Treating Exacerbations of Asthma in Children: The Role of Systemic Corticosteroids
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Treating Exacerbations of Asthma in Children: The Role of Systemic Corticosteroids

Gary Rachelefsky, MD

ABSTRACT. Objective. To review the use of systemic corticosteroids to treat recurrent, acute asthma episodes in children, with a focus on the role of oral corticosteroids.

Methods. A comprehensive review of the literature was performed using the Medline database (January 1966–October 2002) and the Embase database (January 1980–August 2002).

Results. The significant findings of 17 selected, controlled clinical trials of oral corticosteroids (OCSs) for acute exacerbations of asthma in children, compared with placebo or with other formulations of corticosteroids, can be summarized as follows: 1) OCSs are effective for the outpatient treatment of acute asthma, 2) pulmonary function tests may not be the best means of assessing the efficacy of OCSs for acute asthma, 3) early administration of OCSs for acute asthma reduces hospitalizations, 4) the critical factor for a positive outcome is early administration of the corticosteroid, and 5) OCSs are preferred for the outpatient treatment of acute asthma.

Conclusions. Early treatment of acute asthma symptoms with OCSs in children with a pattern of recurrent acute asthma may decrease the severity of acute asthma episodes and reduce the likelihood of subsequent relapses. Attention should be given to identifying these children and standardizing a treatment approach based on accepted, consistent definitions of what constitutes an asthma exacerbation and recurrence. A suggested protocol is described. Pediatrics 2003;112:382–397; acute asthma, asthma exacerbation, asthma therapy, childhood asthma, emergency department, steroids, systemic corticosteroids, upper respiratory tract infection, wheeze.

ABBREVIATIONS. ED, emergency department; OCS, oral corticosteroid; PEF(R), peak expiratory flow (rate); URI, upper respiratory tract infection; ICS, inhaled corticosteroid; IV, intravenous; RSV, respiratory syncytial virus.

Asthma exacerbations are the leading sources of hospital admissions for children in the United States.1–4 Children younger than 5 years have the highest rate of hospital admissions because of asthma, and this population continues to show the greatest increases in morbidity. Between 1980 and 1995, reported asthma increased by >160% in very young children (infants through 4 years of age) compared with the significant but substantially smaller increase of approximately 74% in school-age children (between 5 and 14 years of age). During the same period, hospitalizations for asthma rose by approximately 45% for very young children compared with just >13% for school-age children.2 Children who live in impoverished urban areas are especially at risk, with significant rates of unscheduled urgent care visits and hospitalizations for sudden, severe asthma.5

These increases in asthma and associated morbidity have occurred despite recent advances in treatment and the availability of various national and international guidelines for managing asthma.4,6–14 Although there are several possible explanations for increased disease prevalence (eg, better diagnostic criteria, earlier diagnosis, changing environmental factors), the fact remains that there exists significant variation in medical care for children who experience an asthma exacerbation.5 This is particularly true for the youngest patients. Outpatient emergency care for children with asthma has improved since the first publication of national guidelines in 1992.15,16 The 2 most obvious trends have been increased use of pulmonary function testing in capable children and the early administration of systemic corticosteroids for pediatric acute asthma seen in the emergency department (ED).3,15–19 Nonetheless, there remains considerable heterogeneity in the treatment of acute asthma, particularly for patients younger than 5 years, which may reflect challenges in classifying sudden, severe asthma in this population as well as in administering appropriate therapy and, to some extent, the differences in various guidelines available. Table 1 presents the recommendations for starting corticosteroid treatment, including doses, for children with acute asthma found in selected, commonly used guidelines and practice parameters. Although each recommends initial treatment with a short-acting bronchodilator (preferably inhaled) and oxygen as needed to maintain a saturation level >90% to 94%, no 2 are alike in their corticosteroid recommendations for children.

METHODS

A comprehensive review of the literature was performed on the topic of using oral corticosteroids (OCSs) to treat acute asthma in children. The literature included full-length papers in English published in peer-reviewed medical journals and non-English articles published with English abstracts. The articles were selected on the basis of a broad literature search using the Medline database (January 1966–October 2002) and the Embase database (January 1980–August 2002). Key text words included but were not limited to pediatric asthma, childhood asthma, acute asthma, and corticosteroid. Articles obtained were further searched for relevant references published before 1966.

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measurements. For this reason, the patient can sense significant airflow limitation even when measurements of lung function are obtained. Associated respiratory distress with documented and symptoms of shortness of breath, wheezing, chest tightness, or some combination of these . . . [with] associated respiratory distress with documented and quantified decreases in expiratory airflow when measurements of lung function are obtained.”

Obtaining measurements of lung function is the critical diagnostic factor differentiating evaluation of the very young patient with acute asthma. Most asthma patients—including school-age children—can sense significant airflow limitation even when symptoms seem minimal; the airflow obstruction can be documented by either spirometry or peak flow measurements. For this reason, the patient’s assessment of his or her symptoms is critical to evaluating exacerbation severity. However, for infants and young children who cannot communicate a feeling of airflow limitation, exacerbations may have a rapid and unexpected onset and additional deterioration may occur quickly. Immediate attention is needed and should include the child’s degree of alertness and responsiveness to the environment, the child’s color, and the observed level of respiratory distress. For infants, the ability to feed or suckle and the quality of crying also are important. Exacerbations can be classified as mild, moderate, or severe according to the physiologic and clinical observations described in Table 2.

Objective measures of lung function during an exacerbation are desired but not usually practical in young children. Children who are aged 5 years and older and regularly use a peak flow meter at home may be able to perform the maneuver in the ED. However, it is unrealistic to expect objective measurements in younger children, children with little experience with peak flow meters, or children in significant respiratory distress. Furthermore, even for children who can use a peak flow meter, the measurement may underestimate the degree of obstruction. For these reasons, a validated asthma severity measure such as the Pulmonary Score described by Smith and Strunk may be preferred for young children. This measure uses a scoring scale from 0 (very mild exacerbation) to 9 (very severe exacerbation) and has been tested in children who present to the ED with mild to severe acute asthma and shown to correlate well with the peak expiratory flow rate (PEFR).

Rapid identification and classification of respiratory distress can significantly enhance treatment outcomes and reduce complications. However, a pattern of recurring exacerbations or severe symptoms treated in the ED can signal a child with particular risk factors for morbidity. Thus, once the initial assessment is made and treatment is initiated, the clinician should address the child’s history. For the current exacerbation, significant factors include the duration of symptoms, symptom triggers, recent upper respiratory infections (URIs), vomiting, use of rescue medications (including time of last dose), and use of long-term controller medications. Information should also be obtained regarding previous exacerbations including the number of courses of OCSs, ED visits, and hospitalizations for asthma in the past year; the last ED visit and/or hospital admission; the

### TABLE 1. Recommendations for Using OCSs to Treat Acute Exacerbations of Asthma in Children From Selected, Currently Used Asthma Guidelines

<table>
<thead>
<tr>
<th>Guidelines</th>
<th>Dose</th>
<th>When to Start</th>
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<tr>
<td>BTS (1996)</td>
<td>5–15 y: single dose of 1–2 mg/kg prednisolone, maximum 40 mg; then 1–2 mg/kg/d, maximum 40 mg for 4 d</td>
<td>Patient with incomplete response to initial treatment with short-acting β2-agonist (by nebulization or MDI + spacer ± face mask) 3–4x hourly, after 3–4 h</td>
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<td>Canada (1999)</td>
<td>&lt;1 y: 1–2 mg/kg/d prednisolone for 1–3 d</td>
<td>As soon as possible in all patients with moderate or severe asthma (ie, FEV1 or PEF &lt;60% of predicted)</td>
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<td>NHLBI (1997)</td>
<td>5–15 y: single dose of 40–60 mg prednisone or equivalent; then 30–60 mg/d for 7–14 d</td>
<td>Patient with incomplete response to initial treatment with short-acting β2-agonist, up to 3 treatments of 2–4 puffs by MDI at 20-min intervals</td>
</tr>
<tr>
<td>Child (³12 y)</td>
<td>≤5 y: 1–2 mg/kg/d prednisolone or equivalent, maximum 50 mg/d, for 3–5 d</td>
<td>If the response to initial treatment with a rapid-acting inhaled β2-agonist (up to 3 treatments of 2–4 puffs by MDI at 20-min intervals) is not prompt or sustained (eg, PEF &gt;80% predicted or personal best) after 1 h</td>
</tr>
</tbody>
</table>

BTS indicates British Thoracic Society; NHLBI, National Heart, Lung, and Blood Institute; FEV1, forced expiratory volume in 1 second; MDI, metered dose inhaler.

