

Special considerations for the pregnant woman and senior citizen with airway disease

Michael Schatz, MD San Diego, Calif.

Asthma and rhinitis may occur during pregnancy and in senior citizens. Many aspects of the diagnosis and management of these illnesses do not change in these special circumstances. However, a number of diagnostic and therapeutic considerations are unique to these conditions. This article will review those special considerations in the diagnosis and management of airway disease in pregnant women and senior citizens.

PREGNANCY

Managing asthma and rhinitis during pregnancy is unique because the effect of the illness and its treatment on the developing fetus as well as on the mother must be considered. In addition, physiologic changes associated with pregnancy could affect the upper or lower airways.

Nasal vascular pooling (resulting from an increased circulating blood volume and possibly enhanced by the vasodilating effect of progesterone) and increased nasal glandular activity occur during pregnancy.¹ The most important physiologic change affecting the lower airways during pregnancy is the progesterone-mediated physiologic hyperventilation of pregnancy, associated with an increased tidal volume (V_T), somewhat increased P_O₂ (102 to 196 mm Hg), and markedly decreased P_{CO}₂ (28 to 30 mm Hg).² The rise in free cortisol that occurs with advancing pregnancy could also be relevant to upper or lower airway disease.^{1,2}

The developing fetus is totally dependent on the mother for its oxygen supply. Thus, the hypoxia and other blood gas abnormalities associated with exacerbations of maternal asthma could threaten the fetus. Although rhinitis should not directly affect the fetus, severe gestational nasal symptoms could indirectly affect pregnancy adversely through an effect on eating, sleeping, or emotional well-being, or by exacerbating coexistent asthma.

A major concern in the management of airway disease during pregnancy are the potential adverse effects of medications on the fetus. Unfortunately, assessing the actual risks of medications during pregnancy may be difficult. Ethical and statistical considerations make it virtually impossible to scientifically prove that a medica-

tion is safe during pregnancy. Thus, medication choices during pregnancy must be based on less definitive information, such as animal studies, observational human data, and preferences for topical and older medications.^{2,3} In general, medications are recommended for use during pregnancy when their potential benefits for the mother and/or fetus outweigh their apparent risks, based on the best information available.^{2,3}

Allergen immunotherapy may be indicated in the management of airway disease in women of childbearing age. Immunotherapy appears to be generally safe during pregnancy,^{4,5} although anaphylaxis caused by immunotherapy occasionally occurs and could be a threat to the fetus. It is generally recommended that allergen immunotherapy be continued during pregnancy by women who are deriving benefit from it, are not prone to systemic reactions, and are at maintenance dosage or at least receiving a substantial dosage.² Beginning immunotherapy generally is not recommended during pregnancy because of the unknown potential in the pregnant patient for benefit or systemic reactivity, and because of the usual latency of several months before any substantial clinical benefit from immunotherapy is achieved.²

The presence of specific IgE is usually most practically and accurately detected by skin tests. However, skin testing is associated with a small risk of systemic allergic reactions. Therefore, selective radioimmunosorbent tests may be chosen over skin testing during pregnancy in previously untested patients in whom specific allergen sensitizations cannot be ascertained by a careful history alone.

Asthma

Effect of pregnancy on the course of asthma. Asthma may improve, worsen, or remain unchanged during pregnancy.⁶ Although change in the course of asthma during pregnancy in individual women is unpredictable, studies have suggested that women with more severe asthma before pregnancy may be more likely to experience worsening of their asthma during pregnancy than women with milder disease.⁷ In addition, experience during a previous pregnancy may be somewhat predictive, because in approximately 60% of women, the course of asthma is similar in successive pregnancies.⁸ The variable effect of pregnancy on the course of asthma appears to be more than merely random fluctuation in the natural history of the disease, because the changes in asthma severity that women attribute to pregnancy generally revert toward the prepregnancy course of asthma

From the Department of Medicine, University of California, San Diego School of Medicine, and Department of Allergy, Kaiser-Permanente Medical Center, San Diego.

