

Asthma in Pregnant Women

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Abstract

One of the most common potentially serious and affecting worldwide disease, asthma is quite common to be seen to complicate pregnancy as well. Managing asthma its complications in pregnancy is quite different as both the illness and the treating of the developing fetus must be considered. Most important goal of treating asthma in pregnancy is to optimize fetal as well as maternal health. Well-controlled asthma has been associated with favourable outcomes in pregnancy whereas poorly controlled asthma has been associated with poor outcome during prenatal, natal and post natal period. Proper control of asthma should allow a woman with asthma to maintain a normal pregnancy with little or no increased risk to herself or her fetus. Asthma affects 4%-8% of all pregnant women and is affecting more and more pregnant women each year.

In patients starting inhaled corticosteroids during pregnancy budesonide is recommended as the inhaled corticosteroid of choice. Asthma course worsens in one third, improves in one third or remains unchanged in one third of women during pregnancy. For women with moderate or severe asthma during pregnancy, ultrasound and antenatal fetal testing should be considered. During pregnancy, it is safer for women with asthma to be treated with asthma medications than to have asthma symptoms and exacerbations.

Key words: Asthma, Pregnancy

INTRODUCTION

One of the most common potentially serious and affecting worldwide disease, asthma, is quite common to be seen to complicate pregnancy as well. Asthma can be defined as a chronic inflammatory disorder of the airways characterised by increased responsiveness of tracheobronchial tree to multiplicity of stimuli¹. The symptoms get reversed often require intervention. Many recent reports have suggested a 2- 4 fold rise in the prevalence of asthma². Managing asthma its complications in pregnancy is quite different as both the illness and the treating of the developing fetus

must be considered. Most important goal of treating asthma in pregnancy is to optimize fetal as well as maternal health. Studies have shown that pregnant women with asthma have an increased risk of adverse perinatal outcomes,³ while controlled asthma is associated with reduced risks.^{4,5} Well-controlled asthma has been associated with favourable outcomes in pregnancy whereas poorly controlled asthma has been associated with increased rates of preterm delivery, pre-eclampsia, low birth weight growth restriction, Cesarean delivery, and maternal morbidity mortality as demonstrated by Sorensen et al.,⁷ and Bracken et al.⁸.

The magnitude of risk is related to the severity of the maternal asthma. Nevertheless, most pregnant women with asthma can successfully control their asthma and have a healthy baby. Proper control of

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asthma should allow a woman with asthma to maintain a normal pregnancy with little or no increased risk to herself or her fetus.

PREVALENCE

Lack of precise and universally accepted definition of asthma makes reliable comparison of reported prevalence from different parts of the world problematic¹. Previous estimates of Asthma affects 4%-8% of all pregnant women^{3,4} and is affecting more and more pregnant women each year. Two recent studies have also addressed racial and ethnic disparities in the rate and impact of asthma during pregnancy³.

PHYSIOLOGIC CHANGES DURING PREGNANCY

Both hormonal as well as mechanical changes can influence the respiratory functions and can lead to an exacerbation of asthma.¹ A progesterone mediated first trimester causes an increase in Tidal Volume leading to secondary increase in Minute Ventilation Volume. Pregnancy induced hyperventilation leads to compensatory respiratory alkalosis, increase in pH may lead to more severe respiratory compromise than similar ABG in nonpregnant. Mechanical changes in pregnancy include elevation of uterus, secondary elevation of diaphragm, decreased diameter of chest and increased intraabdominal pressure.

