

UPDATE 2003

From the desk of...

Sachdev HPS

President
Indian Academy of Pediatrics (2003)

 The various Sub-specialty Chapters of the Indian Academy of Pediatrics have an important role of providing evidence-based guidelines for various conditions to help the members impart quality care to their patients. In this context, I am happy to note that the Respiratory Chapter has sustained an effort to bring out the latest aspects of asthma management. The guidelines have been written with the Indian scenario in mind and have been presented in a unique reader friendly format. I am sure that the mainstream members of the Indian Academy of Pediatrics will benefit from this monograph while managing their patients suffering from this common malady.

Sd. Sachdev HPS

Shah NK

Hon. Secretary General
Indian Academy of Pediatrics (2002-2003)

 I have gone through the “Consensus Statement on the Diagnosis and Management of Asthma in Children” prepared by the IAP Respiratory Chapter in December 2001. I very much appreciate the hard work put in by the faculty involved in the revision of this document in Dec 2003.

I am indeed glad that the group of experts has revised the ‘Consensus Statement’. I am sure this new document will be of immense benefit to the member pediatricians while tackling patients with asthma on a day- to- day basis and serve as a ready reckoner for them.

Sd. Shah NK

Khubchandani RP

National Convenor
Asthma by Consensus (2001 and Update 2003)
President Respiratory Chapter (2003-2004)

 Since this publication in 2001 there has been a flurry of evidence based information released in the form of at least 3 international guidelines on asthma management.

The respiratory chapter thus found it fit to update this publication. A draft committee reviewed all the recent literature and modifications were circulated to the entire consensus group.

You are now reading about asthma management as it should be practiced in 2004.

Sd. Khubchandani RP

From the desk of...

Mathur YC

President

Indian Academy of Pediatrics (2001)

 I am extremely happy to know that IAP Respiratory Chapter is coming out with a consensus statement on asthma management in childhood. I congratulate them for this academic document on a very common respiratory problem confronted by all IAP members. This will help in day-to-day practice and for the care of our loved ones.

As you all know, due to industrialization and environmental factors, the incidence of childhood asthma is increasing. Such a document on asthma will ensure uniformity in management. I do hope, as follow up, zonal seminars will be conducted which will involve sharing of experiences in management of asthma. This document will serve as a guide to all practising pediatricians across the country and maintain uniformity and these IAP guidelines will be used as referral material.

Sd. Mathur YC

Hathi GS

Hon. Secretary General

Indian Academy of Pediatrics (1998-2001)

 The rapid rise in environmental pollution, particularly in urban areas, has shown a marked increase in the incidence of pediatric asthma in the last decade.

I am happy to know that the IAP Respiratory Chapter is publishing guidelines on the management of pediatric asthma. The change in understanding of etiopathology of asthma, the easier availability of simple as well as advanced investigations and advances in the management of pediatric asthma has made it necessary for pediatricians to keep abreast, so that the benefits can be transferred to our little patients.

I am happy to note that these guidelines are written in a very lucid manner and the step by step method of discussion has made it very easy to understand and follow.

Pediatricians will find these guidelines very practical and useful.

Sd. Hathi GS

From the desk of...

Sukumaran TU

President
IAP Respiratory Chapter (2001-2002)

*A*s you are aware childhood bronchial asthma is a disease which is underdiagnosed and undertreated. The prevalence of bronchial asthma is increasing all over the world as shown by the ISAAC study. Preventive therapy of bronchial asthma is very essential to prevent further deterioration in pulmonary function. Patient, parent and pediatrician education go a long way in successful asthma management. With this view in mind, we proudly present before you new guidelines for the management of childhood bronchial asthma.

Sd. Sukumaran TU

Kamath SS

Secretary
IAP Respiratory Chapter (2001-2002)

I am extremely glad that we have been able to publish this booklet on management of childhood asthma. This is really a consensus of the opinions of experts from different parts of the country. Here I would like to thank Dr. Raju Khubchandani for taking up the responsibility to co-ordinate and bring out this booklet in record time. I hope that this will be extremely useful to practising pediatricians in the whole country.

Sd. Kamath SS

From the desk of...

Khubchandani RP

National Convener
Asthma By Consensus 2001

A visit to the website, Pub Med, reveals that over the last decade asthma ranks as one of the most frequently written about diseases. The reasons for this are not difficult to seek. A significant increase in prevalence and diagnosis, paradigm changes in principles of management and a wide menu of new drugs and devices are the responsible elements.

The setting in India for children with asthma is unique in more ways than one. Asthma carries a taboo with it and newer concepts of inhaled treatment have been difficult to swallow (!). Add to this the fears regarding cost and adverse effects or the novel triggers that may prevail in our setting and we have a mammoth task of physician-parent-patient education before us. The burden is not lightened when we note the marked paucity of original research data emanating from our midst.

Pediatricians in India interested in pulmonology have been sensitive to these facts and changing trends. Above all they have been aware of the inadequacy of blindly adapting guidelines published in other countries. Soon after the National Heart Lung and Blood Institute (NHLBI), USA, published their revised guidelines in 1997, a consensus group met in Chandigarh in April 1998 to evolve a document, which would address the ground realities that the Indian milieu has to offer. The document (*Indian Pediatrics*, 1999; 36: 157-65) was later endorsed by the IAP Respiratory Chapter and is widely regarded as the first attempt to standardize asthma management in the children of our country. With over 3 years having gone by, the Respiratory Chapter deemed it appropriate to update previously published data and present it in a user friendly manner for a practising pediatrician.

'Are national guidelines followed?', screamed the subtitle of an article that addressed physician practices caring for children with asthma in the US (*Pediatrics* 2000; 106(4): 886-92). Unfortunately, wrote the author, there is evidence that dissemination of guidelines alone has minimal impact on physician behaviour. Although changes in understanding of a condition or treatment do not always result in immediate changes in prescribing practices, guidelines are a pre-requisite for actual practice change. Follow up action to increase compliance with guidelines would be an equally important activity the chapter would now have to undertake.

These consensus guidelines are derived by a team of pediatricians (names appear on the inside back cover) from across the country. I acknowledge the expert comments of Prof. Peter D Sly (MD, FRACP, Head, Division of Clinical Sciences; Director, Clinical Research and Education, Princess Margaret Hospital for Children, Australia).

It has taken a little over a thousand collective man-hours to prepare a document that should probably take a little over an hour to read. It is sincerely hoped that ABC (Asthma By Consensus) will truly become abc (a bedside companion)

Sd. Khubchandani RP

Those who made this book possible

President

IAP Respiratory Chapter
Sukumaran TU *Ettumanoor*

Secretary

IAP Respiratory Chapter
Kamath S Sachidananda *Cochin*

National Convener

Khubchandani RP *Mumbai*

Draft Writing (2001)

Khubchandani RP *Mumbai*
Kenia Priti *Mumbai*
Amdekar YK *Mumbai*
Singh Varinder *Delhi*

Draft Writing Update 2003

Fernandez Daphin *Mumbai*
Gajendragadkar Ajit *Mumbai*
Khare RD *Mumbai*
Khubchandani Raju *Mumbai*

Researcher (2001)

Kenia Priti *Mumbai*

Researcher (2003)

Fernandez *Mumbai*

Working Group

(*zonal convenors)

North

Kabra SK
Delhi
Kumar V
Delhi
Singh Daljit
Ludhiana
Singh Meenu
Chandigarh
Singh Varinder*
Delhi
Tilak Raj
Kanpur

South

Balachandran A*
Chennai
Kamath SS
Cochin
Mahesh Babu R
Bangalore
Nagabhushana S
Bangalore
Narayanan Noel
Thiruvananthapuram
Ranjit Suchitra
Chennai
S.Sushma Bai
Kottayam
Sukumaran TU
Ettumanoor
Suresh Babu
Davangere
Vijayasekaran D
Chennai

East

Bhakta Santanu
Imphal
Chourjit Singh Ksh
Imphal
Das Debashish
Shillong
Ghosh Gautam*
Gupta Atul
Kolkata
Majumdar Nilartan
Kolkata
Mohanty Aswini
Cuttack
Patgiri DK
Dibrugarh
Roy Chowdhury S
Patna
Sahay Mamoranjan
Jharkhand

West

Balsekar M
Mumbai
Deopujari S
Nagpur
Kamath H
Goa
Khatav V
Mumbai
Modak S
Pune
Pherwani A
Mumbai
Shendurnikar N
Baroda
Ugra D*
Mumbai

Central

Agarwal Sanwar
Raipur
Mohana Kumar
Eluru
Rai Ashok
Varanasi
Sihare Pradeep*
Bilaspur

Advisory Group

Amdekar YK <i>Mumbai</i>	Lata Kumar <i>Chandigarh</i>	Paramesh H <i>Bangalore</i>
Bhave Swati <i>Mumbai</i>	Mukherjee Dilip <i>Kolkata</i>	Sethi GR <i>Delhi</i>
Chugh Krishan <i>Delhi</i>	Nair MKC <i>Trivandrum</i>	Somu N <i>Chennai</i>
Krishnan S <i>Chennai</i>	Pandit Anand <i>Pune</i>	Subramanyam L <i>Chennai</i>

Acknowledgement

Sly PD *Australia*

Layout and Production

Art Throb Creations *Mumbai*

Address for correspondence :

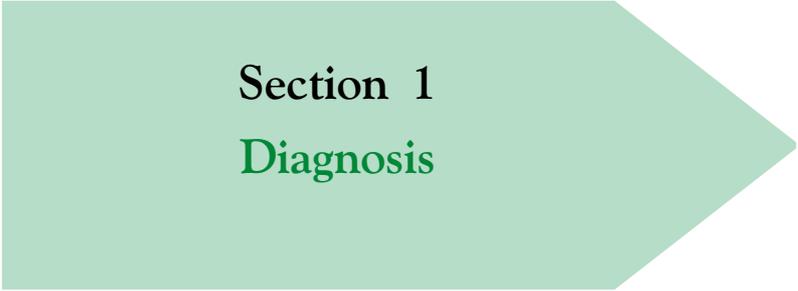
Dr. Raju P Khubchandani (Chairperson, IAP Respiratory Chapter)
31, Kailash Darshan, Opp. Nessbaug, Nanachowk, Mumbai - 400 007
e-mail: dr_rajukay@hotmail.com

How to read this book ?

The RIGHT-SIDED pages are numbered. They carry the 'CORE' knowledge and the matter flows from one right sided page to the next.

The LEFT-SIDED pages are not numbered. They carry 'MORE' information or explanatory notes to the matter on the corresponding right sided page.

Drug information and instructions to parents on usage of various devices are carried in the appendix, which is a continuous text.



Section 1

Diagnosis

more

Step 1 – Qualifying some terms

Recurrent: The adjective 'recurrent' is essential to the clinical definition of asthma. More than three episodes of airflow obstruction are considered significant by several widely followed guidelines.

Cough variant asthma: Recurrent isolated cough of unclear etiology may be a sole and distressing manifestation of asthma.

Nocturnal cough: Owing to circadian rhythms bronchial caliber in all humans is narrowest in the early hours of the morning (4 a.m.). Nocturnal cough may, thus, be the sole manifestation of asthma. In children under treatment, the persistence of nocturnal symptoms suggests the need for better control.

Recurrent pneumonic infiltrates: This is defined as more than two episodes in a year or more than three episodes over any period of time. Consider asthma in the differential diagnosis if the infiltrates recur in different lobes.

Step 2 – Pitfalls in auscultation

Localized wheeze: It is important to differentiate this from generalized wheeze, since it suggests a local obstruction e.g. foreign body.

Stridor: Care should be taken to differentiate stridor from wheeze in very small infants with rapid respiratory rates.

Conducted sounds: Noisy breathing may occur due to upper airway obstruction by enlarged tonsils/adenoids/allergic sinusitis/rhinitis. Snoring, mouth breathing, saliva staining the pillow, restless sleep, long unequal breathing pauses with sudden waking are the features that suggest upper airway obstruction.

Diagnosis and assessment of severity of asthma

Four easy steps

Step 1 Suspect asthma in all children whose presenting symptoms may suggest recurrent airflow obstruction

Symptoms suggestive of recurrent airflow obstruction
<ul style="list-style-type: none"> • Recurrent wheeze • Recurrent isolated cough • Recurrent breathlessness • Nocturnal cough • Tightness of chest

Also consider asthma in the following clinical situations

- Recurrent pneumonic infiltrates in different lobes
- Recurrent 'lower respiratory infections'

Step 2 Identify signs that suggest generalized airflow obstruction

Signs suggestive of generalized airflow obstruction
<ul style="list-style-type: none"> • Generalized rhonchi • Prolonged expiration • Chest hyperinflation

All asthmatic children do not wheeze

Beware of pitfalls in auscultation

Asthma being characteristically episodic, there may be no signs at the time of evaluation

more

Typical features

Afebrile episodes: This feature may help to differentiate asthma from infectious causes of wheezing in early childhood (page 3). Prolonged cough and / or wheeze after viral respiratory infections may suggest asthma.

Personal atopy: If a child has other manifestations of atopic disease, the risk of asthma increases. Look for flexural dermatitis, eczema and allergic rhinoconjunctivitis which are other atopic manifestations. Pre-existing eczema is probably most important – mainly because eczema is common in the first year of life and thus, predates the development of asthma in most individuals.

Atopy / Asthma in a parent or sibling: This doubles the risk of asthma in the child. If both parents have asthma the risk is more than three times as compared to the general population.

Exercise / Activity: In a smaller child, laughing or crying may provoke symptoms.

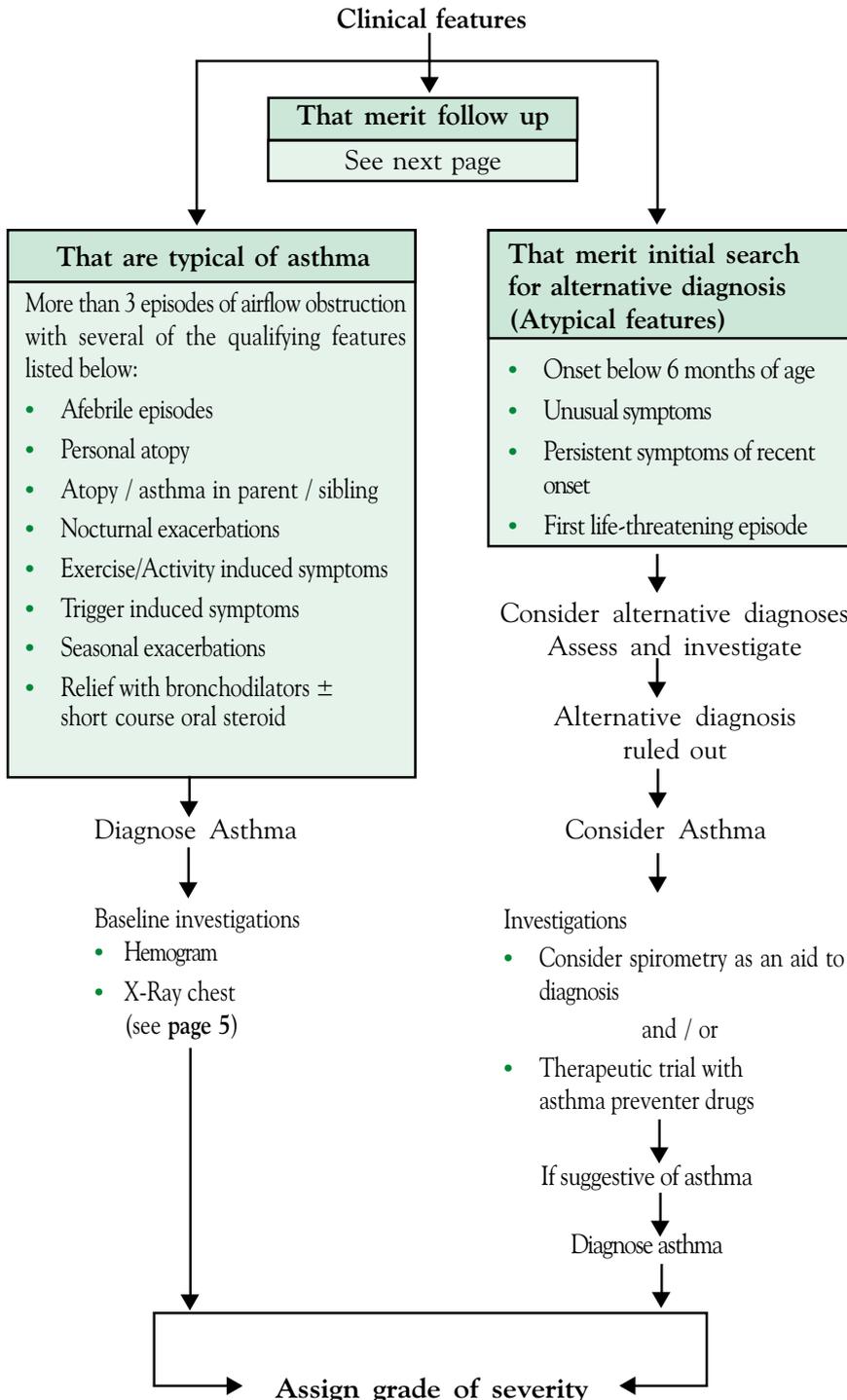
Triggers: These are usually inhaled irritants or aeroallergens (page 10).

