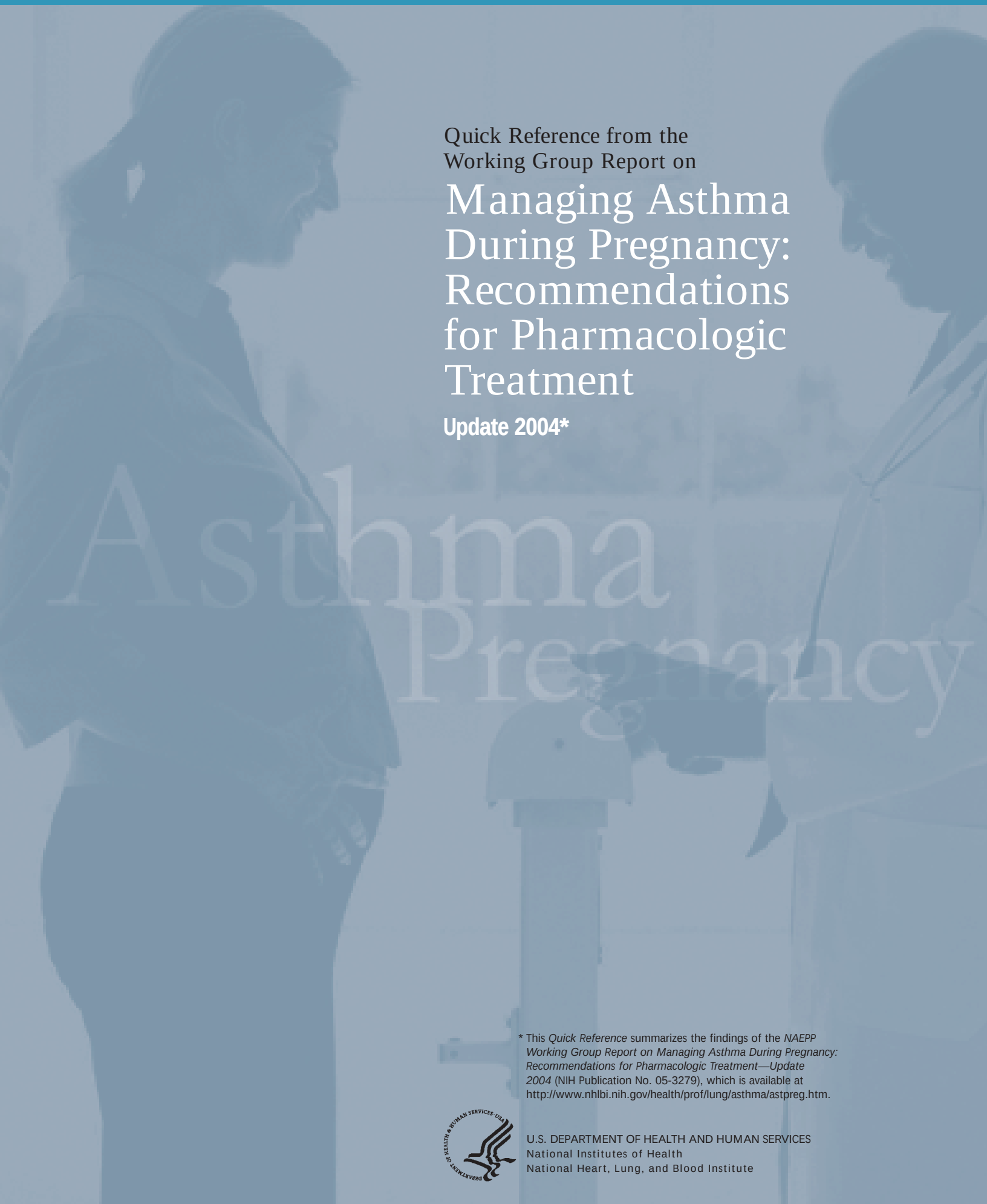

Quick Reference from the
Working Group Report on

Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment

Update 2004*

* This *Quick Reference* summarizes the findings of the *NAEPP Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004* (NIH Publication No. 05-3279), which is available at http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Heart, Lung, and Blood Institute

NATIONAL ASTHMA EDUCATION AND PREVENTION PROGRAM

Quick Reference from the Working Group Report on

Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment

Update 2004

Maintaining adequate control of asthma during pregnancy is important for the health and well-being of both the mother and her baby. Asthma has been reported to affect 3.7 to 8.4 percent of pregnant women,[1] making it potentially the most common serious medical problem to complicate pregnancy. The largest and most recent studies suggest that maternal asthma increases the risk of perinatal mortality, preeclampsia, preterm birth, and low birth weight infants. More severe asthma is associated with increased risks,[2, 3] while better-controlled asthma is associated with decreased risks.[4]

In 1993, the National Asthma Education and Prevention Program (NAEPP) published the *Report of the Working Group on Asthma and Pregnancy* (Asthma and Pregnancy Report 1993),[5] which presented recommendations for the management of asthma during pregnancy. Since then, there have been revisions to the general asthma treatment guidelines, *Guidelines for the Diagnosis and Management of Asthma—Expert Panel Report 2* (EPR-2 1997),[6] and *Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma—Update on Selected Topics 2002* (EPR—Update 2002);[7] release of new asthma medications; and publication of new gestational safety data.

Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004 (Asthma and Pregnancy—Update 2004)[8] reflects the NAEPP's commitment to keep recommendations for clinical practice up to date and based on systematic reviews of the evidence. Asthma and Pregnancy—Update 2004 was developed through the collective expertise of an expert panel on asthma and pregnancy (Working Group). The NAEPP Science Base Committee and NAEPP Coordinating Committee members provided review and comment. The recommendations made in Asthma and Pregnancy—Update 2004 are intended to *assist* clinical decisionmaking; the clinician and patient still need to develop individual treatment plans that are tailored to the specific needs and circumstances of the patient.

The scope of the current systematic review is pharmacologic treatment of asthma in women during their pregnancy; however, highlights from EPR-2 1997 and EPR—Update 2002 relative to other aspects of asthma care are also presented because they should enhance the overall success and safety of managing asthma in pregnancy.

Systematic Review of the Evidence

A systematic review of the evidence on the safety of asthma medications during pregnancy was conducted by drug class. Of 226 articles retrieved in the search of literature published in peer-reviewed journals from January 1990 through May 2003, 42 met criteria for inclusion in the evidence review; 2 additional articles published after May 2003 were included, for a total of 44 articles. A summary of the findings from the evidence, arranged by medication category, follows.

Beta$_2$-Agonists

One experimental animal study[9] and six human studies were included. The six human studies consisted of one case report[10] and five clinical studies[11–15] that included a total of 6,667 pregnant women, of whom 1,929 had asthma and 1,599 had taken beta$_2$-agonists. The data were reassuring regarding the safety of beta$_2$-agonists during pregnancy. More data were available for albuterol. Two long-acting inhaled beta$_2$-agonists have become available since 1993—salmeterol and formoterol. Limited data are available on their use during pregnancy. The pharmacologic and toxicologic profiles of these two drugs are similar to the short-acting inhaled beta$_2$-agonists, with the exception of their prolonged retention in the lungs.

Theophylline

Seven experimental animal studies[16–22] and eight human studies were included. The experimental animal studies confirm the association of high-dose theophylline and adverse pregnancy outcomes in animals. The eight human studies, consisting of two case reports[23, 24] and six clinical studies[11, 13, 25–28] (of which two were randomized controlled trials), included a total of 57,163 pregnant women, of whom 3,616 had asthma and 660 had taken theophylline. Studies and clinical experience confirm the safety of theophylline at recommended doses (to serum concentration of 5–12 mcg/mL) during pregnancy. In a randomized controlled trial, there were no differences in asthma exacerbations or maternal or perinatal outcomes in the theophylline versus the beclomethasone dipropionate treatment groups.

However, in the theophylline treatment group, there were higher levels of reported side effects and discontinuation of the medication and an increase in the proportion of women with forced expiratory volume in 1 second (FEV_1) at less than 80 percent of that predicted.[25]

Anticholinergics

No data on anticholinergics were available for the current evidence review.

Inhaled corticosteroids

Three experimental animal studies[29–31] and 10 human studies were included. The human studies included eight studies of pregnant women. Of the eight studies, five were cohort studies;[11, 13, 32–34] one was a controlled trial;[35] and two were randomized controlled trials.[25, 28] These eight studies included a total of 21,072 pregnant women, of whom 16,900 had asthma and 6,113 had taken inhaled corticosteroids. Also included were two studies of newborns from the Swedish Birth Registry—one compared the rate of abnormalities among 2,014 newborns whose mothers had taken budesonide to the rate of abnormalities in the total newborn population, although the number in that population was not reported;[36] the other study compared 2,900 newborns whose mothers had taken budesonide to the total newborn population of 293,948;[37] there may be some overlap in the populations of these two studies. There are three major conclusions from the evidence review: (1) the risk of asthma exacerbations associated with pregnancy can be reduced and lung function (FEV_1) improved with the use of inhaled corticosteroid therapy;[25, 28, 34] (2) no studies

to date, including studies of large birth registries, have related inhaled corticosteroid use to any increases in congenital malformations or other adverse perinatal outcomes; and (3) the preponderance of data on inhaled corticosteroids during pregnancy is with budesonide. Few or no studies are available on the other inhaled corticosteroid formulations during pregnancy.

Oral (systemic) corticosteroids

Nine experimental animal studies[38–46] and eight human studies were included. The animal studies do not change the previous understanding (Asthma and Pregnancy Report 1993)[5] of the steroid-mediated clefting or decreases in fetal growth in animals. The eight human studies in the current evidence review included one report of two meta-analyses:[47] one meta-analysis used six cohort studies that included 51,380 pregnant women, of whom 535 had taken oral corticosteroids; the other meta-analysis used four case-control studies,[48–51] each of which was also eligible to be included in the evidence review. These four case-control studies included 52,038 pregnant women, of whom 25 had taken oral corticosteroids. The remaining three human studies included one case-control study[52] and two prospective cohort studies[11, 13] that included a total of 4,321 pregnant women, of whom 1,998 had asthma and 213 had taken oral corticosteroids. The findings from the current evidence review are conflicting. Oral corticosteroid use, especially during the first trimester of pregnancy, is associated with an increased risk for isolated cleft lip with or without cleft palate (the risk in the general population is 0.1 percent; the risk in women on oral corticosteroids is 0.3 percent).[47] However, very few pregnant women who had oral steroid-dependent asthma were included in the studies, and the length, timing, and dose of exposure to the drug were not well described. Oral corticosteroid use during pregnancy in patients who have asthma is associated with an increased incidence of preeclampsia and the delivery of both preterm and low birth weight infants.[13, 47, 52] However, the available data make it difficult to separate the effects of the oral corticosteroids on these outcomes from the effects of severe or uncontrolled asthma, which has been associated with maternal and/or fetal mortality.

