

Asthma in Pregnancy

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Abstract: Asthma is an increasingly common problem during pregnancy. Mild and moderate asthma can be associated with excellent maternal and perinatal pregnancy outcomes, especially if patients are managed according to contemporary recommendations of National Asthma Education and Prevention Program. Severe and poorly controlled asthma may be associated with increased prematurity, need for cesarean delivery, preeclampsia, and growth restriction. Severe asthma exacerbations can result in maternal morbidity and mortality, and can have commensurate adverse pregnancy outcomes. The management of asthma during pregnancy should be based upon objective assessment, trigger avoidance, patient education, and step therapy. Asthma medications should be continued during pregnancy and while breast-feeding.

Key words: asthma, medications, exacerbations, step-therapy, pregnancy outcomes

completely reversible. Insight into the pathogenesis of asthma has changed with the recognition that airway inflammation is present in nearly all cases. Current medical management for asthma emphasizes treatment of airway inflammation to decrease airway responsiveness and prevent asthma symptoms. The National Asthma Education and Prevention Program (NAEPP) has found that “it is safer for pregnant women with asthma to be treated with asthma medications than it is for them to have asthma symptoms and exacerbations.”¹

Introduction

Asthma may be the most common potentially serious medical condition to complicate pregnancy, affecting approximately 8% of the pregnant women.¹ Asthma is characterized by chronic airway inflammation with increased airway responsiveness to a variety of stimuli, and airway obstruction that is partially or

Diagnosis

Diagnosis of asthma in pregnancy is no different than for a nonpregnant patient. Asthma typically includes characteristic symptoms (wheezing, chest cough, shortness of breath, chest tightness), temporal relationships (fluctuating intensity, worse at night), and triggers (eg, allergens, exercise, infections). Wheezing on auscultation would support the diagnosis, but its absence does not exclude the diagnosis. Ideally, the diagnosis of asthma would be confirmed by demonstrating airway obstruction on spirometry that is at least partially reversible, [$>12\%$ increase in

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forced expiratory volume in 1 second (FEV₁) after inhalation of albuterol].^{2,3}

In patients presenting with new respiratory symptoms during pregnancy, the most common differential diagnosis would be dyspnea of pregnancy. Dyspnea of pregnancy can usually be differentiated from asthma by its lack of cough, wheezing, chest tightness, or airway obstruction. Other differential diagnosis considerations include gastroesophageal reflux, chronic cough from postnasal drip, and bronchitis.

The most commonly used pulmonary function parameters are the peak expiratory flow rate (PEFR) and FEV₁. Current NAEPP guidelines suggest classifying degree of asthma severity in patients not on controller medication and degree of asthma control in patients on controller medication (Table 1).

Effects of Pregnancy on Asthma

Asthma during pregnancy has been associated with considerable maternal morbidity. In a large prospective study, the effects of pregnancy on asthma were found to be variable, 23% improved and 30% became worse during pregnancy.⁴

Women with mild asthma had an exacerbation rate of 12.6% and hospitalization rate of 2.3%; those with moderate asthma had an exacerbation rate of 25.7% and hospitalization rate of 6.8%; and severe asthmatics had exacerbation of 51.9% and hospitalization rate of 26.9%.⁴

Effects of Asthma on Pregnancy

As compared to women without a history of asthma, women with asthma have been reported to have higher risks for several complications of pregnancy, including preeclampsia, preterm birth, low birth weight or intrauterine growth restriction congenital malformations, and perinatal mortality, even after adjustment for potential confounders.⁵ Although residual confounding or common pathogenetic factors may explain some of these associations, observational data showing strong associations between poor asthma control (based on symptoms, pulmonary function, or exacerbations) and these increased risks suggest potential benefits of improved asthma control in pregnancy in terms of improved pregnancy outcomes.⁶⁻⁹

TABLE 1. *Classification of Asthma Severity and Control in Pregnant Patients*

Asthma Control*	Well Controlled	Not Well Controlled		Very Poorly Controlled
Asthma severity†	Intermittent	Mild persistent	Moderate persistent	Severe persistent
Symptom frequency/albuterol use	≤ 2 d/wk	> 2 d/wk, but not daily	Daily symptoms	Throughout the day
Nighttime awakening	≤ Twice per month	> Twice per month	> Once per week	≥ 4/wk
Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
FEV ₁ or peak flow (% predicted/ personal best)	> 80%	> 80%	60%-80%	< 60%

*Asses asthma control in patients on long-term control medications to determine whether step-up, step-down, or no change in therapy is indicated.