Seasonality: Sudden temperature changes, flowering season and harvesting time are risk situations. This feature can be judged only after observation over a sufficient time period.

Relief with bronchodilator ± short-course oral steroid: A past history of usage of such drugs with relief or a therapeutic trial with these drugs in a case presenting for the first time are of great importance. This is a clinical indicator of reversible airflow obstruction. The regime is discussed under management of an acute attack (page 18).

Alternative diagnoses	Investigations
Onset below 6 months of age	
Choking episodes, vomiting, symptoms related to feeds	Aspiration syndromes e.g. GE reflux
Short prodrome (fever, upper respiratory and gastrointestinal symptoms)	Bronchiolitis
Symptoms and signs suggestive of impending cardiac failure, cyanosis, murmur	Congenital heart disease
Persistent respiratory symptoms	
Persistent cough, upper airway symptoms, fever	Adenoiditis, sinusitis
Persistent cough, constitutional symptoms, tuberculosis contact, adenopathy	Tuberculosis
Unusual symptoms	
Recurrent multifocal bacterial infections including respiratory symptoms	Immunodeficiency states
Recurrent respiratory symptoms, clubbing, unequal lung signs, coarse crepitations	Mucociliary defects
Recurrent respiratory symptoms, consanguinity, malabsorption, failure to thrive	Cystic fibrosis
First life-threatening episode	
History suggestive of foreign body inhalation, localized wheeze, unequal air entry	Foreign body
History suggestive of diet allergy (see page 10)	Diet allergy

Step 3 Assess clinically to qualify the above symptoms



In children, asthma is a clinical diagnosis, made by evaluation over time, either retrospectively or prospectively

Investigations help in confirming or ruling out alternative diagnoses, rather than in diagnosing asthma

more

Situation 1

In children with a strong family/personal history of atopy, asthma may be suspected even after the first afebrile wheezy illness. Early recognition of asthma in this situation promotes an early and active approach in terms of advice to parents, trigger avoidance and pharmacotherapy.

Situation 2

As mentioned earlier, asthma is the commonest cause of recurrent airflow obstruction in the older child. Early onset asthma i.e. onset in infancy / toddlerhood is, however, well recognized.

There exists a group of infants who are born with anatomically small airways. This predisposes them to wheeze with viral infections (wheeze associated with lower respiratory infections). Each viral infection results in an inflamed hyperreactive airway and further narrowing of airway caliber. As these infants grow older, the airways grow in size and the symptoms progressively abate. Thus, not all wheeze and cough are caused by asthma and caution is needed to avoid giving infants and young children inappropriately prolonged asthma therapy.

On the other hand, asthma in early childhood is frequently underdiagnosed (receiving labels such as recurrent bronchitis, asthmatic bronchitis, wheezy bronchitis and recurrent upper respiratory tract infections) and thus, many infants and young children are deprived of the benefits of preventer therapy. Therapeutic strategies for wheezy infants must address the possibility that for those who will go on to develop asthma, a prolonged delay in anti-inflammatory treatment leads to poor growth, school absenteeism, a poor quality of life and possibly to a permanent loss in pulmonary function.

In deciding when to initiate daily long-term control therapy, the clinician must, therefore, weigh the long-term effects of inadequately controlled asthma versus the possible adverse effects of medications given over prolonged periods. Initiation of the long term control therapy should be considered strongly for infants and young children who in the past year have had more than three episodes of wheezing that lasted more than 1 day and affected sleep, AND who in addition have identifiable risk factors for development of persistent asthma as indicated by either a) a physician diagnosis of atopic dermatitis or a parental history of asthma OR b) two of the following conditions: physician diagnosed allergic rhinitis, greater than 4 percent peripheral blood eosinophilia*, or wheezing apart from colds. It should also be considered if they consistently require symptomatic treatment more than two times per week or have severe exacerbations (requiring inhaled beta 2 agonist more frequently than every 4 hours over 24 hours) that occur less than 6 weeks apart. If clear benefit is not observed within 4-6 weeks, alternative diagnoses or therapy must be considered.

* In our setting, parasitic infections are a common cause of peripheral blood eosinophilia

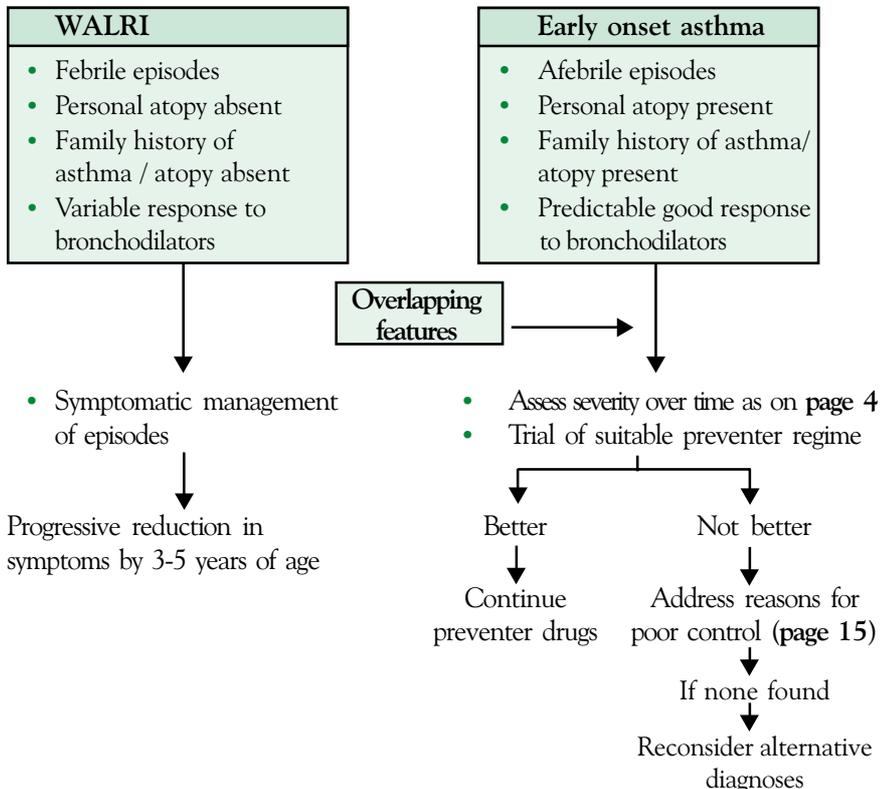
Step 3 continued Clinical features that merit follow up

Situation 1: < 3 episodes of symptoms of airflow obstruction in a child with a family history of asthma / atopy or personal history of atopy

- Action:**
- Follow up this child irrespective of age of onset.
 - Caution parents about future recurrences and advise them to maintain a diary of symptoms.
 - Identify trigger factors that may be operative in the child’s environment and advise avoidance / special actions.
 - Treat acute episodes as on **page 18**.
 - Continue to look for other qualifying features on follow up and assign a diagnosis of asthma.
 - Assess the severity over time prospectively as on **page 4** to plan a long term strategy.

Situation 2: Frequent symptoms of airflow obstruction in a child between 6 months - 3 years of age

Wheeze associated lower respiratory infection (WALRI) and early onset asthma are the common causes of wheezing in this age group. While children with asthma do benefit from a preventer drug regime, preventer therapy in WALRI continues to be subject of debate.



Early recognition of asthma leads to early intervention

Distinct pathogenic processes contribute to bronchoconstriction, but the differing wheezing phenotypes may be difficult to set apart in the clinical setting

The toddler who wheezes frequently is often a management dilemma. "To treat or not to treat is the question"

more

Grading of asthma

In the event of overlapping criteria, it is appropriate to label the patient as belonging to the higher grade.

In each grade the patient may have a mild, moderate or severe exacerbation. Grading the severity of acute episodes is described on **page 17**.

Note that while grading, the patient may be on treatment with preventer drugs.

Since asthma is a dynamic condition, the grade of severity may change over time.

Peak expiratory flow (PEF) in diagnosis (page 5)

Step 4 Having diagnosed asthma, quantify the symptoms over a period of time to assess severity

Grades of severity of asthma	Symptoms of airflow obstruction	Night time symptoms	Peak expiratory flow (PEF)*
Grade 4			
Severe persistent	<ul style="list-style-type: none"> • Continuous • Limited physical activity 	<ul style="list-style-type: none"> • Frequent 	<ul style="list-style-type: none"> • $\leq 60\%$ of personal best • $> 30\%$ diurnal variation**
Grade 3			
Moderate persistent	<ul style="list-style-type: none"> • $>$ once a day • Attacks affect activity 	<ul style="list-style-type: none"> • $>$ once a week 	<ul style="list-style-type: none"> • $> 60\% - < 80\%$ of personal best or • $> 30\%$ diurnal variation**
Grade 2			
Mild persistent	<ul style="list-style-type: none"> • $>$ once a week but $<$ once a day 	<ul style="list-style-type: none"> • $>$ twice a month 	<ul style="list-style-type: none"> • $\geq 80\%$ of personal best • 20-30% diurnal variation**
Grade 1			
Mild intermittent	<ul style="list-style-type: none"> • $<$ once a week • Asymptomatic and normal between attacks 	<ul style="list-style-type: none"> • $<$ twice a month 	<ul style="list-style-type: none"> • $\geq 80\%$ of personal best • $< 20\%$ diurnal variation**

Grading severity helps to decide the optimal preventer regime for long-term control

* Not essential

** A diurnal variation of $< 10\%$ in PEF values is normal. Lowest PEF levels are seen on waking and highest levels about 12 hours later.

Note:

Children with intermittent asthma but severe exacerbations should be treated as having moderate persistent asthma.

more

Investigations in diagnosis

Hemogram: In asthma, as in other atopic states, mild eosinophilia is common. Diethyl-carbamazine is often irrationally prescribed in the setting of wheezy illness with mild eosinophilia. Its use should be reserved for tropical eosinophilia, which should be considered when the absolute eosinophil count exceeds 3000 / cumm.

X-Ray chest: A baseline chest X-Ray is advisable in every case to exclude other diagnostic possibilities mimicking asthma e.g. congenital anomalies, foreign body. Repeat radiographs at frequent intervals or with every exacerbation are not required. In most cases, the chest X-Ray is normal between episodes. Evidence of generalized hyperinflation may be present in those with severe symptoms or in poorly controlled cases.

Spirometry: While spirometry offers objective and sensitive criteria, by no means are these specific to a diagnosis of asthma. Spirometric findings are thus, to be interpreted in concert with the clinical setting. In children below 7-8 years, spirometry is difficult to perform. It is technician dependent and reproducibility of test results is poor. Spirometric results only reflect the lung function on the day of testing and may thus be normal since asthma is a dynamic condition. The procedure is expensive and the equipment is not widely available. For all these reasons, the consensus group feels that spirometry has a very restricted role in the diagnosis of asthma in the Indian setting.

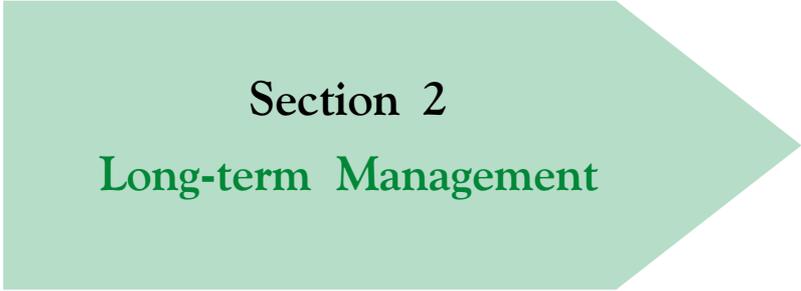
PEF: Standard values for various populations have not been defined. Thus, the currently accepted norm is to utilize 'personal best' values as a benchmark. In order to obtain personal best values, monitoring of PEF should be performed over one to two weeks (8.00 a.m. and 8.00 p.m. daily) during asymptomatic periods. This limits the role of PEF in initial diagnosis and assessment of severity but makes it better suited to monitor therapy and in follow up for reassessment of the grade of severity. Technique, compliance and reproducibility are also difficulties that may be encountered. Children can be trained to use the peak flow meter after approximately 5 years of age. Asthma, being a dynamic condition as mentioned earlier, the only merit of PEF monitoring over spirometry is that it can be performed over a one to two week period at home thereby giving a temporal profile.

Serum IgE, RAST, Skin allergy testing: These tests may help to confirm atopy, but not asthma. The various allergens have not been well standardized and skin allergy testing is cumbersome, expensive and not widely available. Results of these tests seldom contribute additionally to pharmacotherapy in managing most asthmatics. Hence, these tests are not recommended routinely by the consensus group in diagnosis of asthma.

The place of investigations in diagnosis

Which test ?	When ?	What information ?
Hemogram	As a baseline	May reveal mild eosinophilia in asthma
X-Ray chest	As a baseline	Essentially normal in asthma
Spirometry	Use is limited to situations where clinical diagnosis of asthma is in doubt, provided: <ul style="list-style-type: none"> the child can perform the test (Age) the equipment is available (Availability) the cost is permissible (Affordability) 	Establishes a diagnosis if: <ul style="list-style-type: none"> FEV₁ and FEV₁/FVC are reduced (Values relative to reference or predicted. Also examine flow volume curve) Improvement in FEV₁ by ≥ 12 % after inhaling short acting bronchodilator
Peak Expiratory Flow (PEF)	A poor tool for diagnosis. May be used when clinical diagnosis of asthma is in doubt (atypical presentation) and spirometry is unavailable, unaffordable or normal at the time of doctor visit.	Establishes a diagnosis of asthma when: <ul style="list-style-type: none"> >15 % increase in PEF after bronchodilator >15% decrease in PEF after exercise Diurnal variation of >10 % in PEF when not on bronchodilator therapy or diurnal variation of >20 % in PEF when on bronchodilator therapy
Serum IgE levels, RAST, Skin allergy testing	Not routinely indicated.	Indicate atopic state. Skin testing may be required prior to immunotherapy to identify incriminating allergens.

