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*Part I of this series examined the pathophysiology of asthma and emergency department management strategies such as beta agonists, steroids, and magnesium. Part II will continue with management strategies and will also discuss asthma in special populations.*

*As this article's discussion will focus on specific medications for use in the acute asthma patient, the reader should maintain an awareness of the importance of basic patient management. For instance, making sure that an asthma patient is adequately hydrated*

## An Update on the Emergency Department Management of Asthma

Part II: Management Strategies and Special Populations

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*is paramount as the dehydration commonly seen in acute asthma patients can compound the clinical presentation by contributing to increased heart rate, decreased blood pressure, and to decreasing the patient's overall level of comfort and alertness.*

—The Editor

## Additional ED Management Strategies

**Anticholinergics.** Anticholinergics have been used for centuries in the treatment of bronchoconstriction. Relief from pulmonary illnesses often

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was sought by smoking the Datura plant. The plant has a muscarinic antagonist (stramonium) and was smoked to relieve bronchoconstriction. This chemical is structurally similar to atropine. By refining this structure, researchers created an anticholinergic agent, ipratropium bromide (Atrovent), that is active via the inhalatory route. Anticholinergic agents like ipratropium bromide block cholinergic-mediated bronchoconstriction by competitively antagonizing acetylcholine at its receptor sites, and they might also inhibit airway obstruction by interfering with the release of inflammatory mediators from the mast cell. Ipratropium is not as effective as beta agonists alone in reversing acute bronchoconstriction and therefore should not be used alone.

A meta-analysis of all trials using ipratropium in addition to inhaled beta adrenergics showed an improvement in airflow obstruction when both agents were used.<sup>1</sup> The addition of ipratropium is recommended in the management of acute adult and pediatric asthma, especially in the more severe cases.<sup>1-3</sup> Adult dosing is 500 mcg inhaled via metered-dose inhaler (MDI) or nebulizer every 20 minutes for up to three doses. The dose is lowered to 250 mcg if the patient weighs less than 20 kg. Its bronchodilating effect begins 5-15 minutes after administration,

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plateaus at 45-60 minutes, and lasts for up to 6 hours. Because of its very favorable safety profile, wide therapeutic margin, relatively low cost, and the potential for reduction of hospitalization, it often is included in the care of the acute pediatric asthma patient.<sup>4</sup>

**Methylxanthines in Acute Asthma.** Theophylline (Elixophyllin, Uniphyll, Theo-24, T-Phyl, Theo-Dur) is a methylxanthine that has been used as a bronchodilator for many years. Theophylline can help with bronchodilation without inducing the ventilation-perfusion mismatch that the beta adrenergic agents can cause.<sup>5</sup> Also, theophylline enhances diuresis, which may reduce excess alveolar fluid, and increases cardiac output. Theophylline has been shown to increase respiratory drive, improve mucociliary clearance, reduce pulmonary vascular resistance, and improve contractility of the diaphragm, all of which can be useful in the patient with impending respiratory failure.<sup>5</sup>

A meta-analysis of 164 non-critically ill admitted pediatric patients did not show a benefit in the use of theophylline. The patients receiving theophylline had longer lengths of stay (LOS) and more use of beta2 adrenergic agents.<sup>5</sup> More recently, a study of children admitted to the pediatric intensive care unit (PICU) randomized them into three groups (standard treatment with terbutaline and theophylline; standard treatment with theophylline, and standard treatment with IV terbutaline). The authors found no difference in LOS. All groups had significant improvement in asthma scores, and no difference in adverse events. However, both groups treated with terbutaline had significantly more expenses (by about \$3,500 per patient), mainly due to the high cost of terbutaline.<sup>5</sup> Another recent study of theophylline vs. placebo showed a faster improvement in asthma severity scores with no difference in LOS or in adverse effects.<sup>6</sup>

The data are different in the adult population, with a Cochrane systematic review of the available literature showing no benefit from the addition of theophylline. The addition of theophylline also resulted in more adverse effects.<sup>7</sup>

Given the fact that theophylline has a narrow therapeutic window and potential for significant toxicity, it should be used with caution, and serum concentrations must be monitored.<sup>8</sup> One author recommends its use only in children with severe asthma refractory to magnesium therapy.<sup>8</sup> The routine use of theophylline in the ED for adults is not supported by the available literature.