†Assess severity for patients who are not on long-term control medications; see Table 2 to determine starting controller therapy based on severity.

FEV₁ indicates forced expiratory volume in 1 second.

Prospective studies of the effects of asthma during pregnancy have generally had excellent perinatal outcomes^{6,10-13} Preterm birth < 37 weeks was increased among asthmatics who had severe disease or required oral corticosteroids,^{6,11} pre-eclampsia and small for gestational age was increased among those with daily symptoms,⁶ and the rate of cesarean delivery was increased among those with moderate or severe asthma.¹¹ These studies show that the gravida with mild or moderate asthma can have excellent maternal and perinatal outcomes. These findings do not contradict the possibility that suboptimal control of asthma during pregnancy is associated with increased risk to the mother or baby.¹¹ In fact, a significant relationship has been reported between lower FEV₁ during pregnancy and increased risk of low birth weight and prematurity.⁸

ASTHMA MANAGEMENT

The ultimate goal of asthma therapy during pregnancy is to maintain adequate oxygenation of the fetus by prevention of hypoxic episodes in the mother. Other goals include achievement of minimal or no maternal symptoms day or night, minimal or no exacerbations, no limitations of activities, maintenance of normal or near normal pulmonary function, minimal use of albuterol, and minimal or no adverse effects from medications. Consultation or comanagement with an asthma specialist is appropriate, as indicated, for evaluation of the role of allergy and irritants, complete pulmonary function studies, or evaluation of the medication plan if there are difficulties in achieving the goals of therapy or the patient has severe asthma. A team approach is helpful if more than 1 clinician is managing the asthma and the pregnancy. The effective management of asthma during pregnancy relies on 4 integral components: objective measures for assessment and monitoring, patient

education, avoidance or control of asthma triggers, and pharmacologic therapy.

Objective Measures for Assessment and Monitoring

FEV₁ after a maximal inspiration is the single best measure of pulmonary function. When adjusted for confounders, a mean FEV₁ < 80% predicted has been found to be significantly associated with increased preterm delivery < 32 weeks and < 37 weeks, and birth weight < 2500 g.⁸ However, measurement of FEV₁ requires a spirometer. The PEFR correlates well with the FEV₁, and has the advantages that it can be measured reliably with inexpensive, disposable, portable peak flow meters.

Patient self-monitoring of PEFR provides valuable insight to the course of asthma throughout the day, assesses circadian variation in pulmonary function, and helps detect early signs of deterioration so that timely therapy can be instituted. Patients with persistent asthma should be evaluated at least monthly and those with moderate-to-severe asthma should have daily home PEFR monitoring.¹ The typical PEFR in pregnancy should be 380 to 550 L/min. The pregnant woman should establish her "personal best" PEFR, then calculate her individualized PEFR zones: Green Zone > 80% of personal best, Yellow Zone 50% to 80% of personal best, and Red Zone < 50% of personal best PEFR.

Patient Education

Patients should be made aware that controlling asthma during pregnancy is especially important for the well being of the fetus. She should have a basic understanding of the medical management of asthma during pregnancy, including self-monitoring of PEFRs and the correct use of inhalers. She should be instructed on the proper PEFR technique; make the measurement while standing, take a maximum inspiration, and note the reading on

the peak flow meter. Women who smoke must be informed of the potential adverse effects of smoking on the fetus, which may add to the fetal effects of uncontrolled asthma, and should be strongly encouraged to quit. Women should also be instructed to avoid and control other asthma triggers. The importance of adherence to treatment should be stressed.

