or wheezing episodes related solely with viral infections, inhaled corticoids are of dubious benefit[66-68] (Proof B).

Antagonists of Leukotriene receptors: Only two studies on these for children at this age exist. In one of them, treated children had few repeat episodes in the month after the episode of Bronchiolitis[69]; in the other, the drugs reduced bronchial inflammation in atopic children[70]. Therefore, there is not at present a sufficiently sound basis for their use.

Long-term β_2 adrenergic agonists: In this age group, these are not currently recommended in a routine way.

Association of long-term β_2 adrenergic agonists and inhaled Glucocorticoids: There has only been one study (without a control group) of these drugs in children of this age-group[71]. Although its results were positive, more studies on the synergic effect of glucocorticoids and long-term β_2 adrenergic agonists on children under 3 are needed before these two drugs together can be recommended.

Other anti-asthma drugs such as Chromones or Theophylline have proved their use in nursing children[72-78].

Classification

Table 5 indicates the system for classifying asthma in children of this age group.

TABLE 5. **Classification* of asthma in children[49]**

Occasional and episodic	– Episodes of few hours or days of duration < once every 10-12 weeks – Maximum 4-5 crises a year – Asymptomatic in the inter-crisis period with good tolerance to exercise *Respiratory function test:* – Normal in the inter-crisis periods
Frequent and episodic	– Episodes < once every 5-6 weeks (maximum 6-8 crises/year) – Wheezing on intense effort – Asymptomatic inter-crisis *Respiratory function test:* – Normal in the inter-crisis periods
Persistent moderate	– Episodes > once every 4-5 weeks – Mild symptoms in inter-crisis periods – Wheezing on moderate effort – Night symptoms ≤ twice a week – Need for β2 agonists ≤ 3 times a week *Respiratory function test:* – PEF or FEV1 ≥ 70% of predicted value – 20-30% variability of PEF
Persistent grave	– Frequent episodes – Symptoms in inter-crisis periods – β2 agonists required > 3 times a week – Night symptoms ≤ twice a week – Wheezing on minimum effort *Function test in inter-crisis period:* – PEF or FEV_1 < 70% of predicted value – PEF variability > 30%

*To classify children under 6, lung function does not have to be assessed. In nursing children, inter-crisis periods will be assessed by means of their repercussion on normal daily activity (crying, laughter, play and feeding).

Treatment

Table 6 shows the maintenance treatment for children under 3.

Children over 3

General considerations

1. Up to the age of 6, children belonging to the transient asthma group and children with early-onset persistent asthma overlap. Other children will begin to suffer asthma for the first time, making up the persistent late-onset group[16].

2. The role of atopy from this age has to be clarified by means of a proper allergological assessment, since it is the main risk factor for persistent asthma[14].

3. From six years of age, as there are probably few children affected by transient wheezing, most children who suffer persistent wheezing are going to have early-onset or late-onset asthma[14,16,17,19].

Medication

Inhaled Glucocorticoids: their efficacy at these ages has been well contrasted[47,57,79-89] (Proof A).

Long-term β_2 adrenergic agonists: In this age group, various clinical trials with both Salmeterol and Formoterol exist. These found good results, with side-effects that coincide with those of short-acting agonists[90,91].

Antagonists of leukotriene receptors: There are sufficient data on their effectiveness at these ages, although their anti-inflammatory capacity is less than that of inhaled corticoids. The dimensions of their effect on corticoid consumption are still to be determined[92-96] (Proof A).

Chromones: A systematic review of 24 clinical trials concludes that, in long-term treatment, the effect of Sodium Chromoglycate is no greater than that of placebo. Thus, it is of doubtful utility[97] (Proof A).

TABLE 6. **Asthma maintenance treatment in children under 3**

	Basic control of the disease	Symptom relief
Occasional and episodic	Not needed	AA-β_2-AC on demand
Frequent and episodic Without risk factors With risk factors	 Normally not needed Low doses IGC	
Persistent moderate *(Before taking this step, the diagnosis and proper administration of treatment need to be re-checked)*	Medium doses IGC *(Assess response at 3 months. Withdraw if there is no response and there are no risk factors)*	
Persistent grave	High doses IGC If the control is not adequate, consider one or several of: – Add AA-β_2-AL – Add ALTR – Add oral GC	

AA-β_2-AC: short-term β_2 adrenergic agonist; AA-β_2-AL: long-term β_2 adrenergic agonist; ALTR: antagonist of leukotriene receptors; GC: glucocorticoids; IGC: inhaled glucocorticoids; oral: oral pathway.