**SUDDEN SEVERE ASTHMA IN YOUNG CHILDREN**

According to national guidelines, an asthma exacerbation can be defined as an increase in symptoms with a decrease in pulmonary function as measured by spirometry or peak flow and/or increased use of bronchodilators. For children, the American Academy of Pediatrics has defined an asthma exacerbation as “an abrupt and/or progressive worsening of symptoms of shortness of breath, wheezing, chest tightness, or some combination of these . . . [with] associated respiratory distress with documented and quantified decreases in expiratory airflow when measurements of lung function are obtained.”

Obtaining measurements of lung function is the critical diagnostic factor differentiating evaluation of the very young patient with acute asthma. Most asthma patients—including school-age children—can sense significant airflow limitation even when symptoms seem minimal; the airflow obstruction can be documented by either spirometry or peak flow measurements. For this reason, the patient’s assessment of his or her symptoms is critical to evaluating exacerbation severity. However, for infants and young children who cannot communicate a feeling of airflow limitation, exacerbations may have a rapid and unexpected onset and additional deterioration may occur quickly. Immediate attention is needed and should include the child’s degree of alertness and responsiveness to the environment, the child’s color, and the observed level of respiratory distress. For infants, the ability to feed or suckle and the quality of crying also are important. Exacerbations can be classified as mild, moderate, or severe according to the physiologic and clinical observations described in Table 2.

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Rapid identification and classification of respiratory distress can significantly enhance treatment outcomes and reduce complications. However, a pattern of recurring exacerbations or severe symptoms treated in the ED can signal a child with particular risk factors for morbidity. Thus, once the initial assessment is made and treatment is initiated, the clinician should address the child’s history. For the current exacerbation, significant factors include the duration of symptoms, symptom triggers, recent upper respiratory infections (URIs), vomiting, use of rescue medications (including time of last dose), and use of long-term controller medications. Information should also be obtained regarding previous exacerbations including the number of courses of OCSs, ED visits, and hospitalizations for asthma in the past year; the last ED visit and/or hospital admission; the
last course of OCS; and any intensive care unit admissions or intubations. Past ED visits and hospitalizations are red flags indicating children whose asthma is poorly controlled, regardless of age. These patients’ symptoms may be unstable and can deteriorate rapidly and unexpectedly. In addition, the older child whose history includes rapid onset (ie, ≤3 hours) of severe symptoms is at increased risk for sudden deterioration and should be watched carefully and treated aggressively.

**TREATING ACUTE ASTHMA IN CHILDREN**

Asthma exacerbations in children should be treated promptly and aggressively at home (Fig 1) and/or in the ED, depending on symptom severity (Fig 2). The first line of treatment for exacerbations of wheeze at home is adequate dosing with a short-acting β2-agonist, preferably administered by inhalation. As shown in Fig 1, follow-up is determined by the initial response to bronchodilator therapy. In each case, the child’s physician should be notified. If the exacerbation is mild and there is a good response to bronchodilator (ie, PEF returns to normal in a capable child), then nothing more is needed other than observation and continued β-agonist treatment as shown in Fig 1. If the child is using an inhaled corticosteroid (ICS), then a step-up in dose should be considered. For any other outcome, an OCS is added to the initial bronchodilator therapy; the child with a severe exacerbation or poor response to treatment (ie, continued marked wheezing or shortness of breath; PEF <50% predicted in a capable child) needs to be assessed in the ED.

Most children who are seen in an ED for an acute episode of wheezing receive systemic corticosteroids as recommended by national and international guidelines. The current approach to treatment in the United States is shown in Fig 2. However, despite adoption of the national guidelines, significant variation exists in how older and younger children are treated for asthma exacerbations in the ED; older children are more likely to receive corticoste-
Assess Severity

Measure PEF: Value ≤ 50% personal best or predicted suggests severe exacerbation.

Note signs and symptoms: Degrees of cough, breathlessness, wheeze, and chest tightness correlate imperfectly with severity of exacerbation. Accessory muscle use and suprasternal retractions suggest severe exacerbation.

Initial Treatment

- Inhaled short-acting β₂-agonist: up to three treatments of 2-4 puffs by MDI at 20-minute intervals or single nebulizer treatment.

Good Response

Mild Exacerbation
PEF > 80% predicted or personal best
No wheezing or shortness of breath
Response to β₂-agonist sustained for 4 hours
- May continue β₂-agonist every 3-4 h for 24-48 hours.
- For patients on inhaled corticosteroids, double dose for 7-10 days.

- Contact clinician for followup instructions.

Incomplete Response

Moderate Exacerbation
PEF 50-80% predicted or personal best
Persistent wheezing and shortness of breath
- Add oral corticosteroid.
- Continue β₂-agonist.

- Contact clinician urgently (this day) for Instructions.

Poor Response

Severe Exacerbation
PEF < 50% predicted or personal best
Marked wheezing and shortness of breath
- Add oral corticosteroid.
- Repeat β₂-agonist immediately.
- If distress is severe and nonresponsive, call your doctor and proceed to emergency department; consider calling ambulance or 9-1-1.

- Proceed to emergency department.

Fig 1. Home management of an acute exacerbation of asthma in a child. Adapted from the National Asthma Education and Prevention Program’s Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma (1997).10

roids. A cross-sectional ED study of viral-induced exacerbations of wheeze reported administration of systemic corticosteroids to 71% of children older than 2 years but only to 45% of children younger than 24 months.21

The efficacy of systemic corticosteroids to treat exacerbations of asthma in older children and adults is well documented; these agents have been used to treat acute asthma for >50 years.20,22–27 In most cases, clinical improvement has been reported within several hours, and the available data for children support findings in older patients—that is, early treatment with systemic corticosteroids can reduce both the duration and the severity of an acute episode of asthma.20,22,27 Storr et al.28 showed that for 140 children who were older than 2 years and presented with acute asthma in the ED, a single dose of prednisolone (30 mg in children 2–5 years, 60 mg for children 5 years and older) significantly improved clinical outcomes. Twenty children who received prednisolone were discharged within a few hours compared with 2 children in the placebo group (P < .0001). For children who remained in the hospital, the mean duration of stay was 24 hours for the prednisolone group and 39 hours for the children who received placebo (P = .0011). In addition, for the hospitalized children, early administration of the corticosteroid was associated with a reduced need for added corticosteroids: 20 children in the prednisolone group and 44 children in the placebo group required more corticosteroids during their hospital stay (P = .0005).28 Similar results were reported in a double-blind, placebo-controlled trial by Scarfone et al.,29 who showed that 1 dose of oral prednisone (2 mg/kg) administered on admission to the ED significantly decreased the pulmonary index over a 4-hour period (P < .001) in 75 children between the ages of 1 and 17 years. The subsequent hospitalization rates were 31% (11 of 36) for children who were treated with the corticosteroid compared with 49% (19 of 39) for placebo-treated children. The between-treatment difference for hospital admissions increased with ex-
Acute exacerbation: for children who presented with an initial pulmonary index $\geq 10$, the hospitalization rates were 32% and 72% ($P < .05$) in the prednisone and placebo groups, respectively. Other studies suggest that continued administration of oral (or inhaled) corticosteroid for 3 to 7 days after the initial exacerbation may provide added benefit.$^{30-33}$ Table 4 presents the significant findings of con-

