GLOBAL STRATEGY FOR THE DIAGNOSIS AND MANAGEMENT OF ASTHMA IN CHILDREN 5 YEARS AND YOUNGER

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Global Strategy for Asthma Management and Prevention in Children 5 Years and Younger

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PREFACE

Each year, the Global Initiative for Asthma (GINA) updates its guidelines for treatment of asthma, the *Global Strategy for Asthma Management and Prevention*, and makes it available via the GINA Website at www.ginasthma.org. That guideline document provides a unified text and a source document for other GINA documents and resources. Each chapter contains, where relevant, details and management advice for specific age groups including children 5 years and younger, children older than 5 years, adolescents, adults, and the elderly. Most of the differences between these age groups relate to natural history and co-morbidities, but there are also important differences in the approach to diagnosis, measures for assessing severity and monitoring control, responses to different classes of medications, techniques for engaging with the patient and his/her family in establishing and maintaining a treatment plan, and the psychosocial challenges presented at different stages of life.

In January 2008, the GINA Executive Committee convened a panel of pediatric experts* to prepare a conceptual framework for the diagnosis and management of asthma in children 5 years and younger. In this report, *Global Strategy for Asthma Management and Prevention in Children 5 Years and Younger*, an effort has been made to present the special challenges that must be taken into account in managing asthma in children during the first 5 years of life, including difficulties with diagnosis, the efficacy and safety of drugs and drug delivery systems, and the lack of data on new therapies. Approaches to these issues will vary among populations in the world based on socioeconomic conditions, genetic diversity, cultural beliefs, and differences in health care access and delivery. Patients in this age group are often managed by pediatricians and general practitioners who are routinely faced with a wide variety of issues related to childhood diseases. While this report highlights a number of issues specific to the under-5 age group, the reader is referred to the *Global Strategy for Asthma Management and Prevention* for fuller background on asthma pathology, pathophysiology, and medications.

Recommendations in this report are made based on the best evidence currently available, and are intended to serve as an initial reference point with the recognition that some recommendations may need to be modified to adapt to the population characteristics and health care resources present in different clinical practice settings.

The panel was charged with the responsibility of reviewing the available scientific literature and assigning evidence levels (A, B, C, and D) according to the methodology used in previous GINA documents[1] **(Table A)**. Because of the relative paucity of randomized clinical trials in children 5 years and younger, many of the recommendations are identified as **Evidence D**, expert opinion. However, in many of these cases, the expert opinion is based on randomized clinical trial data from studies conducted in older children and adults. The GINA Executive Committee is aware of the trend toward application of GRADE[2] technology and is developing a system to slowly make a transition to this methodology.

Eric Bateman, MD
Chair, GINA Executive Committee

Table A. Description of Levels of Evidence

Evidence Category	Sources of Evidence	Definition
A	Randomized controlled trials (RCTs). Rich body of data.	Evidence is from endpoints of well designed RCTs that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B	Randomized controlled trials (RCTs). Limited body of data.	Evidence is from endpoints of intervention studies that include only a limited number of patients, posthoc or subgroup analysis of RCTs, or meta-analysis of RCTs. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C	Nonrandomized trials. Observational studies.	Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D	Panel consensus judgment.	This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

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INTRODUCTION

Asthma is the most common chronic disease of childhood and the leading cause of childhood morbidity from chronic disease as measured by school absences, emergency department visits, and hospitalizations[3]. Asthma typically begins in early childhood, with an earlier onset in males than females[4-6]. Atopy is present in the majority of children with asthma over the age of 3, and allergen-specific sensitization is one of the most important risk factors for the development of asthma[7]. However, no intervention has yet been shown to prevent the development of asthma or to modify the long-term natural course of the disease[8-16] (**Evidence A**).

Asthma is defined as a chronic inflammatory disorder of the airways and is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing[1]. However, in children 5 years and younger, the clinical symptoms of asthma are variable and non-specific. Furthermore, neither airflow limitation nor airway inflammation, the main pathologic hallmarks of the condition, can be assessed routinely in this age group. For this reason, to aid in the diagnosis of asthma in young children, a symptoms-only descriptive approach that includes the definition of various wheezing phenotypes has been recommended[17].

For all patients with a confirmed diagnosis of asthma, the goal of treatment is to achieve control of the clinical manifestations of the disease, and maintain this control for prolonged periods, with appropriate regard to the safety and cost of the treatment required to achieve this goal. Control of asthma can be achieved in a majority of children 5 years and younger with a pharmacologic intervention strategy developed in partnership between the family/caregiver and the health care practitioner. As in older children and adults, inhaled therapy constitutes the cornerstone of asthma treatment in children 5 years and younger.

I. RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF ASTHMA

Epidemiologic studies have identified a number of risk factors associated with the development of asthma, including (but not limited to) sensitization to aeroallergens, maternal diet during pregnancy and/or lactation, pollutants (particularly environmental tobacco smoke), microbes and their products, and psychosocial factors. However, evidence for avoidance measures to prevent asthma is lacking in many cases.

AEROALLERGENS

Atopic sensitization to common aeroallergens, especially perennial inhalant allergens, is an important risk factor associated with asthma[18]. For some children, the earlier in life they become sensitized to local allergens the greater their risk for asthma later in life[7], especially when sensitization occurs in association with frequent lower respiratory illnesses[8]. Several types of aeroallergens are particularly important in relation to asthma.

House Dust Mites: A Cochrane analysis questioned the effectiveness of house dust mite avoidance for the treatment of established asthma[9]. Moreover, there is no evidence that anti-house dust mite measures prevent the onset of asthma[10-12].

Companion Animal Allergens: The relationship between exposure and sensitization to allergens from companion animals is not clear, and there are insufficent data to recommend for, or against, the presence of a pet in the home unless the child has become sensitized to the pet species[13-15, 18].

Cockroaches: Exposure to cockroach allergen in the living quarters is associated with the development of sensitization, and sensitization to cockroach allergen is associated with an increased risk of developing asthma[16].

Fungi: Sensitization to *Alternaria* is a major risk factor not only for the development of asthma in children, but also for its severity[19,20]. *Alternaria* is usually considered an outdoor aeroallergen, but outdoor and indoor concentrations may be similar[21].

MATERNAL DIET DURING PREGNANCY AND/OR LACTATION

At present, there are insufficient data to support a protective effect of any dietary intervention during pregnancy or lactation in preventing asthma or atopic disease[22,23]. Breastfeeding itself decreases early childhood wheezing syndromes associated with upper and lower respiratory infections. However, although recommended for its general health benefits, there is little evidence that breastfeeding prevents development of persistent asthma[8, 24-26].