Association of long-term β_2 adrenergic agonists and inhaled Glucocorticoids: There are studies on the role of long-term β_2 adrenergic agonists in controlling asthma in combined therapy with inhaled Glucocorticoids in this age-group[53,54,98] (Proof A). The administration of this combination in the same device could be more effective than when administered separately[99].

Specific Immunotherapy (if the indications specified in the section devoted to it are complied with) can help control the disease.

Classification

Asthma in children over 3 is classified in the same way as for children under 3, as shown in table 5.

Treatment

Table 7 shows the maintenance treatment of children over 3.

Specific Immunotherapy

A recent meta-analysis made its beneficial effects clear, in terms of reduction of symptoms, of recovery and maintenance medication, and of bronchial hyper-responsiveness, whether specific or non-specific, but only when biologically standardised extracts were used[100-103] (Proof A).

Specific immunotherapy is indicated when the following criteria are met104 (Proof D):

TABLE 7. **Maintenance treatment of children over 3**

	Basic control of the disease			Alivio síntomas
	Drug treatment		Immunotherapy	
	Choice	Alternative		
Occasional and episodic	Not needed			AA-β_2-AC on demand
Frequent and episodic	IGC low dose	ARLT Chromones	IT*	
Persistent moderate	IGC medium doses + AA-β_2-AL	IGC medium doses + ALTR	IT*	
Persistent grave	IGC high dose + AA-β_2-AL If there is no proper control, consider one or several of: – Increase IGC doses – Add AA-β_2-AL – Add oral GC			

*Assess according to Section 4.2

AA-β_2-AC: short-term β_2 adrenergic agonist; AA-β_2-AL: long-term β_2 adrenergic agonist; ALTR: antagonist of leukotriene receptors; GC: glucocorticoids; IGC: inhaled glucocorticoids; oral: oral pathway.

1. Frequent or persistent moderate episodic asthma, mediated by IgE, when there is sensitisation to a single allergen, a predominant allergen or a group of allergens with crossed reactivity.

2. When the symptoms are not properly controlled by means of avoidance of the allergen and the drug treatment.

3. When the patient has both nasal and lung symptoms.

4. When the patient (or his/her parents or legal guardians) do not want a long-term drug treatment.

5. When the drug treatment causes adverse side-effects.

Specific immunotherapy is counter-indicated[104] (Proof D):

1. In children with grave immunopathies or chronic liver disease.

2. In psychological and social situations that do not permit proper monitoring.

3. As starter therapy in pregnant adolescents, although the corresponding maintenance doses can be administered to girls who begin their treatment before the pregnancy.

Age is not a parameter limiting the use of immunotherapy, if the previous indication criteria are met (Proof D).

Although there are no objective data, the minimum length of treatment should be three years and the maximum five[104] (Proof D).

Subcutaneous can be replaced by sublingual immunotherapy[105,106] (Proof C). The latter does not have the systemic adverse side-effects that on very rare occasions subcutaneous immunotherapy has had[107].

In both subcutaneous and sublingual immunotherapy, only biologically standardised allergen extracts can be used[104] (Proof B).

Subcutaneous immunotherapy must be administered by trained staff. The patient will remain under observation for 30 minutes after the injection.

Systems of inhalation

General considerations

1. The amount of a drug that is administered to a child with asthma depends on the kind of medication, the system of inhalation, the characteristics of the patient and the interaction between these factors.

2. Of the several pathways for drug administration, inhalation is the pathway of choice[108,109] (although not all anti-asthma drugs are available in this form, such as the leukotrienes and methyl-chantines).

3. Prescribing any system of inhalation must occur only after the child and his/her parents have been trained in its use and have demonstrated satisfactory technique (Proof B).

