

# The 'Crashing Asthmatic'

JAMES C. HIGGINS, CAPT, MC, USN, Naval Hospital, Jacksonville, Florida

**Asthma is a common chronic disorder, with a prevalence of 8 to 10 percent in the U.S. population. From 5 to 10 percent of patients have severe disease that does not respond to typical therapeutic interventions. To prevent life-threatening sequelae, it is important to identify patients with severe asthma who will require aggressive management of exacerbations. Objective monitoring of pulmonary status using a peak flow meter is essential in patients with persistent asthma. Patients who have a history of frag- mented health care, intubation, or hospitalization for asthma and those with mental illness or psychosocial stressors are at increased risk for severe asthma. Oxygen, beta<sub>2</sub> agonists, and systemic corticosteroids are the mainstays of acute asthma therapy. Inhaled anticholinergic medications provide additional bronchodilation. In patients who deteriorate despite usual therapeutic efforts, evidence supports individualized use of parenteral beta<sub>2</sub> agonists, magnesium sulfate, aminophylline, leukotriene inhibitors, or positive pressure mask ventilation before intubation. (Am Fam Physician 2003;67:997-1004. Copyright© 2003 American Academy of Family Physicians.)**



See page 907 for definitions of strength-of-evidence levels.

Members of various family practice departments develop articles for "Practical Therapeutics." This article is one in a series coordinated by the Department of Family Medicine at the Naval Hospital, Jacksonville, Fla. Guest editor of the series is Anthony J. Viera, LCDR, MC, USNR.

**A**sthma is one of the most common chronic disorders managed by family physicians. A "crashing asthmatic" is a patient with asthma who is clinically deteriorating into respiratory failure or arrest despite initial treatment. Managing such a patient can be a major challenge. Crucial tasks include rapid assessment of the severity of the asthma attack, objective determination of the response to therapy, and identification of the risk of respiratory failure.

## Background

Over the past decade, the mortality rate for asthma in the United States has increased.<sup>1</sup> Prevalence, morbidity rates, and treatment costs also have risen. These increases have occurred despite the reversible nature of asthma, a heightened awareness of the disease, and an expanding formulary of therapeutic agents for the management of asthma. To reverse these upward trends, national and global guidelines and strategies for the prevention and management of asthma have been developed.<sup>2</sup>

The prevalence of asthma is estimated

to be as high as 8 percent in adults and 10 percent in children.<sup>1,3</sup> From 5 to 10 percent of these patients have severe disease that does not respond to typical asthma medications.<sup>4</sup> The mechanisms that differentiate between easily managed and unresponsive asthma are still being investigated.<sup>5</sup>

## Status Asthmaticus

Status asthmaticus is a condition in which severe airway obstruction and asthmatic symptoms persist despite the administration of standard acute asthma therapy.<sup>6</sup> It can present with little warning and progress rapidly to asphyxiation.

Death can occur when asthma is severe, uncontrolled, and poorly responsive to treatment, with steady deterioration of respiratory status occurring over a period of days.<sup>1,6</sup> Data indicate that in nearly 85 percent of asthma deaths, the final episode lasted longer than 12 hours.<sup>1</sup> This length of time should have allowed ample opportunity for treatment if the patients had presented promptly for care and their respiratory distress had been quickly recognized.<sup>1</sup> Fortunately, only one in 2,000 patients die of asthma; the vast majority survive.<sup>1</sup>

TABLE 1

**Risk Factors for Death from Severe Asthma**


---

Previous asthma attacks with respiratory failure, seizure, loss of consciousness, or intubation
History of hypercapnia, metabolic acidosis, or pneumothorax with previous asthma attacks
Severe asthma attacks despite long-term oral corticosteroid therapy
Psychosocial factors, including mental illness, decreased perception of severity of dyspnea or disease, noncompliance with asthma therapy, substance abuse, or inner-city residence

---

Information from references 1, 3, and 4.

---

**Pathology**

Status asthmaticus can lead to several forms of sudden death. The most common scenario is severe bronchospasm, with mucus plugging leading to asphyxia.

Other reasons for sudden death include cardiac dysrhythmias related to hypoxia, hyperinflation leading to air trapping, and tension pneumothorax.<sup>7</sup> In patients with asthma, deaths also have occurred subsequent to the use of sedatives (respiratory depression), beta blockers (bronchospasm) and, occasionally, nonsteroidal anti-inflammatory drugs (anaphylaxis).<sup>1,6</sup>

Pathologic findings in fatal asthma include bronchial lumen occlusion by mucus, hyperplasia of submucosal glands, basement membrane thickening, and tissue eosinophilia.