Cromolyn

No experimental animal studies and two human studies were included in the current review. The two human studies consisted of prospective cohort studies[11, 13] that included 4,110 pregnant women, of whom 1,917 had asthma and 318 had taken cromolyn. The safety of using cromolyn during pregnancy is supported by the current review of evidence.

Leukotriene modifiers

Leukotriene modifiers include two compounds available as oral tablets (the receptor antagonists montelukast and zafirlukast) and 5-lipoxygenase pathway inhibitors (e.g., zileuton). No animal studies and one human study were available for review. The human study was an observational study of 2,205 pregnant women, 873 with asthma, of whom 9 took leukotriene modifiers, but the specific agent was not identified.[11] The conclusion is that minimal data are currently available on the use of leukotriene modifiers during pregnancy. Reassuring animal studies have been submitted to the Food and Drug Administration (FDA) for leukotriene receptor antagonists but not for the leukotriene lipoxygenase inhibitor.

Recommendations for Managing Asthma During Pregnancy

The Working Group recommends the following principles and stepwise approach to pharmacologic therapy for managing asthma during pregnancy. (See figures 1–6.) The principles and approach are based on the Working Group's interpretation of the current scientific review of the evidence on the safety of asthma medications during pregnancy and consideration of previous NAEPP reports: the Asthma and Pregnancy Report 1993, the EPR-2 1997, and the EPR—Update 2002.

General principles

- The treatment goal for the pregnant asthma patient is to provide optimal therapy to maintain control of asthma for maternal health and quality of life as well as for normal fetal maturation. Asthma control is defined as:
  - Minimal or no chronic symptoms day or night
  - Minimal or no exacerbations
  - No limitations on activities
  - Maintenance of (near) normal pulmonary function
  - Minimal use of short-acting inhaled beta$_2$-agonist
  - Minimal or no adverse effects from medications
- It is safer for pregnant women with asthma to be treated with asthma medications than for them to have asthma symptoms and exacerbations. Monitoring and making appropriate adjustments in therapy may be required to maintain lung function and, hence, blood oxygenation that ensures oxygen supply to the fetus. Inadequate control of asthma is a greater risk to the fetus than asthma medications are. Proper control of asthma should enable a woman with asthma to maintain a normal pregnancy with little or no risk to her or her fetus.
- The obstetrical care provider should be involved in asthma care, including monitoring of asthma status during prenatal visits. A team approach is helpful if more than one clinician is managing a pregnant woman with asthma.
- Asthma treatment is organized around four components of management:
  - **Assessment and monitoring of asthma, including objective measures of pulmonary function.** Because the course of asthma changes for about two-thirds of women during pregnancy,[53] monthly evaluations of asthma history and pulmonary function are recommended. Spirometry tests are recommended at the time of initial assessment. For routine monitoring at most subsequent followup outpatient visits, spirometry is preferable, but measurement of peak expiratory flow (PEF) with a peak flow meter is generally sufficient. Patients should be instructed to be attentive to fetal activity. Serial ultrasound examinations starting at 32 weeks gestation may be considered for patients who have suboptimally controlled asthma and for women with moderate-to-severe asthma. Ultrasound examinations are also helpful after recovery from a severe exacerbation.

- **Control of factors contributing to asthma severity.** Identifying and controlling or avoiding such factors as allergens and irritants, particularly tobacco smoke, that contribute to asthma severity can lead to improved maternal well-being with less need for medications. (See figure 7.)

- **Patient education.** Asthma control is enhanced by ensuring access to education about asthma and about the skills necessary to manage it—such as self-monitoring, correct use of inhalers, and following a plan for managing asthma long term and for promptly handling signs of worsening asthma.

- **A stepwise approach to pharmacologic therapy.** In this approach to achieving and maintaining asthma control, the dose and number of medications and the frequency of administration are increased as necessary, based on the severity of the patient's asthma, and are decreased when possible.

Recommendations for Pharmacologic Treatment of Asthma During Pregnancy

Stepwise approach for managing asthma. To develop recommendations for the stepwise approach to the pharmacologic treatment of asthma in pregnant women, the Working Group first considered the stepwise approach in the EPR—Update 2002, which was based on systematic review of the evidence from medication effectiveness studies in nonpregnant adults and children. The Working Group also considered EPR-2 1997 and the Asthma and Pregnancy Report 1993.

The effectiveness of medications is assumed to be the same in pregnant women as in nonpregnant women, although there are no studies that directly test this assumption. Based on their current systematic review of evidence from safety studies of asthma medications during pregnancy, the Working Group then tailored existing recommendations for stepwise therapy. Refer to figures 1, 2, and 3 for a complete list of recommended therapies and medication dosages in the stepwise approach to managing asthma. The following information highlights the rationale for the preferred medications.

- *Step 1: Mild Intermittent Asthma.* Short-acting bronchodilators, particularly short-acting inhaled beta$_2$-agonists, are recommended as quick-relief medication for treating symptoms as needed in patients with intermittent asthma. Albuterol is the preferred short-acting inhaled beta$_2$-agonist because it has an excellent safety profile and the greatest amount of data related to safety during pregnancy of any currently available inhaled beta$_2$-agonist. Women's experience with these drugs is extensive, and no evidence has been found either of fetal injury from the use of short-acting inhaled beta$_2$-agonists or of contraindication during lactation.

