CHILDHOOD ASTHMA
A PRACTICAL APPROACH TO MANAGEMENT

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Abstract: Asthma is a chronic inflammatory disorder of the airways characterised by recurring symptoms and bronchial hyper-responsiveness, leading to episodic and reversible airway obstruction. Diagnosis is often made clinically, based on the history of symptoms. The goals of management are to i) achieve and maintain control of symptoms, ii) maintain normal activity levels including exercise, iii) and to prevent asthma related morbidity and mortality. The two main groups of medications available are bronchodilators (reliever medication) and anti-inflammatory agents (controller medication like inhaled corticosteroids). Management proceeds in steps, based on the severity of symptoms and response to treatment. Prompt and effective management can lead to good control of symptoms and significant improvement in the quality of life of the child. Practical aspects in inhaler technique, use of corticosteroids and wheeze in infants are outlined.

(Abbreviations: API - Asthma Predictive Index, ICS – Inhaled corticosteroid, MDI – Metered dose inhaler, LABA – Long acting beta agonist, LTRA - Leukotriene receptor antagonist, SABA – Short-acting beta agonist)

Key points in management
• Bronchodilators and corticosteroids form the backbone of asthma pharmacotherapy.
• Pharmacotherapy is only part of the management. Treat the associated modifiable risk factors.
• The pathology of asthma involves inflammation. This has to be treated adequately.
• Patient education regarding symptoms, inhaler technique and avoidance of triggers is vital.
• Follow up – assess response to treatment, review and modify treatment as required.
• Persistent asthma of mild to moderate asthma may be safely and effectively managed in a primary care set up. Severe cases must be referred to a specialist for optimal care.

Introduction:
Childhood asthma is a common clinical problem that has defied a precise definition. It may be broadly defined as a chronic inflammatory disorder of the airways characterised by recurring symptoms and bronchial hyper-responsiveness, leading to episodic and reversible airway obstruction. It is characterised by the history of respiratory symptoms such as “wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation”. The varying nature, recurrence and reversibility of the symptoms are the defining characteristics of asthma (Figure 1).

Pathologically asthma has three important characteristics that contribute to its clinical features
1. Thickening of airways due to chronic inflammation,
2. Secretions that further compromise the airway and
3. Episodic smooth muscle spasm worsening the symptoms.

This article addresses the practical aspects of the management of asthma in children specifically in the outpatient setting.
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DIAGNOSIS OF ASTHMA

The diagnosis of asthma in children is made clinically in most cases (mainly based on the clinical history), with investigations playing only a supportive role. (Box 1).

Key points in history

- The common symptoms in children are wheeze, cough, tightness or pain in the chest.
- The symptoms are often worse at night. This is because bronchi have a normal diurnal variation (they are narrower at night).
- Symptoms may be triggered by viral infections, exercise, changes in environment (cold environment), allergens, emotions etc.
- Symptoms are characteristically episodic and reversible, spontaneously or with medication.
- In most cases, the symptoms are mild. However, they can be severe and persistent to the extent that, it affects the day to day activities of the child, like outdoor play, school performance etc.
- There may be associated atopic features like eczema, allergic rhinitis (bouts of sneezing in the morning is suggestive) and a positive family history.
- In addition to eliciting features which are suggestive of asthma, it is important to rule out other causes of wheeze. Careful history taking to rule out foreign body aspiration, feeding and swallowing difficulties and chronic wet cough is very important. In children, when cough is the only symptom (without wheeze), a detailed evaluation is needed before labelling it as asthma. Chronic wet cough in a child is unlikely due to asthma and must be investigated further. It is also important to carefully listen to the parent’s description of the symptoms as stridor and upper airway sounds may be referred to as wheeze.
- Details of prior treatment and response to such treatments need to be obtained since dramatic response of symptoms to bronchodilators is an important feature that favours the diagnosis of asthma.