![Diagram of ED management of acute exacerbation of asthma in a child.](image-url)
trolled clinical trials of OCSs for acute exacerbations of asthma in children, compared with placebo or with other formulations of corticosteroids. These can be summarized as follows:

1. OCSs are effective for the outpatient treatment of acute asthma. OCSs were more effective than placebo in the outpatient treatment of acute asthma (ie, when administered at home, in the doctor’s office or clinic, or in the ED). Of the 17 outpatient studies included in Table 4, only 2 reported lack of efficacy with corticosteroid treatment.34,35 Both studies involved treatment given at home or in the clinic (ie, milder episodes for which the child was not taken to an ED). Another study reported equivocal results in 28 children who were treated with tapering doses of methylprednisolone or matching placebo over the course of 1 week.36 These children had presented to the clinic with acute exacerbations requiring at least 3 consecutive treatments with bronchodilator and were well enough to go home but still had measurements of forced expiratory volume in 1 second below 80% of their personal baseline. Trends favored the corticosteroid, but statistical significance was not attained. Reviewing the data, the investigators suggested that the between-treatment differences would have been more dramatic with increased exacerbation severity.36 Review of Table 4 supports this: significant between-treatment differences favoring corticosteroid therapy are more likely to be reported for studies of children who present to an ED for their acute asthma.28,30,37 For the majority of the outpatient clinical trials, early treatment was associated with shortened duration of the exacerbation, reduced severity of acute symptoms, and fewer complications—including hospital admissions and relapses requiring additional treatment—after the exacerbation.28,29,31–33,37–44

2. Pulmonary function tests may not be the best means of assessing the efficacy of OCSs for acute asthma. Although OCSs have been shown to improve acute symptoms and reduce arterial hypoxemia in children, clinical trials have not shown consistent improvements in pulmonary function as measured by spirometry or PEF in capable children.28,32,33,39–41,43,44 This is also true when corticosteroids are administered by other routes (eg, intravenous [IV], inhalation).32,33,41,45

3. Early administration of OCSs for acute asthma reduces hospitalizations. Administration of an OCS within 45 minutes of ED arrival was associated with fewer hospital admissions.28,29,32,33,41–44

4. The critical factor for a positive outcome is early administration of the corticosteroid. The most important factor for a positive clinical response to treatment of acute asthma with corticosteroids was early administration at the first sign of symptoms if given at home or within 1 hour of presentation if administered at the ED. For children who had to be hospitalized for their exacerbation, early and continued administration of a corticosteroid was associated with a shorter duration of hospital stay, quicker improvements in arterial oxygen pressure and pulmonary index scores, and fewer relapses after discharge.28,29,32,41,42,46,47 In children with “milder” exacerbations that were not seen at the ED, administration of the corticosteroid on first symptoms was associated with fewer relapses requiring subsequent rescue interventions and/or ED visits or hospitalizations.30,38,39

5. OCSs are preferred for the outpatient treatment of acute asthma. The results of studies comparing different routes of administering corticosteroids for treating acute asthma have been equivocal in terms of objective measures, symptoms, or relapse rates. However, OCSs are usually preferred because of relatively quick onset of action, minimal side effects or complications, and low cost. Seven studies in Table 4 compared different formulations of corticosteroids in the treatment of children with acute asthma seen in the ED.32,33,41–45 All routes of delivery were effective, but there are drawbacks to using IV or inhaled routes of delivery. The former may be preferred for the hospitalized child, although comparisons in this population have shown at least comparable results for IV and oral administration of corticosteroids.45,46,48 In the outpatient setting, IV delivery is not preferred because of its potential for complications and difficult set-up (particularly in young children).27 Intravenous therapy is also more costly than oral treatment. Although studies have not compared costs in the outpatient setting, a study in children who were hospitalized for acute asthma reported substantial savings when an OCS was substituted for IV dosing.47