Avoidance or Control of Asthma Triggers

Limiting adverse environmental exposures during pregnancy is important for controlling asthma. Avoiding or controlling triggers can reduce asthma symptoms, airway hyperresponsiveness, and the need for medical therapy.³ Association of asthma with allergies is common; 75% to 85% of patients with asthma have positive skin tests to common allergens including animal dander, house dust mites, cockroach antigens, pollens, and molds. Other common nonimmunologic triggers include tobacco smoke, strong odors, air pollutants, food additives such as sulfites, and certain drugs including aspirin and β -blockers. Another trigger can be strenuous physical activity. For some patients, exercise-induced asthma can be avoided with inhalation of albuterol, 10 to 30 minutes before exercise.

Specific measures for avoiding asthma triggers include using allergen-impermeable mattress and pillow covers, remove carpeting, weekly washing of bedding in hot water, avoiding tobacco smoke, inhibiting mite and mold growth by reducing humidity, and leaving the house when it is vacuumed. Ideal animal dander control involves removing the pet from the home; allergic women should at least keep furry pets out of the bedroom. Cockroaches can be controlled by poison baits or traps and eliminating exposed food or garbage.

In a patient who is receiving a maintenance or near-maintenance dose of immunotherapy "allergy shots," not experiencing adverse reactions to the injections, and apparently deriving clinical benefit, con-

tinuation is recommended.¹ In such patients, a dose reduction may be considered to further decrease the chance of anaphylaxis. Risk-benefit considerations do not usually favor the start of immunotherapy during pregnancy.

Pharmacologic Therapy

Medications for asthma are divided into long-term controllers that prevent asthma manifestations (inhaled corticosteroids, long-acting β agonists (LABA), leukotriene modifiers, cromolyn and theophylline) and rescue therapy such as albuterol that provides quick relief of symptoms.

Women who have previously been prescribed asthma medications should be asked about their use to classify their current level of therapy according to a stepped care approach (Table 2) and to assess potential adherence problems and barriers. Adherence to inhaled corticosteroids has been reported to be poor in many studies. For example, reported adherence rates were approximately 50% in 1 study of asthmatic adults; decreased adherence was associated with an increased frequency of asthma exacerbations in this study.¹⁴ Women with asthma have been reported to decrease their inhaled corticosteroid use during early pregnancy compared with their pre-pregnancy use,¹⁵ which may be due to their reported concern regarding the safety of inhaled corticosteroids during pregnancy.¹⁶ Moreover, a substantial proportion of asthma exacerbations during pregnancy have been associated with non-adherence to inhaled corticosteroids.¹⁷ In addition to assessing adherence, asking about past medications and their effectiveness and any side effects can help guide subsequent management decisions.

The goals of asthma therapy include: relieving bronchospasm, protecting the airways from irritant stimuli, mitigating pulmonary and inflammatory response to an allergen exposure, and resolving the inflammatory process in the airways

TABLE 2. Step Therapy Medical Management of Asthma During Pregnancy**Step Asthma Severity and Medications†**

Mild intermittent

1. No daily medications, albuterol as needed

Mild persistent

2. Low-dose inhaled corticosteroid (alternative: cromolyn, LTRA, or theophylline*)

Moderate persistent

3. Medium-dose inhaled corticosteroid (alternative: low-dose inhaled corticosteroid and LABA, LTRA, or theophylline*)
4. Medium-dose inhaled corticosteroid and LABA (alternative: medium-dose inhaled corticosteroid plus LTRA, or theophylline*)

Severe persistent

5. High-dose inhaled corticosteroid and LABA
6. High-dose inhaled corticosteroid and LABA and oral prednisone

*Theophylline (serum level 5-12 mcg/mL). We have modified step 3 to reflect the choice of a medium-dose inhaled corticosteroid over a low-dose inhaled corticosteroid plus LABA because of the lack of safety data on the use of LABA during pregnancy.