Investigations are not a pre-requisite to initiating treatment. In indeterminate cases, when spirometry is not feasible, a therapeutic trial with appropriate preventer regime is justified



Section 2

Long-term Management

Goals of long term asthma care

Aim for:

- **Freedom from**
Symptoms, including nocturnal cough
Acute attacks and emergency doctor / hospital visits
Frequent school absenteeism
Adverse drug effects
- **Normal**
Daily activities and sports participation
Growth charts
Peak expiratory flow / spirometry

Towards reaching the goals...

- **Patient education**
- **Pharmacotherapy**
Initiating inhaled therapy
Selecting the optimal preventer regime
- **Dealing with triggers / precipitants**
- **Addressing special situations**
Concurrent medical conditions
Seasonal asthma
Surgery
Exercise induced asthma
- **Follow up**
Periodic assessment / monitoring
Duration of therapy
Place of investigations
- **Dealing with poor asthma control**
- **Other treatment modalities**

*Keep the child
subjectively and
objectively
healthy*

more

*At the first consultation, give the patient
your time, more than your prescription*

Patient education: partnering a long term strategy with the parents

Patient education is the most important facet of management of childhood asthma. Besides parents, involve the child (if possible) and other caregivers in the discussion.

The ten commandments (Checklist of inputs to parents during the first consultation)

- Discuss that asthma is a chronic condition with episodic symptoms and explain the need for continuous preventer drugs for certain grades of asthma.
- Emphasize that the drugs used ‘control’ but do not ‘cure’ asthma. Reassure parents that a majority of children outgrow their symptoms.
- Clear myths and misconceptions regarding inhaled therapy and emphasize merits of the inhaled route.
- Discuss the selected regime and address concerns regarding usage of steroids.
- Discuss the usage and maintenance of the inhaler device selected. Advise the parent to carry the inhaler device at each follow up visit.
- Counsel regarding approximate time taken to note improvement and emphasize the need for compliance with the prescribed preventer drugs.
- Advise regarding dealing with triggers / precipitants. Emphasize that diet has a small role in causation of symptoms.
- Advise the parent to maintain a diary of events and carry it at each follow up visit. They may record days that there are events such as daytime cough, nocturnal cough, wheeze, reliever medication use, doctor /hospital visits. (The prototype asthma diaries described in literature are detailed and need to be logged in daily and may be used in those with persistent symptoms or poor control. Maintaining a daily diary even on ‘well days’ is less likely to be complied with).
- Educate regarding management of acute exacerbations at home prior to doctor contact.
- Schedule the first follow up visit 2-4 weeks after institution of preventer regime. Subsequent visits may be planned 2-8 weekly according to the severity or earlier in case of recurrences.

The eleventh commandment (During follow up)

Identify any lacunae in understanding and reinforce the above in subsequent meetings.

Consider calling these children at protected times; start or end your day with a session

Group education reassures parents that they are not alone and helps them interact. Besides, it saves time

more

More about devices

MDI: Difficulty with coordination of actuation and inhalation precludes the usage of this device without a spacer in most individuals. Direct usage also causes deposition of more than 80 percent of actuated dose in the oropharynx. Usage with a spacer is always strongly recommended.

Chlorofluorocarbons are known to damage the ozone layer and are now being replaced by hydrofluoroalkanes. Inhalers which use propellants other than chlorofluorocarbons have been recently introduced in India. They do not offer any additional patient benefit but are environment-friendly.

MDI with Spacer*: The age at which one may expect the cooperation and understanding of a child to move from an 'active' device i.e. MDI with spacer with mask to a 'passive' device i.e. MDI with spacer is approximately 3 years, as tidal breathing is adequate to ensure delivery of drug to the lower airways. An older child may be taught to breathe in and pause after inspiration to a count of '5'. After each actuation of the MDI, the child should be made to inhale a few times rather than breathing once after multiple actuations.

***Spacers:** Spacers or volume holding chambers eliminate the need for coordinating inhalation and actuation while using an MDI. For a child on a regime containing medium or high dose inhaled steroid, use of a spacer with the MDI minimizes oral steroid deposition and consequently, the local effects of inhaled steroid therapy viz. thrush and dysphonia. Mouth washing and gargling are further effective in reducing the quantity of swallowed drug.

Small and large volume spacers are equally efficacious in drug delivery to lungs. However, small volume spacers may not entirely overcome the problem of coordination of actuation and inhalation. Some children cannot generate the inspiratory flows required to move the valve of the valved spacers. In such children a valved spacer may be used with the child lying down and the spacer vertical so that the valve lies in the open position or alternatively a non-valved spacer may be used. Polyamide spacers are stated to have lesser electrostatic charge lining the inside of the chamber thus making more aerosol available for inhalation.

Spacers should be cleaned monthly rather than weekly as per manufacturers recommendations or performance is adversely affected. They should be washed in soap water solution and allowed to dry in air. The mouthpiece should be wiped clean of detergent before use. Spacers should be replaced yearly for optimum benefit.

Commercially designed spacers give assured drug delivery, though preliminary data on home made spacers (mineral water bottles) is encouraging. Such home made devices may be considered if cost is a barrier to initiating inhaled therapy.

DPI: By the age of 7-8 years, the child can usually be trained to generate appropriate inspiratory flow (30 - 60 L/min) which is required for optimal drug delivery using a DPI. Lower or higher rates lead to either oral or pharyngeal deposition. During acute exacerbations, the patient may not be able to generate flows within the specified range. Thus, in this setting the use of DPIs may lead to sub-optimal drug delivery.

Nebulizer: The purchase of a nebulizer for home use is not routinely recommended. MDI and DPI ensure adequate drug delivery and are significantly cheaper and more convenient for daily preventer therapy. MDIs control the size of droplets of aerosol better than nebulizers and rapidly deliver a measured amount of medication. Even in management of acute episodes at home, the use of MDI with spacer and mask has been found to give results comparable to a nebulizer. Nebulizers, however, do find place for management of acute episodes in emergency room / inpatient settings, since,

- In acute severe episodes inability to generate optimal inspiratory flows and reduced tidal volumes may result in unreliable delivery. The nebulizer delivers the drug over a longer period and overcomes the problems of reduced delivery per breath.
- Mixing of drugs e.g. short acting beta₂ agonist (SA β₂ agonist) with anticholinergic nebulizer solutions is possible.

Initiating inhaled therapy

Select the appropriate device

Device	Age	For preventer regimes (daily use)	For acute episodes	
			Home	Hospital
Metered Dose Inhaler (MDI)	Children > 10-12 years may learn appropriate usage. However, a spacer is still recommended	For regimes incorporating cromoglycate or low dose inhaled steroid with or without long acting beta ₂ -agonist (LA β ₂ agonist)	May treat mild episodes	No role
MDI with Spacer*	Suitable for all age groups. For smaller children (< 3 years) attach a face mask	For all preventer regimes. Recommended for patients on medium to high dose inhaled steroid	Recommended for mild-moderate episodes	Suitable for mild-moderate episodes
Dry Powder Inhaler (DPI)	May be used above 7-8 years of age	For regimes incorporating cromoglycate or low dose inhaled steroid with or without LA β ₂ agonist	May treat mild episodes	No role
Nebulizer	Suitable for all age groups	Do not recommend purchase	May be used if already purchased	Recommended mode for patients with severe episodes or on ventilator

*Spacer devices are inhaler aids used as accessories to MDIs. In smaller children who are unable to understand or co-operate, a facemask can be attached to the mouthpiece of the spacer. Commercially available spacers differ in size (small volume / large volume), design (valved / non-valved) and the material used (polyamide / polycarbonate). For practical purposes drug delivery through any of these is comparable. Home made spacers may provide an option.

Highlight advantages of the inhaled route to the parents

‘Smaller dose’: Contrast the milligram (mg) concentration of syrups and tablets with the microgram (mcg) concentration of the same drug in the inhaled form.

‘Target delivery’ - ‘Quicker action’: Drug is delivered directly to the site of action. Reliever drugs, therefore, act faster.

‘Safer’: Smaller dose and thus, much better safety profile than with oral therapy. This is particularly relevant for steroids.

Clear misconceptions that parents may harbour

Is inhaled therapy **addictive**? Emphasize that addiction liability is a property of the drug rather than device / route. Illustrate with an example that alcohol, though oral, is still addictive. Reiterate that none of the asthma medications are known to cause dependence.

Is inhaled therapy **strong**? Discuss advantages of inhaled treatment as above. Emphasize the microgram concentration of drugs used.

Is inhaled therapy **expensive**? The inhaler device is a one-time purchase. Only drugs need to be purchased subsequently. A few inhaled drugs may be slightly more expensive than oral drugs on a per dose basis but, discuss these in the context of the child’s well being, safety and reduced doctor / hospital visits.

Are inhalers **easy enough for children** to use? Discuss device selected and the ease of training required for usage.

Instruct parents and the child (if possible) regarding usage of the device (see appendix).

The advent of inhaled therapy will be known as the most important milestone in the history of asthma management

When it comes to inhaled therapy in asthma, children are not therapeutic orphans. New drugs and novel devices help children reap rich benefits

The metered dose inhaler with a spacer is the most versatile device. It can be used through all ages, for all the preventer regimes and for management of acute episodes

more

Alternative regimes

Alternative regimes such as cromones, leukotriene receptor antagonists, and SR theophylline are less effective than inhaled corticosteroids in mild persistent asthma. Furthermore, alternative add-on therapies to inhaled corticosteroids in moderate persistent asthma, which include leukotriene receptor antagonists and SR theophylline, are less effective than inhaled LABA.

Oral regimes are not necessarily a cheaper option; the cost per day of oral therapy being similar to regimes consisting of inhaled steroid alone. If initial expense is a constraint, home made spacers may be considered.

The drugs in the various regimes

Inhaled corticosteroids (steroids): Inhaled steroids are the most effective preventer drugs and are hence the 'gold standard'. Beclomethasone dipropionate (BDP), Budesonide (BUD), and Fluticasone propionate (FP) show benefit within 2 to 3 weeks of starting therapy.

Low dose refers to usage of inhaled BDP or BUD at < 400 mcg/day, medium dose at 400-800 mcg/day and high dose > 800 mcg/day. The corresponding dose of FP is half of these. All comparisons use CFC propelled BDP as a reference. When used in equivalent doses the efficacy and adverse effect profile are practically similar. Though twice daily administration of ICS is recommended, having achieved control, one can administer them once daily.

Local adverse effects such as thrush and dysphonia (because of laryngeal myopathy) are occasional. The smallest dose of ICS compatible with maintaining disease control should be used. At higher doses, add on agents, for example LABA, should be actively considered. Administration of ICS at or above 400 mcg per day of BDP or equivalent should be followed up for systemic side effects such as short-term growth suppression and adrenal suppression. Patients on high dose therapy need monitoring of growth and periodic ophthalmic assessment. In practice most patients require low to medium dose of ICS which are safe and devoid of any adverse effects. All the three compounds are also available as nasal spray for managing allergic rhinitis.

Inhaled long acting β_2 agonists (LABAs): Inhaled LABAs are the preferred add-on drugs to ICS for treatment of moderate persistent asthma in children above 5 years of age. Salmeterol / formoterol act synergistically when combined with inhaled steroids and have a steroid sparing role. They are not recommended for use alone in preventer therapy. This class of drugs is particularly effective in children with frequent nocturnal or exercise induced symptoms. For want of clinical data in younger children, package inserts advise their use beyond 4 years (salmeterol) or 5 years (formoterol). Potential for developing tolerance exists.

Sodium Cromoglycate: Cromoglycate has limited effectiveness but a strong safety profile in persistent asthma. It could be considered in treatment of mild persistent asthma as an alternative but inferior option to inhaled corticosteroids. The benefits of cromoglycate are usually evident about 3-4 weeks after starting the drug. Ideally, it should be used in 4 daily doses, but in school going children this is often not practical and 3 daily doses may be acceptable.

Leukotriene receptor antagonists (LTRAs): Zafirlukast (for children ≥ 7 years) and Montelukast (for children ≥ 1 years), are alternative options, but not preferred therapy for treatment of mild persistent asthma. They also may be used with ICS as add-on therapy in the treatment of moderate persistent asthma (preferred in children < 5 years) and as an alternative to inhaled LABAs in children > 5 years.

Theophylline: This drug is no longer recognized as a reliever. It possesses anti-inflammatory and immunomodulator properties and is recommended as an adjunct to inhaled steroids. These effects are seen at serum levels of 5-15 mcg/ml. Syrup formulations have a short duration of action and are, therefore, not suited for preventer therapy. Sustained release formulations are available, but their dosage forms may be suited only for older children.

Oral corticosteroids: If needed, prednisolone may be administered as a single morning dose in order to prevent compromise of the hypothalamic-pituitary axis. The morning dose is convenient for school going children and working parents.

Selecting the optimal preventer regime

Starting therapy:

Assess grade of severity of asthma. Start the regime appropriate to the grade assessed and titrate upwards if control is not achieved.

	Grade 4	First Choice	Other Options
	Severe persistent	Medium to high dose inhaled steroid + LABA <i>If needed</i> Add oral steroid	***
	Grade 3		
	Moderate persistent	Low dose inhaled steroid + LABA* or Medium dose inhaled steroids** <i>If recurring severe exacerbations</i> Medium dose inhaled steroid + LABA*	Low/medium dose steroid + Leukotriene receptor antagonist/SR theophylline*
	Grade 2		
	Mild persistent	Low dose inhaled steroid	Cromolyn, LTRA, SR theophylline* (Listed alphabetically)
	Grade 1		
	Mild intermittent	No daily medication	

* For children above 5 years only

** For children below 5 years

*** Evidence to date does not support using a third long-term control medication added to inhaled corticosteroids and long-acting inhaled β_2 -agonists in order to avoid using systemic corticosteroid therapy.

Note:

- At every grade of severity, acute episodes should be managed with reliever drugs as discussed on page 18.
- If a trial of an add-on treatment is ineffective, stop the drug (or in case of increased inhaled steroid, reduce to the original dose).

Onwards:

If goals of treatment achieved i.e. good control – step down treatment as discussed on page 13.

If goals of treatment not achieved i.e. poor control – step up treatment if required, as discussed on page 15.

Medication plans must accommodate the fact that asthma is both a chronic and a dynamic condition

more

Pets

Animal dander may persist for a few months after the pet is given away. Therefore, improvement in asthma may not be immediately evident.

Weather and temperature changes

In general, most acute episodes of asthma are reported in the winter and the rainy seasons.

Aspirin sensitivity

Aspirin and NSAIDs are not contraindicated in all children with asthma. The triad syndrome is very rare below 8 years of age and may pose an occasional problem in the adolescent. Onset of symptoms ranges from 30 minutes to 2 hours after drug ingestion and is not IgE mediated. There may be accompanying nasal, ocular, dermal or gastrointestinal manifestations.

Diet

The role of diet in the precipitation of asthma symptoms is over-emphasized in our setting. While nuts, eggs, chocolates, sea food and certain preservatives are the commoner food allergens, providing a general avoid list of food items to all patients is irrational.

Suspect food allergy only if :

- Symptoms are recurrent, invariable and occurring rapidly after ingestion of suspected food.
- Ingestion often leads to perioral rash and/or gastrointestinal symptoms in addition to respiratory symptoms.
- Sudden severe life threatening episodes occur without prior warning.
- A child has severe / poorly controlled asthma where other trigger factors have been ruled out or eliminated.

Confirm by avoidance and challenge, if necessary and feasible, with full resuscitative measures available.