POLLUTANTS

Maternal smoking during pregnancy and exposure to environmental tobacco smoke early in life are associated with a greater risk of developing wheezing illnesses in childhood[27], as well as with reduced lung function later in life[6]. Therefore, every effort should be made to avoid exposing children to tobacco smoke[28].

Use of biomass fuels in the home has been associated with an increased risk of asthma, increased severity of asthma, and exercise-induced bronchospasm in children[29,30]. This presents a problem in much of the world where biomass fuels such as wood, charcoal, animal dung, and crop residues are used on a daily basis for cooking and/or heating. Outdoor air pollution related to traffic has been shown to trigger wheezing in the first 3 years of life[31].

MICROBES AND THEIR PRODUCTS

Wheezing in early childhood is predominately linked to viral infections, especially those due to rhinovirus, respiratory synctial virus (RSV), Boca virus, and metapneumovirus (MPV)[32-34].

The impact of bacterial products and their relationship to the development of asthma is increasingly a focus of interest and forms part of the so-called "hygiene hypothesis." Exposure to a farming environment in early life has been associated with a reduced risk of asthma and allergy in children compared to those who have not grown up on a farm[35,36]. In this regard, exposure to the lipopolysaccaride endotoxin from microorganisms encountered in the farming environment appears to be a potential protective factor, particularly in children with specific genetic polymorphisms[37].

Since intestinal flora are the largest source of microbial exposure for most infants and children, the use of probiotics to modify the composition of intestinal flora has been proposed as a method for exploiting this asthma-protective effect of microbes. While probiotics have been shown to be of some benefit in the prevention of atopic dermatitis, no impact on the development of asthma has been demonstrated[38].

Although the use of antibiotics also modifies the composition of intestinal flora, the impact of use of antibiotics early in life on the risk of developing asthma later in life is controversial[39,40]. Based on available data, it is recommended that particularly broad-spectrum antibiotics should be used with circumspection in this young age group, and only for recognized indications (**Evidence D**).

PSYCHOSOCIAL FACTORS

A child's social environment may play a role in the development and severity of asthma[41,42]. Stress in family or other primary caregivers during the first year of life is associated with an atopic profile and wheeze in infants, and is also associated with asthma at age 6 to 8 years[43]. Maternal distress in early life may play a role in the development of childhood asthma, especially if the distress continues beyond the postpartum period[44].

OTHER RISK FACTORS

Children born by Cesarean section have a higher risk of asthma than those born by vaginal delivery[45], particularly children of allergic parents[46]. Paracetamol (acetaminophen) use during pregnancy[47] and for fever in the child's first year of life[48] have been associated with increased prevalence of asthma in children.

SUMMARY

Since the contributions of different risk factors to the development of asthma vary widely in different societies and homes, their relative importance overall may be difficult to assess. Avoidance of some risk factors requires societal and public health interventions. However, measures to avoid other risk factors can be implemented by individual concerned parents as part of their personal preventive strategies for asthma, and these include:

- Avoid exposures to atmospheric pollution and particularly tobacco smoke
- Avoid unnecessary use of antibiotics in young children
- Provide a calm and nurturing environment (**Evidence D**).

II. DIAGNOSIS

Making a diagnosis of asthma in children 5 years and younger may be difficult because episodic respiratory symptoms such as wheezing and cough are also common in children who do not have asthma, particularly in those younger than 3 years[49,50]. Furthermore, it is not possible to routinely assess both airflow limitation and inflammation in this age group. Nevertheless, a diagnosis of asthma in young children can often be made based largely on symptom patterns and on a careful clinical assessment of family history and physical findings. The presence of atopy or allergic sensitization provides additional predictive support, as early allergic sensitization increases the likelihood that a wheezing child will have asthma[7].

SYMPTOMS

Symptoms in this age group that may indicate a diagnosis of asthma include wheeze, cough, breathlessness (typically manifested by patterns of activity limitation), and nocturnal symptoms/awakenings.

Wheeze: Wheeze, the most common symptom associated with asthma in children 5 years and younger, has been strictly defined as a continuous high-pitched sound, sometimes with musical quality, emitting from the chest during expiration[51]. Wheezing occurs in several different patterns but a wheeze that occurs recurrently, during sleep, or with triggers such as activity, laughing, or crying is consistent with a diagnosis of asthma.

Wheezing may be interpreted differently based on the individual observing it (e.g., parent versus clinician), when it is being reported (e.g., retrospectively versus in real time), the environmental context in which it is occurring (e.g., wheeze may have different presentation patterns in areas of the world where parasites with life cycles involving the lung are more prevalent), and the cultural context in which it is occurring (e.g., different cultures assign different relative importance to certain symptoms and to diagnosis and treatment of respiratory tract diseases in general).

Viral respiratory infections are the most common factors responsible for acute wheezing episodes in young children, and some viral infections (RSV and rhinovirus) are associated with recurrent wheeze throughout childhood. Since many young children may wheeze with viral infections, deciding when the presence of wheezing with infections is truly an initial or recurrent clinical presentation of childhood asthma is difficult[5].

Cough: Cough due to asthma is recurrent and/or persistent, and is usually accompanied by some wheezing episodes and breathing difficulties. Nocturnal cough (occurring when the child is asleep) or cough occurring with exercise, laughing, or crying in the absence of an apparent respiratory infection, strongly supports a diagnosis of asthma. The common cold and other respiratory illnesses are also associated with cough.

Breathlessness (Terms often used by parents include difficult breathing, heavy breathing, and shortness of breath): Breathlessness that occurs during exercise and is recurrent increases the likelihood of the presentation being due to asthma. In infants and toddlers, crying and laughing are an exercise equivalent.

CLINICAL HISTORY

For children 5 years and younger with a history of recurrent respiratory symptoms; a strong family history of asthma in first degree relatives (especially the mother); and/or atopy presenting as atopic dermatitis, food allergy, and/or allergic rhinitis also make a diagnosis of asthma more likely.

TESTS FOR DIAGNOSIS AND MONITORING

While no tests diagnose asthma with certainty in young children, the following may be considered as useful adjuncts in making a diagnostic decision.