†Starting therapy for a specific level of severity.^{1,3}

LABA indicates long-acting β agonist; LTRA, leukotriene-receptor antagonist.

leading to improved pulmonary function with reduced airway hyperresponsiveness. It is safer for pregnant women with asthma to be treated with asthma medications than it is for them to have asthma symptoms and exacerbations.¹ Current pharmacologic therapy emphasizes treatment of airway inflammation to decrease airway hyperresponsiveness and prevent asthma symptoms. The step-care therapeutic approach uses the least amount of drug intervention necessary to control a patient's severity of asthma.

Step Therapy

The step-care therapeutic approach increases the number and frequency of medications with increasing asthma severity (Table 2). Based on the clinical trials in patients of varying degrees of severity, medications are considered to be "preferred" or "alternative" at each step of therapy. Patients not optimally responding to treatment should be stepped-up to more intensive medical therapy. Patients with not well-controlled asthma (Table 1) should generally be stepped up 1 step, and those with very poorly controlled asthma (Table 1) should be stepped up 2 steps.

Once control is achieved and sustained for several months, a step-down approach can be considered, but should be undertaken cautiously and gradually to avoid compromising the stability of the asthma control. For some patients, it may be prudent to postpone until after birth attempts to reduce therapy that is effectively controlling the patient's asthma.¹ In the case of a patient who had a favorable response to an alternative drug before becoming pregnant, it would be appropriate to maintain the therapy that successfully controlled the patient's asthma before pregnancy. However, when initiating new treatment for asthma during pregnancy, preferred medications should be considered first, rather than alternative treatment options.¹

Patients with very poorly controlled asthma may require oral corticosteroids. In such cases, a short course of oral prednisone (40 to 60 mg of prednisone per day in a single or 2 divided doses for 3 to 10 d) is recommended.

Inhaled corticosteroids are the preferred treatment for the management of all levels of persistent asthma during pregnancy.¹ Airway inflammation is present

in nearly all cases; therefore, inhaled corticosteroids have been advocated as first-line therapy for patients with even mild asthma. Because there are more data on using budesonide during pregnancy than on using other inhaled corticosteroids, the NAEPP considered budesonide to be the preferred inhaled corticosteroid for use during pregnancy.¹ However, if a woman is well controlled by a different inhaled corticosteroid before pregnancy, it seems reasonable to continue that medication during pregnancy.

As needed, use of inhaled β_2 agonists is currently recommended for all levels of asthma during pregnancy.¹ Albuterol has a rapid onset of effect in the relief of acute bronchospasm via smooth muscle relaxation, and is an excellent broncho-protective agent for pretreatment before exercise. β_2 agonists are associated with tremor, tachycardia, and palpitations. They do not block the development of airway hyperresponsiveness. An increased frequency of bronchodilator use could be an indicator of the need for additional anti-inflammatory therapy. Salmeterol and formoterol are LABA preparations.

Data are lacking regarding the safety of LABAs during human pregnancy, although safety is considered likely based on the inhalational route and the generally reassuring data for short-acting β agonists.¹ Although a possible association between LABA and an increased risk of severe and even fatal asthma exacerbations has been observed in nonpregnant patients, recent information suggests that there is no such increased risk when these agents are used with inhaled corticosteroids,¹⁸ as is recommended during pregnancy.

Theophylline is an alternative treatment for mild persistent asthma and an alternative add on treatment for the Step 3 or 4 management of moderate persistent asthma during pregnancy (Table 2). Inhaled corticosteroids are preferred over theophylline because they led to a greater improvement in FEV₁, had fewer side

effects, and did not require serum monitoring.¹² New dosing guidelines have recommended that serum theophylline concentrations be maintained at 5 to 12 mcg/mL during pregnancy.¹ Theophylline can have significant interactions with other drugs, which can cause decreased clearance with resultant toxicity. For instance, cimetidine can cause a 70% increase in serum levels, whereas erythromycin use can increase theophylline serum levels by 35%. The main advantage of theophylline is the long duration of action, 10 to 12 hours with the use of sustained release preparations, which is especially useful in the management of nocturnal asthma. Theophylline is only indicated for chronic therapy and is not effective for the treatment of acute exacerbations during pregnancy.