Dealing with triggers / precipitants

Advise avoidance and / or special actions

Triggers	Special actions
Allergens	
• Dust mite antigen	• Remove carpets or upholstery that tend to gather dust • Use cotton sheets rather than woolen blankets • Sun the room • Dust mattresses periodically and expose them to sunlight • Encase mattresses and pillows in plastic covers • Keep soft toys away from sleeping area and wash weekly with hot water
• Molds and spores	• Attend to damp walls / leakages • Clean airconditioner filters monthly
• Cockroach antigen	• General hygiene measures to limit cockroach population • Insecticide spraying to be done while child is away
• Animal dander (pets)	• Gentle persuasion to give pet away • Pets not to be allowed in the sleeping area / bedroom • Bathe pet weekly
• Pollen (flowers)	• Avoid flowering plants indoors • Stay indoors during harvesting / flowering seasons
Irritants	
• Smoke* (cigarettes, agarbattis – incense sticks, etc.)	• Make house free from cigarette smoke • If usage absolutely unavoidable, limit to an area where the child is not exposed
• Mosquito repellent mats	• Advise usage of mosquito nets and long clothes, especially in the evening and night
• Chalk, fine dusts, sprays	
• Weather and temperature changes, iced drinks, cold baths	
• Occupational / Environmental**	• May have to consider change of residence / work unit
Precipitants	
• Viral infections	• At the onset of respiratory symptoms commence inhaled / oral short acting beta ₂ agonist • If a child is on a preventer regime of inhaled steroids, double the dose for 5-7 days • If exacerbation is severe or if previous history of severe exacerbation, consider rescue dose of oral steroids • If a child is on theophylline, beware altered levels caused by febrile illness
Drugs	
• Aspirin / NSAIDs	• Total avoidance in only the small subset of children having the triad syndrome- aspirin sensitivity, nasal polyposis / sinusitis and asthma. All cyclo-oxygenase inhibitors are contraindicated. Paracetamol is a safe option
• Propranolol	• Limited indications in pediatric age group
Diet	
• Food additives (sulphites, benzoates, monosodium glutamate, possibly tartrazine)	• Some children are sensitive to monosodium glutamate, an ingredient in Chinese food (ingestion causes Chinese restaurant syndrome)
• Dietary substances	• Make the child aware of his food sensitivity and inform all caregivers • List the possible foods containing the implicated substances • Warn about possible contamination which may occur when a safe food is cooked in the same utensil or stored in proximity to an offending food • Warn about situations with high risk e.g. party / restaurant eating • Educate regarding management of acute episodes

Inhaled allergens/ irritants and viral infections are the most important triggers

* Smoke also includes irritant fumes from kerosene stoves, coal stoves, crackers, fire places etc.

**Cottage industry at home e.g. carpet weaving, bidi / snuff making, flour mill, cow shed / haystack very near home.

more

Concurrent medical conditions

Allergic rhinitis: This is suspected in a child with afebrile episodes of rhinorrhoea, sneezing, stuffiness of nose, features of upper airway obstruction and nocturnal cough (postnasal drip). Examination reveals nasal mucosal edema, hyperemia, clear nasal discharge, post-nasal drip, 'cobblestone' pharyngeal wall, horizontal creases under the eyes (Dennie Morgan lines), bluish/dark discoloration under the eyes (allergic shiners) and a transverse crease across the bridge of the nose.

The dosage of nasal steroid spray should be added to that of inhaled steroid in order to compute the total dose of steroid therapy.

Newer antihistaminics lack anticholinergic and sedative properties and are safe and less troublesome to use in children with allergic rhinitis or eczema accompanying asthma. There is no role for continuing them as therapy in asthma in absence of allergic rhinitis.

Seasonal asthma

A few children experience asthma symptoms only in relation to certain pollens, spores or molds. The time of the year (harvesting or flowering season) may vary from place to place.

Surgery

Children with asthma are at risk for complications during and after surgery. Acute bronchoconstriction may be triggered by intubation, impaired cough reflex, atelectasis or respiratory infections. The likelihood of these complications depends upon the severity of the bronchial hyperresponsiveness, mucous hypersecretion and airflow obstruction.

Addressing special situations

Situation	Action
<p>Concurrent medical conditions</p> <ul style="list-style-type: none"> • Allergic rhinitis / sinusitis • Gastroesophageal reflux (GER) 	<ul style="list-style-type: none"> • Intranasal steroid sprays: Budesonide 100 mcg twice a day or Fluticasone/Mometasone 50 mcg once a day • Oral antihistaminics • Antireflux treatment • Avoid oral bronchodilators / theophylline
<p>Seasonal asthma</p>	<ul style="list-style-type: none"> • Daily preventer regime should be initiated prior to the anticipated onset of symptoms and continued throughout the season • Encourage indoor activities during such seasons
<p>Surgery</p>	<ul style="list-style-type: none"> • Review symptoms and medications used • For those who have received systemic steroids for longer than 2 weeks duration during past six months, intravenous hydrocortisone must be given 8 hourly on the day of surgery reducing the dose within 24 hours following surgery • For others, optimize lung function with oral steroid prior to surgery

Asthma and allergic rhinitis frequently co-exist – the concept of one airway, one disease

Perioperative steroids may be needed in this risk situation

more

Exercise induced asthma (EIA)

In some children, EIA may be the only manifestation of asthma, while in most patients it is an expression of poorly controlled asthma and in them, preventer therapy should be reviewed.

Non-pharmacological advice: Teaching the child the correct breathing technique and avoiding exercise on cold mornings, ensure that warm air reaches the lungs. Each individual has a threshold of activity above which EIA may occur. Initial exercise below that threshold (warming up) induces a latent period of about 1 hour during which span heavier exercise does not provoke symptoms.

Pharmacological advice: Optimal anti-inflammatory preventer medications will reduce airway responsiveness and consequently the occurrence of EIA.

SA β_2 agonist: They are good for those who exercise infrequently or when the exercise is planned. Tachyphylaxis is observed and therefore, these agents are not advisable if exercise is repeated throughout the day or over many days.

Inhaled LA β_2 agonist: They may be added in a child on a preventer regime of inhaled steroid whose exercise induced symptoms are persistent. Administration of short acting inhaled agents before exercise at school is not always practical in our setting and use of LA β_2 agonist with preventer regime is preferred. They may also be used in exercise induced asthma, especially if the time of exercise is not predictable or in children who take part in frequent sporting activities. Formoterol may be considered if exercise is expected early in the day owing to its rapid onset of action. With sustained usage of salmeterol (>1 month duration), the protective effect of each dose may reduce to 6-9 hours after administration.

LTRAs: They are useful whenever the exercise is too frequent or unpredictable or when exercise induced asthma exists in an otherwise well controlled child with mild asthma. Montelukast, in particular, is a long acting once daily drug and covers for the whole day. It can be used above the age of 1 year making it a preferred option in children below 5 years. Unlike with LA β_2 agonist, patients do not exhibit tolerance to the protective effect of LTRA.

Addressing special situations

Situation	Action
Exercise induced asthma (EIA)	<p>Non-pharmacological advice:</p> <ul style="list-style-type: none"> • For those not initiated to a particular game, encourage indoor sports, swimming, yoga • Avoidance of outdoor exercise on winter mornings • Practise nose breathing and slow deep breathing during exercise • Advise a short period of warming up within one hour of main activity • Notify teacher / coach about child's condition and advise the need for inhaled medication prior to activity <p>Pharmacological advice :</p> <p>For prevention</p> <ul style="list-style-type: none"> • Grade severity of asthma and institute suitable preventer regime. • If EIA persists, select additional options from below: <ul style="list-style-type: none"> A) Infrequent exercise: Inhaled SA β_2 agonist given 15-30 minutes before exercise. Helpful for 2-3 hours. B) Frequent exercise: Inhaled LA β_2 agonist. Protective effect observed 2-3 hours after salmeterol and within 1 hour after formoterol dose, lasting for 10-12 hours. <p style="text-align: center;">or</p> Leukotriene receptor antagonists (LTRAs) - Montelukast 4mg OD (children 1-4 years), 5mg OD (children 5-12 years) or 10 mg OD (children > 12 years) <p>For treatment</p> <p>If exercise induces symptoms, treat with inhaled SA β_2 agonists</p>

Exercise is the only trigger the child must be trained to conquer and not avoid

Exercise induced asthma should not limit either participation or success in sport

more

Monitoring weight and height

Untreated / Poorly controlled asthma is an important cause of failure to thrive. Once appropriate treatment is instituted, increase in growth velocity is noted. Growth velocity monitoring is also very important in children on high dose inhaled steroid / continuous oral steroid regimes. Such children also need periodic ophthalmic assessment for development of posterior subcapsular cataracts.

Adverse effects of theophylline

Serum theophylline levels need to be monitored in case of symptoms and signs of toxicity. Risk factors for toxicity are:

- Age less than 3 years
- Dose \geq 16 mg/kg/day
- Acute febrile illness
- Concomitant administration of macrolides, fluoroquinolones, anticonvulsant or antituberculous therapy.

Stepping down therapy

Reduction in therapy should be gradual because asthma can deteriorate at a highly variable rate and intensity.

Brittle asthma

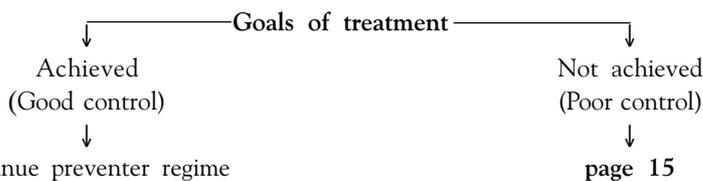
Brittle asthma is characterized by sudden and unpredictable fall in lung function, often with no evident triggers. The suddenness of the attacks suggests a neurogenic origin. Since some children are poor perceivers of initial bronchospasm and since the condition is labile, continuous long term peak expiratory flow monitoring is recommended. Inhaled bronchodilators, rather than rescue steroids, form the mainstay of therapy. Mechanical ventilation may be required for life threatening episodes.

Asthma in remission

A child with a past history consistent with persistent asthma who has neither had symptoms of airflow obstruction nor taken therapy for the past 12 months can be said to be in remission.

Follow up

- Call for first follow up at 1-2 weeks after initiating therapy and subsequent follow up 2-8 weekly.
- Review regime prescribed and diary of events since the past visit. Enquire specifically regarding bronchodilator usage, school absenteeism, limitation of activity and sleep disturbance.
- Assess if symptoms and signs of asthma are present at the time of visit and monitor weight and height.
- Check for adverse effects (relevant especially, if on oral drugs e.g. steroids, theophylline).
- Re-emphasize the need for continued compliance and clarify any doubts regarding asthma and its management (page 7).
- Assess whether goals of treatment (page 6) have been achieved.



- Continue preventer regime
- Follow up 2-8 weekly
- At 3-6 months, good control continues
- Reduce the doses / drugs
Follow the principle “Last in – First out”
In the prescribed regime step down on doses / drugs in reverse order of increase / introduction
Taper inhaled steroid by approx. 25% every 2-3 months
- Step down to the regime suitable for a lower grade of severity
- In moderate – severe persistent categories, consider spirometry annually, if feasible (page 14)
- Good control continues on low dose inhaled steroid (grade 2 regime) for 3-6 months
- Consider stopping preventer regime (remission)
- Advise continued trigger avoidance
- Advise home management plan in case of acute episodes (grade 1 regime)
- Follow up 3-6 monthly for a period of 1-2 years
- Counsel regarding possible future resumption of preventer regime if recurrences

Risk factors for asthma persisting into adulthood
<ul style="list-style-type: none"> • Female sex • Presence of eczema • Onset after the age of three years • Severe disease • Parental history of atopy / asthma

In most cases, follow up is essentially clinical

2 out of 3 children with asthma outgrow their symptoms

Clinic situations:

Recurrence of symptoms and signs of airflow obstruction during follow-up – Assess as mentioned under poor control. Beware the brittle asthmatic.

Irregular follow up – Assess grade of severity on presentation, prescribe appropriate preventer regime and reiterate need for compliance and follow up.

more

Peak expiratory flow (PEF)

In well-controlled children with mild-moderate asthma, routine PEF monitoring is not necessary. Introduction of the concept not only adds to the number of inputs that the parents have to imbibe initially and but also increases the initial cost.

The best time to introduce the concept of PEF monitoring is after an acute episode in response to the question, “How do I know an attack is coming ?” or “How do I judge the severity of an attack at home ?”.

All currently available peak flow meters are comparable. Low reading peak flow meters (those calibrated for a lower range of peak flow) are suited for pediatric use because of better sensitivity.

The norms for different child populations have not been standardized. It is inappropriate to use ‘normals’ in the charts supplied with the devices, since they do not apply to Indian children.

Ascertain what the normal value for the child is by observing the child’s ‘personal best’. This may be done by asking the parents / child to record 8 a.m. and 8 p.m. readings over 7-14 days when the child is asymptomatic. Recheck instrument efficacy and personal best periodically. Readjust personal best values upwards on a yearly basis to account for growth. Parental supervision of recordings is highly desirable because the measurement of PEF is dependent on effort and technique. Patients need instructions, demonstrations and frequent reviews of technique. The procedure is effort dependent – beware a malingering adolescent and ignore a reading when the child has coughed into the device.

Caution:

- PEF monitoring during acute episodes may worsen the symptoms by leading to collapse of peripheral airways during forced expiration.
- In long term daily monitoring, compliance may be an issue to deal with.

Usage of the device is described in the **appendix**.

Spirometry

Spirometry is most helpful to ensure that an apparently well-controlled child has normal lung function. A persistent bronchodilator response in an asymptomatic child is an indicator that preventer therapy should not be reduced.

Place of investigations in follow up

Which test ?	When ?	What information ?
<p>Peak Expiratory Flow (PEF) if:</p> <ul style="list-style-type: none"> • Trainable: Age approximately > 5 years • Tenable: Parents and child well initiated to therapy • Affordable: Able to afford cost of purchase of peak flow meter 	<p>Long term daily monitoring in moderate – severe persistent asthma or in brittle asthma</p> <p>Short term daily monitoring (2-3 weeks) in poorly controlled asthma</p>	<ul style="list-style-type: none"> • Establishes the individual patient’s personal best • Offers a quantitative measure of impairment of airway function • Detects changes in disease status that require reliever / preventer drugs • Evaluates responses to change in preventer therapy • Provides assessment of severity for patients with poor perception of airflow obstruction e.g. brittle asthmatics
<p>Spirometry if:</p> <ul style="list-style-type: none"> • Age: Approximately > 7-8 years • Availability: Equipment available • Affordability: Able to afford cost of test 	<p>Annually after initiation of treatment in moderate-severe persistent asthma</p> <p>Follow up of previous spirometry performed at time of diagnosis</p>	<ul style="list-style-type: none"> • Documents normalization of airway function if initially abnormal • Assesses maintenance of normal airway function • Bronchodilator response

PEF and spirometry may help to follow up older children in select situations

more

Correctable issues

Reasons for non-adherence:

Medication-related factors	Patient-related factors
<ul style="list-style-type: none">• Misunderstanding the need for preventer medication• Awkward regimes, e.g. multiple drugs / frequent dosing• Difficulties in delivering inhaled drugs to young children• Difficulty with device• Fear of side effects• Cost and availability	<ul style="list-style-type: none">• Denial of diagnosis• Inappropriate expectations of cure rather than control• Poor parental supervision• Cultural issues (traditions / beliefs)• Rebellious adolescent

Reasons for poor drug delivery – the 3 D's:

Drug	Device	Delivery
<ul style="list-style-type: none">• Incorrect dosing e.g. patient misunderstanding, school timings etc.	<ul style="list-style-type: none">• Inappropriate device for age• Spacer prescribed, but not being used• Old / Broken spacer• Blocked outlet of MDI• Empty MDI• MDI attached directly to mask• Spacer valve stuck because of humidity and improper cleaning• Nebulizer chamber outlet blocked	<ul style="list-style-type: none">• MDI used directly with poor coordination• Mask not apposed to face• Short quick breaths without inspiratory pause• Frivolous child• Inability to distract child through time taken for nebulization• Inability to generate sufficient inspiratory flow as required by certain devices

Short course steroid

A temporary increase in anti-inflammatory therapy using oral steroids may be indicated to re-establish control. However, one should resist overuse of oral steroid as an alternative to daily inhaled preventers.