Around 30-40% of patients with asthma report perimenstrual worsening of symptoms⁴ Likelihood of female hormones influencing asthma seems obvious though exact mechanism remains undetermined. Considerable evidence suggests that female sex hormones have effects on several cells and cytokines involved in inflammation specifically attributed to estrogens. Increase in B cell differentiation, decrease in T cell suppression activity and number, and increase in antibody production. Evidence suggests that progesterone can act as a glucocorticoid agonist and suppress histamine release from basophils. Both estrogen and progesterone are involved in eosinophilic infiltration in many organs, both can reduce the oxidative burst after the phagocytic stimulus. Estradiol enhances eosinophilic adhesion to human mucus. Microvascular endothelial cells, the

combined effect with the progesterone induces eosinophilic degranulation. There appears to be a cyclic variation in lymphocyte beta-2 adrenoreceptor density in healthy women with higher levels during luteal phase. This upregulation is as a result of progesterone rather than estrogen.⁴

In Asthmatic women in fact there is downregulation of beta-2 adrenoreceptors. As pregnancy progresses and progesterone levels increase similar effects may be seen causing worsening in control of asthma in some pregnant asthmatic women. Maternal plasma cortisol levels increase with pregnancy. Cortisol's effect on asthma during pregnancy are more variable. Several Prostaglandins play a major role in asthma as bronchodilators and bronchoconstrictors, amniotic fluid contains large amounts of these PG's. There is a 10-30 fold increase in PGF₂-alpha during pregnancy. And its levels have been found to correlate with estrogen levels. Chronic hypoxia may lead to small for gestational age infant.¹ In women with asthma there was a twofold increased risk of preterm delivery compared with women who had no history of the condition⁶ (OR = 2.03; 95% CI 1.01-4.09). These data suggest that poor asthma control, by causing acute or chronic maternal hypoxia, may be the most remedial responsible factor for impaired fetal growth and supports the important generalization that adequate asthma control during pregnancy is important in improving maternal fetal outcome.

PREGNANCY ON ASTHMA

Asthma course may worsen, improve or remain unchanged during pregnancy. Overall asthma appeared to revert to the prepregnancy state by 3 months post partum in most women. About one third of women with asthma experience improvement while they are pregnant, about one third get worse, and the other third stay about the same. The symptoms tend to be at their worst during weeks 24-36 (months 6-8). However some patients did not follow the same course of asthma suggesting that the course of an individual during pregnancy remains unpredictable. Two observations may be important regarding the course of asthma during pregnancy. First more severe asthma tends to worsen during pregnancy while less severe asthma tends to remain unchanged or improved. The mechanisms responsible for the altered asthma course

during pregnancy are unknown. The myriad pregnancy associated changes in the levels of sex hormones, cortisol and PG's may contribute to change the asthma course during pregnancy. In addition exposure to fetal antigens leading to alterations in immune functions may predispose some pregnant asthmatic women to worsening asthma. A recent article by Tamasi and colleagues⁵ found that pregnant women with moderate severe asthma had increased numbers of circulating interferon gamma and IL-4 + T cells when compared with non pregnant asthmatic women and healthy controls. (pregnant / non pregnant.) Proliferation of these T lymphocytes may contribute to airway inflammation and may influence fetal development as well. There is also a possible influence of fetal sex and maternal asthma during pregnancy. Reports have suggested that asthma attacks or worsening asthma during pregnancy who are associated with female fetus.¹ The mechanisms leading to changes require further investigation, one possible cause there may be abnormal levels of placental enzymes that may lead to reduced fetal growth in female infants of pregnant asthmatic women.

ASTHMA ON PREGNANCY

The observations that maternal asthma may increase the risk of perinatal complications is confirmed by one of the largest studies to date⁶. Pregnancies in women with asthma are significantly more likely to be complicated by preeclampsia, perinatal mortality, preterm birth and LBW but not suggestive of any congenital malformations caused by asthma. This study also suggests that patients with more severe asthma are at a greater risk. Chronic hypoxia at high altitude is associated with lower birth weight but otherwise normal pregnancy. Therefore hypoxia caused by uncontrolled asthma may be a possible mechanism leading to adverse perinatal outcomes including placenta praevia.

Preplacental hypoxia as a result of smoking, anemia, asthma may directly affect fetal growth. As a result placenta adapts by increasing capillary growth, trophoblastic proliferation and thinning of the placental barrier. Studies have suggested that placental vascular resistance may be prematurely decreased in moderate to severe asthmatics.