**Ketamine.** A recent observational study involving 10 pediatric patients with refractory asthma showed some benefit with the use of ketamine (Ketalar). The authors used ketamine at a loading dose of 1 mg/kg intravenously, followed by a continuous infusion of 0.75 mg/kg/hr (12.5 mcg/kg/min) for one hour. The authors observed a significant improvement in asthma scores, oxygen saturation, and respiratory rate.<sup>9</sup> An adult randomized controlled trial (RCT) showed no clinical benefit of ketamine in acute asthma.<sup>10</sup> Ketamine use, therefore, should be limited to the severely ill pediatric asthma patient.

**Mast Cell Stabilizers.** Cromolyn (Intal, Gastrocrom, Nalcrom) and nedocromil (Tilade) inhibit mediator release from mast cells and are considered non-preferred alternative

monotherapy for children with mild persistent asthma.<sup>11</sup> They have no role in the acute management of asthma.

**Leukotriene Receptor Antagonists (LTRAs).** Leukotrienes are potent pro-inflammatory mediators that induce bronchospasm, mucus secretion, and airway edema, and may be involved in eosinophil recruitment into the asthmatic airway. Montelukast (Singulair), zafirlukast (Accolate), and zileuton (Zyflo) are leukotriene receptor antagonists. Montelukast is approved for use in children as young as 2 years, while zafirlukast is approved for children 7 years and older. Of note, zafirlukast has been associated with hepatotoxicity.<sup>12</sup> Although less effective than inhaled corticosteroids, these agents should be considered for maintenance use in those who cannot or will not take inhaled corticosteroids.<sup>3</sup>

The only ED trial using leukotriene receptor antagonists (zafirlukast) showed decreased relapses and shorter ED stays.<sup>13</sup> A Portuguese study looked at outcomes of ED patients when given montelukast vs. placebo. There was no difference between the groups; however, this study had multiple limitations, including the low use of systemic steroids and low number of patients.<sup>14</sup>

The role of these agents in the acute asthma attack has not been further studied, so the routine use of leukotriene receptor antagonists cannot be recommended.

**Heliox.** Heliox is a mixture of helium and oxygen that decreases turbulent flow in the airway by decreasing airway resistance and increasing laminar flow. This results in decreased work of breathing.<sup>15</sup> Rodrigo published a review of the available literature on the use of heliox in addition to standard care. Most trials only included adult asthma patients with moderate to severe attacks. The author did not find a benefit of using heliox, although the total number of patients was small.<sup>16</sup> A similar study only showed improvement in the patients' perception of dyspnea.<sup>17</sup>

Pediatric data are limited, and the current literature does not yet provide convincing evidence to support the routine use of heliox in the ED management of pediatric asthma. A retrospective study in 28 ventilated pediatric patients showed that heliox decreased peak inspiratory pressures and improved both pH and pCO<sub>2</sub>.<sup>15</sup>

Heliox, on the other hand, was safe and well tolerated when used in the moderate to severe asthma patients.<sup>18</sup>

### Imaging in Acute Asthma

The chest x-ray is not recommended for routing asthma exacerbation and should only be obtained on patients presenting for the first time with asthma, those not responsive to treatment, or when one is suspicious for concomitant or exacerbating factors, such as infections.<sup>19</sup>

### Arterial Blood Gases

There is little role for arterial blood gas (ABG) analysis in the routine asthma patient. Unless the patient is unable to maintain an oxygen saturation of 90%, an ABG is unnecessary. Even when the occasional need for endotracheal intubation arises, a pre-intubation ABG will add little to the patient assessment since

## Table 1. Differential for Asthma in Infants and Toddlers<sup>11</sup>

- Foreign body aspiration
- Congenital airway and heart anomalies
- Abnormalities of the great vessels
- Cystic fibrosis
- Recurrent aspiration
- Immunodeficiency
- Pulmonary infections
- Ciliary dyskinesia
- Mediastinal masses

the need for intubation is based primarily on the patient's level of fatigue and ability to cooperate with therapy.<sup>20</sup>

### The Use of NIPPV in Asthma

Although there has been much written on treatment of chronic obstructive pulmonary disease (COPD) and pulmonary edema with noninvasive positive pressure (NIPPV), relatively few studies have evaluated its utility in asthma.