Physical Examination

- The physical examination is often normal in asthma, as it is a reversible airway obstruction.
- Important clinical clues in favor of the diagnosis include allergic stigmata, like an allergic salute, a transverse crease over the nostril, boggy appearance around the eyes, healed or active eczematous lesions in the popliteal/cubital fossa and on the neck (Figure 2).
- Symptoms during an acute exacerbation - wheeze, decreased breath sounds due to blocked airway and apparent increased work of breathing are the main physical findings. In severe, life-threatening asthma, there may be no breath sounds on auscultation – “silent chest”.
- In addition, tachypnea, tachycardia and features of hypoxia may be present. Clubbing, short stature or severe growth failure, persistent localized lung signs are to be considered as red flags and their presence warrant further investigation.

Box 1: History and examination in asthma

- Common symptoms - wheeze, cough, tightness or pain in the chest.
- Symptoms are often worse at night
- Asthma triggers – exercise, cold weather, emotion, dust and air pollutants
- Symptoms are episodic and reversible with medication.
- All that wheezes is not asthma – rule out other causes.
- Physical examination is often normal.
- Look for allergic stigmata- allergic salute, transverse crease over the nostril, boggy appearance around the eyes, eczematous lesions.
- Red flags - Tachypnea, tachycardia, features of hypoxia, clubbing, short stature or severe growth failure.
ROLE OF INVESTIGATIONS
The role of investigations in the diagnosis of asthma in children is often only supportive. In limited resource settings, where facilities like spirometry are not available, a diagnosis can be reliably made (and treatment initiated) with a good history and physical examination.

**Spirometry**—This is the gold standard test for diagnosis of asthma. It is used to demonstrate airflow obstruction and reversibility after use of a bronchodilator. In children, inability to adhere to the correct technique (which involves deep inspiration and forceful, complete expiration) can lead to misleading results. It is extremely important therefore, that the test is performed under the guidance of an experienced technician/doctor. A child above the age of 7 years can usually perform a reliable spirometry. Total expiration time of 3 sec is acceptable in children (as against 6 sec in adults). The FEV1/FVC (forced expiratory volume in 1 sec/forced vital capacity) ratio is normally >90% in children. A lower value is indicative of obstruction. Reversibility can be demonstrated by FEV1 gain of >12% after administration of a bronchodilator.

**Chest X-Ray**—Helps in ruling out differential diagnosis like foreign body aspiration, tuberculosis, bronchiectasis and congenital cardiac or pulmonary defects. Atopy can be objectively shown by demonstrating an elevated immunoglobulin E (IgE) level or positive skin allergy testing. In children where clinical features point to an alternate cause for a wheeze, other investigations like echocardiogram, swallow studies, bronchoscopy, CT imaging etc. may be necessary.

**MANAGEMENT OUTLINE**
The goals of management are
- To achieve and maintain control of symptoms,
- Maintain normal activity levels including exercise and
- Prevent asthma related morbidity and mortality.

The two main groups of medications available are—
1. **Bronchodilators (reliever medication):** These provide relief of symptoms during an episode and are used when required. Most commonly used drug is salbutamol.
2. **Anti-inflammatory agents (controller medication):** The most effective and widely used agent is inhaled corticosteroids.

**KEY POINTS IN MANAGEMENT**
The hallmark of asthma is airway inflammation and it is like the glowing embers of wood. A flare up can happen any time leading to severe exacerbation of symptoms. Though often mild, they may be serious enough in some cases as to be life threatening.

- There may be a group of patients with mild inflammation, where the symptoms are infrequent and mild with infrequent flare-ups. If they do not have risk factors for severe exacerbation (Box 3), they will require only intermittent need-based bronchodilator therapy.
- In patients with persistent symptoms, with frequent flare-ups that affect the quality of life, the inflammation is significant and the mainstay of treatment is control of inflammation using inhaled steroids. Unless the inflammation is addressed, the patient will not get relief from symptoms of asthma.

- Pharmacotherapy only forms a part of management of asthma. Another important aspect is control of modifiable risk factors like avoidance of allergen exposure, when feasible.
- Patient education about the need for continuous and,
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often prolonged therapy; correct use of devices like metered dose inhaler (MDI) and spacers goes a long way in successful management of these children.

- Asthma management also involves close follow up, assessment of symptom control, review of medication use and compliance.