MANAGING ASTHMA DURING PREGNANCY

General Principles

The treatment goal for the pregnant asthma patient is to provide optimal therapy to maintain good control of asthma for maternal health and quality of life as well as for normal fetal maturation throughout gestation. The ultimate goal of asthma therapy during pregnancy is to prevent hypoxic episodes in the mother, thereby maintaining adequate fetal oxygenation.

Asthma control is defined as:

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no work missed
- Maintenance of (near) normal pulmonary function
- Minimal use of short-acting inhaled beta₂-agonist (salbutamol)
- Minimal or no adverse effects from medications

Asthma is highly variable. Specific therapy should be tailored to the needs and circumstances of individual patients. A general stepwise approach to therapy is recommended in which the number and dose of medications used are increased as necessary and decreased when possible, based on the severity of the patient's asthma. Pharmacologic therapy should be accompanied at every step of severity by patient education and measures to control the factors that contribute to the severity of the asthma. The step-care therapeutic approach uses the lowest amount of drug intervention needed to control asthma, with specific recommendations based on degree of severity of asthma. Asthma care should be integrated with obstetrics care. The obstetrician should be involved in asthma care and should obtain information on asthma status during prenatal visits. Information should include day and night time symptoms, peak flow measurements or spirometry reading, and medication usage. Consultation or co-management 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 complications in achieving the goals of

therapy or the patient having severe asthma. A team approach is helpful if more than one clinician is managing the asthma and the pregnancy. Optimal management of asthma during pregnancy includes objective monitoring of lung function, avoiding or controlling asthma triggers, patient education, and individualizing pharmacotherapy to maintain normal pulmonary function.

FOUR KEY COMPONENTS OF ASTHMA MANAGEMENT

Assessment and Monitoring of Asthma: objective measures of pulmonary functions

Evaluation should include a history (symptom frequency, nocturnal asthma, interference with activities, exacerbations, and medications), lung auscultation, and pulmonary function. The dyspnea in pregnancy is not associated with the chest tightness, wheezing, and airway obstruction characteristic of asthma. Spirometry tests are recommended and preferable for routine monitoring, initial assessment. measurement of peak expiratory flow (PEF) with a peak flow meter is generally sufficient. Forced expiratory volume in one second (FEV₁) of less than 60 percent predicted are at even greater risk. FEV₁ and PEF do not change appreciably due to pregnancy. PEF may still be a useful monitoring tool for pregnant women with asthma. additional fetal surveillance in the form of ultrasound examinations and antenatal fetal testing. Since asthma has been associated with intrauterine growth rate (IUGR) and preterm birth, it is useful to establish pregnancy dating accurately by first trimester ultrasound where possible. The evaluation of fetal activity and growth by serial ultrasound examinations may be considered for (1) women who have suboptimally controlled asthma, (2) women with moderate to severe asthma (starting at 32 weeks), and (3) women after recovery from a severe asthma exacerbation. All patients should be instructed to be attentive to fetal activity.

Avoidance of Triggers

Avoidance leads to improved maternal well-being with less need for medications. Skin prick tests (SPT) or in vitro (radioallergosorbent test [RAST] or enzyme-linked immunosorbent assay [ELISA]) tests may be performed to identify relevant allergens for

which specific environmental control instructions can be given. Benefit-risk considerations do not generally favour start of immunotherapy during pregnancy because the initiation of immunotherapy can be associated with anaphylaxis, which can be fatal to the mother and fetus. Smokers must be encouraged to discontinue smoking, avoid as much as possible, exposure to environmental tobacco smoke and other potential irritants. Furthermore, maternal smoking may be associated with increased risk for wheezing and development of asthma in her child.

Patient Education

To understand potential interrelationships between asthma and pregnancy. Controlling asthma during pregnancy is important for the well-being of the fetus. The woman should understand that it is safer to be treated with asthma medications than it is to have asthma symptoms and exacerbations. She should be able to recognize and promptly treat signs of worsening asthma. She should have a basic understanding of medical management during pregnancy, including self monitoring and the correct use of inhalers.