Reprint requests: Michael Schatz, MD, Department of Allergy, Kaiser-Permanente Medical Center, 7060 Clairemont Mesa Blvd., San Diego, CA 92111.

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TABLE I. Potential mechanisms of increased adverse perinatal outcomes associated with maternal asthma

Hypothetical mechanism	Outcome	Supporting data
Severely uncontrolled asthma	Perinatal mortality	Severe asthma during pregnancy has been associated with perinatal mortality, ⁹ whereas asthma managed by asthma specialists during pregnancy has not been associated with increased perinatal mortality. ¹⁰⁻¹²
Moderately uncontrolled asthma	Intrauterine growth	Infants of mothers hospitalized during pregnancy for status asthmaticus weighed significantly less than did infants of mothers who did not require emergency therapy for asthma ¹³ ; poorer maternal pulmonary function during pregnancy in asthmatic women was associated with an increased risk of intrauterine growth retardation. ¹⁴
Medication	Pre-eclampsia	Incidence of pre-eclampsia increased in asthmatic subjects treated with prednisone in one series, ¹⁰ theophylline in another. ¹¹
Medication	Prematurity	Increased incidence of preterm and low-birth-weight infants in orally corticosteroid-dependent asthmatic subjects compared with non-corticosteroid-treated controls. ¹⁵
Medication	Intrauterine growth	Lower birth weight in infants of mothers treated with prednisone 10 mg daily throughout pregnancy (for pregnancy maintenance) compared to control infants. ¹⁶
Common pathogenetic factors	Preterm birth	Increased bronchial hyperreactivity demonstrated in 68% of women delivering preterm infants for no identifiable reasons ¹⁷ ; increased incidence of preterm births in patients with more severe asthma requiring oral corticosteroids. ¹⁵
Common pathogenetic factors	Pre-eclampsia	Vascular α -adrenergic hyperreactivity and β -adrenergic hyporeactivity demonstrated in asthmatic subjects ² ; increased pre-eclampsia in patients with more severe asthma requiring corticosteroids. ¹⁰

From Schatz M, Hoffman CP, Zeiger RS, Falkoff R, Macy E, Mellon M. The course and management of asthma and allergic diseases during pregnancy. In: Middleton E, Reed CE, Ellis EF, Adkinson NF, Yunginger JW, Busse WW, editors. *Allergy: principles and practices*. 5th ed. St. Louis: Mosby (In press). By permission.

within 3 months postpartum.⁸ The exact mechanisms involved in the change of course of asthma during pregnancy have not been defined, but a number of gestational physiologic changes have the potential to affect asthma.⁶ It does appear that upper respiratory infections are the most common precipitants of severe gestational asthma.

Several observations have been made regarding the course of asthma and the stage of pregnancy. The peak incidence of flares during pregnancy appears to occur between 24 and 36 weeks' gestation, especially in women whose asthma worsens during pregnancy.^{7, 8} In contrast, women with asthma tend to experience fewer symptoms during the last 4 weeks of pregnancy than during any other 4-week gestational period.⁸ Additionally, troublesome asthma during labor and delivery is extremely rare in prospectively managed asthmatic women.⁸

Outcome of pregnancy in pregnant asthmatic women. Controlled studies comparing the outcome of pregnancy in patients with asthma to outcomes in concurrently followed nonasthmatic women have been recently reviewed.⁹ Maternal asthma, especially more severe or uncontrolled asthma, may increase the risk of perinatal complications, such as pre-eclampsia, perinatal mortality, preterm birth, and low-birth-weight infants.

Potential mechanisms for the apparent increase in

perinatal risks in the pregnancies of asthmatic women include hypoxia and other adverse physiologic consequences of uncontrolled asthma, asthma medications, and/or common pathogenetic factors. The latter could include factors that predispose to bronchial hyperreactivity as well as vascular and uterine muscle hyperreactivity, such as circulating mediators that act on smooth muscle, or autonomic nervous system (ANS) abnormalities. The data supporting these various mechanisms are summarized in Table I.^{2, 9-17} It is particularly difficult to differentiate the effects of corticosteroids, used to treat more severe asthma, from the effects of uncontrolled asthma itself or from associated extrapulmonary smooth-muscle hyperreactivity in patients with more severe asthma. Although the mechanisms responsible for it remain undefined, the absence of increased incidence of adverse fetal and infant outcomes in three prospective studies in which asthma was managed by allergy or pulmonary specialists supports the hypothesis that optimal control of asthma during pregnancy improves perinatal outcome.¹⁰⁻¹²