4. Re-evaluation of the technique must be a part of the clinical monitoring sessions.

5. In children from 0 to 5, there is little or no evidence on which to base the recommendations indicated.

6. In general, and a priori, age is what will orient us towards using one kind of system or another, and the line of division lies between the ages of 4 and 6[110] (table 8).

Pressurised inhalers

Common problems with the administration technique mean that over 50 % of the children who receive treatment with a direct-application (without chamber) pressurised inhaler benefit much less than when they use other systems[111]. Therefore, pressurised inhalers directly applied to the mouth must NOT be used in infancy; they must always be used with spacers.

Spacer chambers

The use of a spacer chamber with a pressurised inhaler solves the problem of coordination, reduces oropharyngeal impact and improves the distribution and amount of medication that reaches the bronchial tree[112] (Proof A). Its use with inhaled corticoids reduces the systemic bioavailability of these and the risk of systemic effects[113] (Proof B).

Up to 4 years of age small-volume chambers are recommended: these are the ones with a face mask attached. As nasal respiration in these cases greatly reduces lung

TABLE 8 **Systems of inhalation for children[8]**

	Choice	Alternative
< 4 years	Pressurised inhaler with chamber and face mask	Nebuliser with face mask
4-6 years	Pressurised inhaler with spacer chamber with mouthpiece	Pressurised inhaler with chamber and face mask Nebuliser with face mask
> 6 years	Dry-powder inhaler Pressurised inhaler with spacer chamber with mouthpiece	Nebuliser with mouthpiece Pressurised inhaler activated by inspiration

*In children between 5 and 12, there is no significant difference in terms of effectiveness between the pressurised inhaler with chamber and the dry-powder inhaler[120] (Proof A).

deposit[114], from 4 years on, if possible and if the child is sufficiently cooperative, the patient should move on to a large-volume chamber without a mask[115,116].

Dry-powder inhalers

Dry-powder inhalers do not contain propellants and the doses are homogeneous, the inhalation technique is easier than with the pressurised inhaler and they are small and manageable, which makes it easy for the child to carry with him/her. Lung deposit is higher than that with pressurised inhalers, but the results are similar when the latter is used with a spacer chamber.

The amount of drug lodged in the oropharynx is higher than with pressurised inhalers with inhalation chamber, but lower than with pressurised inhalers without a chamber[117,118]. The risk of side-effects increases with oropharyngeal deposit. The most common inhalers used are those with a multi-dose system (Accuhaler and Turbuhaler). With both systems an inspiratory flow of 30 L/min is sufficient. These devices are recommended from 5-6 years up.

Nebulisers

At present, the use of nebulisers at home in maintenance treatment is restricted to special cases[119]. The oxygen-driven "jet" kinds of nebuliser are used by the Emergency Services.

Relationship between Primary and Specialist Care

1. Care of asthmatic children must be coordinated between Specialist and Primary Care.

2. Each health area will need to make this coordination concrete, depending on the resources it has.

3. The organisation of plans to care for asthmatic children must include both Primary and Specialist Care.

4. The main principles of this coordination are as follows:

a) Specialist care will be greater, depending on whether the asthma is more serious or vice versa.

b) The Primary Care paediatrician will refer the child to the Allergy or Pneumology Unit when:

– An allergological and/or function assessment is needed.

– He/she cannot control the asthma properly.

– There are personal and/or family circumstances of the child that make referral advisable.

c) The Specialist Care paediatrician (allergologist or pneumologist):

– Will make a function/allergological appraisal, which he/she will report to the Primary Care paediatrician.

– Will recommend treatment guidelines that the PC paediatrician will try to follow, whilst not losing sight of the aim of controlling the disease.

5. Forced spirometry with the bronchodilation test may be a useful technique in Primary Care Paediatrics both for diagnosis and for monitoring the asthmatic child.

6. The Phadiatop and/or the prick test could be useful in allergy screening in Primary Care.

7. However, to perform forced spirometry and the prick test, particular equipment and proper training (acquired in Paediatric Pneumology or Allergology Units) are needed.

Levels of proof used in this document

Level	Sources of proof[6]
A	Randomised trials, with abundance of data in large and representative groups with an exemplary method
B	Randomised trials, but with amount of data limited
C	Non-randomised trials, observational studies
D	Consensus among experts

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