Pharmacologic Therapy

It is safer for pregnant women with asthma to be treated with asthma medications than to have asthma symptoms or exacerbations and reduced lung function that may potentially impair oxygenation for the fetus. Medications are categorized in two general classes: (1) long-term-control medications (inhaled corticosteroids, LABA-salmeterol/formoterol, combination therapy) to achieve and maintain control of persistent asthma; especially important is daily medication to suppress the inflammation that is considered an early and persistent component in the pathogenesis of asthma; and (2) quick-relief medications (inhaled beta₂-agonist-salbutamol, inhaled anticholinergic- Ipratropium bromide) that are taken as needed to treat exacerbations.

STEPWISE APPROACH FOR MANAGING ASTHMA DURING PREGNANCY

As per global initiative for asthma (GINA) guidelines¹³, clinicians can use the day time and night time symptoms given by the asthmatics as well as spirometry (FEV₁) and Peak flow meter (PEFR) to

Table 1. Classification Of Asthma Severity (Gina 2007¹³)

	Symptoms/Day	Symptoms/Night	PEF or FEV ₁	PEF variability
STEP 1	< 1 time a week			
Mild Intermittent	Asymptomatic and normal PEF between attacks	<= 2 times a month	>= 80%	< 20%
STEP 2	> 1 time a week			
Mild Persistent	but < 1 time a day Attacks may affect activity	> 2 times a month	>= 80%	20-30%
STEP 3	Daily			
Moderate Persistent	Attacks affect activity	> 1 time a week	60%-80%	> 30%
STEP 4	Continuous			
Severe Persistent	Limited physical activity	Frequent	<= 60%	> 30%

PEF, Peak Expiratory Flow; FEV₁, Forced Expiratory Volume in the first second.

classify asthma (Table 1).

- The presence of one of the features of severity is sufficient to place a patient in that category.
- Patients at any level of severity-even intermittent asthma-can have severe attacks.

For patients who require long-term systemic corticosteroid:

- Use the lowest possible dose (single dose daily or on alternate days).
- Monitor patients closely for adverse side effects of corticosteroids.
- When control of asthma is achieved, make persistent attempts to reduce the dose of or discontinue systemic corticosteroid. High-dose inhaled corticosteroid is preferable to systemic corticosteroid administration¹⁸. Depending on the duration of systemic corticosteroid administration, care must be exercised in their withdrawal to avoid disease exacerbation and/or serious hypothalamic-pituitary-adrenal (HPA) crisis.
- Consultation with an asthma specialist is recommended.

MANAGEMENT OF ASTHMA DURING LABOUR AND DELIVERY

Although asthma exacerbations during labor are uncommon, patients should continue their medical therapy during labor. Patients experiencing some asthma symptoms during labor usually either require no medication or are adequately controlled by inhaled beta-agonists. If the patient's asthma responds poorly to inhaled beta-agonists, methylprednisone should be administered intravenously. Patients receiving regular glucocorticoids or who have received frequent courses during pregnancy should receive supplemental steroids for the stress of labor, delivery, and the puerperium. Consequently, although such infants should be carefully observed for any evidence of adrenal hypofunction, prophylactic treatment is not warranted.

However, 15-methyl PGF₂-alpha and methylergonovine can cause bronchospasm. Magnesium sulfate, which is a bronchodilator, and beta-adrenergic agents such as terbutaline can be used to treat preterm labor. Indomethacin, however, can induce bronchospasm in the aspirin-sensitive patient. No reports were found of the use of calcium channel blockers for tocolysis among patients with asthma. Epidural analgesia has the benefit

of reducing oxygen consumption and minute ventilation during labour. Meperidine causes histamine release but rarely causes bronchospasm during labour. A 2 percent incidence of bronchospasm has been reported with regional anesthesia.