The leukotriene receptor antagonists, zafirlukast (Accolate) and montelukast (Singulair) are both pregnancy category B drugs. Human data are limited for leukotriene receptor antagonist use in pregnancy.¹⁹ Leukotriene modifiers are less effective as single agents than inhaled corticosteroids and less effective than LABA as add on therapy.³

Oral corticosteroid use during the first trimester of pregnancy has been associated with a 3-fold increased risk for isolated cleft lip with or without cleft palate; however, most of these observations were among women who did not have asthma. With a background incidence of about 0.1%, the excess risk attributable to oral steroids would thus be 0.2% to 0.3%.²⁰ Oral corticosteroid use during pregnancy in patients who have asthma has been associated with an increased incidence of preeclampsia, preterm delivery, and low birth weight.^{6,20,21} A recent prospective study found that systemic corticosteroids resulted in a deficit of about 200 g in birth weight compared with nonasthmatic controls and asthmatic women exclusively treated with β_2 agonists.¹⁹ However, it is difficult to separate the effects of the oral

corticosteroids on these outcomes from the effects of severe or uncontrolled asthma.

Because of the uncertainties in these data and the definite risks of severe uncontrolled asthma to the mother and fetus, the NAEPP Working Group recommends the use of oral corticosteroids when indicated for the long-term management of severe asthma or for exacerbations during pregnancy.¹

Management of Allergic Rhinitis and Gastroesophageal Reflux

Rhinitis, sinusitis, and gastroesophageal reflux may exacerbate asthma symptoms, and their management should be considered an integral aspect of asthma care. Intranasal corticosteroids are the most effective medications for control of allergic rhinitis. Loratadine (Claritin) or cetirizine (Zyrtec) are recommended second-generation antihistamines. Oral decongestant ingestion during the first trimester has been associated with gastroschisis; therefore, short-term (≤ 3 d) intranasal decongestants or intranasal corticosteroids should be considered before use of oral decongestants.¹ Controlling gastroesophageal reflux may improve asthma control.

ANTENATAL MANAGEMENT

In general, data are lacking to guide the optimal obstetric management of the woman with asthma, and recommendations are based on extrapolation of data from other clinical settings and expert opinion. Women with asthma that is not well-controlled may benefit from increased fetal surveillance. Patients with moderate and severe asthma should be considered to be at risk for pregnancy complications. Adverse outcomes can be increased by underestimation of asthma severity and undertreatment of asthma. Gravidas with moderate or severe asthma should have scheduling of prenatal visits based upon clinical judgment. In addition to routine

care, monthly or more frequent evaluations of asthma history (emergency visits, hospital admissions, symptom frequency, symptom interference with sleep or activity, medications, dosages, and compliance) and pulmonary function (FEV_1 or PEFR) are recommended. Patients should be instructed on proper dosing and administration of their asthma medications.

Women with asthma that is not well-controlled may benefit from additional fetal surveillance in the form of ultrasound examinations and antenatal fetal testing. Because asthma has been associated with intrauterine growth restriction and preterm birth, it is useful to establish pregnancy dating accurately by first trimester ultrasound where possible. In the opinion of the Working Group,¹ the evaluation of fetal activity and growth by serial ultrasound examinations may be considered for women who have suboptimally controlled asthma, with moderate to severe asthma (starting at 32 wk), and after recovery from a severe asthma exacerbation. The intensity of antenatal surveillance of fetal well-being should be considered on the basis of the severity of the asthma as well as any other high-risk features of the pregnancy that may be present.