Diagnostic considerations. Most women of childbearing age who complain of wheezing associated with chest tightness, cough, or dyspnea have asthma. The diagnosis of asthma can generally be confirmed by the demonstration of reversible obstructive airway disease on pulmo-

nary function testing. If methacholine testing is required to confirm a diagnosis of asthma, it should be deferred until after childbirth. Important triggering factors for asthma can usually be ascertained from a history. Confirmation of specific IgE during pregnancy is discussed earlier.

Several conditions unique to pregnancy must be considered in the differential diagnosis of asthma.¹⁸ Dyspnea of pregnancy may occur in early pregnancy (presumably because of the hyperventilation of pregnancy) or in late pregnancy (presumably because of the effects of the expanding uterus on the diaphragm). Such dyspnea is not associated with cough, wheezing, or airway obstruction. Peripartum cardiomyopathy or tocolytic therapy (i.e., therapy that inhibits uterine contractions) may cause pulmonary edema during pregnancy, which may be associated with wheezing. Additionally, amniotic fluid embolism, which usually presents with acute respiratory distress during labor or delivery, may rarely cause wheezing.

Therapeutic considerations. Avoidance of triggering factors is an obvious but often underused modality in the management of asthma. Avoidance measures are particularly beneficial during pregnancy because they may improve clinical well-being while reducing the need for pharmacologic intervention. It is especially important for the pregnant asthmatic woman to discontinue smoking during pregnancy because smoking may predispose to increased asthma, bronchitis, or sinusitis, and increase the need for medication; the increased morbidity attributed to smoking may be additive to that conferred by maternal asthma.¹⁴

The pharmacologic management of asthma during pregnancy is not substantially different from such management in nonpregnant patients, and the usual goals of therapy (i.e., achieving symptomatic control, preventing acute episodes, optimizing pulmonary function) appear to be beneficial for the fetus and for the mother.⁶ However, data on the use of asthma medications during pregnancy have led to certain specific recommendations for the pharmacologic management of asthma in pregnant women (Table II).³

Medications recommended for the outpatient management of mild, moderate, and severe chronic asthma are shown in Table III.^{3, 19} Medications generally should be added one by one until adequate control is achieved. Recent data confirm that inhaled corticosteroids reduce the frequency of asthma exacerbations during pregnancy.^{20, 21} Although the data suggest that systemic corticosteroids could increase the risk of preeclampsia,¹⁰ reduced intrauterine growth,^{15, 16} or infant prematurity,¹⁵ since severe asthma can be associated with maternal and/or fetal mortality,⁹ benefit-risk considerations still favor using systemic corticosteroids when indicated for severe asthma during pregnancy.³

The recommended management of acute asthma during pregnancy is described in Table IV.^{3, 19} In addition to medications, oxygen (to maintain a $PO_2 \geq 70$ mm Hg or pulse oximetry $\geq 95\%$) and intravenous hydration (at

TABLE II. Preferred medications for the management of asthma during pregnancy

Bronchodilators
Inhaled short-acting β_2 -agonist
Theophylline
Terbutaline if systemic β_2 -agonist required
Antiinflammatory Agents
Cromolyn
Beclomethasone
Prednisone

From National Asthma Education Program of the Working Group on Asthma During Pregnancy: management of asthma during pregnancy. September 1993. Bethesda, Md.: NIH publication 93-3279A.

least 100 ml/hour initially) are important in the management of acute gestational asthma. Additional information about the management of acute gestational asthma has been recently presented elsewhere.⁹

Rhinitis

Substantial symptoms of rhinitis have been reported in approximately 30% of pregnant women.²² Essentially, any of the recognized forms of rhinitis may occur during pregnancy, but the most common types appear to be allergic rhinitis, bacterial rhinosinusitis, rhinitis medicamentosa, and vasomotor rhinitis.¹

Many women notice some increase in nasal congestion associated with nasal dryness and epistaxis during pregnancy. These symptoms are apparently caused by the previously mentioned nasal vascular pooling. In some women, this nasal congestion becomes very troublesome and requires treatment; such vasomotor rhinitis usually improves postpartum.