Therapeutic Trial: A trial of treatment with short-acting bronchodilators and inhaled glucocorticosteroids for at least 8 to 12 weeks may provide some guidance as to the presence of asthma (**Evidence D**). These interventions should be evaluated in terms of how they affect control of daytime and nocturnal symptoms as well as the frequency of exacerbations requiring increasing doses of inhaled or systemic glucocorticosteroids. Marked clinical improvement during the treatment and deterioration when it is stopped supports a diagnosis of asthma. Due to the variable nature of asthma in young children, a therapeutic trial may need to be repeated more than once in order to be certain of the diagnosis.

Tests for Atopy: Sensitization to allergens can be assessed using either immediate hypersensitivity skin testing or an in vitro method that detects antigen-specific IgE antibody. Skin-prick testing is less reliable for confirming atopy in infants.

Chest Radiograph (X-ray): If there is doubt about the diagnosis of asthma in a wheezing child, a plain chest radiograph may help to exclude structural abnormalities of the airway (e.g., congenital malformations such as congenital lobar emphysema, vascular ring), chronic infection (e.g. tuberculosis), or other diagnoses.

Lung function testing, bronchial challenge, and other physiological tests do not have a major role in the diagnosis of asthma in children 5 years and younger due to the inability of children this age to perform reproducible expiratory maneuvers. Such tests are only possible in specialized centers, and are undertaken mainly for research purposes.

DIFFERENTIAL DIAGNOSIS

Although a variety of tools have been described above to aid the clinician in making a diagnosis of asthma in children 5 years and younger, it must be emphasized that a definite diagnosis in this young age group is challenging and has important clinical consequences. Thus, alternative causes that can lead to respiratory symptoms of wheeze, cough, and breathlessness must be considered and excluded before an asthma diagnosis is arrived at[49] **(Table 1)**.

TABLE 1: Differential Diagnosis of Asthma in Children 5 Years and Younger

Infections
- Recurrent respiratory tract infections
- Chronic rhino-sinusitis
- Tuberculosis

Congenital problems
- Tracheomalacia
- Cystic fibrosis
- Bronchopulmonary dysplasia
- Congenital malformation causing narrowing of the intrathoracic airways
- Primary ciliary dyskinesia syndrome
- Immune deficiency
- Congenital heart disease

Mechanical problems
- Foreign body aspiration
- Gastroesophageal reflux

Neonatal or very early onset of symptoms (associated with failure to thrive), symptoms associated with vomiting, or focal lung or cardiovascular signs, suggest an alternative diagnosis and indicate the need for further investigations.

WHEEZING PHENOTYPES

Recurrent wheezing occurs in a large proportion of children five years and younger. However, not all of this wheezing indicates asthma. Several phenotypes of wheezing disorders in this age group have been recognized in epidemiologic studies.

Early childhood wheezing has been classified by a Task Group convened by the European Respiratory Society (ERS)[17] as either episodic wheeze (wheezing during discrete time periods, often in association with clinical evidence of a common cold, with absence of wheeze between episodes) or multiple-trigger wheeze (wheezing that occurs as episodic exacerbations as above, but also with symptoms including cough and wheeze occurring between these episodes, during sleep or with triggers such as activity, laughing, or crying).

Data from a U.S. cohort study[6] led to the description of three wheezing phenotypes: transient wheeze (symptoms begin and end before the age of 3 years), persistent wheeze (symptoms begin before the age of 3 years and continue beyond the age of 6 years), and late-onset wheeze (symptoms begin after the age of 3 years).

The clinical usefulness of the phenotypes described by the ERS Task Group[17] or based on data from the U.S. cohort study[6] remains a subject of active investigation. Children with asthma may have any of these phenotypes, but asthma occurs much more rarely in the episodic wheeze and transient wheeze phenotypes compared to the other phenotypes. A number of other publications provide additional insights into wheezing phenotypes and their relationship to children 5 years and younger with asthma[6,52,53].

To aid in the early identification, in the clinical setting, of children 5 years and younger who wheeze and are at high risk of developing persistent asthma symptoms, a number of risk profiles have been evaluated[54-57]. One such predictive assessment, the Asthma Predictive Index (API), is recommended for children with four or more wheezing episodes in a year and is based on information obtained from the Tucson (USA) Respiratory Study[55]. One study has shown that a child with a positive API has a 4- to 10-fold greater chance of developing asthma between the ages of 6 and 13, while 95% of children with a negative API remained free of asthma[55,57] **(Evidence C)**. . The applicability and validation of the API in other countries and clinical situations is awaited.

III. MANAGEMENT AND PHARMACOLOGIC CONTROL

For all patients with a confirmed diagnosis of asthma, the goal of treatment is to achieve control of the clinical manifestations of the disease, and maintain this control for prolonged periods, with appropriate regard to the safety and cost of the treatment required to achieve this goal. Control of asthma can be achieved in a majority of children 5 years and younger with a pharmacologic intervention strategy developed in partnership between the family/caregiver and the health care practitioner. As in older children and adults, inhaled therapy constitutes the cornerstone of asthma treatment in children 5 years and younger **(Evidence A)**.

ASTHMA EDUCATION

Asthma education should be provided to family members and caregivers of wheezy children 5 years and younger when wheeze is suspected to be caused by asthma (**Evidence D**). An educational package should contain a basic explanation about asthma and the factors that influence it, instruction about correct inhalation technique and the importance of adherence to the prescribed medication regime, and a description of how to recognize when asthma control is deteriorating and the medications to administer when this occurs. Randomized controlled trials in older children and adults have demonstrated that the use of a written asthma management plan along with careful verbal explanation of the treatment regime can improve asthma control. For children 5 years and younger who cannot reliably perform lung function measurements, asthma management plans based on the levels of respiratory symptoms have been shown to be just as effective as plans based on self-monitoring of lung function[58] (**Evidence B**). Crucial to a successful asthma education program are a **patient-doctor partnership** featuring a high level of agreement between family or caregiver and healthcare practitioner regarding the goals of treatment for the child, as well as **intensive follow-up**[59] (**Evidence D**).

ASTHMA CONTROL

For all patients with a confirmed diagnosis of asthma, the goal of treatment is to achieve control of the clinical manifestations of the disease and maintain this control for prolonged periods, with appropriate regard to the safety and cost of the treatment required to achieve this goal.