**Risk Factors for Severe Asthma**

Risk factors for death from asthma are listed in *Table 1*.<sup>1,3,4</sup> Additional markers include frequent emergency department visits, wide variations in lung function, and use of multiple medications.

Studies<sup>1,8,9</sup> have shown that patients with severe asthma are 10 times more likely to present to emergency departments during nighttime hours, and that the highest fatality rates are in inner-city young adults. The risk of death is greatest in patients who have severe, unstable disease that is not being objectively monitored.<sup>1</sup> The National Heart, Lung, and Blood Institute (Expert Panel report 2)<sup>8</sup> addresses these problems in a discussion of key preventive issues, including patient education, objective measurements, environmental considerations, and home action plans.

Evidence indicates that patients with a history of nearly fatal asthma attack may have a blunted perception of increasing airway resistance and worsening bronchospasm.<sup>4,10</sup> Thus, these patients may be unable to sense critical worsening of airflow obstruction. Inadequate allergen control, insufficient use of inhaled corticosteroids, lack of objective monitoring criteria (e.g., home monitoring of peak flow), psychosocial or economic problems, and underuse of emergency ambulance services are well-documented risk factors for severe asthma exacerbations.<sup>11,12</sup>

Viral upper respiratory tract infection is the most common precipitant of an asthma attack. In addition to the usual common cold viruses, chlamydial pneumonia and herpes simplex virus infections may play a role in exacerbations of bronchospasm in patients with and without asthma. In some patients, allergic reactions to foods (e.g., peanuts) can result in life-threatening asthma attacks.<sup>6</sup>

TABLE 2

**Guidelines for Assessing Severity of Asthma Exacerbation****Symptoms**

Breathlessness while at rest  
Talking in words, not full sentences  
Agitation (usually)

**Signs**

Respiratory rate >30 per minute in adults  
Use of accessory muscles for breathing  
Wheezing during inhalation and exhalation  
Pulse rate >120 per minute  
Pulsus paradoxus

**Functional assessment**

PEF rate <150 to 200 mL in adults, or <50% of predicted or personal best effort  
Oxygen saturation <91% on room air  
PaO<sub>2</sub> <60 mm Hg on room air or Pco<sub>2</sub> >42 mm Hg

---

PEF = peak expiratory flow; PaO<sub>2</sub> = partial pressure of oxygen; Pco<sub>2</sub> = partial pressure of carbon dioxide.

Adapted with permission from Expert Panel report 2: guidelines for the diagnosis and management of asthma. Bethesda, Md.: National Institutes of Health, National Heart, Lung, and Blood Institute, 1997; NIH publication no. 97-4051.

---

**TABLE 3**  
**Predicted Average PEF Rates**  
**in Normal Children and Adolescents**

Height (inches)	Average PEF rate (L per minute)	Height (inches)	Average PEF rate (L per minute)
43	147	56	320
44	160	57	334
45	173	58	347
46	187	59	360
47	200	60	373
48	214	61	387
49	227	62	400
50	240	63	413
51	254	64	427
52	267	65	440
53	280	66	454
54	293	67	467
55	307	—	—

PEF = peak expiratory flow.  
Information from reference 13.

### Recognition of the “Crashing Asthmatic”

#### CLINICAL FINDINGS AND PEF VALUES

Asthma is a clinical diagnosis. While episodic and reversible symptoms of airflow obstruction are the primary clinical features, presentations can vary widely. However, the diagnosis of asthma is secure when key clinical elements are present and alternative diagnoses have been excluded. The physician must rapidly assess the severity of an asthma attack, objectively determine the response to therapy, and identify the risk of respiratory failure.

Criteria for diagnosing a severe asthma attack, including peak expiratory flow (PEF) rates, are listed in *Table 2*.<sup>8</sup> Predicted average PEF rates for normal children, adolescents, and adults are provided in *Tables 3*<sup>13</sup> and *4*.<sup>14</sup> Although predicted PEF values are useful in patients with asthma who do not have a known “personal best” peak flow, they should be interpreted with caution. Predicted normal PEF rates can vary substantially according to different formulas, and patients with chronically impaired lung function typically cannot attain these values.<sup>15</sup>

**TABLE 4**  
**Predicted Average PEF Rates in Normal Adults**

Age (years)	Men		Women	
	Height (inches)	Average PEF rate (L per minute)	Height (inches)	Average PEF rate (L per minute)
25	65	520	60	365
	70	592	65	401
	75	664	70	439
30	65	510	60	357
	70	581	65	394
	75	653	70	431
40	65	489	60	342
	70	561	65	379
	75	632	70	416
50	65	468	60	327
	70	543	65	364
	75	611	70	401
60	65	447	60	312
	70	519	65	349
	75	590	70	386

PEF = peak expiratory flow.  
Information from reference 14.