- *Step 2: Mild Persistent Asthma.* The preferred treatment for long-term-control medication in Step 2 is daily low-dose inhaled corticosteroid. This preference is based on the strong effectiveness data in nonpregnant women[6, 7] as well as effectiveness and safety data in pregnant women that show no increased risk of adverse perinatal outcomes. Budesonide is the preferred inhaled corticosteroid because more data are available on using budesonide in pregnant women than are available on other inhaled corticosteroids, and the data are reassuring. It is important to note that there are no data indicating that the other inhaled corticosteroid preparations are unsafe during pregnancy. Therefore, inhaled corticosteroids other than budesonide may be continued in patients who were well controlled by these agents prior to pregnancy, especially if it is thought that changing formulations may jeopardize asthma control.

  Cromolyn, leukotriene receptor antagonists, and theophylline are listed as alternative but not preferred therapies. Cromolyn has an excellent safety profile, but it has limited effectiveness compared with inhaled corticosteroids. Leukotriene receptor antagonists have been demonstrated to provide statistically significant but modest improvements in children and nonpregnant adults with asthma, although in studies comparing overall efficacy of the two drugs, most outcomes clearly favor inhaled corticosteroids. Published data are minimal on using leukotriene receptor antagonists during pregnancy; however, animal safety data submitted to the FDA are reassuring. Thus, leukotriene receptor antagonists are an alternative but not preferred treatment for pregnant women whose asthma was successfully controlled with this medication prior to their pregnancy. Theophylline has demonstrated clinical effectiveness in some studies and has been used for years in pregnant women with asthma. It also, however, has the potential for serious toxicity resulting from excessive dosing and/or select drug-drug interactions (e.g., with erythromycin). Using theophylline during pregnancy requires careful titration of the dose and regular monitoring to maintain the recommended serum theophylline concentration range of 5–12 mcg/mL.

- *Step 3: Moderate Persistent Asthma.* Two preferred treatment options are noted: either a combination of low-dose inhaled corticosteroid and a long-acting inhaled beta$_2$-agonist, or increasing the dose of inhaled corticosteroid to the medium dose range. No data from studies during pregnancy clearly delineate that one option is recommended over the other.

  Limited data describe the effectiveness and/or safety of using combination therapy during pregnancy, but strong evidence from randomized controlled trials in nonpregnant adults shows that adding long-acting inhaled beta$_2$-agonist to a low dose of inhaled corticosteroid provides greater asthma control than only increasing the dose of corticosteroid.[7] The pharmacologic and toxicologic profiles of long-acting and short-acting inhaled beta$_2$-agonists are similar; there is justification for expecting long-acting inhaled beta$_2$-agonists to have a safety profile similar to that of albuterol, for which there are data related to safety during pregnancy. Two long-acting inhaled beta$_2$-agonists are available—salmeterol and formoterol. Limited observational data exist on their use during pregnancy; salmeterol might be chosen because it has been available longer in the United States.

  Increasing the dose of inhaled corticosteroid to medium dose will benefit many patients, and, as noted previously, the data on using inhaled corticosteroids during pregnancy—including studies of large birth registries—are reassuring.

- *Step 4: Severe Persistent Asthma.* If additional medication is required after carefully assessing patient technique and adherence with using Step 3

medication, then the inhaled corticosteroid dose should be increased within the high-dose range, and the use of budesonide is preferred. If this is insufficient to manage asthma symptoms, then the addition of systemic corticosteroid is warranted; although the data are uncertain about some risks of oral corticosteroids during pregnancy, severe uncontrolled asthma poses a definite risk to the mother and fetus.

Management of acute exacerbations. Asthma exacerbations have the potential to lead to severe problems for the fetus. Therefore, asthma exacerbations during pregnancy should be managed aggressively. Refer to figure 4 for home treatment of asthma exacerbation, figure 5 for emergency department and hospital management, and figure 6 for medications and dosages.

Pharmacologic management of allergic rhinitis. Rhinitis, sinusitis, and gastroesophageal reflux are conditions that are often associated with asthma, are frequently more troublesome during pregnancy, and may exacerbate coexisting asthma. If these conditions are present, appropriate treatment is an integral part of asthma management. These topics were outside the scope of the current evidence-based review, but relevant studies on the safety of rhinitis medications during pregnancy were reviewed in order to present the following recommendations.

- Intranasal corticosteroids are the most effective medications for the management of allergic rhinitis and have a low risk of systemic effect when used at recommended doses. Montelukast, a leukotriene receptor antagonist, can be used for the treatment of allergic rhinitis—but minimal data are available on the use of this medication during pregnancy.
- The current second-generation antihistamines of choice are loratadine or cetirizine.
- There may be a relationship between use of oral decongestants in early pregnancy and a rare birth defect, gastroschisis; however, the absolute risk of gastroschisis in exposed fetuses is still extremely small. If nasal decongestion is indicated in early pregnancy, an external nasal dilator, short-term topical oxymetazoline, or intranasal corticosteroid can be considered before use of oral decongestants.

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Dr. Dombrowski has none.

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Dr. Schatz has served on the Speakers' Bureaus of AstraZeneca and Merck; he has received funding/grant support for research projects from Aventis and GlaxoSmithKline.

Dr. Scialli has none.

Dr. Stoloff has served on the Speakers' Bureaus of Alcon, AstraZeneca, Aventis, Genentech, GlaxoSmithKline, Pfizer, and Schering; he has served as a consultant for Alcon, AstraZeneca, Aventis, Genentech, GlaxoSmithKline, Pfizer, and Schering.