The goal behind using a noninvasive means of ventilation is to delay or avoid the need for endotracheal intubation. NIPPV can help to unload the respiratory muscles of their workload, dilating the bronchial tree and improving the sensation of dyspnea along with the goal of increasing alveoli recruitment.<sup>21</sup>

One Cochrane review published in 2005 was unable to reach a recommendation other than that NIPPV may be beneficial. It was otherwise inconclusive. This review, however only included data from one study, excluding the other 11 trials that also have been published.<sup>22</sup> In a study cited by the review, NIPPV was used very early in 30 patients with severe asthma. The patients were randomized into NIPPV or a sham device, in addition to standard management.<sup>23</sup> The NIPPV group had significantly improved pulmonary function tests, less need for hospitalization (17.6% vs 62.5%), and faster improvement than the sham group. None of the patients in the NIPPV group required intubation.<sup>23</sup> With a small sample size and infrequent intubations, the study is too limited to derive definitive recommendations.

### Managing Asthma in Special Populations

**Asthma in Children.** Despite the growing literature and available treatment options, pediatric asthma continues to be one of the greatest challenges facing emergency physicians in the United States today. Asthma is one of the most common diseases of childhood, with a prevalence rate of 5.4%. It is 44% more common in African-American children than among Caucasians, with African-American children hospitalized at a rate more than three times that of Caucasian children. Asthma accounts for 17% of pediatric encounters in EDs in the United States, and the financial cost of pediatric asthma is measured in billions of dollars. Between 1980 and 1996, mortality rates from pediatric asthma more than doubled, with a disproportionate share of those deaths occurring in inner city areas.<sup>4</sup>

**Table 2. Information to be Obtained in the Pediatric Asthma Patient's History and Physical Exam**

HISTORY	PHYSICAL EXAMINATION
• Duration and severity of exacerbation	• Increased respiratory rate
• Associated symptoms and fluid intake	• Increased heart rate
• Frequency and severity of previous attacks as well as response to specific therapies	• Use of accessory muscles (substernal, suprasternal, and intercostal retractions)
• Previous hospitalizations or intensive care unit admissions	• Nasal flaring
• History of intubations	• Poor quality of air entry
• Usual precipitants of exacerbations	• Presence of wheezing
• Use of steroids in the past year or any recent change in steroid dosage	• Prolonged expiratory phase
• Current medications (type, amount, and time of last dose)	• Inability to talk in complete sentences
• Other underlying cardio-pulmonary illnesses	
• Other atopic illnesses (a consistent risk factor for the development of asthma)	
• Previous adverse drug reactions	
• Family history	
• Potential triggers (allergens such as dust, mites, and pollen; irritants such as smoke and perfumes; physical environment factors such as exercise and cold air; physiologic triggers such as viral infections; and pharmacologic therapies such as beta-blockers, aspirin, or NSAIDs)	

The “new” diagnosis of asthma in those younger than 6 years of age is based on physical examination and history. Look for the following: severe wheezing or dyspnea; wheezing after 1 year of age; three or more episodes of wheezing; chronic cough (especially at night or exercise-induced); and clinical benefit of asthma medications.<sup>3</sup> The majority of children with asthma develop symptoms before 5 years of age.<sup>24</sup> Lung function testing, while

**Table 3. Differential Diagnosis of Asthma in Elderly Patients<sup>41</sup>**

- Congestive heart failure
- Chronic obstructive pulmonary disease (COPD)
- Emphysema
- Chronic bronchitis
- Chronic aspiration
- Gastroesophageal reflux disease (GERD)
- Tracheobronchial tumors

very useful in adults and older children, is not useful for diagnosing asthma in younger patients.<sup>3</sup>

The differential for asthma in infants and toddlers differs slightly from that of older children and adults. It includes foreign body aspiration, congenital airway and heart anomalies, abnormalities of the great vessels, cystic fibrosis, recurrent aspiration, immunodeficiency, pulmonary infections, ciliary dyskinesia, and mediastinal masses.<sup>11</sup> (See Table 1.) Information that should be obtained in the pediatric patient's history and physical examination include those listed in Table 2.