A number of good guidelines formulated based on well conducted studies are available and these provide an evidence based approach to efficacious asthma control while highlighting patient safety. It is important to understand the principles on which these guidelines are based and make sure they are not compromised when clinician decides to make a deviation from it due to specific patient needs or circumstances.

STEP WISE MANAGEMENT

The GINA (Global Initiative for Asthma) report 2015 provides a set of excellent updated guidelines for management of asthma. The tables used in this discussion are borrowed from GINA website (used with permission). It suggests the use of a step wise approach for initiation of pharmacotherapy (Figure 3). The steps are based on the severity and frequency of symptoms in an ascending order. Steps 1 to 3 can be safely administered by a general practitioner. When considering stepping up treatment to level 4 or 5, it is advisable to refer to a specialist.

Step 1: (When symptoms are minor and far apart)
Short acting beta agonists (SABA) when required

All patients with the diagnosis of asthma are advised short acting bronchodilators (salbutamol inhaler) when the child has symptoms (Reliever medication). This option should be reserved for patients with occasional daytime symptoms (e.g. less than twice a month) of

Figure 3: Step wise management (In order of severity of disease)

- Step 1 - Bronchodilators (when needed)
- Step 2 - Low dose ICS (plus bronchodilators when needed)
- Step 3 - Low dose ICS + LTRA/ Medium dose ICS/Low dose ICS+LABA (for older children)
- Step 4 - Medium/ high dose ICS +LABA or high dose ICS +LTRA
- Step 5 - Step 4 plus oral steroids, theophylline, other add-on agents

Steps 1 to 3 can be safely administered by a general practitioner. When considering stepping up treatment to level 4 or 5, it is advisable to refer to a specialist.

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short duration, with no night waking and with normal lung function.

Dosage of SABA
Parents are advised to give 2-4 puffs of inhaled salbutamol for wheeze and cough. This must be given as soon as symptoms are noticed and need to be repeated every 2-4 hours in usual circumstances. They must understand that use of this drug is need based. The dose may be increased to 6-12 puffs in one sitting if symptoms worsen. Frequency can be as often as every 1 hour or as infrequent as once in 6-8 hours depending on the severity. Oral preparations are better avoided. Inhaler form (with spacer) does not need any electrical supply for delivery, works well at low doses, is cheaper in the long term and can be life-saving during an asthma attack.

Step 2: (When there is persistent inflammation causing frequent and severe symptoms)
Regular low dose inhaled corticosteroids (ICS) plus SABA when required

Treatment with low dose reduces asthma symptoms, increases lung function, improves quality of life, and reduces the risk of exacerbations and asthma-related hospitalizations or death.

When do you use step 2?
For best outcomes, controller treatment (ICS), when indicated, should be initiated as early as possible after making the diagnosis of asthma. Indications for regular low-dose ICS include
- Asthma symptoms more than twice a month
- Waking due to asthma more than once a month
- Any asthma symptoms plus any risk factors for exacerbations

It is to be noted that steroids exhibit most of their benefit at low dose and unnecessary prescription of a high dose should be avoided (See Box 2 for dosage). Most ICS are administered in two divided doses per day (Mometasone is an exception and is used once daily).

Monteleukast (oral) may be an alternative to low dose corticosteroids, especially when the symptoms are very mild but persistent, when there is accompanying allergic rhinitis or exercise induced symptoms. One has to remember that it is not as effective as inhaled steroids and should not be used as monotherapy in patients with risk factors (Box 3).

Step 3: (children 6–11 years)
Daily moderate dose ICS plus SABA when required
Daily low dose ICS/Long acting beta agonists (LABA) combination plus SABA when required

Before considering a step up, check for common problems such as incorrect inhaler technique, poor adherence, and environmental exposures, and confirm that the symptoms are due to asthma. Leukotriene receptor antagonists (LTRA) like Monteleukast may be used instead of ICS for patients who do not tolerate ICS but they are less effective.

Before stepping up, it is important to
- Review the diagnosis of asthma, check compliance to medications, and inhaler technique
- Look for co-morbid conditions that may complicate asthma like allergic rhinitis, adenoiditis etc.