Interrelationships between rhinitis and pregnancy. Few data exist on the clinical effect of pregnancy on rhinitis or the effect of rhinitis on pregnancy. As mentioned earlier, it seems unlikely that gestational rhinitis would have any direct adverse effect on the course of pregnancy, but severe rhinitis could indirectly affect pregnancy adversely.

Diagnostic considerations. The etiology of rhinitis during pregnancy can usually be determined from the history, physical examination, and nasal cytology.¹ The use of blood tests to confirm the presence of specific IgE has been discussed previously. Because the classic symptoms and signs of sinusitis were absent in nearly one half of the pregnant women with proven sinusitis in one study,²³ clinical findings and a high index of suspicion may be supplemented by other diagnostic procedures. The use of A-mode ultrasonography is limited by the occurrence of false-negative and false-positive results.¹ Because the radiation exposure associated with sinus radiographs is small and is reduced by abdominal or pelvic shielding,² sinus radiographs may be used during pregnancy when necessary to confirm or establish the diagnosis of sinusitis, especially if the patient is not responding adequately to treatment. Diagnostic sinus irrigations may be necessary during pregnancy in pa-

TABLE III. Pharmacologic step therapy of chronic asthma during pregnancy

Category	Frequency/severity of symptoms	Pulmonary function* (untreated)	Step therapy
Mild	<3 Times per week; nocturnal symptoms <2 Times per month	>80%	Inhaled β_2 -antagonists as needed
Moderate	≥ 3 Times per week; exacerbations affect sleep or activity	60-80%	Inhaled cromolyn; substitute inhaled beclomethasone; add oral theophylline
Severe	Daily; limited activity; frequent nocturnal symptoms; frequent acute exacerbations	<60%	Above plus oral corticosteroids (burst for active symptoms, alternate day or daily if necessary)

*FEV₁ or PEF based on the norm for the patient, which may be standardized norms or personal best. FEV₁, forced expiratory volume in 1 second; PEF, peak expiratory flow.

From Schatz M, Zeiger RS. Asthma and allergy during pregnancy. In: Bierman CW, Pearlman DS, Schapiro GG, Busse WW, editors. Allergy, asthma, and immunology from infancy to adulthood. 3rd ed. Orlando, FL: WB Saunders, 1996. p. 727-42. By permission.

TABLE IV. Pharmacologic management of acute asthma during pregnancy

Nebulized β_2 -agonist bronchodilator
Up to three doses in first 60 to 90 minutes
Every 1 to 2 hours thereafter until adequate response
Nebulized ipratropium
Intravenous methylprednisone (with initial therapy in patients on regular corticosteroids and for those with poor response during the first hour of treatment)
1 mg/kg every 6 to 8 hours
Taper as patient improves
Consider intravenous aminophylline in hospitalized patients not responding to the above. If it is to be used:
6 mg/kg loading dose
0.5 mg/kg per hour initial maintenance dosage
Adjust rate to keep theophylline level between 8 to 12 μ g/mL
Consider subcutaneous terbutaline 0.25 mg if patient not responding to the foregoing therapy

From Schatz M, Zeiger RS. Asthma and allergy during pregnancy. In: Bierman CW, Pearlman DS, Schapiro GG, Busse WW, editors. Allergy, asthma, and immunology from infancy to adulthood. 3rd ed. Orlando, FL: WB Saunders. 1996. p. 727-42. By permission.

tients with abnormal sinus radiographs who are not responding to therapy.