As with adults, short acting beta2 adrenergics should be used for acute symptom relief, on demand, and at the lowest dose and frequency needed for relief.<sup>3</sup> Systemic corticosteroids are safe and effective for pediatric patients and should be used routinely. Ipratropium should be added for those with severe asthma. Intravenous magnesium also should be considered in severe cases.

There are important considerations when discharging the pediatric asthma patient from the ED. If MDIs will be prescribed, they should be used with spacers and a mouth piece, although supportive information is scant.<sup>3</sup> When possible, children should be allowed to select the inhaler device of their choice, as this improves compliance and allows for better technique. The use of more than one type of device has been shown to reduce the quality of the technique. As with adults, education is essential to achieve proper use of the device.<sup>3</sup> Nebulizers rarely are needed, as with adults, as long as MDIs are used properly.<sup>25</sup> Children also can use dry powder inhalers (Turbuhaler and Diskus).<sup>25</sup>

Inhaled corticosteroids are the first-line maintenance therapy for patients with anything more than intermittent asthma. They can be used as monotherapy.<sup>3</sup> LTRAs are an alternative for those who cannot or will not use inhaled corticosteroids.<sup>3</sup> LTRAs were shown to be superior to placebo in three pediatric RCTs.<sup>26-28</sup> When compared to inhaled corticosteroids, LTRAs resulted in more relapses requiring systemic steroids. Most of these trials have excluded pediatric patients.<sup>3,29</sup> LABAs, however, are not recommended for maintenance monotherapy, but these can be added if there is not a good response to inhaled corticosteroids.<sup>3,29,30</sup> Theophylline is less effective when added to inhaled corticosteroids than LABAs or LTRAs, although limited data are available.<sup>31</sup> It should not be prescribed routinely in the ED.

**Asthma in Pregnancy.** Asthma is one of the most common medical problems complicating pregnancy.

Between 3.7% and 8.4% of pregnant patients in the United

**Table 4. Outpatient Management Strategies According to the Levels of Asthma**

	MILD INTERMITTENT	MILD PERSISTENT	MODERATE PERSISTENT	SEVERE PERSISTENT
<b>Beta adrenergics</b>	SABAs as needed	SABAs as needed	SABAs as needed Can add LABA	SABAs as needed Add LABA
<b>Steroids</b>		Inhaled preferred (low dose)	Inhaled preferred, can increase dose (low to medium dose)	Inhaled preferred (high dose) May need oral steroids
<b>Leukotriene inhibitors</b>	Alternative	Add to therapy	Add to therapy	
<b>Cromolyn</b>		Alternative		
<b>Theophylline</b>			Consider adding	Consider adding

SABA = short-acting beta agonists; LABAs = long-acting beta agonists<sup>43</sup>

States have asthma.<sup>32</sup> About 18% of all pregnant asthma patients have at least one ED visit. Approximately 62% of pregnant patients with acute severe asthma will require hospitalization.<sup>33</sup>

Some of the normal changes in pregnancy are relevant to asthma. There is a 50% increase in minute ventilation in late pregnancy (progesterone-mediated). This results in a normal maternal pCO<sub>2</sub> of about 28-32 mmHg. When interpreting ABGs, remember that pregnant women normally have a compensated respiratory alkalosis. Functional residual capacity (FRC) decreases by as much as 18% in late pregnancy. Keep this in mind during intubation—poor oxygen reserve may result in a precipitous drop in oxygen saturation when apnea ensues. Also, ventilator volumes must be kept low to avoid volutrauma and barotrauma.<sup>33</sup> Plasma volume increases more than red blood cell mass, resulting in the physiologic anemia of pregnancy. This decreases oxygen-carrying capacity.<sup>33</sup> Finally, chronic maternal hypoxia is known to cause intrauterine growth retardation, and maternal hypercarbia causes profound fetal acidosis.<sup>33</sup> Thus, maternal hypoxemia and hypercarbia should be avoided at all costs.