The relevance of distinguishing between current control (as assessed by the control or elimination of clinical features of asthma in the recent weeks or months) from "future risk" (the likelihood of future worsening, exacerbations, impaired lung development), and the relationship between these two concepts, have not been carefully studied in small children. However, a combination of increased daytime cough, daytime wheeze, and nighttime β_2-agonist use has been found to be a strong predictor of an exacerbation in children 5 years and younger (predicting around 70% of exacerbations, with a low false positive rate of 14%[60]). In contrast, no individual symptom was predictive of an imminent asthma exacerbation. This finding indirectly supports the importance of good daily asthma control and the use of composite outcomes in the assessment of asthma control in this age group.

Although exacerbations may occur in children after months of apparent clinical control, the risk is greater in patients whose current control is poor. On the other hand, the "future risk" of harm caused by excessive doses of medications, or inappropriate treatment such as the prolonged use of high doses of inhaled or systemic glucocorticosteroids, must also be avoided by ensuring that treatment is appropriate and reduced to the lowest level that maintains satisfactory current clinical control.

Defining satisfactory current clinical asthma control in children 5 years and younger is problematic, since health care providers are almost exclusively dependent on the reports of the child's family members and caregivers who might be unaware either of the presence of asthma symptoms, or of the fact that they represent uncontrolled asthma. Moreover, as with the diagnosis of asthma, lung function testing is not feasible as a means to monitor control in children of this age. No objective measures to assess clinical control have been validated for children younger than 4 years (one such measure has been developed for children aged 4-11[61]). However, a working scheme based on current expert opinion presents characteristics of controlled, partly controlled, and uncontrolled asthma for children 5 years and younger based on symptoms recognized by family members/caregivers and the child's need for reliever/rescue treatment (**Table 2**) (**Evidence D**).

PHARMACOTHERAPY

Inhaled therapy constitutes the cornerstone of asthma treatment in children 5 years and younger. A general strategy for choosing inhalers in children is provided in **Table 3**. A pressurized metered-dose inhaler (MDI) with a valved spacer (with or without a face mask, depending on the child's age) is the preferred delivery system[62] (**Evidence A**). This recommendation is based on studies with performed with β_2-agonists.

Spacers come in different designs and, since the dose received may vary considerably from one device to another, a spacer device that has documented efficacy in young children is recommended. Nebulizers, the only viable alternative delivery systems in children, should be reserved for the minority of children who cannot be taught effective use of a spacer device.

Table 2. Levels of Asthma Control in Children 5 Years and Younger*			
Characteristic	**Controlled (All of the following)**	**Partly Controlled (Any measure present in any week)**	**Uncontrolled (3 or more of features of partly controlled asthma in any week)**
Daytime symptoms: wheezing, cough, difficult breathing	None (less than twice/week, typically for short periods on the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator)	More than twice/week (typically for short periods on the order of minutes and rapidly relieved by use of a rapid-acting bronchodilator)	More than twice/week (typically last minutes or hours or recur, but partially or fully relieved with rapid-acting bronchodilator)
Limitations of activities	None (child is fully active, plays and runs without limitation or symptoms)	Any (may cough, wheeze, or have difficulty breathing during exercise, vigorous play, or laughing)	Any (may cough, wheeze, or have difficulty breathing during exercise, vigorous play, or laughing)
Nocturnal symptoms/awakening	None (including no nocturnal coughing during sleep)	Any (typically coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)	Any (typically coughs during sleep or wakes with cough, wheezing, and/or difficult breathing)
Need for reliever/rescue treatment	≤ 2 days/week	> 2 days/week	> 2 days/week

**Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate. Although patients with current clinical control are less likely to experience exacerbations, they are still at risk during viral upper respiratory tract infections and may still have one or more exacerbations per year.*

Table 3: Choosing an Inhaler Device for Children with Asthma		
Age Group	**Preferred Device**	**Alternative Device**
Younger than 4 years	Pressurized metered-dose inhaler *plus* dedicated spacer with face mask	Nebulizer with face mask
4-5 years	Pressurized metered-dose inhaler *plus* dedicated spacer with mouthpiece	Pressurized metered-dose inhaler *plus* dedicated spacer with face mask, *or* Nebulizer with mouthpiece or face mask

Controlled trials in children 5 years and younger are rather limited, the patient populations have often not been well characterized with respect to phenotype (including wheezy children who may or may not have asthma), and different studies have used different outcomes and definitions of exacerbations. However, based on literature that is available, extrapolations from studies in older children and adults, and on expert opinion, the following sections provide recommendations for controller medications (taken daily on a long-term basis to keep asthma under control) and reliever medications (for use on an as-needed basis) for the pharmacologic treatment of asthma in children 5 years and younger.

Controller Medications

Inhaled glucocorticosteroids

Efficacy: As in older children, several placebo-controlled studies of inhaled glucocorticosteroids in children 5 years and younger with asthma have found statistically significant clinical effects on a variety of outcomes, including increased lung function and number of symptom-free days, and reduced symptoms, need for additional medication, caregiver burden, systemic glucocorticosteroid use, and exacerbations[57,63-73] (**Evidence A**). However, the dose-response relationships have been less well studied. The clinical response may differ depending on the specific device used for delivery and the child's ability to use it correctly. With correct use of a spacer device, twice the recommended initial low dose of inhaled glucocorticosteroid results in near-maximum benefits as regular, long-term treatment in the majority of patients (**Table 4**)[64,68]. Use of inhaled glucocorticosteroids for up to 2 years has not been documented to induce remission of asthma; symptoms almost always return when treatment is stopped[57] (**Evidence B**).

Safety: The majority of studies evaluating the systemic effects of inhaled glucocorticosteroids have been undertaken in children older than 5 years. However, the available data in children 5 years and younger suggest that, as in older children, clinically effective doses of inhaled glucocorticosteroids are safe and the potential risks are well balanced by the clinical benefits[57,63,73]. Generally, low doses of inhaled glucocorticosteroids (**Table 4**) have not been associated with any clinically serious adverse systemic effects in clinical trials and are considered safe[63-73] (**Evidence A**). However, higher doses have been associated with detectable systemic effects on both growth and the hypothalamic-pituitary-adrenal (HPA) axis[57,63-73]. These effects are similar to those reported in studies of older children, which find no evidence of long-term clinical impact[74,75]. Local side effects, such as hoarseness and candidiasis, are rare in children 5 years and younger[68].