It is difficult to draw conclusions from the available outpatient comparisons of oral and ICSs for acute asthma because of the variability in study methods and outcome measures used. In the studies included in Table 4, inhaled therapy was associated with a range of outcomes, which may be attributed to differences in route of administration (eg, face mask vs mouthpiece) and the child’s ability to inhale medication effectively. Six of the 7 studies compared inhaled and oral formulations. Three showed no significant differences in outcomes when using an OCS or an ICS in the ED treatment of acute asthma.33,43,44 One study suggested some advantages with high-dose inhaled budesonide compared with oral prednisolone,42 and another indicated better outcomes with nebulized dexamethasone compared with prednisone.31 Schuh et al32 reported oral prednisone to be better than inhaled fluticasone propionate in reducing the signs and symptoms of an acute exacerbation of asthma evaluated at 4 hours posttreatment. The use of different inhaled medications, different means of delivery, and different doses and frequency of dosing makes generalizations about efficacy problematic. There is no effective way to determine how much inhaled medication reached the airways in these studies or how much had relevant systemic effects.49,50 A meta-analysis of the efficacy of ICSs to treat acute asthma presenting in the ED in older children and adults reported a lack of evidence to
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<th>Study</th>
<th>Design</th>
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<th>Study Population</th>
<th>Outcomes (Favoring OCS Unless Indicated)</th>
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<td><strong>Studies of OCS only with treatment given at home or in office/clinic</strong></td>
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<tr>
<td>Webb et al&lt;sup&gt;35&lt;/sup&gt;</td>
<td>DBPC, partial</td>
<td>Pred (1.0 mg/kg) bid for 5 d or P w/crossover if child showed no improvement 8 d after starting Tx or for a subsequent attack</td>
<td>N = 38; Age: 32–17 mo; Age: 32–17 mo; At entry: ≥2 acute wheezing episodes diagnosed as asthma (30 children had required previous hospitalization for wheezing)</td>
<td>No between-Tx differences for parent assessments of AM and PM cough, wheeze, dyspnea, hospitalization for study population or for subanalyses by age (0–6 mo, 6–12 mo, 12–18 mo)</td>
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<td></td>
<td>crossover</td>
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<tr>
<td>Brunette et al&lt;sup&gt;38&lt;/sup&gt;</td>
<td>2 y, unblinded</td>
<td>Tx for acute episodes: Y 1: nebulized albuterol + OCS, if needed, for 7–14 d</td>
<td>N = 2; Age: &lt;72 mo at end of 2-y observation period; Controller Tx: theophylline</td>
<td>Group 1: no significant differences Y 1 vs Y 2 for no. episodes, no. wheezing days, ED visits, hospitalizations, duration of hospital stay</td>
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<td></td>
<td>controlled</td>
<td>Y 2: group 1 = same as Y 1; group 2 = Pred (1 mg/kg) at first sign of URI (even before wheezing)</td>
<td>At entry: ≥4 acute severe wheezing episodes (or ≥2 requiring hospitalization) w/URI during previous year</td>
<td>Group 2: significant reductions in Y 2 vs Y 1 for no. episodes (&lt;.002); no. wheezing days (&lt;.001); ED visits (&lt;.001); hospitalizations (&lt;.001); duration of hospital stay (&lt;.001)</td>
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<td><strong>Studies including school-age children (with or without preschool children)</strong></td>
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<tr>
<td>Shapiro et al&lt;sup&gt;36&lt;/sup&gt;</td>
<td>DBPC</td>
<td>Day 1: 8 tablets MP (4 mg/tablet) or P</td>
<td>N = 28; Age: 5.1–14.4 y (mean: 8.1 y); All subjects were PFT capable; Controller Tx: theophylline</td>
<td>During 14 d of observation: all patients improved; no ED visits or hospitalizations; trends favored MP for wheezing (days 7, 14) and FEV&lt;sub&gt;1&lt;/sub&gt; (day 7)</td>
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<td>Days 2–8: Decrease by 1 tablet/d (down to 1 tablet on day 8) Followed for additional 7 d</td>
<td>At entry: acute exacerbation requiring 3 consecutive bronchodilator Tx in which patient responded well enough to go home, but with FEV&lt;sub&gt;1&lt;/sub&gt; &lt;80% personal BL</td>
<td>Authors commented that differences may have been more dramatic if “sicker” children had been included.</td>
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<tr>
<td>Deshpande et al&lt;sup&gt;30&lt;/sup&gt;</td>
<td>DBPC</td>
<td>3 d oral Pred (day 1: 2.0 mg/kg; day 2: 1.0 mg/kg; day 3: 0.5 mg/kg) or P</td>
<td>N = 44; Age: 5–15 y (mean: 10.5 y); All subjects were PFT capable; Control Tx: BDP, cromolyn, theophylline</td>
<td>Compared with BL, both Tx improved Sx score: Pred, P &lt; .001; P, P &lt; .01 Compared with P, Pred improved AM and PM PEFR on days 2.3 (P &lt; .05) Hospitalized, day 4: Pred = 0; P = 5</td>
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<td>At entry: acute wheezing episode with PEFR 15–80% of personal BL</td>
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<td>Harris et al&lt;sup&gt;39&lt;/sup&gt;</td>
<td>DBPC</td>
<td>Pred (6–12 y: 30 mg; &gt;12 y: 40 mg) or P bid for 7 d Followed for additional 11 wk</td>
<td>N = 42; Age: 6–28 y (median; 12 y; all but 2 were &lt;18 y) All subjects were PFT capable; Controller Tx: theophylline</td>
<td>At day 7: no between-Tx differences in FEV&lt;sub&gt;1&lt;/sub&gt;, PEFR, bronchodilator use, Sx Relapse (rescue intervention w/Pred): Wk 1–2: Pred = 1 (45%); P = 8 (42%) (P = .004) Wk 3–11 for subjects without relapse in wk 1–2: Pred = 7 (33%); P = 3 (27%) (NS)</td>
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<td>At entry: ≥1 course (≤10 d) OCS for exacerbation incompletely responsive to bronchodilator&lt;sup&gt;a&lt;/sup&gt; during previous 12 mo (*Increased Sx + ≥20% decrease in PEFR or FEV&lt;sub&gt;1&lt;/sub&gt; w/failure to improve after 2 consecutive albuterol Tx OR to maintain improvement for 4 h after repeated albuterol over 24 h)</td>
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<tr>
<td>Study</td>
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<tr>
<td>Horowitz et al\textsuperscript{a}</td>
<td>DBPC</td>
<td>Single dose Pred (&lt;5 y; 20 mg; \geq 5 y; 40 mg) or P (observed for 72 h)</td>
<td>N = 67; Age: 4-16 y; 55 subjects were PFT capable; Controller Tx: 47 = none; others = theophylline, cromolyn, ketotifen</td>
<td>Accessory respiratory muscle use + dyspnea (P &lt; .01); Changes in respiratory rate (P &lt; .05); Changes in pulse rate (P &lt; .05); Trend toward improved PEFR in capable children (NS)</td>
</tr>
<tr>
<td>Grant et al\textsuperscript{a}</td>
<td>DBPC, crossover</td>
<td>Single dose Pred (2 mg/kg; max = 60 mg) or P Tx given at home within 3 h of incomplete response to bronchodilator</td>
<td>N = 78; Age: 2-14 y; Controller Tx: cromolyn = 15, theophylline = 18, BDP = 4; At entry: moderately severe asthma; \geq 2 outpatient visits for acute asthma in prior yr; incomplete response to home bronchodilator</td>
<td>Compared with P phase, Pred phase has more: Attacks resulting in outpatient visit (clinic or ED P = .004); children &lt;6 y, P = .009; children \geq 6 y NS Proportion of attacks resulting in outpatient visits (P = .04); children &lt;6 y, P = .04; children \geq 6 y, NS Attacks requiring ED visit (P = .04)</td>
</tr>
</tbody>
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Studies of OCS only with treatment given in the ED (all children received oxygen and bronchodilator therapy according to the protocol of the ED); all studies included school-age children (with or without preschool children)