The effects of pregnancy on the course of asthma are unpredictable, with instances in which the asthma worsens, improves, and remains the same.<sup>33</sup> In three large studies, asthma symptoms have reportedly improved in 18-34% of patients, have remained unchanged in 26-40%, and have worsened in 20-40% of patients.<sup>34-36</sup> The worsening is thought to be related to baseline asthma severity.<sup>33</sup> Acute asthma exacerbations are more likely to occur during the second and third trimesters.<sup>33</sup>

One study described a two-fold higher risk of pre-term delivery in women with asthma compared to those without.<sup>37</sup> However, pregnancy outcome is equal to those who don't have asthma if the symptoms are controlled and complications are prevented.<sup>33</sup>

Concerns with adverse or teratogenic effects of asthma medications to the fetus have resulted in less-than-optimal management of asthma.<sup>38</sup> However, in cohort studies, asthma medicines have not been associated with adverse pregnancy outcomes.<sup>39,40</sup> Finally, always involve the obstetrician early in the case, and

ensure adequate monitoring of both mother and baby.

**Asthma in the Elderly.** It is estimated that 7-9% of those older than 70 years of age have asthma. There are more asthma-related deaths in the elderly than in other age group.<sup>41</sup> Studies have shown that many of these patients have delays in seeking care, mainly due to the fear of losing independence, fear of being institutionalized, and fear of dying. In addition, they have decreased perception of dyspnea and often do not recognize the early or subtle symptoms of asthma.

Even when recognized by the patient, underdiagnosis and misdiagnoses are common. Also, these patients tend to be treated less aggressively than their younger counterparts. The differential diagnosis in the elderly has several common medical conditions with very similar symptom profiles. These include congestive heart failure, COPD, emphysema, chronic bronchitis, chronic aspiration, gastroesophageal reflux disease (GERD), and tracheobronchial tumors.<sup>41</sup> (See Table 3.)

In many respects, asthma in the elderly is similar to that of other adults. The reported symptoms are similar: cough, wheezing, and dyspnea. However, a few key factors must be appreciated. The elderly tend to have reduced beta adrenergic responsiveness. Although beta adrenergic agents still are critical to management, these patients may not respond as well. Also, the prevalence of beta-blocker use makes them more susceptible to bronchospasm. When using steroids, consider that the oral treatment can aggravate or accelerate other medical problems, such as diabetes and osteoporosis. Metered-dose inhalers are preferred, but the elderly often have problems using them.<sup>41</sup> The use of spacers improves the technique, and thus should be encouraged when possible.

Despite proper treatment in the ED, this demographic group has high rates of non-compliance and high health care utilization rates.<sup>41</sup>

### Discharge Strategies and Follow-Up

Use the "Rule of Twos" to determine the severity of the patient's disease process: anyone who has symptoms more than

two times per week or more than two nights per month should be considered to have persistent asthma and managed as such.<sup>42</sup> Table 4 describes medications with which patients should be discharged depending upon the classification level of their asthma.

The available combination of an inhaled steroid and a long-acting bronchodilator product (such as Advair—inhaled fluticasone and salmeterol) as a dry powder inhaler is approved for use in children as young as 4-5 years old.

Studies have shown that emergency physicians do a poor job of prescribing appropriate controller medications to patients with asthma classified as persistent.<sup>44</sup> Furthermore, when emergency physicians do appropriately prescribe controller medications to patients being discharged from the ED, the primary care physician almost universally continues these medications. Otherwise the primary care physician often fails to prescribe these medications at the patient's follow-up visit despite guidelines that indicate they are necessary.<sup>44</sup>

It should be noted that asthma in young children is most commonly intermittent and triggered by viral respiratory infections (VRI). In this particular scenario, conventional doses of inhaled corticosteroids do not prevent exacerbations of VRI-induced asthma, and oral corticosteroids are a more appropriate alternative with which to send the patient home. In fact, a good strategy in this particular scenario is to prescribe an inhaled beta2 agonist and give a prescription for oral corticosteroids to be filled by the parents only if inhaled beta agonists appear to be inadequate.<sup>45</sup> It often is necessary to send older children and adults home with a course of oral steroids after an acute exacerbation, usually for 3-10 days. As stated before, this short "burst" therapy does not need to be tapered.<sup>46</sup> A common oral corticosteroid regimen used for adults is prednisone up to 60 mg daily for 5 days. In patients in whom compliance is an issue, however, a viable alternative is to give a single-dose IM injection of corticosteroid prior to discharge.<sup>47</sup> The available combination of an inhaled steroid and a long-acting bronchodilator product (such as inhaled fluticasone and salmeterol) as a dry powder inhaler is approved for use in children as young as 4-5 years old and can be considered as an alternative. All patients should follow up with their primary care physicians within a week of discharge.