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Figure 1 Stepwise Approach for Managing Asthma During Pregnancy and Lactation: Treatment

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/ Day Symptoms/ Night	PEF or FEV_1 PEF Variability	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 Severe Persistent	Continual Frequent	≤60% >30%	• Preferred treatment: - High-dose inhaled corticosteroid AND - Long-acting inhaled $beta_2$-agonist AND, if needed, - Corticosteroid tablets or syrup long term (2 mg/kg per day, generally not to exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroid and maintain control with high-dose inhaled corticosteroid.*) • Alternative treatment: - High-dose inhaled corticosteroid* AND - Sustained release theophylline to serum concentration of 5–12 mcg/mL.
Step 3 Moderate Persistent	Daily >1 night/week	>60%–<80% >30%	• Preferred treatment: EITHER - Low-dose inhaled corticosteroid* and long-acting inhaled $beta_2$-agonist OR - Medium-dose inhaled corticosteroid.* If needed (particularly in patients with recurring severe exacerbations): - Medium-dose inhaled corticosteroid* and long-acting inhaled $beta_2$-agonist. • Alternative treatment: - Low-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist.† If needed: - Medium-dose inhaled corticosteroid* and either theophylline or leukotriene receptor antagonist.†
Step 2 Mild Persistent	>2 days/week but <daily >2 nights/month	≥80% 20%–30%	• Preferred treatment: - Low-dose inhaled corticosteroid.* • Alternative treatment (listed alphabetically): cromolyn, leukotriene receptor antagonist† OR sustained-release theophylline to serum concentration of 5–12 mcg/mL.
Step 1 Mild Intermittent	≤2 days/week ≤2 nights/month	≥80% <20%	• No daily medication needed. • Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroid is recommended.
Quick Relief All Patients	• Short-acting bronchodilator: 2–4 puffs **short-acting inhaled $beta_2$-agonist**‡ as needed for symptoms. • Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroid may be needed. • Use of short-acting inhaled $beta_2$-agonist‡ >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.		

Step down
Review treatment every 1–6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/work missed
- Maintain (near) normal pulmonary function
- Minimal use of short-acting inhaled $beta_2$-agonist‡
- Minimal or no adverse effects from medications

Notes

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is percent of personal best; FEV_1 is percent predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroid), then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled $beta_2$-agonist‡ (e.g., use of approximately one canister a month even if not using it every day indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy).
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens, irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if Step 4 care is required. Referral may be considered if Step 3 care is required.

* There are more data on using budesonide during pregnancy than on using other inhaled corticosteroids.
† There are minimal data on using leukotriene receptor antagonists in humans during pregnancy, although there are reassuring animal data submitted to FDA.
‡ There are more data on using albuterol during pregnancy than on using other short-acting inhaled $beta_2$-agonists.

Figure 2 Usual Dosages for Long-Term-Control Medications During Pregnancy and Lactation*

Medication	Dosage Form	Adult Dose
Inhaled Corticosteroids (See Estimated Comparative Daily Dosages for Inhaled Corticosteroids [Figure 3].)		
Systemic Corticosteroids		**(Applies to all three corticosteroids.)**
Methylprednisolone **Prednisolone** **Prednisone**	2, 4, 8, 16, 32 mg tablets 5 mg tablets, 5 mg/5 cc, 15 mg/5 cc 1, 2.5, 5, 10, 20, 50 mg tablets 5 mg/cc, 5 mg/5 cc	• 7.5–60 mg daily in a single dose in a.m. or qod as needed for control • Short-course "burst" to achieve control: 40–60 mg per day as single dose or 2 divided doses for 3–10 days
Long-Acting Inhaled Beta$_2$-Agonists (Should not be used for symptom relief or for exacerbations. Use with inhaled corticosteroids.)		
Salmeterol **Formoterol**	MDI 21 mcg/puff DPI 50 mcg/blister DPI 12 mcg/single-use capsule	2 puffs q 12 hours 1 blister q 12 hours 1 capsule q 12 hours
Combined Medication		
Fluticasone/Salmeterol	DPI 100, 250, or 500 mcg/50 mcg	1 inhalation bid; dose depends on severity of asthma
Cromolyn		
Cromolyn	MDI 1 mg/puff Nebulizer 20 mg/ampule	2–4 puffs tid-qid 1 ampule tid-qid
Leukotriene Receptor Antagonists		
Montelukast **Zafirlukast**	10 mg tablet 10 or 20 mg tablet	10 mg qhs 40 mg daily (20 mg tablet bid)
Methylxanthines (Serum monitoring is important [serum concentration of 5–12 mcg/mL at steady state].)		
Theophylline	Liquids, sustained-release tablets, and capsules	Starting dose 10 mg/kg/day up to 300 mg max; usual max 800 mg/day