<table>
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<tr>
<th>Study</th>
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<td>Storr et al\textsuperscript{a}</td>
<td>DBPC</td>
<td>Single dose Pred (&lt;5 y; 30 mg; \geq 5 y; 60 mg) or P given “soon” after ED admission; Assessed at 4+ h after admission</td>
<td>N = 40; Age: mean: 5.3 y; 61 subjects were PFT capable; Controller Tx: ICS = 34; cromolyn = 5; At entry: acute asthma, most were self (parent)-referrals</td>
<td>Clinical scores\textsuperscript{a} at 5 h (P &lt; .0001); PEFR in capable children (P = .006); Discharged at assessment: Pred = 30%; P = 3% (P &lt; .0001); Median stay: Pred = 24 h; P = 39 h (P = .0011); Supplemental OCS: Predl = 30%; P = 60% (P = .0005)</td>
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<tr>
<td>Scarfone et al\textsuperscript{a}</td>
<td>DBPC</td>
<td>Pred (2 mg/kg; max 60 mg) or P within 5 min of nebulized albuterol on admission to ED; Assessed every 30 min for 2 h and at 4 h</td>
<td>N = 75; Age: 1-17 y (mean: 59-63 mo); Controller Tx: theophylline = 6; At entry: = 1 previous exacerbation; present with moderate exacerbation (PI: 9-13, max = 15)</td>
<td>Decrease in median PI (P &lt; .001); Hospitalized: Overall: Pred = 31%; P = 49% (NS); Patients with initial PI &gt; 10: Pred = 32%; P = 72% (P &lt; .05); Patients with initial suboptimal response to bronchodilator: Pred = 45%; P = 83% (P &lt; .05)</td>
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<tr>
<td>Qureshi et al\textsuperscript{a}</td>
<td>Parallel group</td>
<td>Single dose of oral Pred (2 mg/kg, max = 60 mg) or oral Dex (0.6 mg/kg, max 16 mg) given with second dose nebulized albuterol in ED; At discharge: Pred group received 4 daily doses Pred (1 mg/kg, max 60 mg) for d 2-5; Dex group received 1 dose Dex (0.6 mg/kg, max 16 mg) for day 2; Followed for 10 d after discharge</td>
<td>N = 533; Age: 2-18 y (mean: 6.5 y); 96 subjects were PFT capable; Controller Tx: ICS = 88; At entry: acute asthma exacerbation requiring \geq 2 nebulizations in the ED</td>
<td>At discharge: no significant between-Tx differences in asthma severity, time in ED At 10 d: no significant between-Tx differences in relapse rates (primary efficacy variable), hospitalizations, 5x persistence Side effects: Increased vomiting with Pred (P = .008); Parents more likely to be noncompliant with Pred (P = .004)</td>
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<td>Study</td>
<td>Design</td>
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<td>Outcomes (Favoring OCS Unless Indicated)</td>
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<td>Barnett et al41</td>
<td>DBPC</td>
<td>Oral MP (2 mg/kg) + saline i.v. or i.v. MP (2 mg/kg) within 30 min of nebulized albuterol on admission to ED</td>
<td>N = 49</td>
<td>At entry: ≥2 previous exacerbations; present with moderate to severe exacerbation (≥6 years; FEV₁ &lt;60% pred; &lt;6 y: PI, 6-11 with max 12)</td>
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<td></td>
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<td>Assessed at 4 h</td>
<td></td>
<td>No between-Tx differences for respiratory rates, oxygen saturation, PI, FEV₁, hospitalization, relapses during week post-ED visit</td>
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<tr>
<td>Scarfone et al38</td>
<td>DBPC</td>
<td>Pred (2 mg/kg, max 60 mg) + P nebsol or nebulized Dex (1.5 mg/kg) + P tablets within 5 min of nebulized albuterol on admission to ED</td>
<td>N = 11, Age: 1–17 y (mean: 55–64 mo; 62% &lt; 5 y)</td>
<td>Discharged at 2 h: Pred = 7%; Dex = 23% (P = .02) Relapse within 48 h postdischarge: Pred = 16%; Dex = 0% (P = .008)</td>
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<td>At discharge: Pred (2 mg/kg/d) in 2 divided doses for 5 d</td>
<td>Controller Tx: theophylline = 19; corticosteroids (type and duration not indicated) = 75</td>
<td>Trends favored Dex for PI, hospitalizations Side effects: vomiting; Pred = 15%; Dex = 0% (P = .001)</td>
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<td>Devidayal et al12</td>
<td>DBPC</td>
<td>Single dose Predl (2 mg/kg, max 60 mg) + P inhaler or P tablets + Bud (1600 µg by Turbuhaler) upon admission</td>
<td>N = 80, Age: 2–12 y (mean: 6.5 y; 44% were 2–5 y)</td>
<td>Compared with BL, at 4 h, both Tx significantly improved: PEFR (P &lt; .01 for both) PI (P &lt; .001 for both) Wheezeing (P &lt; .05 for both) Accessory muscle use (P &lt; .001 for both) Oxygen saturation (P &lt; .05 for both)</td>
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<td>Assessed hourly for 4 h</td>
<td>44 subjects were PFT capable</td>
<td>No relapses or hospitalizations in either group HPA axis effects: serum cortisol pre/post stimulation (nmol/L): Wk 1–2 Predl = 21/333; Bud = 300/669 (P = .0003/ &lt;.00001) After 2 wk, serum cortisol levels were normal in both Tx groups Both Tx improved status of children At assessment, no. patients with SaO₂ &gt;95%: Bud = 40; Predl = 19 (P &lt; .01) SaO₂ &gt;90%: Bud = 41; Predl = 39 (NS) 0 Respiratory distress grade: Bud = 34; Predl = 15 (P &lt; .01) Mild accessory muscle usage: Bud = 7; Predl = 19 (P &lt; .01) Expiratory wheeze only: Bud = 7, Predl = 19 (P &lt; .01) Full recovery: Bud = 40; Predl = 32 (P &lt; .01) Need for i.v. hydrocortisone: Bud = 1; Predl = 8 (P &lt; .001) Requiring longer stay: Bud = 1; Predl = 5 (NS) Duration of stay (h): Bud = 2.9; Predl = 5.5 (P &lt; .001)</td>
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<td>Study</td>
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<td>Schuh et al 12</td>
<td>DBPC</td>
<td>Single dose (FP, 2 mg) by MDI + spacer + P tablet or Pred (2 mg/kg) + P inhalation</td>
<td>N = 100&lt;br&gt;Age: ≥ 5 y (mean; 9.4 y)&lt;br&gt;All subjects were PFT capable&lt;br&gt;At entry: severe acute asthma (FEV₁ &lt;60% pred)</td>
<td>At 4 h:&lt;br&gt;% Increase in FEV₁: FP = 9.4; Pred = 18.9 (P &lt; .001)&lt;br&gt;% Children with excellent response (increase in FEV₁ ≥25%): FP = 10; Pred = 27 (P = .002)&lt;br&gt;% Children with poor response (increase in FEV₁ &lt;5%): FP = 31; Pred = 8 (P = .002)&lt;br&gt;% Children with reduction in FEV₁: FP = 25; Pred = 0 (P &lt; .001)&lt;br&gt;% Hospitalized: FP = 31%; Pred = 10% (P = .01)&lt;br&gt;Side effects: vomiting: FP = 24; Pred = 8 (P = .001)</td>
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<td>Manjra et al 13</td>
<td>DBPC</td>
<td>Nebulized FP (1 mg) bid + P tablets for 7 d or Pred (2 mg/kg/d) for 4 d, then 1 mg/kg/d for 3 d + bid P nebulizations</td>
<td>N = 321&lt;br&gt;Age: 4-16 y (mean: 9.0 y)&lt;br&gt;All subjects were PFT capable&lt;br&gt;At entry: acute exacerbation of asthma (PEFR 40%-75% Pred + clinical score ≥2)</td>
<td>&lt;br&gt;No local or systemic side effects in any group&lt;br&gt;Compared with P, all Tx provided some clinical benefit: Days in hospital: Pred = 3.5 P = .04; P = 4.1&lt;br&gt;Total Sx score (wheezing, accessory respiratory muscle use, prolonged expiration): Pred = 2.2 (NS); Bud = 2.1 (P = .04); Terb = 2.4 (NS); P = 3.1 Tx failures: Pred = 16.13% (P = .002); P = 61.85%&lt;br&gt;No local or systemic side effects in any group</td>
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<td>Nuhoglu et al 14</td>
<td>Parallel group</td>
<td>MP (1 mg/kg/d) bid + Bud (800 µg/d by Turbuhaler) or Bud (1600 µg/d) for 3 d (both groups also used terbutaline, 2000 µg/d)</td>
<td>N = 60&lt;br&gt;Age: 4-17 y (mean: 8.9-9.5 y)&lt;br&gt;At entry: asthma exacerbation not responsive to home bronchodilator TX but not severe enough to hospitalize; PI: 2-6 (max 12)</td>
<td>&lt;br&gt;Compared with BL, both Tx showed statistically significant improvements in PI, FEV₁&lt;br&gt;Significant between-Tx difference for PI favoring high-dose Bud (P = .038)</td>
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<td>Study</td>
<td>Design</td>
<td>Treatments</td>
<td>Study Population</td>
<td>Outcomes (Favoring OCS Unless Indicated)</td>
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| Gleeson et al[^48]    | DBPC      | Hydrocortisone (6 mg/kg) i.v. at 0 h followed by 2 mg/kg every 4 h for 24 + h (continued at least 12 h post oral medication) + Pred (1 mg/kg, max 25 mg) or P bid starting 12-24 h post-i.v. | N = 39  
Age: 2-11 y (mean; 4.9 y)  
26 subjects were PFT capable  
Controller Tx: theophylline = 7; cromolyn = 3  
At entry: hospitalized for acute asthma unresponsive to 2 doses of nebulized salbutamol | No. patients wheeze-free at discharge (P < .05)  
Day 2 PEFR (P < .05)  
No between-Tx differences for duration of hospital stay, relapse rates over 3 mo post discharge, or PEF at discharge |
| Becker et al[^46]     | DBPC      | Oral Pred (2 mg/kg/dose, max 120 mg) bid or i.v. MP (1 mg/kg/dose, max 60 mg) qid | N = 66  
Age: 2-18 y (mean: 6.7-8.1; 35<6 y)  
31 subjects were PFT capable  
Controller Tx: inhaled anti-inflammatory = 45  
At entry: hospitalized for acute asthma | PEFR improved in both groups (P < .001)  
No between-Tx differences for duration of hospital stay, duration of treatment, or PEFR  
Time to weaning to bronchodilators: Pred = 59 h, MP = 68 h (NS)  
Significant difference favoring Pred for duration of supplemental oxygen (P = .014)  
Costs per indicated dose  
Community hospital costs: Pred $2-4/120 mg; MP $14-180/60 mg  
University hospital costs: Pred $8-22/120 mg; MP = $63-252/60 mg | |
| Matthews et al[^47]   | DBPC      | Pred (2 mg/kg, max 40 mg, at 0 and 24 h) + P nebulizing solution or P tablets (0 and 24 h) + Bud nebulizing suspension (2 mg, every 8 h Turbohaler) then Bud nebulizing suspension (800 µg/d) for 24 d (both groups) | N = 46  
Age: 5-16 y  
All subjects were PFT capable  
At entry: hospitalized with severe acute asthma and evidence of tachypnea and tachycardia | At 24 h, significant improvements in cough, wheeze, shortness of breath in both groups (P ≤ .01 for all); significant between-Tx difference favoring Bud for shortness of breath (P < .05)  
No significant between-Tx differences in FEV₁ (primary efficacy variable), SaO₂, PEFR, bronchodilator usage | |

DBPC indicates double-blind, placebo-controlled; bid, twice daily; Tx, treatment; Predl, prednisolone; Pred, prednisone; MP, methylprednisolone; PFT, pulmonary function test; Sx, symptoms; BDP, beclomethasone dipropionate; NS, not significant; Dex, dexamethasone; Bud, budesonide; HPA, hypothalamic pituitary axis; FP, fluticasone propionate; SaO₂, arterial oxygen percent saturation; Terb, terbutaline; qid, 4 times daily.
support use of these medications alone (ie, without addition of systemic corticosteroids).51

As for intravenous treatment, ICs have higher acquisition costs than oral formulations. Thus, OCSs remain the preferred treatment for most children with acute asthma in the outpatient setting.