Immunotherapy (such as omalizumab [Xolair]) as an adjunct to standard medical therapy can improve asthma control, although the role of immunotherapy in the ED has not been studied. The use of antihistamines also may be routine in the future, but their use cannot be recommended at this time.<sup>24</sup>

## Conclusion

Knowledge of asthma has improved dramatically in the past 25 years. Despite this, and the wide armamentarium of drugs available, asthma patients still have high rates of ED utilization, morbidity, and mortality. It is in the patient's best interest for the emergency physician to know the latest recommendations regarding the acute management of asthma, including the management of the asthma patient who is not responding to treatment or whose condition is deteriorating rapidly. Knowledge of proper discharge regimens and appropriate follow-up also are important.

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### Physician CME Questions

41. Ipratropium is not as effective as a beta agonist alone in reversing acute bronchoconstriction and therefore should not be used alone.
  - A. True
  - B. False
42. Which of the following statements is true regarding the use of theophylline for acute asthma?
  - A. It can help with bronchodilation without the ventilation-perfu-

### *Emergency Medicine Reports* CME Objectives

*To help physicians:*

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- apply state-of-the-art diagnostic and therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur.

- sion mismatch that beta adrenergic agonists can cause.
- B. It enhances diuresis, which may reduce excess alveolar fluid.
- C. It should be used with caution because of its narrow therapeutic window and potential for significant toxicity.
- D. It has been shown to increase respiratory drive, improve mucociliary clearance, reduce pulmonary vascular resistance, and improve contractility of the diaphragm.
- E. All of the above are true.
43. Which of the following is included in the differential diagnosis of asthma in infants and toddlers?
- A. Chronic bronchitis
- B. Tracheobronchial tumors
- C. Cystic fibrosis
- D. Gastroesophageal reflux disease
44. Although leukotriene receptor antagonists are less effective than inhaled corticosteroids, they should be considered for maintenance therapy in patients who cannot or will not take inhaled corticosteroids.
- A. True
- B. False
45. Which of the following is true regarding asthma in children?
- A. The majority of children develop symptoms after age 5.
- B. Lung function testing is not useful for the diagnosis of asthma in younger children.
- C. The differential diagnosis of asthma for infants and toddlers is the same as it is for older children and adults.
- D. When discharging pediatric asthma patients, nebulizers frequently are needed for treatment.
46. Which of the following is considered the appropriate treatment for a patient with mild intermittent asthma?
- A. Steroids
- B. Cromolyn
- C. Beta adrenergics
- D. Theophylline

47. Which of the following statements is true regarding the effects of asthma on pregnancy?
- A. Acute asthma exacerbations are more likely to occur during the first trimester.
- B. Asthma typically worsens during pregnancy.
- C. Asthma typically improves during pregnancy.
- D. In cohort studies, asthma medications have not been associated with adverse pregnancy outcomes.
48. Which of the following is included in the differential diagnosis of asthma in elderly patients?
- A. Mediastinal masses
- B. Chronic obstructive pulmonary disease
- C. Ciliary dyskinesia
- D. Foreign body aspiration
49. Which of the following statements is true regarding asthma treatment in elderly patients?
- A. Elderly patients tend to have improved responsiveness to beta adrenergics.
- B. They often recognize the early symptoms of asthma.
- C. Elderly patients tend to be treated more aggressively for asthma than younger patients are.
- D. Physicians should consider that oral steroids can aggravate or accelerate other medical problems such as diabetes and osteoporosis.
50. Which of the following statements is true regarding the changes in pregnancy that are relevant to asthma?
- A. Pregnant women have a compensated respiratory alkalosis.
- B. Functional residual capacity is decreased, which decreases oxygen reserve.
- C. Maternal hypercarbia results in profound fetal acidosis.
- D. Chronic maternal hypoxia is known to cause intrauterine growth retardation.
- E. All of the above

## CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

## In Future Issues:

## Diabetic Emergencies

### CME Answer Key

- |       |       |
|-------|-------|
| 41. A | 46. C |
| 42. E | 47. D |
| 43. C | 48. B |
| 44. A | 49. D |
| 45. B | 50. E |