Leukotriene modifiers

Efficacy: Leukotriene modifiers reduce viral-induced asthma symptoms in children ages 2-5 years with a history of intermittent asthma[76] by reducing the number of protocol-defined exacerbations, but do not reduce the frequency of hospitalizations, use of prednisolone, duration of exacerbations, or days without asthma symptoms. Moreover, no effect on post-bronchiolitic wheeze or cough is seen following hospitalization with RSV bronchiolitis[77]. In a three-month study of children with persistent wheeze, montelukast reduced symptoms and rescue β_2-agonist use by approximately 6%. The percentage of patients experiencing an asthma attack was not significantly reduced, but the need for a course of prednisolone was significantly reduced from 28% to 19% of patients[78]. Montelukast has also been shown to reduce airway hyperresponsiveness to methacholine[76] or hyperventilation with cold dry air[79]. A randomized, placebo-controlled trial of the addition of montelukast to usual asthma therapy among 42 children aged 2-5[80] found that this treatment reduced the number of days with worsening of asthma symptoms in boys but not in girls, the number of days with symptoms in the two groups being 7.8% and 3.5%, respectively. In summary, leukotriene modifiers improve some asthma outcomes in young children (**Evidence A**). However, the role of leukotriene modifiers as add-on therapy in children 5 years and younger whose asthma is uncontrolled on inhaled glucocorticosteroids has not been specifically evaluated.

Safety: No safety concerns have been demonstrated from the use of leukotriene modifiers in young children.

Theophylline

Although a few studies in children 5 years and younger suggest clinical benefit from regular use of theophylline, the effects are small and mostly non-significant[81]. The efficacy of theophylline is less than that of low-dose inhaled glucocorticosteroids, and side effects are more common (**Evidence D**).

Long-acting inhaled β_2-agonists

Long-acting inhaled β_2-agonists (LABAs) are bronchodilators, but as long-term therapy for asthma they are only prescribed in combination with an inhaled glucocorticosteroid and are therefore considered controller medications. The effect of long-acting inhaled β_2-agonists or combination (LABA/glucocorticosteroid) products has not been adequately studied in children 5 years and younger. Formoterol and salmeterol have shown long-lasting bronchodilatory and bronchoprotective effects in this age group[82]. However, there are no published randomized placebo-controlled trials in this age group on the addition of long-acting inhaled β_2-adrenergic agents to inhaled glucocorticosteroids. Therefore, long-acting inhaled β_2-agonists cannot be recommended in this age group (**Evidence D**).

Cromolyn and nedocromil sodium

A Cochrane Review concluded that there was no beneficial effect of cromolyn therapy in preschool children[83,84] and nedocromil has not been studied in preschool children. Therefore, cromones cannot be recommended in this age group (**Evidence A**).

Oral and systemic glucocorticosteroids

Because of the side effects associated with prolonged use, oral glucocorticosteroids in young children with asthma should be restricted to the treatment of acute severe exacerbations, whether viral-induced or otherwise (**Evidence D**).

Immunotherapy

No studies of immunotherapy for asthma have been performed in this age group. Therefore, immunotherapy is not recommended for the treatment or prophylaxis of asthma in children 5 years and younger (**Evidence D**).

Comparisons Between Controller Medications

In older children and adults, regular treatment with inhaled glucocorticosteroids has been well documented to be clinically more effective than other controller treatments for asthma. Moreover, they attenuate the decline in lung function seen in association with severe exacerbations[85]. Fewer comparative studies have been conducted in children 5 years and younger. However, two studies of nearly 1,000 children in this age group[86,87] confirmed the superiority of inhaled glucocorticosteroids over cromones for almost all endpoints assessing asthma control (**Evidence A**).

Two additional studies compared inhaled glucocorticosteroids with leukotriene modifiers. A one-year, randomized, open study compared montelukast with nebulized budesonide in 400 children; overall measures favored budesonide[88]. In the second, a blinded, placebo-controlled study of 63 children, only the fluticasone propionate treatment significantly improved symptoms over placebo, whereas montelukast did not, and fluticasone propionate also improved lung function after three months[89] (**Evidence B**).

Reliever Medications

Rapid-acting inhaled β_2-agonists are the most effective bronchodilators available and therefore the preferred reliever treatment for asthma in children 5 years and younger. An MDI with spacer is, in most cases, an effective way for delivering reliever therapy[62,90] (**Evidence A**). When delivery is not optimal because of lack of cooperation or distress, or when the child is hypoxic, nebulizer therapy is also an option. Oral therapy is not recommended due to its slower onset of action and its tendency to produce more side effects.

There is no evidence that inhaled ipratropium has an important role in the daily management of asthma in children 5 years and younger[91] (**Evidence A**).

TREATMENT STRATEGY

The goal of asthma treatment, to achieve and maintain control of the disease, can be reached in a majority of children 5 years and younger with a pharmacologic intervention strategy[86] developed in partnership between the family/caregiver and the health care practitioner. Although validated tools for assessment of asthma control have not been developed for young children, it is recommended that both current impairment (day and night symptoms, activity level impairment, need for rescue medications) and future risk (likelihood of acute exacerbation in the future) be assessed and controlled (Table 2) (**Evidence B**).

Who Should be Treated

Regular controller treatment is normally recommended for children 5 years and younger whose frequency and severity of asthma symptoms without treatment indicates that their asthma is not controlled (**Table 2**).

Selecting Initial Therapy

A low-dose inhaled glucocorticosteroid is recommended as the preferred initial treatment to control asthma in children 5 years and younger[57,70,88] (**Table 4**) (**Evidence A**).

Table 4: Low Daily Doses* of Inhaled Glucocorticosteriods for Children 5 Years and Younger

Drug	Low Daily Dose (µg)
Beclomethasone dipropionate	100
Budesonide MDI+spacer Budesonide nebulized	200 500
†Ciclesonide	NS
Fluticasone propionate	100
†Mometasone furoate	NS
†Triamcinolone acetonide	NS

* A low daily dose is defined as the dose which has not been associated with clinically adverse effects in trials including measures of safety. This is not a table of clinical equivalence.

†NS = Not studied in this age group.

This initial treatment should be given for at least 3 months to establish its effectiveness in reaching control. If at the end of this period the low dose of inhaled glucocorticosteroid does not control symptoms, and the child is using optimal technique and is adherent to therapy, doubling the initial dose of glucocorticosteroid given in **Table 4** may be the best option[64] (**Evidence C**). Addition of a leukotriene modifier to the low-dose inhaled glucocorticosteroid may also be considered, although this has not been studied in this age group (**Evidence D**).

Table 5 presents a management approach based on asthma control for children 5 years and younger.