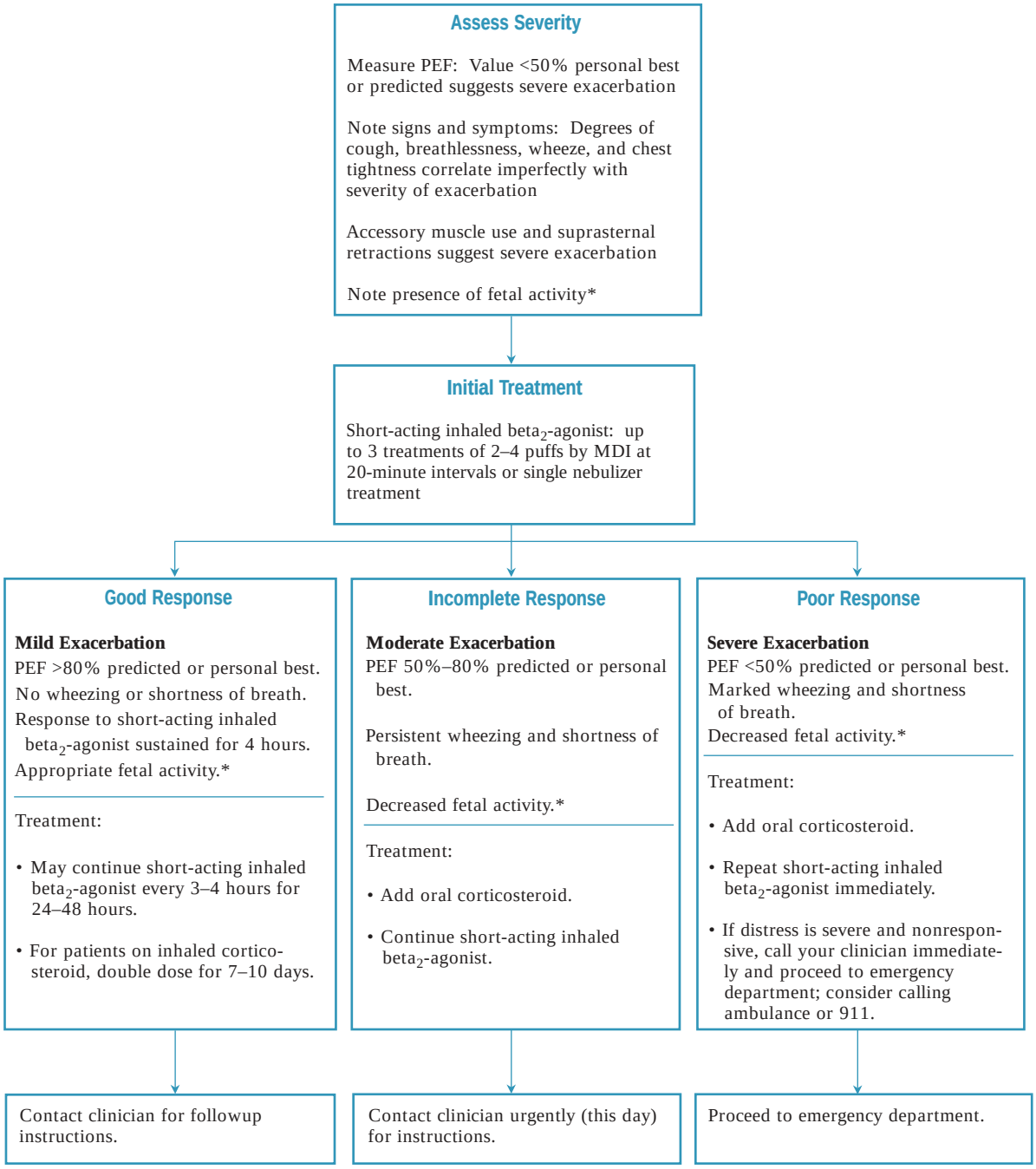
DPI, dry powder inhaler; MDI, metered-dose inhaler.
*Adapted from EPR—Update 2002.
Notes: • The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.
• Some doses may be outside package labeling, especially in the high-dose range.

Figure 3 Estimated Comparative Daily Dosages for Inhaled Corticosteroids*

Drug	Adult Low Daily Dose	Adult Medium Daily Dose	Adult High Daily Dose
Beclomethasone CFC			
42 or 84 mcg/puff	168–504 mcg	504–840 mcg	>840 mcg
Beclomethasone HFA			
40 or 80 mcg/puff	80–240 mcg	240–480 mcg	>480 mcg
Budesonide DPI			
200 mcg/inhalation	200–600 mcg	600–1,200 mcg	>1,200 mcg
Flunisolide			
250 mcg/puff	500–1,000 mcg	1,000–2,000 mcg	>2,000 mcg
Fluticasone			
MDI: 44, 110, or 220 mcg/puff	88–264 mcg	264–660 mcg	>660 mcg
DPI: 50, 100, or 250 mcg/inhalation	100–300 mcg	300–750 mcg	>750 mcg
Triamcinolone acetonide			
100 mcg/puff	400–1,000 mcg	1,000–2,000 mcg	>2,000 mcg