All patients who wheeze do not necessarily have asthma. Therefore, the physician must question the diagnosis of asthma, particularly when initial interventions fail. In children, wheezing can be associated with bronchiolitis, foreign-body aspiration, tracheomalacia, and congenital heart or lung abnormalities. Wheezing in adults may be caused by chronic obstructive pulmonary disease, respiratory infection, congestive heart failure, pulmonary embolism, aspiration, and vocal cord dysfunction. It is also important to look for comorbid conditions (e.g., coronary artery disease) that may complicate management.

#### ADDITIONAL FINDINGS

Hyperinflation is the most common finding on chest radiographs in patients hospitalized for treatment of asthma.<sup>6</sup> Possible abnormalities include pneumonia, con-

*Continuous nebulization of beta<sub>2</sub> agonists may be useful in the treatment of severe asthma.*

gestive heart failure, atelectasis, pneumothorax, and pneumomediastinum.

Arterial blood gas (ABG) parameters are often used to guide treatment in patients with severe asthma. However, the decision to intubate should be based on clinical grounds, rather than on ABG determinations alone. Close observations of respiratory effort, level of consciousness, and pulse oximetry serve as clinical correlates of pulmonary gas exchange. ABG measurements may aid in decision-making by providing quantitative information on pulmonary gas exchange. Initial findings during an asthma exacerbation typically include hypoxemia and hypocapnia. Hypercapnia is usually a later finding that reflects increasing airflow obstruction and fatigue because of the increased work of breathing; it may indicate impending respiratory failure. However, mechanical ventilation is required in fewer than 10 percent of patients who present with hypercapnia.<sup>6</sup>

Eosinophilia is a common finding in patients with asthma or allergy. Hypokalemia and hypermagnesemia may occur with heavy use of beta<sub>2</sub> agonists. Serum creatine kinase MM isoenzyme levels may be elevated because of extreme exertion of the ventilatory muscles.<sup>6</sup>

Patients who regularly measure peak flows at home usually document at least several days of depressed values and greater morning-to-evening variability in PEF rates before an exacerbation.<sup>6</sup> During a severe asthma attack,

patients may be unable to check their PEF because of marked dyspnea.

### **Conventional Management**

The goals of acute asthma management are to relieve bronchospasm, improve gas exchange, treat the underlying cause, and prevent complications. Before an in-depth history is obtained, treatment of patients with acute dyspnea should be initiated to prevent further deterioration.

Close monitoring and objective reevaluation for response to therapy are essential. The PEF rate is a key quantitative measure for assessing airflow; however, marked dyspnea initially may prevent proper use of the peak flow meter in patients who are experiencing severe asthma flares.

### **BETA<sub>2</sub> AGONISTS**

Inhaled beta<sub>2</sub>-adrenergic agonists are the mainstays of bronchodilator therapy. These agents provide the most rapid relief of bronchospasm with the fewest side effects.<sup>16,17</sup> [Reference 17—Evidence level B, uncontrolled trial] If patients can coordinate hand motion and breathing, albuterol (Ventolin) delivered by metered-dose inhaler (MDI) with a spacer (four to eight puffs every 20 to 30 minutes for three doses) compares favorably with nebulization (2.5 to 5 mg every 20 minutes).<sup>16</sup> In patients with more severe asthma, MDI dosing can be increased to one puff every 30 to 60 seconds, or continuous nebulization can be instituted (10 to 15 mg per hour) to improve symptoms.<sup>16,18</sup>

### **ANTICHOLINERGIC MEDICATIONS**

Anticholinergic drugs, especially when given in combination with inhaled beta<sub>2</sub> agonists, are associated with significantly improved pulmonary function and decreased hospitalization rates in patients with acute asthma.<sup>3,16,19</sup> [Reference 19—Evidence level A, meta-analysis] Ipratropium bromide (Atrovent) initially can be given by MDI (four to eight puffs) or nebulized solution (three doses of 250 mcg each). The recommended follow-up dosing of 250 to 500 mcg at six-hour intervals is well tolerated.<sup>3</sup> Atropine solution should not be nebulized because atropine crosses the blood-brain barrier, leading to sedation and worsening of asthma.<sup>20</sup>

### **CORTICOSTEROIDS**

Corticosteroids are potent anti-inflammatory drugs that are highly effective in the treatment of severe asthma. Sys-

---

### **The Author**

JAMES C. HIGGINS, CAPT, MC, USN, is staff physician in the family practice residency program at Naval Hospital, Jacksonville, Fla., and assistant clinical professor of family medicine at the Uniformed Services University of the Health Sciences F. Edward Hébert School of Medicine, Bethesda, Md. After graduating from the Philadelphia College of Osteopathic Medicine, Dr. Higgins completed a family practice residency at Naval Hospital, Jacksonville, and a faculty development fellowship in family medicine at the University of North Carolina, Chapel Hill.