Home Management of Asthma Exacerbations

An abnormal fetal heart rate tracing may be the initial manifestation of an asthmatic exacerbation. To avoid fetal hypoxia, maternal pulse oximetry should be 95% or higher. Therefore, asthma exacerbations in pregnancy should be optimally managed. Patients should be instructed on rescue management, and educated to recognize signs and symptoms of early asthma exacerbations such as coughing, chest tightness, dyspnea, or wheezing, or by a 20% decrease in their PEFR. This is important so that prompt home rescue treatment may be instituted to avoid maternal and fetal

hypoxia. In general, patients should use inhaled albuterol 2 to 4 puffs every 20 minutes up to 1 hour. A good response is considered if symptoms are resolved or become subjectively mild, normal activities can be resumed, and the PEFr is $> 80\%$ of the personal best. The patient should seek further medical attention if the response is incomplete, or if fetal activity is decreased.

Hospital and Clinic Management

The principal goal should be the prevention of hypoxia. Measurement of oxygenation via pulse oximetry is essential, arterial blood gases should be obtained if oxygen saturation remains $< 95\%$, and chest x-rays are not commonly needed. Continuous electronic fetal monitoring should be initiated if gestation has advanced to the point of potential fetal viability. Albuterol (2.5 to 5 mg) is given every 20 minutes for 3 doses. For an incomplete response (FEV_1 or PEFr $< 70\%$), therapy should include: albuterol 2.5 to 10 mg every 1 to 4 hours as needed, or 10 to 15 mg/h continuously by nebulizer driven with oxygen, systemic (oral or intravenous) corticosteroids, and inhaled ipratropium bromide.¹ Occasionally, nebulized treatment is not effective because the patient is moving air poorly; in such cases, terbutaline 0.25 mg can be administered subcutaneously every 20 minutes for 3 doses. The patient should be assessed for general level of activity, color, pulse rate, use of accessory muscles, and airflow obstruction determined by auscultation and FEV_1 and/or PEFr before and after each bronchodilator treatment.

LABOR AND DELIVERY MANAGEMENT

Asthma medications should not be discontinued during labor and delivery. It is commonly recommended that women who currently or recently (during the previous

4 wk) received systemic corticosteroids should be given intravenous corticosteroids (eg, hydrocortisone 100 mg 8 h) during labor and for the 24-hour period after delivery to prevent adrenal crisis.¹ An elective delivery should be postponed if the patient is having an exacerbation. It is rarely necessary to perform a cesarean section for an acute asthma exacerbation; maternal and fetal compromise usually responds to aggressive medical management.

Prostaglandin (PG) E₂ or PGE₁ can be used for cervical ripening, the management of spontaneous or induced abortions, or postpartum hemorrhage, although the patient's respiratory status should be monitored. Carboprost (15-methyl PGF₂- α) and ergonovine and methylergonovine (methergine) can cause bronchospasm.² If tocolysis is needed, magnesium sulfate and terbutaline are preferable because they are bronchodilators; in contrast, indomethacin might induce bronchospasm in the aspirin-sensitive patient.² There are no reports of the use of calcium channel blockers for tocolysis among patients with asthma, although an association with bronchospasm has not been observed with wide clinical use. Nonselective β -blockers may trigger bronchospasm.

Breast-feeding

In general, only small amounts of asthma medications enter breast milk. Prednisone, theophylline, antihistamines, inhaled corticosteroids, leukotriene receptor antagonists, β_2 agonists, and cromolyn are not considered to be contraindications for breast-feeding.¹ However, among sensitive individuals, theophylline may cause neonatal vomiting, feeding difficulties, jitteriness, and cardiac arrhythmias.

Summary

Asthma is an increasingly common problem during pregnancy. Mild and moderate

asthma can be associated with excellent maternal and perinatal pregnancy outcomes, especially if patients are managed according to contemporary NAEPP recommendations. Severe and poorly controlled asthma may be associated with increased prematurity, need for cesarean delivery, preeclampsia, and growth restriction. Severe asthma exacerbations can result in maternal morbidity and mortality, and can have commensurate adverse pregnancy outcomes. The management of asthma during pregnancy should be based upon objective assessment, trigger avoidance, patient education, and step therapy. Asthma medications should be continued during pregnancy and while breast-feeding.