Stepping up doses / grades

While stepping up, first step up in the same grade towards the higher range of doses and after this has been achieved, consider stepping up to a higher grade of preventer regime. At each step, give sufficient time for action of drugs.

Dealing with poor asthma control

A deterioration of asthma may be characterized by reduction in PEF, by failure of inhaled bronchodilators to produce a sustained response, by a reduced tolerance to exercise or activity or by the development of increasing nocturnal symptoms. In case of poor response to preventer treatment, the following steps are needed.

Rule out alternative diagnosis

Review the history, clinical features and investigations as indicated on page 2



Identify correctable issues

Adherence: Ascertain adherence with prescribed preventer regime. This may be done by questioning the parents or by comparing the prescribed dose count over a period of time with the number of canisters of inhalers used.

Drug delivery: Ask the parent / patient to demonstrate the technique of usage of the inhaler device in your presence.

Trigger elimination: Review the list of triggers. A detailed description of the child's environment may uncover a less obvious cause.



Concurrent medical conditions

Reassess the child for concurrent medical conditions viz. allergic rhinitis or gastroesophageal reflux that may be responsible for poor control.



Consider short course steroid

To regain control, a short course of oral prednisolone (1-2 mg / kg / day, maximum 60 mg / day, for 3-10 days) is often effective. If asthma symptoms do not recur and PEF remains normal, no additional therapy is necessary. However, if the prednisolone burst does not control symptoms, is effective only for a short period of time (less than 1-2 weeks) or needs to be repeated frequently, proceed to the next step.



Step up preventer dose regime after objective monitoring

In children with poor control, an objective assessment of daily trends in peak flow is desirable. Besides comparing with personal best values, diurnal variations need to be studied (page 4). Suitable changes in preventer regime can then be effected.



Specialist referral

If poor control still persists, repeat steps described above and consider specialist referral and infrequently needed treatment options e.g. methotrexate, immunotherapy (page 16). Consider complications of asthma such as allergic bronchopulmonary aspergillosis or bronchiectasis.

*Usually,
'difficult'
asthma has easy
solutions*

more

Immunotherapy

The course of allergen immunotherapy is typically of 3-5 years duration. Reactions to immunotherapy, especially bronchoconstriction are more frequent among patients with poorly controlled asthma compared to those with other atopic conditions such as allergic rhinitis. It is, therefore, important to have the asthma relatively stable when starting immunotherapy.

Immunomodulators

Immunomodulator drugs that reduce oral systemic steroid dependence should be used only in selected patients who are under the supervision of an asthma specialist. Although, some of the compounds have steroid sparing effects, their use in asthma remains complicated because of highly variable effects, potential toxicity and limited clinical experience. The drugs tried include troleandomycin, cyclosporine, methotrexate, gold, intravenous immunoglobulin, dapsone and hydroxychloroquine.

Complementary medicine

A review of multiple trials on the use of acupuncture in asthma concluded that they lacked quality and that the effectiveness of acupuncture in treating asthma has not been established. One trial, however, demonstrated benefit in EIA. Homeopathy, based on the "law of similars" and the use of infinitesimally small doses is as yet unproven for asthma. No controlled clinical trials have been reported on herbal medicines and the claims of effectiveness of western plant derivatives for asthma remain unsubstantiated.

Efficacy of 'Asmaron', an ayurvedic drug developed by CSIR is yet to be substantiated by scientific trials in children.

Other treatment modalities

Immunotherapy

- Usage:** • As an adjunct to preventer therapy.
- Indications:** • Poorly controlled asthmatics on maximal preventer therapy in whom allergy testing shows sensitivity to one or at the most two unavoidable indoor allergens e.g. dust mite.
- Prerequisites:** • Child > 5 years age.
• Only in a hospital setting with full resuscitative measures available.
• Experienced personnel.
• Asthma is relatively stable at the time of administration.
- Timing:** • Relatively early in the natural history of the disease before irreversible changes have occurred.

Immunosuppressive drugs

Metothrexate and gold salts have the best evidence for positive effects.

- Usage:** • As an adjunct to preventer therapy.
- Indications:** • Poorly controlled asthmatics on optimal preventer therapy with good compliance and elimination of triggers or in whom side effects of oral steroid are not tolerable.
- Prerequisites:** • Hospital setting.
• Experienced personnel.

Other modalities

Ketotifen: This oral mast-cell stabilizer has been used as a preventer drug. Its role in asthma is not well defined.

Yoga: Some qualitative research performed without including control groups has shown beneficial effect. It may be used as a supplement to pharmacotherapy.

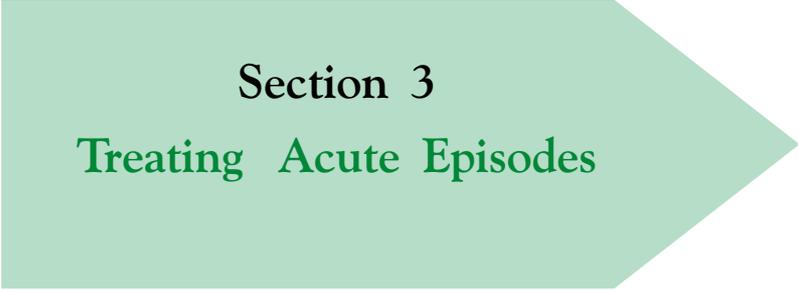
Acupuncture: Results of published trials examining long-term benefit are conflicting. Acupuncture has been demonstrated to have a mild bronchodilator effect superior to 'placebo' and 'no treatment' when measuring its effect on methacholine induced bronchoconstriction.

Lack of scientific evidence and experience prevents mention or discussion of other modalities such as homeopathy, ayurveda, fish therapy, heavy metal therapy etc.

Immunotherapy and immunomodulator drugs have definite evidence of benefit but find use in a very small select group

There is some preliminary evidence of the adjunctive role of yoga and acupuncture

No data exists to support other forms of complementary medicine



Section 3
Treating Acute Episodes

Assessment of severity of an acute episode

Assess for presence of 'Red flag' signs which suggest threat to life:

- Altered sensorium (drowsy or very agitated)
- Bradycardia
- Poor pulse volume
- Cyanosis (with 60 % oxygen)
- Excessive use of accessory muscles or state of exhaustion (vocalization limited to 1-2 words)
- Excessive diaphoresis
- Silent chest on auscultation
- ABG: rate of rise of $pCO_2 > 5$ mm Hg/hr, $pCO_2 > 40$ mm Hg, $pO_2 < 60$ mm Hg, metabolic acidosis ($-BE > 7-10$)
- SaO_2 on room air $< 92\%$

Assessment is clinical and has to be quick

If Red flag signs are absent, grade severity of exacerbation as below :

Score	Respiratory rate		Wheezing present*	Accessory muscle usage
	< 6 yrs	> 6 yrs		
0	< 30	< 20	None	No apparent activity
1	31-45	21-35	Terminal expiration with stethoscope	Questionable increase
2	46-60	36-50	Entire expiration with stethoscope	Increase apparent
3	>60	>50	During inspiration and expiration without stethoscope	Maximum activity
Add Score	0-3 Mild 4-6 Moderate >6 Severe		*If wheezing absent (due to minimal air flow), score > 3	

Ascertain the following information:

- Duration of episode
- Medications the child is already using as preventers
- Reliever medications taken before reporting to doctor
- Precipitating factors

Identify risk factors for acute severe asthma:

- Previous exacerbations:**
- Chronic steroid-dependent asthma
 - Prior intensive care admission / mechanical ventilation / life threatening episode
 - Poor compliance with preventer therapy
- Current exacerbation:**
- Rapid onset and progress of symptoms
 - Frequent visits to doctor in preceding few days
 - Visit to emergency room in past 48 hours
 - Economic and logistic constraints to healthcare access

The decision-making involves two parts; how to treat and where to treat

more

Oxygen

Hypoxia is due to ventilation-perfusion mismatch. SA β_2 agonists may increase the mismatch by attenuating the hypoxic pulmonary vasoconstriction. Hence, oxygen must always be administered along with nebulized SA β_2 agonists. Oxygen saturation must be maintained $> 91\%$.

Hydration

The child may need more than maintenance fluids initially due to increased insensible losses. Fluids are also required to make secretions less viscous. The amount required reduces when the patient is ventilated. SIADH must be anticipated, especially if the patient is on positive pressure ventilation.

Drugs used in management

Short-acting β_2 agonists (SA β_2 agonists): Salbutamol and terbutaline are similar in their efficacy, actions, kinetics and adverse effects. An isomer of salbutamol (Laevalbuterol), which is now available in the Indian market, is equipotent to salbutamol at half the dose but there is no added advantage as far as side effects or efficacy are concerned. While inhalation is the method of choice, oral alternatives may be justified in children whose symptoms are mild and infrequent. High dose / frequent nebulization with β_2 agonists may result in hypokalemia. This has been postulated as a cause for the occurrence of arrhythmia and sudden death. Long-acting β_2 agonists have no role in the management of acute episodes. If a child is on a preventer regime containing this class of drugs, there is an additional need for SA β_2 agonists for relief from acute symptoms.

Rescue steroid: Advent of this regime of steroid usage has drastically reduced morbidity and hospitalization in children with acute exacerbations. Steroid therapy directly reduces inflammation and also induces expression of β_2 agonist receptors. Rescue steroids take about 6-8 hours to document an effect, irrespective of route of administration and in situations assessed to be moderate to severe, it is justified to initiate usage early. Underuse of steroids has been incriminated in fatal cases. Oral prednisolone is the best option. Rescue therapy used for 3-7 days has no contraindications and adverse effects with such usage are insignificant. No tapering of dose is necessary. Parenteral steroids do not confer any advantage in an outpatient setting but may be used in hospitalized children who are severely distressed, drowsy or unable to retain oral medication. High dose inhaled steroids are under trial for their role as rescue agents and some studies have reported encouraging results.

Ipratropium bromide: Inhaled ipratropium may add to the bronchodilator benefits seen with inhaled β_2 agonists but is less effective when used alone. Usage may be limited to 24-48 hours to minimize incidence of atropine-like side-effects.

Aminophylline: Aminophylline still finds place in the management of acute severe episodes in a ward / ICU setting. Improved diaphragm contractility and mucociliary clearance may be beneficial effects. The risk for adverse effects is high, especially in those who are on long acting theophylline as a preventer drug and a loading dose must be avoided in such patients. A calculated intravenous drip rather than a bolus dose is a safer option.

Practices not routinely followed

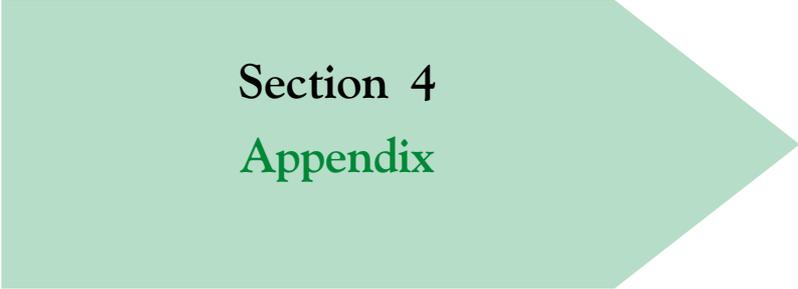
Antibiotics: Antibiotics are not routinely required since bacterial infections seldom trigger asthma. Consider antibiotics only in those who do not improve in response to bronchodilators, have purulent secretions or have radiological hematological evidence of infection.

Mucolytics: These may dislodge thick secretions and increase airflow obstruction.

Sedatives: This group of drugs may depress the respiratory drive, suppress the cough reflex and mask the vital sign of deterioration of sensorium.

Chest physiotherapy: This is not routinely indicated. It may actually add to the child's discomfort. If there is evidence of collapse (invariably due to a mucous plug), gentle cupping and vibration with the palm of the hand is helpful.

open gatefold for core (page 18)



Section 4

Appendix

Contents

Drug information

- Relievers A1-A4
- Preventers A5-A8

Instructions for usage of devices A9-A12

Drug	Formulations available in India	Dose
Short acting β_2 agonists		
Salbutamol	MDI 100 mcg/dose	2-4 puffs as needed. May be repeated thrice at 20 min interval and then 1-4 hourly as needed
	DPI Rotacap 200 mcg/dose	1-2 Rotacaps as needed. May be repeated thrice at 20 min intervals and then 1-4 hourly if needed
	Neb respirator solution 5 mg/ml	0.15 mg/kg, minimum 0.25 ml < 6 months age , 0.5 ml > 6 months age, 0.5-1 ml older children. For continuous nebulization 10 mg /10 ml saline via jet nebulizer
	Neb respule 2.5 mg/2.5 ml 2.5 mg/3 ml	Use equivalent doses as respirator solution
	Syp 2 mg/5 ml Tab 2 mg, 4 mg, 8 mg	0.15 mg/kg/dose 3-4 times a day
Laevalbuterol	Neb respule 0.63 mg/2.5 ml 1.25 mg/2.5 ml	3 times a day
	Terbutaline	MDI 250 mcg/dose
	Neb respirator solution 10 mg/ml	2-5 mg diluted and nebulized
	Syp 1.5 mg/5ml Tab 2.5 mg, 5 mg	0.075 mg/kg/dose may be repeated thrice at 20 min intervals
	Inj 0.5 mg/ml	0.01 mg/kg sc Bolus 5-10 mcg/kg over 10 minutes followed by 2-10 mcg/kg/hour iv (1ml terbutaline + 50 ml 5% dextrose, thus, 1ml = 10 mcg terbutaline)

Non-selective β_2 agonists

Adrenaline	Inj 1 mg/ml (1:1000 solution)	0.01 mg/kg sc
-------------------	----------------------------------	---------------

MDI - Metered Dose Inhaler
DPI - Dry Powder Inhaler
Neb - Nebulizer

Tab - Tablet
Syp - Syrup
Inj - Injection

relievers

Possible adverse effects

Comments

Tachycardia, tremors, headache, hypokalemia, hyperglycemia.

Inhaled route minimizes systemic adverse effects.

- Nebulizer solution of salbutamol is compatible with nebulizer solution of sodium cromoglycate and ipratropium (can be mixed).
- Subcutaneous terbutaline is not recommended below the age of two years.
- IV terbutaline drip necessitates continuous heart rate and ECG monitoring. If heart rate $> 180/\text{min}$ or if ECG changes develop, halve the drip rate.
- Discontinue nebulized β_2 agonist if using high infusion rates of iv terbutaline.
- Dose of iv terbutaline is to be halved if concurrently used with theophylline drip.
- Since dry powder devices require an optimal inspiratory flow rate they may not be suited to manage acute episodes. May be used for mild episodes.