Consider starting at a higher step if:
- There are troublesome asthma symptoms on most days
- Waking from asthma once or more a week, especially if any risk factors for exacerbations

When do you use Step 4 or 5?
As shown in Figure 3, higher steps of therapy involve use of higher doses of ICS/LABA in older children, addition of Monteleukast and in severe cases, daily oral steroids, theophylline and other drugs. A patient who needs such treatment should be assessed by a specialist.

How often should the patients be reviewed?
After initiating a management plan, it’s desirable to review the patient after 1-2 months. The response to therapy will be evident by this time and parents often tend to discontinue therapy around this time, as the child seems to be doing well. Subsequent reviews may be planned according to the response to treatment. A patient on inhaled corticosteroids should be seen at least twice a year.

At each visit:
- The symptom control is assessed
- Details of any events like exacerbations is sought and documented
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- The technique of inhaler use is reviewed and the action plan is revised
- The need for ongoing treatment and compliance is reinforced
- It is a good practice to observe the inhaler technique during each visit

When feasible, spirometry may be repeated 6 months after initiating therapy to objectively assess improvement.

**Box 2: Low, medium and high dose inhaled corticosteroids for children aged 6–11 years**

<table>
<thead>
<tr>
<th>Inhaled corticosteroid</th>
<th>Total daily dose (mcg)</th>
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<tbody>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td>Beclometasone dipropionate (CFC)</td>
<td>100–200</td>
</tr>
<tr>
<td>Beclometasone dipropionate (HFA)</td>
<td>50–100</td>
</tr>
<tr>
<td>Budesonide (DPI)</td>
<td>100–200</td>
</tr>
<tr>
<td>Budesonide (nebul)</td>
<td>250–500</td>
</tr>
<tr>
<td>Ciclesonide (HFA)</td>
<td>80</td>
</tr>
<tr>
<td>Fluticasone propionate (DPI)</td>
<td>100–200</td>
</tr>
<tr>
<td>Fluticasone propionate (HFA)</td>
<td>100–200</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>110</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>400–800</td>
</tr>
</tbody>
</table>

Most ICS are administered in 2 divided doses (except mometasone)
This is not a table of equivalence, but of estimated clinical comparability
Most of the clinical benefit from ICS is seen at low doses
High doses are arbitrary, but for most ICS are those that, with prolonged use, are associated with increased risk of systemic side-effects
CFC: Chlorofluorocarbon; HFA: Hydrofluoroalkane; From the *Global Strategy for Asthma Management and Prevention 2015*, © Global Initiative for Asthma (GINA), all rights reserved.

**Box 3: Risk factors for poor asthma outcomes** (GINA 2015)
Potentially modifiable independent risk factors for flare-ups (exacerbations)
- Uncontrolled asthma symptoms
- High SABA use (with increased mortality if >1 x 200-dose canister/month)
- Inadequate ICS: not prescribed ICS; poor adherence; incorrect inhaler technique
- Low FEV1, especially if<60% predicted
- Major psychological or socioeconomic problems
- Exposures: smoking, allergen exposure if sensitized
- Co-morbidities: obesity; rhinosinusitis, confirmed food allergy

**Other major independent risk factors for flare-ups (exacerbations)**
- Ever intubated or in intensive care unit for asthma
- ≥1 severe exacerbation in last 12 months

**When do you step down?**
Stepping down refers to decreasing controller treatment from higher doses or combinations to a lower level. Step down may be considered after at least 3 months of good control(Figure 4) in children with no risk factors for poor asthma control (Box 3).
If the patient is already on a low dose ICS, there is no step down. In these individuals, stepping down to once a day dosing or alternate day dosing of inhaled steroid is not advisable. If initial asthma presentation is with an exacerbation, it is a preferable option to give a short
course of oral steroids and start regular controller treatment and then step down once control is achieved. It is important to arrange a follow-up when step down is initiated, for timely recognition of any worsening.

**How long to treat?**

It is important to discuss the plan of therapy with the patients at the commencement of treatment. This helps to avoid unrealistic expectations. One cannot predict how long child will need controller inhaler treatment. Instead of promising cure at a certain age or discontinuation of inhalers after a few months, the clinician should emphasize the need for symptom control and explain that treatment will continue as long as the child needs symptom control (many months to years).