References

1. National Asthma Education and Prevention Program Expert Panel Report: Managing asthma during pregnancy: recommendations for pharmacologic treatment—2004 update. *J Allergy Clin Immunol.* 2005;115:34–46. Available at <http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg.htm> (last accessed 12-30-09).
2. Dombrowski MP, Schatz M, ACOG Practice Bulletin: Asthma in pregnancy. *Obstet Gynecol.* 2008;111:457–464.
3. National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. Available at <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdl.pdf> (last accessed 12-30-09).
4. Schatz M, Dombrowski MP, Wise R, et al, for The NICHD Maternal-Fetal Medicine Units Network, and NHLBI. Asthma morbidity during pregnancy can be predicted by severity classification. *J Allergy Clin Immunol.* 2003;112:283–288.
5. Schatz M, Dombrowski MP. Asthma in pregnancy. *N Engl J Med.* 2009;360:1862–1869.
6. Bracken MB, Triche EW, Belanger K, et al. Asthma symptoms, severity, and drug therapy: a prospective study of effects on 2205 pregnancies. *Obstet Gynecol.* 2003;102:739–752.
7. Bakhirebva LN, Schatz M, Jones KL, et al. Asthma control during pregnancy and the risk of preterm delivery or impaired fetal growth. *Ann Allergy Asthma Immunol.* 2008;101:137–143.
8. Schatz MS, Dombrowski MP, Wise R, et al, for The NICHD Maternal-Fetal Medicine Units Network, and The NHLBI, Bethesda, MD. Spirometry is related to perinatal outcomes in pregnant women with asthma. *Am J Obstet Gynecol.* 2006;194:120–126.
9. Murphy VE, Clifton VL, Gibson PG. Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. *Thorax.* 2006;61:169–176.
10. Mihrshani S, Belousov E, Marks GB, et al. Pregnancy and birth outcomes in families with asthma. *J Asthma.* 2003;40:181–187.
11. Dombrowski MP, Schatz M, Wise R, et al, for The NICHD Maternal-Fetal Medicine Units Network, and The NHLBI. Asthma during pregnancy. *Obstet Gynecol.* 2004;103:5–12.
12. Dombrowski MP, Schatz M, Wise R, et al, for The NICHD Maternal-Fetal Medicine Units Network, and The NHLBI. Randomized trial of inhaled beclomethasone dipropionate versus theophylline for moderate asthma during pregnancy. *Am J Obstet Gynecol.* 2004;190:737–744.
13. Triche EW, Saftlas AF, Belanger D, et al. Association of asthma diagnosis, severity, symptoms, and treatment with risk of preeclampsia. *Obstet Gynecol.* 2004;104:585–593.
14. Williams LK, Pladevall M, Xi H, et al. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol.* 2004;114:1288–1293.
15. Enriquez R, Pingsheng W, Griffen MR, et al. Cessation of asthma medication in early pregnancy. *Am J Obstet Gynecol.* 2006;195:149–153.
16. Chambers K. Asthma education and outcomes for women of child-bearing age. *Case Manager.* 2003;14:58–61.

17. Murphy VE, Gibson P, Talbot PI, et al. Severe asthma exacerbations during pregnancy. *Obstet Gynecol.* 2005;106:1046–1054.
18. Nelson HS, Carr W, Nathan R, et al. ACAAI/AAAAI Joint Task Force Report: update on the safety of long-acting B-agonists in combination with inhaled corticosteroids for the treatment of asthma. *Ann Allergy Asthma Immunol.* 2009;102:11–15.
19. Bakhireva LN, Jones KL, Schatz M, et al. Safety of leukotriene receptor antagonists in pregnancy. *J Allergy Asthma Immunol.* 2007;119:618–625.
20. Park-Wyllie L, Mazzotta P, Pastuszak A, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. *Teratology.* 2000;62:385–392.
21. Schatz M, Dombrowski MP, Wise R, et al. The NICHD Maternal-Fetal Medicine Units Network, and The NHLBI. The relationship of asthma medication use to perinatal outcomes. *J Allergy Clin Immunol.* 2004;113:1040–1045.