The limited use of OCSs for asthma exacerbations in young children contrasts with the 50+ -year history of positive outcomes in adults and older children. This probably reflects both fears of side effects and inconsistencies in reported clinical data between children and adults. Controlled studies of therapy for acute asthma are limited in children younger than 5 years, and this population would not be expected to provide objective lung function data because of difficulties in detecting small changes in function in children’s airways.10,14,26 However, clinical benefits have been observed for some infants and toddlers with the corticosteroid administered either at home at the first sign of an exacerbation or in the hospital (Table 4).38-40 For young children who present with acute, severe wheezing in the ED, a controlled trial showed that corticosteroid treatment within 30 minutes of arriving at the ED was associated with a significant improvement in pulmonary index scores (P < .01) at 3 hours and lower hospitalization rates in children younger than 24 months.52 In this case, methylprednisolone was administered intramuscularly (4 mg/kg). The hospitalization rates were 18% for the infants and toddlers who received the corticosteroid and 50% for those who were treated with placebo (P < .05).52

The effect of single doses or short-term courses of systemic corticosteroids on acute asthma is 2-fold: 1) interfering with the inflammatory cascade underlying the asthmatic response and 2) enhancing the responsiveness of the β2 receptor in the bronchial smooth muscle.10,23,53,54 The latter probably accounts for the rapid (ie, within hours) efficacy of corticosteroids for asthma exacerbations, particularly in patients with incomplete responses to bronchodilator therapy—children as well as adults.4,10,23,37,39,44

CONSIDERATIONS FOR CHILDREN WITH RECURRENT VIRUS-INDUCED EXACERBATIONS OF ASTHMA

Viral respiratory infections are associated with wheezing illnesses and asthma exacerbations in children and adults and are estimated to account for up to 85% of acute childhood asthma episodes. It is not uncommon for children who present with an “asthma attack” to have a history of a URI just before symptom onset.30,55-58 A 12-month prospective study looked at the relationship between symptomatic URIs and asthma in 20 school-aged children (7–13 years) and 37 older subjects (14–55 years).36 URI symptoms, asthma symptoms, medications, and peak flow rates were recorded twice daily on diary cards. A total of 139 symptomatic URIs were reported; 44% (61) immediately preceded (within 24 hours) or coincided with the onset of an asthma exacerbation, and 47% of all asthma exacerbations were associated with viral symptoms. Compared with acute asthma episodes not associated with URIs, the viral-associated exacerbations had significantly greater asthma symptom and severity scores (P < .05, P < .001, respectively; Fig 3). URIs also were associated with trends toward lower peak flow rates and use of more asthma controller medication.56

An earlier community-based, longitudinal study of 108 school-aged children (9–11 years) reported a substantially higher association between viral respiratory infections and acute asthma episodes.58 This study looked at 292 asthma exacerbations over 13 months and included viral analyses using reverse transcription-polymerase chain reaction. In this school-age population, URIs were associated with 80% to 85% of the exacerbations. Picornaviruses (predominantly rhinovirus) were the most common infective agents.58

Similar observations have been made for very young children for whom the occurrence of asthma-like symptoms (eg, wheezing, nocturnal cough, difficulty breathing) is more frequently reported with viral respiratory infection than with environmental exposures.4,10 In fact, viral respiratory infections are the most common cause of asthma exacerbations among children younger than 5 years—the population with the highest ED visit and hospitalization rates for asthma.4,10

In reviewing the data on viral-induced asthma exacerbations in school-aged children and toddlers, 3 points of differentiation are evident. First, most toddlers with asthma have symptoms only during the viral season and not year round.57,58 Second, unlike older children, few toddlers show positive skin tests to aeroallergens. Third, respiratory syncytial virus (RSV), not rhinovirus, predominates as the infectious trigger.31,56-59 Similar to the study in school children reported by Johnston et al,21 a cross-sectional ED study of 22 wheezing infants (0–24 months), 48 wheezing children (2–16 years), and 59 matched control subjects reported an association between asthma exacerbations and respiratory viral infection in 82%
to 83% of all children with wheeze. Viral analysis of nasal washes by reverse transcription-polymerase chain reaction demonstrated positive antigen for RSV in 68% of the wheezing infants (≥24 months) and for rhinovirus in 71% of the children older than 2 years. Also, although nasal eosinophilia, serum eosinophil cationic protein levels, and total immunoglobulin E—characteristics of allergic inflammation—were not correlated with wheezing in the infants, all were significantly associated with asthma exacerbations in the 2- to 16-year group and were substantially higher in older children who were rhinovirus positive.21

In North America, RSV and influenza virus infections usually peak in early winter to early spring; the peak season for rhinovirus infections is early autumn. Asthma exacerbations related to symptomatic URIs are more likely to occur at these times (ie, the “cold season”), and a temporal relationship has been determined for pediatric ED visits for wheeze and peak viral activities.21,57

The clinical implications of asthma exacerbations caused by viral infection relate to the sudden onset of severe symptoms, increased airway responsiveness, and the potential for future asthma.4,59–62 It is not unusual for asthma symptoms to occur suddenly and unexpectedly for children with respiratory infections, even normally asymptomatic children with very mild asthma.4,21,57 In the community-based study reported by Johnston et al,56 most of the children had stable baseline PEFR (median: 312 L/min) but experienced a sudden severe fall (median maximal fall: >81 L/min) with viral infection. PEFRs returned to baseline levels during a 7- to 24-day period. However, although PEFRs may return to baseline, increased airway responsiveness as a result of respiratory infections can linger, resulting in heightened sensitivity to environmental factors (eg, temperature, humidity, allergens, pollutants) for extended periods of time.57 Results of the Tucson Children’s Respiratory Study and the Melbourne Asthma Study suggest that respiratory infections very early in life, particularly those caused by RSV, may have a negative impact on lung function for years after the initial episode.63,64 RSV-induced bronchiolitis severe enough to cause hospitalization in infants and toddlers has been associated with a significantly increased risk for developing asthma in the preschool and early school years (by age 7.5 years); the risk ratio for future asthma was greater than a family history of atopy or asthma.62

The argument for early administration of corticosteroid to the child with recurrent viral-related exacerbations of asthma thus reflects the potential for increased severity of airway obstruction later in life, as well as the potential for sudden severe loss of airway function despite minimal disease. Table 5 shows the US recommendations for treating children who have acute asthma with recurrent URIs.4

Despite these recommendations, children with established patterns of recurrent asthma episodes with viral infections are frequently undertreated. Review of the data on corticosteroids for acute, pediatric asthma suggest that giving an OCS at home could prevent some ED visits for acute asthma.30,38–40 However, this remains the exception rather than the rule, and often the young patient with viral episodes of acute asthma is started on long-term inhaled therapy. Although ICSs are the recommended treatment for persistent asthma, data on continuous treatment with ICS for virus-induced wheezing in preschool children is equivocal.4,10,65–68 Data for older children with predominantly intermittent asthma and several viral-induced exacerbations of symptoms per year are more difficult to interpret, being dependent on the investigators’ definitions of persistent and intermittent asthma.55,67–69 However, on the basis of a review of the acute asthma literature, it is likely that early administration of an OCS might help prevent virus-induced severe exacerbations of asthma in children who are susceptible to these episodes.