-
- Non-selective β_2 agents such as isoproterenol and adrenaline are used infrequently because of cardiac stimulation.
 - May be used when inhaled therapy is not feasible or as an adjunct to inhaled therapy in very severe attacks.
-

Drug	Formulations available in India	Dose
Anticholinergics		
Ipratropium bromide	MDI 20 mcg/dose, 40 mcg/dose DPI Rotacap 40 mcg/dose	2-4 puffs as needed, may be repeated thrice at 20 mins interval and then 6-8 hourly as needed 1-2 Rotacaps as needed
	Neb respirator solution 0.25 mg/ml	0.5 ml < 1 year, 1 ml >1 year every 20 mins for 3 doses, then every 6-8 hours
	Neb respule 0.5 mg/2 ml	Use equivalent doses as respirator solution
Corticosteroids		
Prednisolone	Tab 5 mg, 10 mg Syp 5 mg/5 ml, 15 mg/5 ml	1-2 mg/kg/day max. 60 mg/day
Hydrocortisone	Inj 100 mg/vial	10 mg/kg stat followed by 5 mg/kg every 6 hourly iv
Methylxanthines		
Aminophylline	Inj 250 mg/10 ml	0.5-1 mg/kg/hr continuous infusion in 5 % dextrose
Other drugs		
Magnesium sulphate	Inj 25 % (250 mg/ml), 50 % (500 mg/ml) 1 ml ampoule	25-50 mg/kg in normal saline infused over 30 minutes

MDI - Metered Dose Inhaler
DPI - Dry Powder Inhaler
Neb - Nebulizer

Tab - Tablet
Syp - Syrup
Inj - Injection

e v e r s (contd.)

Possible adverse effects

Comments

Dryness of mouth, increased wheezing in some, blurred vision if sprayed in eyes (atropine effect).

- Slower onset of action than β_2 agonists but may provide additive effect in severe exacerbations.
 - Alternative in children intolerant to β_2 agonist.
 - Treatment of choice in bronchospasm due to β blocker medication.
-

Seldom any with short-term use.

Infrequently, increased appetite, abnormalities in glucose metabolism, fluid retention, mood alteration may be observed.

Consideration should be given to co-existing conditions such as herpes, varicella or tuberculosis which may be worsened by steroids.

Rescue therapy or burst therapy :

- Short-term therapy should continue till symptoms resolve. May be required for three to seven days.
 - Tapering is not necessary.
 - Inhaled steroids are not yet proven effective for rescue therapy.
 - Injectable steroids do not confer quicker benefit but may be used in acute severe episodes or when the child is likely to vomit oral drugs.
-

See next section.

- Aminophylline is superfluous for routine treatment of acute exacerbations in patients receiving optimal β_2 agonists and steroids. Use justified only in children with respiratory failure since studies for efficacy have excluded such patients for ethical reasons. Improvement of mucociliary clearance and diaphragm contractility may be important mechanisms in this setting.
 - Theophylline mg/kg = aminophylline mg/kg x 0.8.
-

Tachycardia, hypotension, muscle weakness.

- Calcium channel modulation by this drug results in decreased histamine and acetyl-choline release.
-

Drug	Formulations available in India	Dose
Mast cell stabilizers		
Sodium cromoglycate	MDI 5 mg/dose	1-2 puffs 3-4 times a day
	DPI Rotacap 20 mg/dose	1 Rotacap 3-4 times a day
Inhaled corticosteroids		
Beclomethasone dipropionate	MDI 50, 100, 200, 250 mcg/dose	50-400 mcg twice a day
	DPI Rotacap 100,200, 400 mcg/dose	50-400 mcg twice a day
Budesonide	MDI 100, 200, mcg/dose	50-400 mcg twice a day
	DPI Rotacap 100, 200, 400 mcg/dose	50-400 mcg twice a day
	Neb respirator solution 0.5 mg/2ml 1 mg/2 ml	Initiating dose : 0.5-1 mg twice a day Maintenance dose : 0.25-0.5 mg twice a day
Fluticasone propionate	MDI 25, 50, 125 mcg/dose	25-200 mcg twice a day
	DPI Rotacap 50, 100, 250 mcg/dose	25-200 mcg twice a day
	Neb respule 0.5 mg/2 ml 2 mg/2 ml	1 mg twice a day
Leukotriene receptor antagonists		
Montelukast	4 mg, 5 mg dispersible/mouth dissolving tablets 10 mg tablets	1-5yrs : 4 mg once daily 6-14 yrs : 5 mg once daily > 14 yrs : 10 mg once daily

MDI - Metered Dose Inhaler
DPI - Dry Powder Inhaler
Neb - Nebulizer

Tab - Tablet
Syp - Syrup
Inj - Injection

pre venters

Possible adverse effects

Comments

Hardly any. Medicinal taste and reflex coughing are minimized by gargling/spacer use.

- 4 times daily regime is difficult to implement. For practical purposes three times daily regime may be tried.
 - A dose half hour prior to exercise provides protection from EIA for about 4-6 hours.
-

Cough, dysphonia (laryngeal myopathy), oral thrush. Gargling/spacer use decreases local side effects, oropharyngeal deposition and systemic effects. Low (<400 mcg/day and medium (400 to 800 mcg/day) doses of beclomethasone dipropionate and budesonide have negligible systemic effects. In high doses (> 800 mcg / day), systemic effects may occur though studies are not conclusive. These effects include adrenal suppression, growth suppression, skin thinning, cataracts etc.

- Systemic effects of inhaled steroids may occur due to pulmonary absorption and intestinal absorption of orally deposited drug. The newer steroids-budesonide and fluticasone propionate are almost completely inactivated by the liver during first-pass metabolism and thus have negligible systemic effects. Fluticasone is not absorbed from the intestinal tract.
 - When using inhaled fluticasone propionate, the corresponding dose is half that of beclomethasone dipropionate or budesonide by similar delivery systems.
 - Growth monitoring is important if high doses are used.
 - Injectable dexamethasone is not recommended for inhalation since systemic absorption is considerable.
-

Comparable to placebo. Uncommonly, may cause headache, stomach pain, hypersensitivity reactions.

- Bioavailability not affected by food intake.
- Effect starts soon after initiation of therapy(1st dose)

Rarely-(on patients on oral steroids) – Churg Strauss syndrome (eosinophilic vasculitis) has been documented on tapering oral steroids

Drug	Formulations available in India	Dose
Inhaled corticosteroids + Long-acting β_2 agonists		
Fluticasone (FP) + Salmeterol (Sml)	MDI	
	a) FP 50 mcg + Sml 25 mcg/dose	1-2 puffs twice a day
	b) FP 125 mcg + Sml 25 mcg/dose	1-2 puffs twice a day
	c) FP 250 mcg + Sml 25 mcg/dose	1-2 puffs twice a day
	<hr/>	
	DPI Accuhaler	
	a) FP 100 mcg + Sml 50 mcg/dose	1 puff twice a day
	b) FP 250 mcg + Sml 50 mcg/dose	1 puff twice a day
	c) FP 500 mcg + Sml 50 mcg/dose	1 puff twice a day
	<hr/>	
	DPI Rotacaps	
	a) FP 100 mcg + Sml 50 mcg/dose	1-2 Rotacaps twice a day
b) FP 250 mcg + Sml 50 mcg/dose	1 Rotacap twice a day	
c) FP 500 mcg + Sml 50 mcg/dose	1 Rotacap twice a day	
<hr/>		
Budesonide (BUD) + Formoterol (Form)	DPI Rotacap BUD 100 mcg + Form 6 mcg/dose	1-2 Rotacaps twice a day
<hr/>		
Methylxanthines		
Theophylline	Sustained-release anhydrous theophylline tab/cap 100 mg, 200 mg, 300 mg, 450 mg	Getting started >1 year: (rule of 3's) Starting dose 10 mg/kg Increments 3 mg/kg Space the increments 3 days apart Monitor levels 3 days after any increment and then only periodically if poor control/suspicion of adverse effects
	Syp 50 mg/5 ml	<1 year: 0.2 x age in weeks + 5 (gives the dose in mg/kg) Obese: Use average weight for height
<hr/>		
Oral corticosteroids		
Prednisolone	Tab 5 mg, 10 mg Syp 5 mg/5 ml, 15 mg/5 ml	1-2 mg/kg/day max. 60 mg/day
<hr/>		
MDI - Metered Dose Inhaler	Tab - Tablet	
DPI - Dry Powder Inhaler	Syp - Syrup	
Neb - Nebulizer	Inj - Injection	

enters (contd.)

Possible adverse effects

Comments

Inhaled corticosteroids

See previous page

- Combination of inhaled steroid with long acting β_2 agonists has been shown to have a synergistic effect.

Inhaled long acting β_2 agonists

Similar to short acting
 β_2 agonist

- Not to be used for treatment of acute symptoms.
- Potential for developing tolerance exists but clinical significance is probably not relevant.
- To be used with inhaled steroid therapy and not alone.
- Literature recommends usage only for children above the age of four years.

Potential for serious toxicity at serum level > 20 mcg/ml. Early caffeine-like adverse effects are non-specific and include nausea, headache, tachycardia or insomnia.

Drowsiness and seizures are late manifestations.

- Doses less than 12 mg/kg being used - monitoring is not necessary.
- Doses more than 28 mg/kg being used - consider change of drug.
- Several drugs and clinical situations alter theophylline kinetics (particular care to be taken with macrolides, fluoroquinolones, antitubercular and anticonvulsant therapy).
- Introducing the drug gradually reduces incidence of initial caffeine-like effects.

Increased appetite, abnormalities in glucose metabolism, fluid retention, mood alteration, growth retardation and cataract. Consideration should be given to co-existing conditions such as herpes, varicella or tuberculosis which may be worsened by steroids.

- Significant side effects may occur with prolonged use.
- Low doses for prolonged duration may occasionally be required in severe steroid dependent cases.
- Use minimum possible dose to control symptoms. Single morning dose is convenient.
- Betamethasone and dexamethasone are expensive and do not confer additional benefit.

Spacer / Volume holding chamber

Ask the child / parent to:

1. Assemble the spacer, lining up the notch of one half with the slot of the other half. Then, push the two parts firmly together.
2. Remove the cap of the inhaler, shake the inhaler and insert it into one end of the spacer device.
3. Place the mouthpiece of the spacer in the child's mouth. Seal the child's lips around the mouthpiece by gently placing the finger of one hand around the lips.
4. Encourage the child to breathe in and out slowly and gently. This will make a 'clicking' sound as the valve opens and closes. Once the breathing pattern is well established, depress the canister with the free hand and leave the device in the same position as the child continues to breathe (tidal breathing) 4 to 5 times. An older child may be taught to breathe in deeply and pause after inspiration to a count of '5'.
5. Remove the device from the child's mouth.
6. If a second puff is required, wait for about one minute before repeating steps 1-5.
7. For children below about three years, a face mask should be attached to the mouthpiece of the spacer and apposed closely to the face before repeating steps 4-7.

Cleaning the spacer:

Wash with a mild soap / detergent solution every month. Allow to drip dry. Do not rinse or use a cloth to dry. This minimizes the static charge and thus, reduces drug deposition on the spacer wall.

Metered Dose Inhaler

Ask the child / parent to:

1. Remove the mouthpiece cover and shake the inhaler.
2. Breathe out gently.
3. Place the mouthpiece of the inhaler in the mouth between the teeth and seal lips around it taking care not to bite.
4. Start breathing in, slow and deep. Press the canister and continue to inhale deeply.
5. Remove the inhaler from the mouth and hold the breath for about 10 seconds.
6. Wait for at least one minute before taking another inhalation.

Parents must assist and supervise those children who need help in using their MDI correctly. The MDI may be used without spacer only in older children.

usage of devices

Accuhaler

Ask the child / parent to:

1. Slide the purple dust cover to open the device.
2. Hold the Accuhaler with the dose counter facing upward and the mouthpiece pointed towards the child.
3. Use the thumb to push the lever back till you hear a click.
4. Purse the lips around the mouthpiece and breathe in normally.
5. Close the device by sliding back the cover.

Parents must assist and supervise those children who need help in using their Accuhaler correctly.

Rotahaler

Ask the child / parent to:

1. Hold the Rotahaler vertically and insert a Rotacap, transparent end first, into the small raised square hole of the Rotahaler. Make sure that the top of the Rotacap is level with the top of the hole. (If the shell from previous use is still lodged in the square hole, it will be pushed out when the fresh Rotacap is inserted.)
2. Hold the mouthpiece and rotate the base. The fin separates the two halves of the Rotacap.
3. Instruct the child to breathe out gently. Let the child grip the mouthpiece between the teeth (without biting) and seal his/her lips around it. Then, let the child breathe in the powder slowly and deeply. (If the child is doing this correctly, the Rotacap shell will make a low rattling sound inside the Rotahaler.)
4. Remove the Rotahaler from the child's mouth and ask him/her to hold the breath for about 10 seconds.

Parents must assist and supervise those children who need help in using their Rotahaler correctly.

Nebulizer

Prerequisites:

- Optimal volume of solution in nebulizer chamber is 2 to 4 ml
- Particle size is 2-5 microns
- Driven by O₂ or air
- Flow is 4 to 8 L/ min
- Electric (220V AC) or battery powered

Instructions for

Practical points on usage:

- Saline should be used as the diluent and not distilled water. This is because hypo-osmolar solutions can lead to reflex bronchospasm.
- Delivery may be effected through a mouthpiece or mask, depending upon the child's age and level of cooperation.
- If a mask is used, it should be held as close to the face as is comfortable for the child. Any gap reduces drug delivery significantly.

Cleaning the nebulizer:

After each treatment	After each day
<ol style="list-style-type: none">1. Disassemble the nebulizer completely.2. Rinse the tubing, medication cup, and mouthpiece / mask in hot water.3. Shake off excess water and allow to air-dry between a folded paper towel. Avoid drying in dusty or smoky areas.	<ol style="list-style-type: none">1. Disassemble the nebulizer completely.2. Submerge the tubing, medication cup and mouthpiece / mask in a mild liquid detergent and warm water for a couple of minutes.3. Using a small bristle brush, scrub all parts to remove any sediment that may have accumulated.4. Rinse parts thoroughly after washing, to remove all residual soap.5. Immerse all parts in acetic acid* disinfectant solution for 10 minutes.6. Remove all parts and rinse under a strong stream of warm water.7. Air-dry all parts between folded paper towels in a clean area.

Note : If the equipment is not likely to be used again for a few days, it should be placed in a plastic bag with a twist tie and stored in a clean area.

**Acetic acid solution is made by mixing one part white vinegar and three parts water and should be freshly prepared every day.*

usage of devices

Peak flow meter

There are several types of peak flow meters available in the Indian market. The steps for using a peak flow meter are similar for all types.

Ask the parent to:

1. Fit the mouthpiece to the peak flow meter.
2. Ensure that the child stands up and holds the peak flow meter horizontally without restricting movement of the pointer. Adjust the pointer to zero.
3. Nose clips are unnecessary. Ask the child to breathe in deeply (as far as possible) with the mouth wide open. Place the mouthpiece in the child's mouth and seal his / her lips around it.
4. Ask the child to blow out as hard and fast as possible. The child should be told to blow out vigorously, as if blowing out candles on his birthday cake. In case the child coughs, disregard that reading. Make sure that the child's tongue is not blocking the mouthpiece. Record the result.
5. Make the child repeat steps 2-4 thrice and record the highest of three readings.