The risk factors need to be assessed before deciding to stop treatment. A child with risk factors for poor control is not a suitable candidate for a cessation of treatment. It is important to choose a favorable time, in terms of environmental and social factors for stopping treatment; it is unwise to plan it during winter month, during, a flu epidemic, before travel etc. Whenever possible, a spirometry to document a good pulmonary function test (PFT) is desirable before trial of treatment cessation. The reliever therapy with as-needed bronchodilators will be required by these patients even after stopping controller medications and this needs to be discussed beforehand. Children with milder phenotype show better success of treatment cessation.

**INHALER TECHNIQUE**

**Key points**

- Always use a valved spacer with metered dose inhaler.
- Children less than 3 years will need a mask as they cannot reliably breathe through mouth. (Figures 5-7)

- Shake the MDI, fix on to spacer and keep the mouth piece in child’s mouth.
- Do 1-2 practice breaths while parent observes that child is breathing slowly and deeply in –right into the chest. They can watch the valve opening as child breathes in and closing as child breathes out.
- After the actuation of the inhaler, the child must breathe 4-5 times to ensure that the drug in the spacer has been completely inhaled.
- After inhaled corticosteroids, the child should immediately rinse the mouth with tap water and spit out to avoid systemic absorption of the medication.

In small babies movement of the valve may not be very obvious, but it does not matter. If you provide an airtight seal, the baby will get the medicine from the spacer. Do not use a valveless spacer or manually remove the valve of the spacer “to make it easier”.

**ALTERNATIVE OPTIONS**

- **LTRA alone:** A leukotriene antagonist like monteleukast alone may be used in patients with mild persistent symptoms with variable success rates.
- **Intermittent ICS:** This involves use of high dose steroids (1-1.6 mg per day) started at the beginning of symptoms and continued for 7-10 days, rather than daily low dose steroids. Although trials have shown at least similar benefit for this regime as compared to standard daily low dose ICS, the candidates for this should be chosen wisely. A child without risk factors with reliable parents, who will...
strictly follow the instructions, may be offered this option. But in most cases the standard daily regime will be a better option.

- **Use of theophylline derivatives:** Theophylline derivatives are not preferred for use in children as controller treatment.

**SOME COMMON CONCERNS**

- **Food:** Parents are often concerned that certain food items like milk, fruits etc., may be asthma exacerbating agents. In most cases children can be allowed to consume these healthy food items and once asthma treatment is initiated parents will appreciate that it is not the food items which cause the exacerbation. However, if the child has had a true anaphylaxis to any food item, it should never be given again.

- **Physical activity:** Many children have exercise induced symptoms. The solution to this is not to restrict exercise, but to control asthma to the level that normal physical activity is tolerated. It is to be emphasized that outdoor play and physical activity is important for a child’s development. All children with exercise induced symptoms should be instructed to use a short acting bronchodilator inhaler 10 minutes before a planned sports activity. School authorities also should be informed about child’s asthma and instructed about what needs to be done in case of an emergency.

- **Bath:** The need for daily bath and frequent hair wash must be discussed.

- **Allergen avoidance:** It is important to decrease exposure to cigarette smoke, dust and fungus in the home environment. Avoidance of numerous food items based on positive sensitization on allergy panels is not advisable. Those children with proven food allergy are better managed by a specialist.

- **Immunotherapy:** There is varying level of evidence regarding this. It can be tried in select candidates by experienced allergy specialists.

- **Side effects of inhaled steroids on growth:** Side effects are negligible with low dose steroids when taken by correct technique. The benefits far outweigh the risks. Fear of side effects should never be a reason to withhold treatment. There may be a drop in height velocity in the initial years after initiating higher doses inhaled corticosteroid therapy, but there is no change in adult height.\(^8,9\)

- **Addiction to asthma medication:** is a myth and some time has to be spent in explaining this to parents.