Brunette et al38 reported the results of a 2-year study showing that preschool children who experienced repeated asthma episodes associated with viral infections benefited from early administration of short courses of OCSs. During the first year, all of the children received bronchodilators on a continuous basis or intermittently for acute attacks, according to the child’s symptoms. For severe exacerbations, albuterol was also given by nebulization and corticosteroids were occasionally added (up to 14 days). During the second year, the children were randomized to 2 groups: one that continued on the previous year’s treatment protocol and another that was given a short course of prednisone (1 mg/kg) at the first sign of an URI and before any sign of wheezing. Compared with year 1, children who were treated with OCS in year 2 had significant decreases in the numbers of wheezing days (65%; P < .001), exacerbations (56%; P < .002), ED visits (61%; P < .001), and hospitalizations (90%; P < .001). The investigators concluded that preschool children who experience repeated asthma attacks related to URIs might benefit from preventive administration of OCSs.38

| TABLE 5. US Recommendations for Treating Viral-Induced Asthma Exacerbations in Children |
|----------------------------------|----------------------------------|
| **Symptom**               | **Recommended Treatment**            |
| **Severity**             |                                    |
| Mild                   | Short-acting, inhaled β2-agonist every 4–6 h for 24 h (longer with physician consult) |
| Moderate               | Short (3- to 10-d) course of OCSs*  |
| Severe                 | Short (3- to 10-d) course of OCSs*  |
| Recurrent, severe      | Consider initiating short (3- to 10-d) course of OCSs* at first sign of respiratory infection |

Adapted from Pediatric Asthma: Promoting Best Practice. *1–2 mg/kg/d.

**DEVELOPING A PROTOCOL BASED ON EFFICACY AND SAFETY**

The advantage of early use of OCSs relates to the importance of timing when treating an asthma exacerbation. Efficacy is best with early treatment; for children with viral-induced wheezing, data and clinical experience suggest that prevention is conceivable only when treatment can be given at the first sign of upper respiratory symptoms (ie, at home).38
Although more clinical data are needed, it is likely that administration of a short course of OCSs (3 to 5 days) early during a viral infection will decrease the number of young children who are seen at the ED as well as related hospital admissions.

Whether early use of OCSs in children with mild asthma and viral-induced exacerbations can slow the development and/or progression of disease severity over time remains a topic for study. Related to this are the questions of how long and how often therapy can be given safely. The choice of medication for infants and toddlers, in particular, requires careful assessment, balancing efficacy and safety as well as the child’s ability to tolerate the delivery system and to comply with dosing. 4 Although oral administration may be the optimal means of treating very young children with asthma, existing observations suggest that the oral route may be preferable for acute exacerbations in older children as well. The real questions are how much and how often medication can safely be given, balancing the known risks associated with OCS use. There is no doubt that daily administration for extended periods, such as is used for treating severe, persistent asthma, is associated with adverse events. However, to date, short-term, limited use of OCSs—even several times per year—has not been associated with significant side effects in most children. 28–45

Controlled data on the safety of short courses of OCSs to treat children with acute asthma are limited and largely anecdotal, and data on the adverse events associated with pediatric corticosteroid use in other diseases has largely been reported ad hoc. Regular treatment with OCSs for periods of 2 to 6 months has been reported to reduce morbidity and mortality in children with nephrotic syndrome; compared with 2 months of treatment, 3 months or more is associated with fewer relapses, while not increasing adverse events. 70,71 Short courses of OCSs to treat exacerbations for asthma last for days, not months. When used infrequently, this therapy has no serious systemic side effects in most children; however, frequent short courses increase the potential risk of adrenal suppression, depression of linear growth, and osteoporosis. 4,10 The issue is the definition of “frequent.” Empirically, there are no statistics showing that doses of 1 to 2 mg/kg/d (to a maximum daily dose of 4–50 mg) for up to 30 to 40 d/y have any long-term adverse effects in children. 4,10,14,72 However, some children may be more sensitive to the systemic side effects of corticosteroids, and growth should be followed regularly by stadiometry in all children with asthma. 4,10,72 If growth abnormality occurs, then it is important to assess carefully the severity of the disease and the dose and frequency of the corticosteroid treatment. For predominantly asymptomatic children who have several acute, severe asthma episodes yearly, this may be an indicator to start long-term controller therapy. 4,10 It is well documented that regular treatment of persistent asthma with low to moderate doses of ICSs can reduce ED visits and hospital admissions in children and adults. 72–74

A study of 86 children (2–16 years) who were treated for an acute exacerbation of asthma reported some behavioral changes associated with use of a higher dose of OCS. 75 These children had moderate, persistent asthma and were using daily ICSs. They were given a 5-day course of oral prednisone (1 or 2 mg/kg/d) after an incomplete response to bronchodilator and ICS treatment of an acute asthma episode. Both doses resolved the acute symptoms; however, more aggressive behavior (P = .002) and anxiety (P = .02) were reported by parents of children using the 2 mg/kg/d dose. 75

**CONCLUSIONS**

Review of the literature, including current guidelines for managing asthma, suggests that early treatment of acute asthma symptoms with OCSs in children with a pattern of recurrent acute asthma may decrease the severity of acute asthma episodes, reduce the risk of subsequent relapses, and thereby improve the quality of life for these children and their families. Attention should be given to identifying these children and standardizing a treatment approach based on accepted, consistent definitions of what constitutes an asthma exacerbation and recurrence. The following are suggested as a starting point for discussion:

1. **Definition of an asthma exacerbation:** an abrupt and/or progressive worsening of asthma symptoms with associated respiratory distress documented by reduction in PEFR (in capable children) of at least 20% and/or an increased need for short-acting bronchodilator.

2. **Definition of recurrent asthma exacerbations:** >2 acute asthma episodes during the previous 12 months.

3. **A suggested 3-step treatment plan for children with recurrent asthma exacerbations:** The following 3 steps are recommended to be taken by the parent or caregiver at the first sign of an exacerbation (as defined above) or at the first symptoms of a URI in children with recurrent URI-induced acute asthma (even before wheezing is evident): 1) initiate or increase dose of short-acting bronchodilator as directed in asthma management plan; 2) unless contraindicated, start OCS, 1 to 2 mg/kg/d (maximum: 60 mg/d) in 2 to 3 divided doses per day; 3) call the physician.

These recommendations are based on review of the literature and current guidelines for managing asthma as reported here. Validation is required, preferably through controlled and prospective studies designed to address the following questions:

1. What are the appropriate indicators to document outcomes accurately for a) the child with relatively mild acute episodes of asthma usually treated at home, b) the child with more severe acute asthma seen in the ED, and c) the child with recurrent episodes of acute asthma related to respiratory infections? The studies included in Table 4 indicate that at the mild end of the spectrum, results can be difficult to interpret; for these patients, in particular, careful consideration needs to
be given to the specific outcome measures as well as to study power for statistical analyses. Also, because pulmonary function tests may not be the best measure for assessing outcomes (and are not appropriate for studies of young children), which objective parameters should be used (eg, relapses over a period of time, ED visits posttreatment)?

2. How long should treatment be given? The studies in Table 4 present a range of treatment options, with similar positive outcomes in many cases: from a single dose of OCS at the start of an acute asthma episode to 7 days of OCS to mixed treatment with oral and ICSs. To minimize side effects, all corticosteroids should be used at the lowest dose possible, and OCSs should be used in short bursts. However, the definition of “short” remains a topic for discussion that must be included in developing a protocol for using OCSs to manage recurrent, acute asthma in children.