References

- Abramson M, Voight T. Ambient air pollution and respiratory disease. *Med J Aust* 1991; 154: 543-53.
- Abramson MJ, Puy RM, Weiner JM. Is allergen immunotherapy effective in asthma? A meta-analysis of randomized controlled trials. *Am J Respir Crit Care Med* 1995; 151: 969-74.
- Adkinson FN, Eggleston PA, Eney D et al. A controlled trial of immunotherapy for asthma in allergic children. *N Engl J Med* 1997; 336: 324-31.
- Agertoft L, Pedersen S. Effects of long-term treatment with an inhaled corticosteroid on growth and pulmonary function in asthmatic children. *Respir Med* 1994; 88: 373-81.
- Agertoft L, Pedersen S. Importance of the inhalation device on the effect of budesonide. *Arch Dis Child* 1993; 69: 130-3.
- Ahrens R, Lux C, Bahl T, Han SH. Choosing the metered-dose inhaler spacer or holding chamber that matches the patient's need: evidence that the specific drug being delivered is an important consideration. *J Allergy Clin Immunol* 1995; 96: 288-94.
- Allen DB, Mullen M, Mullen B. A meta-analysis of the effect of oral and inhaled corticosteroids on growth. *J Allergy Clin Immunol* 1994; 93: 967-76.
- American Academy of Allergy, Asthma and Immunology Position Statement: environmental allergen avoidance in allergic asthma. *J Allergy Clin Immunol* 1999; 103: 203-5.
- American Thoracic Society. Lung function testing: selection of reference values and interpretive strategies. *Am Rev Respir Dis* 1991; 144: 1202-18.
- American Thoracic Society. Standardization of spirometry : 1994 update *Am J Respir Crit Care Med* 1995; 152: 1107-36.
- Anderson SD, Rodwell LT, Du Toit J, Young IH. Duration of protection of inhaled salmeterol in exercise-induced asthma. *Chest* 1991; 100: 1254-60.
- Anderson SD. Exercise-induced asthma. In: *Allergy and Allergic Diseases*, AB Kay (ed.). Oxford: Blackwell Scientific, 1997, pp 692-711.
- Anderson SD. Issues in exercise-induced asthma. *J Allergy Clin Immunol* 1985; 76: 763-72.
- Aubier M, Levy J, Clerici C, Neukirch F, Herman D. Different effects of nasal and bronchial glucocorticosteroid administration on bronchial hyperresponsiveness in patients with allergic rhinitis. *Am Rev Respir Dis*, 1992; 146: 122-6.
- Balfour-Lynn I. Difficult asthma: beyond the guidelines. *Arch Dis Child* 1999; 80: 201-6.
- Barnes NC, Marone G, Di Maria GU, Visser S, Utama I, Payne SL. A comparison of fluticasone propionate, 1 mg daily, with beclomethasone dipropionate, 2 mg daily, in the treatment of severe asthma. *Eur Respir J* 1993; 6: 877-85.
- Barnes PJ, Ghung KF. Difficult asthma. *BMJ* 1989; 299: 695-8
- Barnes PJ, Pauwels RA. Theophylline in the management of asthma: time for reappraisal? *Eur Respir J* 1994; 7: 579-91
- Barnes PJ, Pedersen S. Efficacy and safety of inhaled corticosteroids in asthma. *Am Rev Respir Dis* 1993; 148: S1-S26.
- Barnes PJ. Immunomodulation as asthma therapy: where do we stand ? *Eur Respir J* 1996; 9: 154-9.
- Barnes PJ. Inhaled corticosteroids for asthma. *New Engl J Med* 1995; 332: 868-75.
- Barnes PJ. Inhaled glucocorticoids: new developments relevant to updating of the Asthma Management Guidelines. *Respir Med* 1996; 90: 379-84
- Barnes PJ. Mechanisms of action of glucocorticoids in asthma. *Am J Respir Crit Care Med* 1996; 154: S21-7.
- Barnes PJ. Poorly perceived asthma. *Thorax* 1992; 47: 408-9.
- Beam WR, Weiner DE, Martin RJ. Timing of prednisone and alterations of airways inflammation in nocturnal asthma. *Am Rev Respir Dis* 1992; 146(6): 1524-30.
- Becker JM, Arora A, Scarfone RJ, et al. Oral versus intravenous corticosteroids in children hospitalized with asthma. *J Allergy Clin Immunol* 1999; 103: 586-90
- Bisgaard H. leukotriene modifiers in pediatric asthma management. *Pediatrics* 2001; 13(3): 128-37

- Bloch H, Silverman R, Mancherje N, Grant S, Jagminas L, Scharf SM. Intravenous magnesium sulfate as an adjunct in the treatment of acute asthma. *Chest* 1995; 107: 1576-81.
- Blumenthal MN, Yunis E, Mendell N, Elston RC. Preventive allergy: genetics of IgE-mediated diseases. *J Allergy Clin Immunol* 1986; 78: 962-8.
- Boorsma M, Andersson N, Larsson P, Ullman A. Assessment of the relative systemic potency of inhaled fluticasone and budesonide. *Eur Respir J* 1996; 9: 1427-32.
- British Thoracic Society. The British Guidelines on Asthma Management: 1995 Review and Position Statement. *Thorax* 1997; 52: S1-21.
- Brown PH, Blundell G, Greening AP, Crompton GK. Do large volume spacer devices reduce the systemic effects of high dose inhaled corticosteroids? *Thorax* 1990; 45: 736-9.
- Burney PGJ, Luczynska C, Chinn S, Jarvis D. The European Community Respiratory Health Survey. *Eur Respir J* 1994; 7: 954-60.
- Busse WW. What role for inhaled steroids in chronic asthma? *Chest* 1993; 104: 1565-71.
- Bye MR, Kerstein D, Barsh E. The importance of spirometry in the assessment of childhood asthma. *Am J Dis Child* 1992; 146: 977-8.
- Calpin C, Macarthur C, Stephens D, Feldman W, Parkin PC. Effectiveness of prophylactic inhaled steroids in childhood asthma: a systemic review of the literature. *J Allergy Clin Immunol* 1997; 100: 452-7.
- Carter E, Cruz M, Chesrown S, Shieh G, Reilly K, Hendeles L. Efficacy of intravenously administered theophylline in children hospitalized with severe asthma. *J Pediatr* 1993; 122: 470-6.
- Chapman KR, Verbeek PR, White JG, Rebuck AS. Effect of a short course of prednisone in the prevention of early relapse after the emergency room treatment of acute asthma. *N Engl Med* 1991; 324: 788-94.
- Chavasse RJ, Bastian- Lee Y, Richter H, Hilliard T, Seddon P. Inhaled salbutamol for wheezy infants: a randomised controlled trial. *Arch Dis Child* 2000; 82: 370-5
- Cheriyian S, Greenberger PA, Patterson R. Outcome of cough variant asthma treated with inhaled steroids. *Ann Allergy* 1994; 73: 478-80.
- Closa RM, Ceballos JM, Gomez-Papi A, Galiana AS, Gutierrez C, Marti-Henneber C. Efficacy of bronchodilators administered by nebulizers versus spacer devices in infants with acute wheezing. *Pediatr Pulmonol* 1998; 26: 344-8.
- Clough JB. Bronchodilators in infancy. *Thorax* 1993; 48: 308.
- Colacone A, Afilalo M, Wolkove N, Kreisman H. A comparison of albuterol administered by metered dose inhaler (and holding chamber) or wet nebulizer in acute asthma. *Chest* 1993; 104: 835-41.
- Condemi J, Goldstein S, Kalberg C, Yancey S, Emmett A, Rickard K, Salmeterol Study Group. The addition of salmeterol to fluticasone propionate versus increasing the dose of fluticasone propionate in patients with persistent asthma. *Ann Allergy Asthma Immunol* 1999; 82: 383-9
- Connett GJ, Lenney W. Use of pulse oximetry in the hospital management of acute asthma in childhood. *Pediatr Pulmonol* 1993; 15(6): 345-9.
- Connett GJ, Warde C, Wooler E, Lenney W. Prednisolone and salbutamol in the hospital treatment of acute asthma. *Arch Dis Child* 1994; 70: 170-3.
- Cook DG, Strachan DP. Health effects of passive smoking, 3: parental smoking and prevalence of respiratory symptoms and asthma in school age children. *Thorax* 1997; 52: 1081-94.
- Creer TL, Backial MA, Burns KL, et al. Living with asthma. I. Genesis and development of a self-management program for childhood asthma. *J Asthma* 1988; 25: 335-62.
- Daniels SE, Bhattacharya S, James A et al. A genome-wide search for quantitative trait loci underlying asthma. *Nature* 1996; 383: 247-50.
- Davies H, Olsen L, Gibson P. Methotrexate as a steroid sparing agent in adult asthma (Cochrane Review). In: *The Cochrane Library, Issue 2*. Oxford: Update Software, 1999.
- Denicola L, Monem G, Gayle M, et al: Treatment of critical status asthmaticus in children. *Pediatr Clin North Am* 1994; 41: 293.
- Deshpande A, McKenzie SA. Short course of steroids in home treatment of children with acute asthma. *BMJ* 1986; 293: 169-71.
- DiGiulio GA, Kerckmar CM, Krug SE, Alpert SE, Marx CM. Hospital treatment of asthma: lack of benefit from theophylline given in addition to nebulized albuterol and intravenously administered corticosteroid. *J Pediatr* 1993; 122: 464-9.

- Djukanovic R, Wilson TW, Britten KM, et al. Effect of an inhaled corticosteroid on airway inflammation and symptoms of asthma. *Am Rev Respir Dis* 1992; 145: 669-74.
- Dolovich M, Ruffin RE, Roberts R, Newhouse MT. Optimal delivery of aerosols from metered dose inhalers. *Chest* 1981; 80(6): 911-5.
- Dorsch W, Wagner H. New antiasthmatic drugs from traditional medicine ? *Int Arch Allergy Anal Immunol* 1991; 94: 262-5.
- Douglass JA, Thien FCK, O'Hehir RE. Immunotherapy in asthma. *Thorax* 1997; 52: S22-9.
- Editorial. Acupuncture, Asthma and Breathlessness. *Lancet* 1986; 2: 1427-8.
- Eigen H. Pulmonary function testing: A practical guide to its use in pediatric practice. *Pediatr in Rev* 1986; 7(8): 235-45
- Enright PL, Sherrill DL, Lebowitz MD. Ambulatory monitoring of peak expiratory flow. Reproducibility and quality control. *Chest* 1995; 107: 657-61.
- Erika von Mutius. The burden of childhood asthma: *Arch Dis Child* 2000; 82(SupplIII): 112-5
- Evans D. To help patients control asthma the clinician must be a good listener and teacher [editorial]. *Thorax* 1993; 48: 685-7.
- Everard ML, Clark AR, Milner AD. Drug delivery from holding chambers with attached facemask. *Arch Dis Child* 1992; 67: 580-5.
- Fabbri L, Burge PS, Croonenborgh L, et al. on behalf of an International Study Group. Comparison of fluticasone propionate with beclomethasone dipropionate in moderate or severe asthma treated for one year. *Thorax* 1993; 49: 817-23.
- Faniran AO, Peat JK, Woolcock AJ. Persistent cough: is it asthma? *Arch Dis Child* 1998; 79: 411-14.
- Ferguson AC, Spier S, Manjra A, Versteegh FGA, Mark S, Zhang P. efficacy and safety of High-dose inhaled steroids in children with asthma: A comparison of fluticasone propionate with budesonide. *J Pediatr* 1999; 134: 422-7
- Fiel SB, Swartz MA, Glanz K, Francis ME. Efficacy of short-term corticosteroid therapy in outpatient treatment of acute bronchial asthma. *Am J Med* 1983; 75: 259-62.
- Frischer T, Kuehr J, Meinert R, et al. Maternal smoking in early childhood: a risk factor for bronchial responsiveness to exercise in primary-school children. *J Pediatr* 1992; 121: 17-22.
- Fung KP, Chow OK, So SY. Attenuation of exercise-induced asthma by acupuncture. *Lancet* 1986; 2: 1419-22.
- Gawchik SM, Saccar CL, Noonan M, Reasner DS, DeGraw SS. The safety and efficacy of nebulized levalbuterol compared with racemic albuterol and placebo in the treatment of asthma in pediatric patients. *J Allergy Clin Immunol* 1999; 103: 615-21.
- Geelhoed GC, Landau LI, Le Souef PN. Evaluation of SaO₂ as a predictor of outcome in 280 children presenting with acute asthma. *Ann Emerg Med* 1994; 23: 1236-41.
- Golbert TM, Patterson R, Pruzansky JJ. Systemic allergic reactions to ingested antigens. *J Allergy* 1969; 44: 966-107.
- Grampian Asthma Study of Integrated Care. Effectiveness of routine self-monitoring of peak flow in patients with asthma. *BMJ* 1994; 308: 564-7.
- Green CP, Price JF. Prevention of exercise induced asthma by inhaled salmeterol xinafoate. *Arch Dis Child* 1992; 67: 1014-7.
- Guidelines on Management of Common Pediatric Problems*. S. Sachidananda Kamath, Swati Y. Bhave, M.K.C. Nair (Eds.), First edition, IAP, pp 196
- Gustafsson P, Tsanakas J, Gold M, Primhak R, Radford M, Gillies E. Comparison of the efficacy and safety of inhaled fluticasone 200 mcg/day with inhaled beclomethasone dipropionate 400 mcg/day in mild and moderate asthma. *Arch Dis Child* 1993; 69: 206-11.
- Hanrahan JP, Tager IB, Segal MR, Tosteson TD, Castile RG, Van Vunakis H, Weiss ST, Speizer FE. The effect of maternal smoking during pregnancy on early infant lung function. *Am Rev Respir Dis* 1992; 145: 1129-35.
- Harris JB, Weinberger MM, Nassif E, Smith G, Milavetz G, Stillerman A. Early intervention with short courses of prednisone to prevent progression of asthma in ambulatory patients incompletely responsive to bronchodilators. *J Pediatr* 1987; 110: 627-33.
- Hegewald MJ, Crapo RO, Jensen RL. Intraindividual peak flow variability. *Chest* 1995; 107: 156-61.