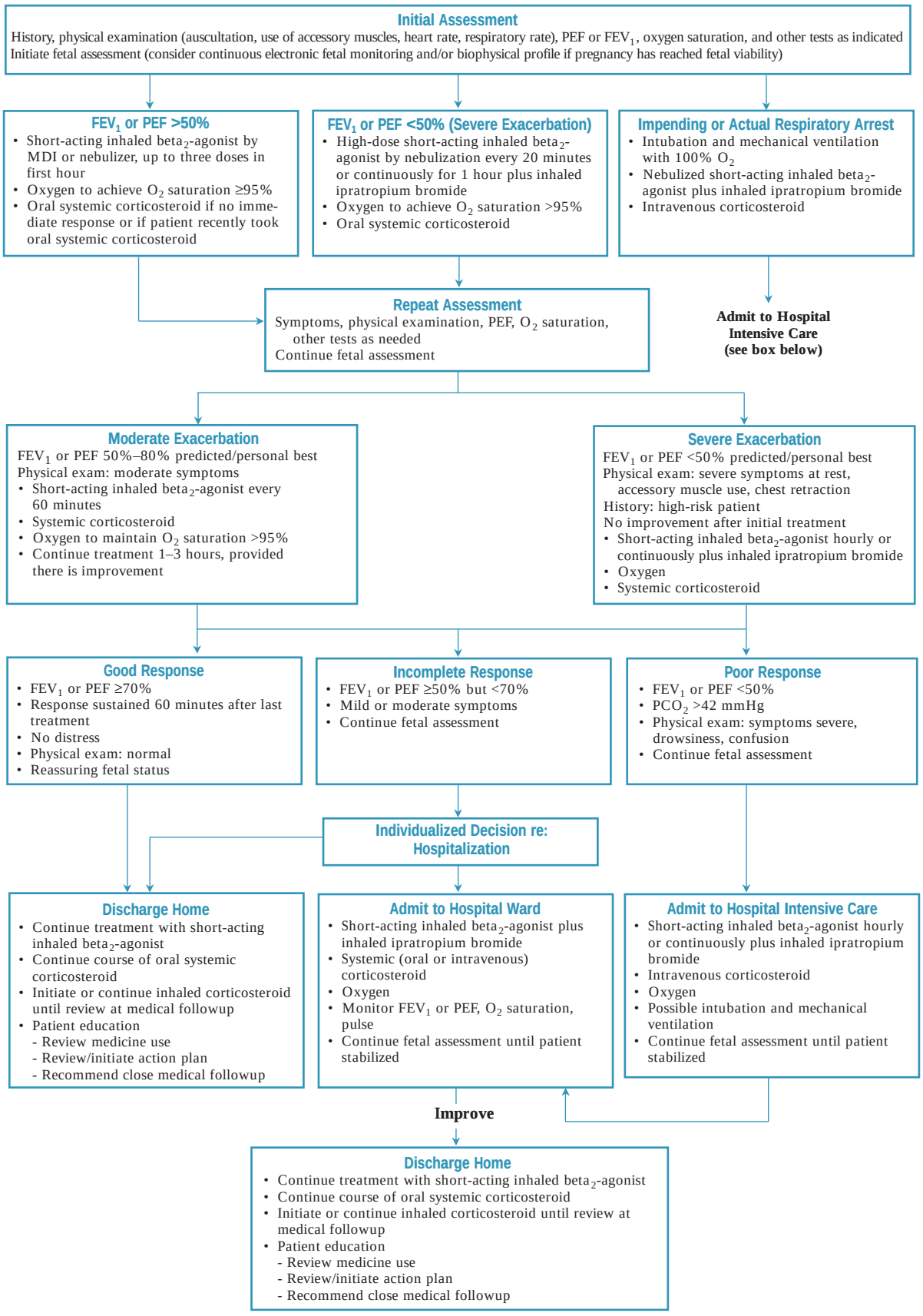
DPI, dry powder inhaler; MDI, metered-dose inhaler.
*Adapted from EPR—Update 2002.

Figure 4 Management of Asthma Exacerbations During Pregnancy and Lactation: Home Treatment



MDI, metered-dose inhaler; PEF, peak expiratory flow.
*Fetal activity is monitored by observing whether fetal kick counts decrease over time.

Figure 5 Management of Asthma Exacerbations During Pregnancy and Lactation: Emergency Department and Hospital-Based Care*



FEV_1, forced expiratory volume in 1 second; MDI, metered-dose inhaler; PCO_2, carbon dioxide partial pressure; PEF, peak expiratory flow.
*Adapted from EPR-2 1997.

Figure 6 Medications and Dosages for Asthma Exacerbations During Pregnancy and Lactation*