Table 5. Asthma Management Approach Based on Control for Children 5 Years and Younger

Asthma education Environmental control As needed rapid-acting β_2-agonists		
Controlled on as needed rapid-acting β_2-agonists	**Partly controlled on as needed rapid- acting β_2-agonists**	**Uncontrolled or only partly controlled on low-dose inhaled glucocorticosteroid***
Controller options		
Continue as needed rapid-acting β_2-agonists	Low-dose inhaled glucocorticosteroid	Double low-dose inhaled glucocorticosteroid
	Leukotriene modifier	Low-dose inhaled glucocorticosteroid plus leukotriene modifier

*Oral glucocorticosteroids should be used only for treatment of acute severe exacerbations of asthma.
Shaded boxes represent the preferred treatment options.

When Control is not Achieved: When doubling the initial dose of inhaled glucocorticosteroids fails to achieve and maintain asthma control, the child's inhalation technique and compliance with the medication regimen should be carefully assessed and monitored, as these are common problems in this age group. Furthermore, control of environmental factors should be assessed and addressed appropriately, and the asthma diagnosis reconsidered.

The best treatment for children whose asthma is not controlled on twice the initial dose of inhaled glucocorticosteroid has not been established. Options to consider are to further increase the dose of inhaled glucocorticosteroid (perhaps combined with more frequent dosing), or to add a leukotriene modifier, theophylline, or a low dose of oral glucocorticosteroid for a few weeks until the control of the child's asthma improves (**Evidence D**). The need for this additional treatment should be re-evaluated at each visit and maintained for as short a period as possible. Furthermore, the treatment goal or level of control that is feasible for each child must be considered and discussed with the family/caregivers, since a compromise might be necessary–accepting a level of persisting symptoms to avoid excessive and harmful doses of oral and inhaled glucocorticosteroids or theophylline.

Duration and Adjustments to Treatment: Asthma symptoms remit in a substantial proportion of children 5 years and younger, and marked seasonal variations are seen in chronic symptoms and the risk of exacerbations. For children with seasonal symptoms, if daily long-term control therapy is discontinued after the season a written action plan detailing specific signs of worsening asthma, and therapeutic interventions that should be subsequently initiated, should be reviewed with the caregivers. It is recommended that the continued need for asthma treatment in children under age 5 should be regularly assessed (e.g., every three to six months) (**Evidence D**). A follow-up visit should be scheduled 3-6 weeks after discontinuation of therapy to ascertain whether the remission of symptoms persists and there is no need for reinstitution of therapy.

Approach to the Child with Intermittent Wheezing Episodes: Intermittent episodic wheezing of any severity may represent unrecognized uncontrolled asthma, an isolated viral-induced wheezing episode, or an episode of seasonal or allergen-induced asthma. The initial treatment is identical in any case: a dose of rapid-acting inhaled β_2-agonist every 4–6 hours as needed for a day or more until symptoms disappear (**Evidence A**). However, uncertainty surrounds the addition of other drugs, especially when the nature of the episode is unclear.

If a detailed history suggests the diagnosis of asthma, and wheezing episodes are frequent (e.g., 3 in a season), regular controller treatment should be initiated (**Evidence D**). Regular controller treatment may also be indicated in a child with less frequent, but more severe, episodes of viral-induced wheeze (**Evidence D**).

Where the diagnosis is in doubt, and when rapid-acting inhaled β_2-agonist therapy needs to be repeated more frequently than every 6-8 weeks, a diagnostic trial of regular controller therapy should be considered to confirm whether the symptoms are due to asthma (**Evidence D**).

The treatment of intermittent episodic wheezing that occurs in children where a diagnosis of asthma cannot be confirmed, or is unlikely, is controversial. The short-term addition of a controller medication–inhaled glucocorticosteroid, leukotriene modifier, or oral glucocorticosteroid–has demonstrated no effects on wheezing symptoms or progression to asthma[92-100]. However, in one study treating wheezing episodes with 1,500 µg of fluticasone proprionate daily for 10 days reduced the need for oral glucocorticosteroids for the episode (18% in the untreated arm versus 8% in the treated arm)[101]. Therefore, although these treatments are widely practiced, based on current evidence, their continued use cannot be recommended (**Evidence D**).

ACUTE EXACERBATIONS

The management of acute exacerbations of asthma in children 5 years and younger includes an action plan to enable the child's family members and caregivers to recognize an asthma attack and initiate treatment, recognize a severe episode, identify when urgent hospitalized treatment is necessary, and provide specific recommendations for follow-up. (**Evidence D**).

Definition: An acute exacerbation of asthma in children 5 years and younger is defined as an acute or subacute deterioration in symptom control that is sufficient to cause distress or risk to health necessitating a visit to a health care provider or requiring treatment with systemic glucocorticosteroids[102]. Early symptoms of an acute exacerbation may include any of the following :

- An increase in wheeze and shortness of breath
- An increase in coughing, especially nocturnal cough
- Lethargy or reduced exercise tolerance
- Impairment of daily activities, including feeding
- A poor response to reliever medication

Upper respiratory symptoms frequently precede the onset of an asthma exacerbation, indicating the important role of upper respiratory tract viral infections in precipitating exacerbations in many, although not all, asthmatic children.

Home Action Plan for Family/Caregivers

An asthma action plan should be considered for use by the family/caregivers of children 5 years and younger (**Evidence D**). Developed through collaboration between an asthma educator, the health care provider, and the family, action plans have been shown to be of value in older children[103-106], although they have not been sufficiently studied in this younger age group. An asthma action plan should contain details that will enable those who care for the child to recognize exacerbations early, and know what interventions are required, including when medical help should be sought. The home action plan should also provide details (including telephone numbers) of services available for emergencies – doctors' offices, emergency rooms and hospitals, ambulance services, and, where relevant, emergency pharmacies. Treatments that can be initiated at home are inhaled rapid-acting β_2–agonist and oral glucocorticosteroids, but specific instructions on their use must be provided in the action plan.

Initial home management: Inhaled rapid-acting β_2-agonist via a mask or spacer device and observation. Treatment should be initiated with two puffs (200µg salbutamol or the equivalent) of inhaled rapid-acting β_2-agonist, given one puff at a time via a mask or spacer device (**Evidence D**). The child should be observed by the family/caregiver and maintained in a restful and reassuring atmosphere for an hour or more. Medical attention should be sought the same day if the inhaled bronchodilator is required for symptom relief more than every 3 hours or for more than 24 hours.