- Helfaer MA, Nichols DG, Rogers MC. Lower airway disease: Bronchiolitis and Asthma. In : Rogers MC (ed.). *Textbook of Pediatric Intensive Care*. Baltimore. Williams and Wilkins, 1996; 127.
- Helms PJ. Wheezing infants. *Clin Exper Allergy* 1994; 24: 97-9.
- Hendeles L, Weinberger M, Szefer S, Ellis E. safety and efficacy of theophylline in children with asthma. *J Pediatr* 1992; 120(2): 177-83
- Hixson LJ, Kelly CL, Jones WN, Tuohy CD. Current trends in the pharmacotherapy for gastroesophageal reflux disease. *Arch Intern Med* 1992; 152: 717-23.
- Idris AH, Mc Dermott MF, Raucci JC, Morrabel A, McGorray S, Hendeles L. Emergency department treatment of severe asthma. Metered-dose inhaler plus holding chamber is equivalent in effectiveness to nebulizer. *Chest* 1993; 103: 665-72.
- Jackson AC. Accuracy, reproducibility, and variability of portable peak flow meters. *Chest* 1995; 107: 648-51.
- Johnson M. Pharmacodynamics and pharmacokinetics of inhaled glucocorticoids. *J Allergy Clin Immunol* 1996; 97(1 Pt 2): 169-76.
- Kallenbach JM, Frankel AH, Lapinsky SE, et al. Determinants of near fatality in acute severe asthma. *Am J Med* 1993; 95: 265-72.
- Kamada AK, Szefer SJ, Martin RJ, et al. and the Asthma Clinical Research Network. Issues in the use of inhaled glucocorticoids. *Am J Respir Crit Care Med* 1996; 153: 1739-48.
- Karpel JP, Schacter EN, Fanta C, et al. A comparison of ipratropium and albuterol vs. albuterol alone for the treatment of acute asthma. *Chest* 1996; 110: 611-6.
- Katellaris CH. How to investigate and manage a patient with possible food allergy. *Mod Med Aust* 1993; 36: 118-20.
- Kemp JP. Making best use of today's bronchodilators. *J Resp Dis* 1994; 15: 521-7
- Kerem E, Levison H, Schuh S, et al. Efficacy of albuterol administered by nebulizer versus spacer device in children with acute asthma. *J Pediatr* 1993; 123: 313-7.
- Kim CS, Eldridge MA, Sackner MA. Oropharyngeal deposition and delivery aspects of metered-dose inhaler aerosols. *Am Rev Respir Dis* 1987; 135: 157-64.
- Kingston HG, Hirshman CA. Perioperative management of the patient with asthma. *Anesth Analg* 1984; 63: 844-55.
- Kleijnen J, ter Riet G, Knipschild P. Acupuncture and asthma: a review of controlled trials. *Thorax* 1991; 46: 799-802.
- Larsen GL. Asthma in children. *N Engl J Med* 1992; 326: 1540-5.
- Larsen GL. Focusing on childhood asthma: the childhood asthma management program (CAMP). *J Allergy Clin Immunol* 1999; 10: 371-373.
- Li JT, O'Connell EJ. Clinical evaluation of asthma. *Ann Allergy Asthma Immunol* 1996; 76: 1-13.
- Lipworth B. New perspectives on inhaled drug delivery and systemic bioactivity. *Thorax* 1995; 50: 105-110.
- Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy: A systemic review and meta-analysis. *Arch Intern Med* 1999; 159: 941-55
- Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy. *Arch Intern Med* 1999; 159: 941-55
- Maguire JF, O'Rourke PP, Colan SD, Geha RS, Crone R. Cardiotoxicity during treatment of severe childhood asthma. *Pediatrics* 1991; 88: 1180-6.
- Malo JL, L'Archeveque J, Trudeau C, d'Aquino C, Cartier A. Should we monitor peak expiratory flow rates or record symptoms with a simple diary in the management of asthma ? *J Allergy Clin Immunol* 1993; 91: 702-9.
- Martin ME, Grunstein MM, Larsen GL. The relationship of gastroesophageal reflux to nocturnal wheezing in children with asthma. *Ann Allergy* 1982; 49: 318-22.
- Martinez F. Definitions, risk factors, and early natural history. Early childhood asthma: What are the questions? *Am J Respir Crit Care Med* 1995; 151: S2-3.
- Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *N Engl J Med* 1995; 332: 133-8.
- Martinez FD. Present and future treatment of asthma in infants and young children. *J Allergy Clin Immunol* 1999; 104: 169-74.
- Martinez FD. Recognizing early asthma. *Allergy* 1999; 54 (Suppl 49): 24-8.

Martinez FD. Viral infections and the development of asthma. *Am J Respir Crit Care Med* 1995; 151: 1644-7.

McCubbin MM, Mitzvetz G, Grandgeorge S, et al. A bioassay for topical and systemic effect of three inhaled corticosteroids. *Clin Pharmacol Ther* 1995; 57: 455-60.

McFadden ER Jr, Gilbert IA. Exercise-induced asthma. *N Engl J Med* 1994; 330: 1362-7.

Mellins RB. Patients education is key to successful management of asthma. *J Rev Respir Dis* 1989; (Suppl): S47-52.

Miles IF, Bright P, Ayres JG, Cayton RM, Miller MR. The performance of Mini Wright peak flow meters after prolonged use. *Respir Med* 1995; 89: 603-5.

Milgrom H, Wood RI, Ingram D. Respiratory conditions that mimic asthma. *Immunol Allergy Clin North Am* 1998; 18: 113-32.

Milne ST, Newman KB. Acute asthma exacerbations: Strategy for early assessment and aggressive management. *Consultant* 1995; 1787-93

Mullarkey ME, Blumenstein BA, Andrade WP, Bailey GA, Olason I, Wetzel CE. Methotrexate in the treatment of corticosteroid-dependent asthma. *N Engl J Med* 1988; 318: 603-7.

Murray AB, Ferguson AC. Dust-free bedrooms in the management of asthmatic children with house dust or house dust mite allergy: a controlled trial. *Pediatrics* 1983; 71: 418-22.

Nagarathna R, Nagendra HR. Yoga for bronchial asthma: a controlled trial. *Br Med J* 1985; 291: 1077-9.

Nasser S, Christie PE, Sousa AR et al. Effect of endobronchial aspirin challenge on inflammatory cells in bronchial biopsy samples from aspirin-sensitive asthmatic subjects. *Thorax* 1996; 51: 64-70.

National Asthma Education and Prevention Program, Expert Panel Report II. *Guidelines for the Diagnosis and Management of Asthma*. National Institutes of Health, Bethesda, US Department of Health & Human Services, 1997.

National Institutes of Health, National Heart, Lung, and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. 1997; Publ. No. 97-4051.

Nelson HS, Bensch G, Pleskow WW, et al. Improved bronchodilation with levalbuterol compared with racemic albuterol in patients with asthma. Nelson HS, Bensch G, Pleskow WW, et al. *J Allergy Clin Immunol* 1998; 102: 943-52

Newhouse MT, Dolovich MB. Control of asthma by aerosols. *N Engl J Med* 1986; 315: 870-4.

Ninan TK, Russell G. Asthma, inhaled corticosteroid treatment, and growth. *Arch Dis Child* 1992; 67(6): 703-5.

Nordic consensus on asthma management. *Respir Med* 2000; 94: 299-327

Oswald H, Phelan PD, Lanigan A et al. Outcome of childhood asthma in mid-adult life. *Br Med J* 1994; 309: 95-6.

Ownby DR. Environmental factors versus genetic determinants of childhood inhalant allergies. *J Allergy Clin Immunol* 1990; 86: 279-87.

Pederson S, Mortensen S. Use of different inhalation devices in children. *Lung* 1990; 168 (Suppl): 653-7.

Platts-Mills TAE, Solomon WR. Aerobiology and inhalant allergens. In: *Allergy: Principles and Practice*.

Middleton EM, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, Busse WW (eds). Chicago: Mosby-Year Book, 1993, pp 469-528.

Rau JL, Restrepo RD, Deshpand EV. Inhalation of single vs. multiple metered dose bronchodilator actuations from reservoir devices. An in vitro study. *Chest* 1996; 109: 969-74.

Recent Advances in Pediatrics(19). London, Harcourt Publishers, David TJ

Rees J, Price J. Asthma in children: Treatment. *BMJ* 1995; 310: 1522

Rees J, Price J. Chronic asthma - general management. *BMJ* 1995; 310: 1400

Reiff DB, Choudry NB, Pride NB, Ind PW. The effect of prolonged submaximal warm-up exercise on exercise-induced asthma. *Am Rev Respir Dis* 1989; 139: 479-84.

Reilly DT, McSharry C, Taylor MA, Aitchison T. Is homeopathy a placebo response? Controlled trial of homeopathic potency, with pollen in hayfever as model. *Lancet* 1986; 2: 881-6.

Rodrigo C, Rodrigo G. Treatment of acute asthma. Lack of therapeutic benefit and increase of the toxicity from aminophylline given in addition to high doses of salbutamol delivered by metered-dose inhaler with a spacer. *Chest* 1994; 106: 1071-6.

Roorda RJ, Gerritsen J, Van Aalderen WM, et al. Risk factors for the persistence of respiratory symptoms in childhood asthma. *Am Rev Respir Dis* 1993; 148: 1490-5.

- Rosenstreich, Eggleston P, Kattan M, et al. for the National Cooperative Inner-City Asthma Study. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 1997; 336: 1356-63.
- Rossing TH, Fanta CH, Goldstein DH, Snapper JR, McFadden ER Jr. Emergency therapy of asthma: comparison of the acute effects of parenteral and inhaled sympathomimetics and infused aminophylline. *Am Rev Respir Dis* 1980; 122: 365-71.
- Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. *N Engl J. Med* 1992; 327: 380-4.
- Scarfone RJ, Fuchs SM, Nager AL, Shane SA. Controlled trial of oral prednisone in the emergency department treatment of children with acute asthma. *Pediatrics* 1993; 2: 513-8.
- Schuh S, Johnson DW, Cailahan S, Canny G, Levison H. Efficacy of frequent nebulized ipratropium bromide added to frequent high-dose albuterol therapy in severe childhood asthma. *J Pediatr* 1995; 126: 639-45.
- Schuh S, Johnson DW, Stephens D, Callaban S, Winders P, Canny G. Comparison of albuterol delivered by metered dose inhaler with spacer versus a nebulizer in children with mild acute asthma. *J Pediatrics* 1999; 35: 22-7
- Selroos O, Halme M. Effect of a volumatic spacer and mouth rinsing on systemic absorption of inhaled corticosteroids from a metered dose inhaler and dry powder inhaler. *Thorax* 1991; 46: 891-4.
- Selroos O, Pietinalho A, Lofroos A-B, Riska H. Effect of early versus late intervention with inhaled corticosteroids in asthma. *Chest* 1995; 108: 1228-34.
- Selvadurai H, Mellis C. Practical management of wheezy infants and toddlers. *Modern Medicine* 1998; 41: 18-32.
- Shirley J, Murphy, William HK, Pharm D. Advances in the management of acute asthma in children. *Pediatrics in Rev* 1996; 17(7): 227-35
- Silverman R. Treatment of acute asthma. *Clinics in Chest Medicine* 2000; 21(2): 361-395
- Silverstein MD, Yunginger JW, Reed CE et al. Attained adult height after childhood asthma: effect of glucocorticoid therapy. *J Allergy Clin Immunol* 1997; 99: 466-74.
- Simon RA, Stevenson DD. Adverse reactions to food and drug additives. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, Busse WW (eds), *Allergy: Principle and Practice*. St Louis: Mosby, 1993.
- Simons FE, Gerstner TV, Cheang MS. Tolerance to the bronchoprotective effect of salmeterol in adolescents with exercise-induced asthma using concurrent inhaled glucocorticoid treatment. *Pediatrics* 1997; 99: 655-9.
- Singhal T, Garg H et al. Efficacy of Home Made Spacer for Asthma. *Indian J Ped* 2001; 68(1): 37 –40
- Sly PD, Cahill P, Willet K, Burton P. Accuracy of mini peak flow meters in indicating changes in lung function in children with asthma. *BMJ* 1994; 308: 572-4.
- Smith SR, Strunk RC : Acute asthma in the Pediatric Emergency Department. *Pediatr Clin North Am* 1997; 46: 1145.
- Spector SL. Alternative treatments in the patient with intractable asthma. *Curr Opin Pulmon Med* 1997; 3: 23-9.
- Sporik R, Holgate ST, Cogswell JJ. Natural history of asthma in childhood-a birth cohort study. *Arch Dis Child* 1991; 66: 1050-3.
- Stempel DA. Management of acute. *Pediatric Clin North Am* 1992; 39: 1311-25
- Strauss RE, Wertheim DL, Bonagura VR, Valacer DJ. Aminophylline therapy dose not improve outcome and increases adverse effects in children hospitalized with acute asthmatic exacerbations. *Pediatrics* 1994; 93: 205-10.
- Szczeklik A, Gryglewski RJ, Czerniawska-Mysik G. Clinical patterns of hypersensitivity to nonsteroidal anti-inflammatory drugs and their pathogenesis. *J Allergy Clin Immunol* 1977; 60: 276-84.
- Szeffler S. Asthma-the new advances. *Adv Pediatr* 2000; 47: 273-308.
- Szeffler SJ, Nelson HS. Alternative agents for anti-inflammatory treatment of asthma. *J Allergy Clin Immunol* 1998; 102: S23-35.
- Tandon MK, Soh PFT, Wood AT. Acupuncture for bronchial asthma ? *Med J Aust* 1991; 154: 409-12.
- The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; 351: 1225-32.
- Tovey ER. Environmental control. In: *Asthma*. Barnes PJ, Grunstein MM, Leff AR, Woolcock AJ (eds). Philadelphia: Lippincott-Raven, 1997, pp 1883-904.

- Tsou Yau KI, Fang LJ, Sheih KH. Factors predisposing infants to lower respiratory tract infections with wheezing in the first two years of life. *Ann Allergy Asthma Immunol* 1999; 82: 5
- Ullah MI, Newman GB, Saunders KB. Influences of age on response to ipratropium and salbutamol in asthma. *Thorax* 1981; 36: 523-9.
- Understanding Asthma (A Management Companion)* Ronald S Walls, Christine R Jenkins (eds.); Sydney. MacLennan and Petty. pp19
- Warner JO, Gotz ML, Landau LI, Levison H, Milner AD, Pedersen S, Silverman M. Management of asthma: A consensus statement. *Arch Dis Child* 1989; 64: 1065-79
- Warner JO, Naspitz CK. Third International Pediatric Consensus Statement on the Management of Childhood Asthma. International Pediatric Asthma Consensus Group. *Pediatr Pulmonol* 1998; 25: 1-17.
- Weinberger M, Hendeles L. Theophylline in asthma. *N Engl J Med* 1996; 334: 1380-8.
- Wildhaber JH, Devason SG, Eber E, Hayden MJ, Everard ML, Summers QA, Le Souef PN. Effect of electrostatic charge, flow delay and multiple actuations on the in vitro delivery of salbutamol from different small volume spacers. *Thorax* 1996; 51: 985-8.
- Wildhaber JH, Dore ND, Davadson SG, LeSouef PN. Inhalation therapy in asthma: nebulizer or pressurized metered-dose inhaler with holding chamber? In vivo comparison of lung deposition in children. *J Pediatrics* 1999; 135: 28-33
- Wolthers OD. Long-, intermediate-and short-term growth studies in asthmatic children treated with inhaled glucocorticosteroids. *Eur Respir J* 1996; 9: 821-7.
- Woolcock A, Lundback B, Ringdas N, Jacques LA. Comparison of addition of salmeterol to inhaled steroids with doubling of the dose of inhaled steroid. *Am J Respir Crit Care Med* 1996; 153: 1481-8.
- Zar HJ, Brown G, Donson H, Brathwaite N, Mann MD, Weinberg EG. Homemade spacers for bronchodilator therapy in children with acute asthma: a randomized trial. *Lancet* 1999; 354: 979-82
- Zeiger RS. Prevention of allergic disease in infancy. In: Schatz M, Zeiger RS, Claman HN (eds), *Asthma and Immunological Diseases in Pregnancy and Early Infancy. Lung Biology in Health and Disease*, Vol. 110. New York: Marcel Dekker, 1998.
- Ziment I, Stein M. Inappropriate and unusual remedies. In: Weiss EB, Stein M (eds) *Bronchial Asthma*. Boston:Little, Brown and Company, 1993; pp. 1145-51.
- Zorc JJ, Pusic MV, Ogborn CJ, Lebet R, Duggan AK. Ipratropium bromide and asthma treatment in pediatric emergency department. *Pediatrics* 1999; 103: 748-52

UPDATE 2003

- British Thoracic Society (BTS) and the Scottish Intercollegiate Guideline Network (SIGN). British Guidelines on the Management of Asthma - *Thorax* 2003; 58: (Suppl I) i1-i92.
- Global Initiative for Asthma (GINA): Global Strategy for Asthma Management and Prevention, Revised 2002. National Institutes Of Health, National Heart, Lung, and Blood Institute. Updated from: NHLBI/WHO Workshop Report: Global Strategy for Asthma Management and Prevention Issued January, 1995. NIH Publication No 02-3659. www.ginasthma.com
- National Asthma Education and Prevention Program. The NAEPP Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma, Update on Selected Topics—2002. National Institutes of Health, Bethesda, US Department of Health and Human Services. *J Allergy Clin Immunol* 2002; 110(5): (Suppl) S142-S219