CONSTRAINTS IN MANAGING ASTHMA DURING PREGNANCY

Poorly controlled asthma is associated with significant morbidity and is also potentially fatal for both the mother and the fetus. But reluctance to the regular inhaled treatment due to ignorance and low illiteracy among the asthma patients in India is a major challenge to the treating physician. The cost of diagnosis and inhaled medicines is beyond the reach of the majority and therefore international guidelines (GINA) may not be appropriate for such patients. Also, a large prevalence of tuberculosis, which is an important cause of cough, adds to the difficulties of diagnosis and management in India. The asthma patients with pregnancy should be managed with affordable medicines early and aggressively for any exacerbations to prevent resultant damage to the fetus in the long run. Since exposures to tobacco smoke and air pollution leads to increase in severity of asthma symptoms, decreased response to treatment and accelerated decline in lung functions; thus all pregnant asthmatics should be advised to avoid both active and passive smoking as well as air pollution (outdoor/indoor) in the form of smoke and fumes especially due to the use of biomass fuels for cooking in the rural areas. Dyspnea or breathlessness during pregnancy is quite common among Indian women due to many causes like anaemia, CHF, hypertension besides asthma and this remains a challenge among the treating physician to differentiate and classify the patient correctly.

All the above factors associated with the constraints of managing a pregnant asthmatic can be dealt with by following the solutions listed below:

- Treat exacerbations aggressively and prevent future exacerbations with regular controller options (inhaled and oral).
- Avoid the use of antibiotics, except to control bacterial infections and infectious exacerbations.
- The addition of oral theophylline and other oral

medication should normally be considered only if inhaled treatments have failed to provide adequate relief.

If optimal control of asthma is not achieved and sustained at any step of care (as indicated by nocturnal symptoms, urgent care visits, or an increased need for short-acting β_2 -agonists), several actions may be considered. Assess the patient's technique in using medications correctly. Increase anti-inflammatory therapy temporarily if needed to reestablish control. The addition of oral theophylline should normally be considered only if inhaled treatments have failed to provide adequate relief as several studies have evaluated the risk of congenital malformations in infants of mothers using theophylline during pregnancy. No significant increased risk was reported in any of the studies^{18,19}. Theophylline exposure is not independently associated with an increased risk of preeclampsia, preterm birth, or low birth weight infants in 429 women from one study after adjusting for confounders.¹⁹ Other perinatal outcomes have also been evaluated. One study demonstrated no increased risk of fetal deaths in infants of 410 exposed mothers.²⁰ Theophylline may be used as alternative add-on therapy in addition to inhaled corticosteroid medication in those pregnant patients with moderate persistent asthma not controlled by inhaled steroids alone.¹⁸ A deterioration of asthma control may be characterized by gradual reduction in PEF or FEV₁, failure of inhaled β_2 -agonist therapy to produce a sustained response, reduced tolerance to activities, or increasing nocturnal symptoms. To regain control of asthma, a short course of oral prednisone may be warranted. Specifically, the type of asthma and degree of severity are of primary importance and must be determined in the preoperative period.

Finally, several drugs commonly used for sedation or during anesthesia have the potential to provoke an acute episode. Aspirin and penicillin are commonly prescribed drugs that have the potential to induce an asthmatic attack. Preoperative use of H₂ receptor antagonists such as cimetidine may again be discouraged due to the potential of unmasking H₁ mediated bronchoconstriction. Also, patients who report the use of non-selective beta-adrenergic blocking agents (propranolol) or the intraoperative use of these agents for the treatment of hypertension

or tachycardia may inadvertently create bronchoconstriction by inhibiting beta-2 mediated smooth muscle relaxation. Theophylline clearance is slowed in the presence concurrent use of cigarettes or and treatment with cimetidine, erythromycin, or beta-adrenergic receptor antagonists. Use of cimetidine may contribute to the supra-therapeutic serum levels of theophylline and subsequently to the dysrhythmias observed during monitored treatment. Therefore, the concomitant use of the H₂ receptor antagonist cimetidine and theophylline together pre-operatively should be closely monitored or reconsidered.