Therapeutic considerations. Medication choices are based on available data regarding the use of antihistamines and decongestants during pregnancy, data on the gestational use of asthma medications (i.e., cromolyn, inhaled corticosteroids) that have been adapted for topical intranasal use, and the relative efficacy of the various medications for specific rhinitis syndromes.²

A recent detailed review of gestational antihistamine data²⁴ concluded that chlorpheniramine should be considered the antihistamine of choice during pregnancy. If chlorpheniramine proves ineffective or is poorly tolerated, tripeleminamine was suggested. Newer second-generation antihistamines would generally be reserved for patients who clearly need an antihistamine but who are experiencing intolerable side effects from chlorpheniramine or tripeleminamine; ideally, these second-generation antihistamines would be used only after the first

trimester. The optimal specific second-generation antihistamine to use is less clear.²⁴ Cetirizine and loratadine do not cause adverse effects in animals, but there are minimal data on their human effects; although some reassuring human data exist for terfenadine, animal studies have revealed some adverse effects of this drug.

Pseudoephedrine is considered the oral decongestant of choice for use during pregnancy.³ However, recent case-control studies have associated first-trimester pseudoephedrine (and other decongestant) use with an increased risk of infant gastroschisis.^{25, 26} The baseline risk of 1 to 2 per 10,000 births in the general population appears to increase to 2 to 6 in 10,000 births in women receiving pseudoephedrine in the first trimester. Although this potential risk should be disclosed to the patient, and some patients may wish to defer the use of any decongestant until after the first trimester on this basis, the potential benefit of pseudoephedrine may warrant this degree of increased risk in other patients.

Cultures of sinus aspirates obtained during pregnancy have shown the most common sinus pathogens to be *Haemophilus influenzae* and *Streptococcus pneumoniae*.²³ Amoxicillin is thus the initial antibiotic of choice in the management of sinusitis during pregnancy in women who are not allergic to penicillin. Erythromycin is recommended for the penicillin-allergic patient with gestational sinusitis, and the addition of sulfisoxazole may be considered in early or midpregnancy if the patient does not respond in 5 to 7 days. Our experience suggests that 3 weeks of therapy is superior to a 10- to 14-day course for preventing the development of recurrent sinusitis during pregnancy. Oxymetazoline nose spray or drops (for <5 days) and pseudoephedrine may also be helpful as adjunctive and symptomatic therapy for gestational bacterial rhinosinusitis.

Amoxicillin plus clavulanate, cefaclor, cefuroxime, or possibly erythromycin plus sulfisoxazole (in early or midpregnancy) may be considered for women with unequivocal clinical sinusitis who are not responding to amoxicillin. If improvement does not ensue, sinus radiographs should be obtained, and sinus irrigation may be

TABLE V. Side effects of asthma medications of particular concern in the elderly

Medication	Side effects	Comment
β -Agonists	Electrocardiographic changes, hypokalemia, tremor, hypoxemia	Avoid long-acting oral β -agonists; ipratropium may cause fewer side effects
Theophylline	Cardiac arrhythmias, nausea, insomnia, liver disease	Target level 8-12 mg/ml recommended
Inhaled corticosteroids	Dermal thinning at high dose, decreased bone density	>1000 μ g/day, dose dependent
Oral corticosteroids	Depression, hypokalemia, hypertension, hyperglycemia, adrenal insufficiency, osteoporosis,* increased intraocular pressure,* cataracts, ulcer aggravation	

*After long-term use.

From National Asthma Education Program Working Group Report: considerations for diagnosing and managing asthma in the elderly. February 1996. Bethesda, Md.: NIH publication 96-3662.

necessary as both a diagnostic and a therapeutic modality.

SENIOR CITIZENS

The diagnosis and management of airway disease in the senior citizen requires special consideration because of the physiologic, psychologic, and psychosocial changes that accompany normal aging.²⁷ In addition, senior citizens have an increased frequency of concomitant medical conditions that may influence the diagnosis or therapy of asthma or rhinitis.