Need for urgent medical attention.
Immediate medical attention should be sought:

- For children younger than 1 year requiring repeated rapid-acting inhaled β_2-agonists over the course of hours
- If the child is acutely distressed
- If the symptoms are not relieved promptly by inhaled bronchodilator
- If the period of relief after a dose of inhaled β_2-agonist becomes progressively shorter[107]

Family/Caregiver Initiated Oral Glucocorticosteroids.
Although practiced in some parts of the world, the evidence to support the initiation of oral glucocorticosteroid treatment by family/caregivers in the home management of asthma exacerbations in children is weak, and should be considered only where the physician is confident that they will be used appropriately (**Evidence D**).

Assessment of Severity

Features that indicate that an exacerbation is severe are provided in **Table 6** and the presence of any of these features is an indication of the need for urgent treatment (**Evidence A**). Agitation, drowsiness, and confusion are features of cerebral hypoxemia. Percutaneous oxygen saturation of 92% or less on presentation (before oxygen or bronchodilator treatment) is associated with higher morbidity and greater likelihood of the need for hospitalization. Other clinical features of a severe attack requiring immediate treatment are inability to talk in sentences or phrases, tachycardia (200 beats per minute or more for children 0-3 years, and 180 beats per minute or more for children 4-5 years), central cyanosis, and a quiet chest on auscultation (indicating minimal ventilation – insufficient to produce a wheeze).

Indications for Hospitalization

Indications for hospitalization of children 5 years and younger are presented in **Table 7**. Children with features of a severe exacerbation that fail to resolve in 1 to 2 hours in spite of repeated dosing with rapid-acting inhaled β_2-agonists, with or without the addition of oral glucocorticosteroids, must be referred for observation and further treatment in the hospital (**Evidence D**). Other indications are respiratory arrest or impending arrest, lack of supervision in the home or rooms, and recurrence of signs of severity within 48 hours of the initial exacerbation (particularly if treatment with systemic glucocorticosteroids has been given). In addition, early medical attention should be sought in children under 2 years of age where the risk of dehydration and respiratory fatigue is increased.

Table 6. Initial Assessment of Acute Asthma in Children Five Years and Younger

Symptoms	Mild	Severe[a]
Altered consciousness	No	Agitated, confused or drowsy
Oximetry on presentation[b] (SaO_2)	≥ 94%	< 90%
Talks in[c]	Sentences	Words
Pulse rate	< 100 bpm[d]	> 200 bpm (0-3 years) > 180 bpm (4-5 years)
Central cyanosis	Absent	Likely to be present
Wheeze intensity	Variable	May be quiet

[a] Any of these features indicates a severe asthma exacerbation

[b] Oximetry performed before treatment with oxygen or bronchodilator

[c] The normal developmental capability of the child must be taken into account.

[d] bpm = beats per minute.

Table 7. Indications for Immediate Referral to Hospital

ANY of the following:

- No response to three (3) administrations of an inhaled short-acting β_2-agonist within 1-2 hours
- Tachypnea despite 3 administrations of an inhaled short-acting β_2-agonist (Normal respiratory rate < 60 breaths per minute in children 0 – 2 months; < 50 in children 2 –12 months; < 40 in children 1 – 5 years)
- Child is unable to speak or drink or is breathless
- Cyanosis
- Subcostal retractions
- Oxygen saturation when breathing room air < 92%
- Social environment that impairs delivery of acute treatment; caregivers unable to manage acute asthma at home

Emergency Treatment and Pharmacotherapy

Treat hypoxemia: The presence of hypoxemia must be treated urgently with oxygen delivered by face mask, to achieve and maintain percutaneous oxygen saturation above 94% (Evidence A). A 24% facemask is usually adequate with oxygen flow set to manufacturer's instructions (usually 4 L per minute). To avoid hypoxemia during changes in treatment, children who are acutely distressed should be treated immediately with oxygen and rapid-acting bronchodilator (2.5 mg of salbutamol or equivalent diluted in 3 ml of sterile normal saline) delivered by an oxygen-driven nebulizer (if available). This treatment should not be delayed, and may be given before the full assessment is completed.

Bronchodilator therapy: The initial dose of rapid-acting bronchodilator may be given by oxygen-driven nebulizer (as described above), or if hypoxemia is absent (or an oxygen-driven nebulizer not available) by either an air-driven nebulizer or a pressurized MDI with spacer and mask or mouthpiece. For most children, the MDI plus spacer is favored as it is more efficient than the nebulizer[62,108,109] (Evidence A) for bronchodilator delivery. The initial dose is two puffs of salbutamol (100 μg per puff) or equivalent. A dose of 2.5 mg salbutamol solution is recommended when a nebulizer is used. The frequency of dosing depends on the response observed over 1 to 4 hours (see below).

Inhaled glucocorticosteroids or leukotriene modifier: Children who have been prescribed maintenance therapy with inhaled glucocorticosteroids, leukotriene modifier, or both should continue to take the prescribed dose during and after an exacerbation (Evidence D).

Assessment of Treatment Response

Children with a severe exacerbation must be observed for at least 1 hour after initiation of treatment, at which time further treatment can be planned.

- If symptoms persist, a further 2 puffs of salbutamol may be given 20 minutes after the first dose and repeated at 20-minute intervals for an hour. Failure to respond to this at 1 hour, or earlier if the child deteriorates, should prompt urgent admission to the hospital and a short course of oral glucocorticosteroids (Evidence D).

- If symptoms improve at 1 hour, but recur within 3 or 4 hours, more frequent doses of bronchodilator may be given (2 or 3 puffs hourly), and oral glucocorticosteroids should be administered. The child should be observed by the family/caregiver and might need to remain in the emergency room or have ready access to emergency care. Children who fail to respond to 10 puffs of inhaled rapid acting β_2-agonist should be referred to the hospital (Evidence D).

- If the symptoms resolve rapidly and do not recur for 1 or 2 hours, no further treatment might be required. The dose of bronchodilator may be repeated every 3 to 4 hours (up to a total of 10 puffs per 24 hours) and, if symptoms persist beyond 1 day, other treatments including inhaled or oral glucocorticosteroids are indicated (Evidence D).

Additional Treatment

The addition of a short course of oral glucocorticosteriods or leukotriene modifiers is of doubtful value. Although such interventions have been shown to result in statistically significant benefits in several studies, their clinical benefit, particularly on such endpoints as hospitalizations and longer-term outcomes, have been inconsistent[92-99,109] . The exception to this pattern is one study of 1,500 μg of fluticasone proprionate daily, which reduced the need for oral glucocorticosteroids from 18% to 8% of subjects[101] (Evidence D).