A complete preoperative evaluation, attentive monitoring of the cardiovascular and respiratory systems, and the ability to treat potential medical emergencies are of equal importance when planning treatment for pregnant asthmatic patients. It is generally accepted that anesthetics such as barbiturates and narcotics, particularly meperidine, are histamine-releasing drugs and have the potential to provoke an acute episode in susceptible individuals. Thiamyl and thiopental evoke histamine release from human mast cell preparations, whereas methohexital and pentobarbital are devoid of this effect. For this reason, methohexital may be preferred in asthmatic or highly allergic patients. All opiates and sedative/hypnotics should be absolutely avoided in the acutely ill asthmatic because the risk of depressing alveolar ventilation is great and respiratory arrest can occur following administration.

Other factors that inhibit control may need to be identified and addressed. Reassessment of specific asthma triggers or the identification of previously uninvolved triggers should be undertaken. Evaluate possible allergens, environmental pollution or smoking, patient or family barriers to adequate self-management behaviors, psychosocial problems, or newly prescribed or over-the-counter or herbal medications that might influence patient response. *A step up to the next higher step of care may be necessary. Consultation with an asthma specialist may be indicated especially in case of repeated exacerbations.* Immunotherapy against identified allergens should not be started during pregnancy. Continuing immunotherapy is recommended for women who are at or near a maintenance dose, who are not having adverse reactions to the injections, and who seem to be deriving clinical benefit.

SUMMARY

During pregnancy, the doctor must classify severity of asthma and should ensure that stepwise treatment be started as quickly as possible (upregulation or downregulation). Minimize use of short-acting inhaled beta₂-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). For persistent asthma during pregnancy, first-line controller therapy consists of inhaled corticosteroids. During pregnancy, budesonide is the preferred inhaled corticosteroid. For pregnant women with asthma, recommended rescue therapy is inhaled salbutamol. Maternal and fetal well-being can be improved by identifying and controlling or avoiding exposure to tobacco smoke²⁰ and other allergens and irritants. Risk-benefit considerations do not usually favour beginning allergen immunotherapy during pregnancy. In general, only small amounts of asthma medications enter breast milk during breast-feeding. Use of prednisone, theophylline, antihistamines, inhaled corticosteroids, beta₂-agonists, and cromolyn is not contraindicated^{21,22}.

SALIENT MESSAGES

1. During pregnancy, it is safer for women with asthma to be treated with asthma medications than to have asthma symptoms and exacerbations^{23,24}. The main goal of asthma treatment is to maintain sufficient oxygenation of the fetus by preventing hypoxic episodes in the mother.
2. Asthma course worsens in one third, improves in one third or remains unchanged in one third of women during pregnancy. For women with moderate or severe asthma during pregnancy, ultrasound and antenatal fetal testing should be considered.
3. Pregnant asthmatic women have an increased risk of perinatal mortality, preeclampsia, low birth weight infants and preterm births compared to non asthmatic women. In patients starting inhaled corticosteroids during pregnancy budesonide has been recommended as the inhaled corticosteroid of choice.

ANNEXURE I

Classify Severity: Clinical Features Before Treatment or Adequate Control			Medications Required To Maintain Long-Term Control
	Symptoms/ Day Symptoms/ Night	PEF or FEV ₁ PEF Variability	Daily Medications
Step 4 Severe Persistent	Continual Frequent	≤60% >30%	- Preferred treatment: - High-dose inhaled corticosteroid AND - Long-acting inhaled beta₂-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 beta₂-agonist OR - Medium-dose inhaled corticosteroid.* - If needed (particularly in patients with recurring severe exacerbations): - Medium-dose inhaled corticosteroid* and long-acting inhaled beta₂-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 beta₂-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 beta₂-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.	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; FEV₁ 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 beta₂-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.
	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 beta₂-agonist‡ • Minimal or no adverse effects from medications		

* 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 beta₂-agonists.

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