Asthma

Diagnostic considerations. In the elderly, the differential diagnosis of asthma is more likely to include chronic obstructive pulmonary disease (COPD), "cardiac asthma" due to left ventricular failure,²⁸ myocardial ischemia, or pulmonary embolism.²⁷ Many elderly patients with asthma have a persistent degree of airflow obstruction, even when optimally treated.^{29, 30} Differentiating asthma with a component of fixed obstruction from COPD may be particularly challenging. A 2-week trial of oral corticosteroid therapy, monitoring both the subjective and pulmonary-function response, may be necessary to reliably differentiate asthma from COPD.²⁷

Therapeutic considerations. Home peak-flow monitoring can be useful in elderly patients as in other patients, especially in those who are poor perceivers of symptom severity, those who require emergency-department care for exacerbations, or those who have coexistent heart or lung diseases that peak-flow monitoring may help differentiate. However, the usefulness of home monitoring by senior citizens with asthma may be limited by certain effects of the aging process, such as pulmonary physiologic changes or physical or cognitive disabilities.²⁷ Symptom diaries represent an alternative to home peak-flow monitoring that may be more appropriate for some senior citizens with asthma. Clinical experience and some studies show that the following symptom-diary changes are particularly indicative of poor asthma control²⁷: nocturnal or early-morning awakenings with wheeze or cough, increased cough and/or sputum, increased use of inhaled β -agonists, decreased tolerance to

exercise or daily activities, and increased intensity of dyspnea.

Several nonpharmacologic aspects of asthma management may require modification or special emphasis in the senior citizen with asthma.²⁷ Because of mental or physical impairments that may accompany aging, elderly patients may require additional education to understand the proper use of medication, especially regarding the use of metered-dose inhalers. Avoiding asthma triggers may more frequently include avoiding certain medications, used for other diseases, that may exacerbate asthma (e.g., β -blockers, nonsteroidal antiinflammatory drugs in aspirin-sensitive subjects) or cough (e.g., angiotensin converting enzyme [ACE] inhibitors). In addition, since respiratory infections are important asthma triggers, influenza and pneumococcal immunizations are strongly recommended for elderly patients with asthma.

Therapeutic considerations for the senior citizen with asthma include special considerations with regard to efficacy and side effects. Regarding efficacy, inhaled corticosteroids may be the inhaled anti-inflammatory medications of choice, since nedocromil and cromolyn have been primarily studied in younger, more allergic patients.²⁷ Moreover, as compared with patients without COPD, patients with mixed asthma and COPD may need more bronchodilators, be more responsive to ipratropium, and be less responsive to anti-inflammatory therapy.²⁴ The side effects of asthma medications that may be more problematic or more frequent in senior citizens with asthma are summarized in Table V.²⁷

Rhinitis

Diagnostic considerations. Allergic rhinitis is an uncommon cause of perennial rhinitis in senior citizens over 65 years of age.³¹ More commonly, rhinitis in the elderly is due to cholinergic hyperreactivity (associated with profuse watery rhinorrhea, which may be triggered by eating), α -adrenergic hyporeactivity (congestion associated with antihypertensive drug therapy), or sinusitis.

Therapeutic considerations. Watery rhinorrhea in the elderly commonly responds to intranasal ipratropium.³² Discontinuation of the causative drug would be the ideal

treatment of congestion due to an antihypertensive agent, but this is frequently not possible. Although α -adrenergic agonists must be used with caution in hypertensive patients, recent data suggest that pseudoephedrine may not increase the blood pressure in patients with controlled hypertension.³³ Other possible decongestant side effects of concern in the elderly include urinary retention in patients with prostatic hypertrophy, cardiac stimulation, and central nervous system stimulation.³¹

The anticholinergic effects of first-generation antihistamines may cause bladder disturbances or problems with visual accommodation in senior citizens, and sedation may also be a problem. Second-generation antihistamines, which lack anticholinergic or sedative properties, would generally be preferred.³⁴ However, terfenadine and astemizole may cause cardiac arrhythmias under certain circumstances,³⁴ especially with hypokalemia or hypomagnesemia.²⁷ Elderly patients may also be more likely to be treated with β -blockers, which generally contraindicate immunotherapy.

CONCLUSION

Pregnancy and aging are conditions that may affect the diagnosis and management of asthma and rhinitis. However, knowledge of the interactions between these conditions and diseases of the airways should facilitate safe and effective therapy, even under these special circumstances.

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