**INFANT AND PRESCHOOL WHEEZE**

It is worthwhile to discuss the entity of infant and preschool wheeze in little more detail. An infant/pre-school child visits the Emergency Department an average of 2.5 times more than a child/adult for wheeze. Not all such episodes are “asthma”. Many such episodes are transient wheeze due to smaller caliber of
the airways in these children. Other common causes are acute viral infections (due to edema, bronchospasm), aspiration (due to poor feeding technique, swallowing dysfunction, gastro-oesophageal reflux), congenital heart disease, congenital anomalies of the respiratory tract etc. Management of a wheezy infant is not easy. The most important step is to rule out progressive lung disease, underlying pathology (watch for danger signs). Unindicated (harmful) treatment is to be avoided (eg. unindicated oral steroids and long acting beta agonists, anti tuberculous treatment etc.). Most of these episodes are mild and self-limiting and counseling of the parents is a vital part of management.

A phenotypic classification for such wheezes do exist
- Viral episodic wheeze – Where the infant/child wheezes only during acute viral infections and is well in between.
- Multi trigger wheeze – Where a wheeze is triggered by both viruses and other triggers like environmental changes, exercise etc. These children are more likely to be atopic and have family history of asthma/atopy.

This classification is not exact nor do children remain in the same group over time. The management guidelines based on such classification are not very evidence based, and are based on consensus and expert opinion—which is due to the inherent difficulty in classification and design of studies on these conditions. The modified Asthma Predictive Index (API) (Figure 8)\textsuperscript{10} is a useful tool to use, to predict the development of asthma in these children. A negative score is reassuring as it indicates that the children will usually grow out of the wheeze.

In case of infrequent wheezes, mild episodes, with a negative API it is safe to treat when necessary with bronchodilators. If they symptoms are more frequent and severe with a positive API, inhaled steroids using metered dose inhaler with spacer+/- mask can be used daily. Nebulized steroids are better avoided for prolonged use.

<table>
<thead>
<tr>
<th>Mandatory</th>
<th>Major Criteria (1/2)</th>
<th>Minor Criteria (2/3)</th>
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<tbody>
<tr>
<td>Strigent: Children with 3+ episodes of wheezing before the age of 3 years</td>
<td>Parental Asthma</td>
<td>Allergic sensitization to milk, eggs, or peanuts</td>
</tr>
<tr>
<td>Loose: Children with &lt;3 episodes of wheezing before the age of 3 years</td>
<td>Eczema</td>
<td>Wheezing apart from colds</td>
</tr>
<tr>
<td></td>
<td>Allergic sensitization to 1 or more aeroallergens</td>
<td>Eosinophilia (&gt;4%)</td>
</tr>
</tbody>
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Figure 8 – Modified Asthma Predictive Index (API)\textsuperscript{10}

In borderline cases, a trial of treatment is justified. A trial of 2-3 months of LTRA/ICS with follow up may be planned. The improvement is assessed and documented at the follow-up visit. If not beneficial, the treatment is stopped. The diagnosis is to be reviewed at each visit. Take into consideration, the new co-morbidities as age changes. If there is history of severe wheezing episodes or past admissions in ICU, it is better to treat with inhaled steroids even if it has occurred infrequently.

What should we do? Remember these ‘rules’
- Infrequent wheezes, mild episodes, less API – safe to treat with as needed bronchodilators only
- More frequent symptoms, more severe episodes, more risk factors, higher API - use inhaled steroids daily
- Intermittent high dose steroids may have a role when episodes are infrequent but of moderate severity.
- LTRA – May work well for some young children. This can be tried (8-12 weeks) and if useful can be continued.
- Nebulised steroids are better avoided for prolonged use.

References:
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TAKE HOME POINTS

- Asthma in school aged children – follow same principles as adult asthma
- Recognize the importance of history and limitations of investigations.
- Start ICS in low dose and do not withhold it in a child who requires it, for fear of side effects.
- Compliance and technique of administration decides success of treatment. Inhalers with valved spacer should be used in all asthmatics for delivery of bronchodilators or ICS. Oral bronchodilators are best avoided and nebulizer bronchodilators should be reserved for severe exacerbations in emergency department. Using nebulizer at home should be an exception rather than rule.
- All children must use a valved spacer for delivery of bronchodilators and inhaled steroids.
- Wheeze in small infants and preschoolers – rule out differentials.
- Continued treatment and regular follow up is important.


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