Inhaled glucocorticosteroids: For children not previously on inhaled glucocorticosteroids, an initial dose of inhaled glucocorticosteroid twice the low daily dose indicated in Table 4 may be given and continued for a few weeks or months (Evidence D). For those already on inhaled glucocorticosteroids, doubling the dose has not been documented to be effective in older children and there is no evidence to support this approach in children 5 years and younger (Evidence D).

Oral glucocorticosteroids: If used, oral glucocorticosteroids (syrup or tablets) are preferred to systemic (intramuscular or intravenous) administration, but are most effective when administered early in an exacerbation. A dose equivalent to prednisolone 1-2 mg/kg/day, with a maximum of 20 mg in children under 2 years of age and 30 mg for children 2-5 years, is recommended (Evidence D). A 3-5 day course is sufficient in most children and can be stopped abruptly (Evidence D).

Table 8 provides a summary of management of acute severe asthma in children 5 years and younger.

Table 8: Initial Management of Acute Severe Asthma in Children 5 Years and Younger*

Therapy	Dose and Administration
Supplemental oxygen	Deliver by 24% face mask (flow set to manufacturer's instructions, usually 4L/minute) Maintain oxygen saturation above 94%
Short-acting β_2-agonist	2 puffs salbutamol by spacer, or 2.5 mg salbutamol by nebulizer Every 20 minutes for first hours[a]
Ipratropium	2 puffs every 20 minutes for first hour only
Systemic glucocorticosteroids	Oral prednisolone (1-2 mg/kg daily for up to 5 days) or Intravenous methylprednisolone (1 mg/kg every 6 hours on day 1; every 12 hours on day 2; then daily)
Aminophylline[b]	Consider in ICU: loading dose 6-10mg/kg lean body weight Initial maintenance: 0.9 mg/kg/hour Adjustment according to plasma theophylline levels
Oral β_2-agonist	No
Long-acting β_2-agonist	No

[a] If inhalation is not possible an intravenous bolus of 5 µg/kg given over 5 minutes, followed by continuous infusion of 5 µg/kg/hour. The dose should be adjusted according to clinical effect and side effects[84].

[b] Loading dose should not be given to patients already receiving theophylline.

Follow-up of Exacerbations

Children who have recently had an asthma exacerbation are at risk of further episodes and require follow-up to ensure complete recovery, to establish the cause of the exacerbation, and, when necessary, to establish appropriate maintenance treatment (**Evidence D**). Prior to discharge from the emergency department or hospital, family/caregivers should receive the following (all are **Evidence D**):

- Instruction on recognition of signs of recurrence and worsening of asthma. The factors that precipitated the exacerbation should be identified and strategies for future avoidance of these factors implemented
- A written individualized action plan including details of accessible emergency services
- A supply of bronchodilator and, where applicable, the remainder of the course of oral or inhaled glucocorticosteroids or leukotriene modifier
- Careful review of inhaler technique
- Further treatment advice:
  - The bronchodilator should be used on an as-needed basis, but the daily requirement should be recorded to assure it is being decreased over time to pre-exacerbation levels
  - Initiate or continued inhaled glucocorticosteroids (for first month after discharge, 3 times low initial dose, then adjust dose as needed)
- A follow-up appointment within 1 week and another within 1-2 months depending on the clinical, social, and practical context of the exacerbation

Before discharge, the condition of the patient should be stable, e.g., out of bed and able to eat and drink without problem.

SUMMARY: KEY MESSAGES

1. The goal of asthma treatment, to achieve and maintain control of the disease, can be achieved in a majority of children 5 years and younger with a pharmacologic intervention strategy developed in partnership between the family/caregiver and the health care practitioner.

2. Maternal smoking during pregnancy and exposure to environmental tobacco smoke early in life are associated with a greater risk of developing wheezing illnesses in childhood, as well as with reduced lung function later in life. Therefore, every effort should be made to avoid exposing children to tobacco smoke.

3. Making a diagnosis of asthma in children 5 years and younger may be difficult because episodic respiratory symptoms such as wheezing and cough are also common in children who do not have asthma, particularly in those younger than 3 years.

4. A diagnosis of asthma in young children can often be made based largely on symptom patterns and on a careful clinical assessment of family history and physical findings. The presence of atopy or allergic sensitization provides additional predictive support, as early allergic sensitization increases the likelihood that a wheezing child will have asthma.

5. Asthma education should be provided to family members and caregivers of wheezy children 5 years and younger when wheeze is suspected to be caused by asthma.

6. For all patients with a confirmed diagnosis of asthma, the goal of treatment is to achieve control of the clinical manifestations of the disease and maintain this control for prolonged periods, with appropriate regard to the safety and cost of the treatment required to achieve this goal.

7. The prolonged use of high doses of inhaled or systemic glucocorticosteroids must be avoided by ensuring that treatment is appropriate and reduced to the lowest level that maintains satisfactory current clinical control.

8. A pressurized metered-dose inhaler (MDI) with a valved spacer (with or without a face mask, depending on the child's age) is the preferred delivery system.

9. Several placebo-controlled studies of inhaled glucocorticosteroids in children 5 years and younger with asthma have found statistically significant clinical effects on a variety of outcomes, including increased lung function and number of symptom-free days, and reduced symptoms, need for additional medication, caregiver burden, systemic glucocorticosteroid use, and exacerbations.

10. Because of the side effects associated with prolonged use, oral glucocorticosteroids in young children with asthma should be restricted to the treatment of acute severe exacerbations, whether viral-induced or otherwise.

11. Rapid-acting inhaled β_2-agonists are the most effective bronchodilators available and therefore the preferred reliever treatment for asthma in children 5 years and younger.

12. A low-dose inhaled glucocorticosteroid is recommended as the preferred initial treatment to control asthma in children 5 years and younger.

13. If low dose of inhaled glucocorticosteroid does not control symptoms, and the child is using optimal technique and is adherent to therapy, doubling the initial dose of inhaled glucocorticosteroid may be the best option.

14. When doubling the initial dose of inhaled glucocorticosteroids fails to achieve and maintain asthma control, the child's inhalation technique and compliance with the medication regimen should be carefully assessed and monitored, as these are common problems in this age group.

15. Continued need for asthma treatment in children under age 5 should be regularly assessed (e.g., every three to six months).

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