3. What dose should be used to treat recurrent acute asthma episodes in children? The recommendations of commonly used guidelines range from 0.5 mg/kg/d to 2 mg/kg/d, and the studies included in Table 4 all fall within this range. Although it is agreed that corticosteroids should always be used at the lowest dose possible, defining an “appropriate lowest dose” to treat the child with acute asthma remains an open question. Between-study comparisons from Table 4 and data from other investigators suggest that doses of 1.0 mg/kg/d to 2 mg/kg/d provide similar clinical benefits for most children. If true, then the lower dose would be preferred because of less risk for side effects. A well-controlled, prospective trial is necessary to address this issue.

Asthma exacerbations represent a failure of overall asthma management, and children with recurrent episodes of acute asthma symptoms should be evaluated and treated appropriately for persistent asthma. This is a challenge in preschool children, for whom diagnosing of asthma can be difficult because of other conditions with similar symptoms and the inability to obtain pulmonary function tests. However, the increasing numbers of preschool children who are seen in the ED for acute asthma indicate that asthma treatment overall is unsatisfactory in this group. There is room for improvement in care pathways for pediatric asthma, and early use of OCSs for children with recurrent acute wheezing may be one approach with significant clinical benefits.

Acknowledgments

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References

4. Pediatric Asthma: Promoting Best Practice. AAAAI; 1999
7. Canadian Asthma Guidelines. Management of patients with asthma in the emergency department and in hospital. CMAJ. 1999;161:533–559
15. 1994 Survey of Directors of Pediatric Emergency Medicine in Pediatric Residency Training Programs. NHANES; 1994
23. Lipworth BJ. Treatment of acute asthma. Lancet. 1997;350:18–23
33. Vollwoitz B, Bentur L, Finkelstein Y, et al. Effectiveness and safety of inhaled corticosteroids in controlling acute asthma attacks in children who were treated in the emergency department: a controlled compar-
34. Grant CC, Duggan AK, DeAngelis C. Independent parental administra-
35. Webb MSC, Henry RL, Milner AD. Oral corticosteroids for wheezing
attacks under 18 months. Arch Dis Child. 1986;61:15–19
36. Shapiro GC, Furukawa CT, Pierson WE, Gardinier R, Bierman CW.
Double-blind evaluation of methylprednisolone versus placebo for acute
37. Qureshi F, Zartisky A, Poirier MP. Comparative efficacy of oral dexam-
ethasone versus oral prednisone in acute pediatric asthma. J Pediatr.
2001;139:20–26
38. Brunette MG, Lands L, Thibodeau LP. Childhood asthma: prevention of
attacks with short-term corticosteroid treatment of upper respiratory
Early intervention with short courses of prednisolone to prevent pro-
gression of asthma in ambulatory patients incompletely responsive to
153:526–530
41. Barnett PL, Caputo GL, Baskin M, Kuppermann N. Intravenous versus
oral corticosteroids in the management of acute asthma in children. Ann
42. Devidayal, Singhi S, Kumar L, Jayshree M. Efficacy of nebulized budes-
onide compared to oral prednisolone in acute bronchial asthma. Acta
Paediatr. 1999;88:835–840
43. Manjra AI, Price J, Lenney W, Hughes S, Barnacle H. Efficacy of nebu-
lized fluticasone propionate compared with oral prednisolone in chil-
dren with an acute exacerbation of asthma. Respir Med. 2000;94:
626–631
44. Nuhoglu Y, Bahceciler NN, Barlan IB, Basaran MM. The effectiveness of
high-dose inhaled budesonide therapy in the treatment of acute asthma
45. Younger RE, Gerber PS, Herrod HG, Cohen RM, Crawford LV. Intra-
venous methylprednisolone efficacy in status asthmaticus of childhood.
Pediatrics. 1987;80:225–230
46. Becker JM, Arora A, Scarfone RJ, et al. Oral versus intravenous corti-
1999;103:586–590
47. Matthews EE, Curtis PD, McLain BI, Morris LS, Turbitt ML. Nebulized
budesonide versus oral steroid in severe exacerbations of childhood
48. Gleeson JGA, Loftus BG, Price JF. Placebo controlled trial of systemic
corticosteroids in acute childhood asthma. Acta Paediatr Scand. 1990;79:
1052–1058
nebulized terbutaline, nebulized corticosteroid and systemic corticoste-
1993;82:547–551
50. Carlsen KCL, Nikander K, Carlsen K-H. How much nebulised budes-
51. Edmonds ML, Camargo CA, Pollack CV, Rowe BH. The effectiveness of
inhaled corticosteroids in the emergency department treatment of acute
52. Tal A, Levy N, Bearman JE. Methylprednisolone therapy for acute
1990;86:350–356
53. Tang R-B, Chen S-J. Soluble interleukin-2 receptor and interleukin-4 in
serum of asthmatic children before and after a prednisolone course. Ann
54. Gibson PG, Nozrila MZ, Fakes K, Simpson J, Henry RL. Pattern of
airway inflammation and its determinants in children with acute severe
of inhaled corticosteroids on episodes of wheezing associated with viral
infection in school-age children: randomized double-blind placebo-
controlled trial. BMJ. 1997;315:858–862
role of viral infections in exacerbations of asthma in 9–11 year old
children. BMJ. 1995;310:1225–1229
57. Tarlo SM, Broder I, Corey P, et al. The role of symptomatic colds in
asthma exacerbations: influence of outdoor allergens and air pollutants.
58. Horn MEC, Brain EA, Gregg I, Inglis JM, Yealland SJ, Taylor P. Respi-
ratory viral infection and wheezy bronchiolitis in childhood. Thorax. 1979;
34:23–28
59. Martinez FD. Links between pediatric and adult asthma. J Allergy Clin
60. Germ JE, Busse WW. The role of viral infections in the natural history
61. Martinez FD. Viral infections and the development of asthma. Am J
Respir Crit Care Med. 1995;151:1644–1647
62. Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman R. Respiratory syn-
cytial virus bronchiolitis in infancy is an important risk factor for asthma
and allergy at age 7. Am J Respir Crit Care Med. 2000;161:
1501–1507
WJ. Asthma and wheezing in the first six years of life. The Group Health
64. Phelan PD, Roberson CF, Olimsky A. The Melbourne asthma study:
65. Wilson N, Silverman M. Treatment of acute episodic asthma in pre-
school children using intermittent high dose inhaled steroids at home.
Arch Dis Child. 1990;65:407–410
66. Wilson N, Sloper K, Silverman M. Effect of continuous treatment with
topical corticosteroid on episodic viral wheezing in preschool children.
Arch Dis Child. 1995;72:317–320
67. Garrett J, Williams S, Wong C, Holdaway D. Treatment of acute asth-
matic exacerbations with an increased dose of inhaled steroid. Arch Dis
Child. 1998;79:12–17
68. Connett G, Lenney W. Prevention of viral induced asthma attacks using
69. Svedmyr J, Nyberg E, Ashrink-Nilsson E, Hedlin G. Intermittent treat-
ment with inhaled steroids for deterioration of asthma due to upper
70. Hodson EM, Knight JP, Willis NS, Craig JC. Corticosteroid therapy for
nephritic syndrome in children. Cochrane Database Syst Rev. 2001:
CD001533
71. Ksiazek J, Wyszymska T. Short versus long initial prednisone treatment
84:889–893
72. Childhood Asthma Management Program Research Group. Long-term
effects of budesonide or nedocromil in children with asthma. The Child-
2000;343:1054–1063
73. Adams RJ, Fulbright J, Finkelstein NA, et al. Impact of inhaled anti-
inflammatory therapy on hospitalization and emergency department
74. Blais L, Suisse S, Boivin J-F, Ernst P. First treatment with inhaled
corticosteroids and the prevention of admissions to hospital for asthma.
Thorax. 1998;53:1025–1029
75. Kayani S, Shannon DC. Adverse behavioral effects of treatment for
acute exacerbation of asthma in children. A comparison of two doses of
oral steroids. Chest. 2002;122:624–628

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