Medications	Dosages		Comments
	Adult Dose	Child Dose	
Short-Acting Inhaled Beta$_2$-Agonists			
Albuterol			
Nebulizer solution (5.0 mg/mL, 2.5 mg/3mL, 1.25 mg/3mL, 0.63 mg/3 mL)	2.5–5 mg every 20 minutes for 3 doses, then 2.5–10 mg every 1–4 hours as needed, or 10–15 mg/hour continuously	0.15 mg/kg (minimum dose 2.5 mg) every 20 minutes for 3 doses, then 0.15–0.3 mg/kg up to 10 mg every 1–4 hours as needed, or 0.5 mg/kg/hour by continuous nebulization	Only selective beta$_2$-agonists are recommended. For optimal delivery, dilute aerosols to minimum of 3 mL at gas flow of 6–8 L/min.
MDI (90 mcg/puff)	4–8 puffs every 20 minutes up to 4 hours, then every 1–4 hours as needed	4–8 puffs every 20 minutes for 3 doses, then every 1–4 hours inhalation maneuver; use spacer/holding chamber	As effective as nebulized therapy if patient is able to coordinate.
Bitolterol			
Nebulizer solution (2 mg/mL)	See albuterol dose.	See albuterol dose; thought to be half as potent as albuterol on a mg basis.	Has not been studied in severe asthma exacerbations. Do not mix with other drugs.
MDI (370 mcg/puff)	See albuterol dose.	See albuterol dose.	Has not been studied in severe asthma exacerbations.
Levalbuterol (R-albuterol)			
Nebulizer solution (0.63 mg/3 mL, 1.25 mg/3 mL)	1.25–2.5 mg every 20 minutes for 3 doses, then 1.25–5 mg every 1–4 hours as needed, or 5–7.5 mg/hour continuously	0.075 mg/kg (minimum dose 1.25 mg) every 20 minutes for 3 doses, then 0.075–0.15 mg/kg up to 5 mg every 1–4 hours as needed, or 0.25 mg/kg/hour by continuous nebulization	0.63 mg of levalbuterol is equivalent to 1.25 mg of racemic albuterol for both efficacy and side effects.
Pirbuterol			
MDI (200 mcg/puff)	See albuterol dose.	See albuterol dose; thought to be half as potent as albuterol on a mg basis.	Has not been studied in severe asthma exacerbations.
Systemic (Injected) Beta$_2$-Agonists			
Epinephrine			
1:1000 (1 mg/mL)	0.3–0.5 mg every 20 minutes for 3 doses sq	0.01 mg/kg up to 0.3–0.5 mg every 20 minutes for 3 doses sq	No proven advantage of systemic therapy over aerosol.
Terbutaline			
(1 mg/mL)	0.25 mg every 20 minutes for 3 doses sq	0.01 mg/kg every 20 minutes for 3 doses, then every 2–6 hours as needed sq	No proven advantage of systemic therapy over aerosol.
Anticholinergics			
Ipratropium bromide			
Nebulizer solution (0.25 mg/mL)	0.5 mg every 30 minutes for 3 doses, then every 2–4 hours as needed	0.25 mg every 20 minutes for 3 doses, then every 2 to 4 hours	May mix in same nebulizer with albuterol. Should not be used as first-line therapy; should be added to beta$_2$-agonist therapy.
MDI (18 mcg/puff)	4–8 puffs as needed	4–8 puffs as needed	Dose delivered from MDI is low and has not been studied in asthma exacerbations.
Ipratropium with albuterol			
Nebulizer solution (Each 3 mL vial contains 0.5 mg ipratropium bromide and 2.5 mg albuterol)	3 mL every 30 minutes for 3 doses, then every 2–4 hours as needed	1.5 mL every 20 minutes for 3 doses, then every 2–4 hours	Contains EDTA to prevent discoloration. This additive does not induce bronchospasm.
MDI (Each puff contains 18 mcg ipratropium bromide and 90 mcg albuterol)	4–8 puffs as needed	4–8 puffs as needed	
Systemic Corticosteroids	(Dosages and comments apply to all three corticosteroids)		
Prednisone **Methylprednisolone** **Prednisolone**	120–180 mg/day in 3 or 4 divided doses for 48 hours, then 60–80 mg/day until PEF reaches 70% of predicted or personal best	1 mg/kg every 6 hours for 48 hours, then 1–2 mg/kg/day (maximum = 60 mg/day) in 2 divided doses until PEF is 70% of predicted or personal best	For outpatient "burst" use 40–60 mg in single or 2 divided doses for adults (children: 1–2 mg/kg/day, maximum 60 mg/day) for 3–10 days.

* Adapted from EPR—Update 2002.

Notes:
- The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.
- No advantage has been found for higher dose corticosteroids in severe asthma exacerbations, nor is there any advantage for intravenous administration over oral therapy provided gastrointestinal transit time or absorption is not impaired. The usual regimen is to continue the frequent multiple daily dose until the patient achieves an FEV_1 or PEF of 50 percent of predicted or personal best and then lower the dose to twice daily. This usually occurs within 48 hours. Therapy following a hospitalization or emergency department visit may last from 3 to 10 days. If patients are then started on inhaled corticosteroids, studies indicate there is no need to taper the systemic corticosteroid dose. If the followup systemic corticosteroid therapy is to be given once daily, one study indicates that it may be more clinically effective to give the dose in the afternoon at 3 p.m., with no increase in adrenal suppression.[54]

Figure 7 Summary of Control Measures for Environmental Factors That Can Make Asthma Worse*

Allergens:

Reduce or eliminate exposure to the allergen(s) the patient is sensitive to, including:

- **Animal dander:** Remove animal from house, or, at a minimum, keep animal out of patient's bedroom and seal or cover with a filter the air ducts that lead to the bedroom.
- **House-dust mites:**
  - Essential: Encase mattress in an allergen-impermeable cover; encase pillow in an allergen–impermeable cover or wash it weekly; wash sheets and blankets on the patient's bed in hot water weekly (water temperature of >130°F is necessary for killing mites).
  - Desirable: Reduce indoor humidity to less than 50 percent; remove carpets from the bedroom; avoid sleeping or lying on upholstered furniture; remove carpets that are laid on concrete.
- **Cockroaches:** Use poison bait or traps to control. Do not leave food or garbage exposed.
- **Pollens** (from trees, grass, or weeds) and outdoor molds: To avoid exposure, adults should stay indoors—especially during the afternoon—with the windows closed during the season in which they have problems with outdoor allergens.
- **Indoor mold:** Fix all leaks and eliminate water sources associated with mold growth; clean moldy surfaces. Consider reducing indoor humidity to less than 50 percent.

Tobacco Smoke:

Advise patients and others in the home who smoke to stop smoking or to smoke outside the home. Discuss ways to reduce exposure to other sources of tobacco smoke, such as from daycare providers and the workplace.

Indoor/Outdoor Pollutants and Irritants:

Discuss ways to reduce exposures to the following:

- Wood-burning stoves or fireplaces
- Unvented stoves or heaters
- Other irritants (e.g., perfumes, cleaning agents, sprays)

*Adapted from EPR-2 1997.

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