*Address correspondence to James C. Higgins, CAPT, MC, USN, 428 Oak Pond Dr., Jacksonville, FL 32259 (e-mail: jchiggdo@aol.com). Reprints are not available from the author.*

temic corticosteroid therapy should be administered promptly to all patients with signs of severe asthma.<sup>21</sup> [Evidence level A, systematic review of randomized controlled trials]

In patients who can tolerate oral medications, oral corticosteroid therapy is as effective as intravenous therapy.<sup>22</sup> Typically, prednisone is given orally in a dosage of 1 to 2 mg per kg once daily (usual maximum: 60 to 80 mg per day) for five to seven days. For intravenous treatment, methylprednisolone sodium succinate (Solu-Medrol) is administered in a dosage of 0.5 to 2 mg per kg every six hours (usual maximum: 125 mg per day), or hydrocortisone is given in a dosage of 2 to 4 mg per kg every four to six hours.<sup>3</sup>

#### OXYGEN

Patients with severe asthma have a ventilation-perfusion mismatch and, thus, benefit from supplemental oxygen therapy. High-flow supplemental oxygen is best delivered using a partial or complete nonrebreather mask. The objective is to maintain the partial pressure of oxygen at a minimum of 92 mm Hg (oxygen saturation greater than 95 percent).<sup>8,16</sup> [References 8 and 16—Evidence level C, expert guidelines] There is no evidence that oxygen suppresses the respiratory drive in the absence of preexisting chronic pulmonary disease.<sup>3</sup>

#### CRITERIA FOR HOSPITALIZATION

Factors to consider in determining the need for hospitalization include disease severity, socioeconomic factors, clinical features, pulmonary function, and response to treatment.<sup>16</sup> Hospitalization is indicated in patients with a pretreatment arterial oxygen saturation of less than 90 percent, persistent respiratory acidosis, or severe obstruction that does not improve (or worsens) with the administration of sympathomimetic agents (i.e., the PEF rate remains at less than 70 percent of the predicted value).<sup>1</sup>

#### TREATMENT OF NONRESPONDING PATIENTS

Patients with severe asthma who do not respond to initial therapy require aggressive treatment to prevent cardiopulmonary arrest. In general, cardiorespiratory monitoring is necessary in patients who have status asthmaticus. A comfortable and supportive environment should be provided.

Pulse oximetry, blood pressure, and cardiac rhythm should be monitored continuously when initial acute

*In patients with severe asthma exacerbation who fail to improve with initial therapy, intravenous access should be established, and pulse oximetry, blood pressure, and cardiac rhythm should be monitored continuously.*

asthma therapy fails. Intravenous access should be secured in patients with severe asthma. Although hypoxemia and anxiety may cause agitation and restlessness, anxiolytic medications should be administered only when the physician is prepared to intubate.

The key concern is to actively manage the airway by being prepared for the next intervention if the patient fails to respond. An overview of the management of acute severe asthma is provided in *Figure 1*.<sup>20</sup>

#### PARENTERAL BETA<sub>2</sub> AGONISTS

Delivery of beta<sub>2</sub> agonists by inhalation is the most effective treatment for asthma exacerbations. Unfortunately, some patients with severe exacerbations may not respond to this treatment. Inhaled beta<sub>2</sub> agonists may be less effective in patients who have a strong inflammatory response or a history of long-term heavy use of beta<sub>2</sub> agonists. Subcutaneous or intravenous administration of beta<sub>2</sub> agonists may be indicated in patients who are coughing excessively, too weak to inspire adequately, or moribund.<sup>3,12</sup>

Terbutaline (Brethine) is given subcutaneously (0.1 to 0.25 mg) or intravenously (0.1 to 10 mcg per kg per minute).<sup>3</sup> In one study<sup>4</sup> of patients with “brittle asthma” (defined by wide diurnal variations in PEF rates), twice-daily subcutaneous administration of terbutaline improved symptoms, medication use, and PEF rates.<sup>4</sup> The findings of this study suggest that some beta receptors may not be accessible by the aerosolized route.

Intravenously or subcutaneously administered epinephrine may help avoid the need for mechanical ventilation in patients with status asthmaticus.<sup>7</sup> However, cardiovascular effects limit the use of epinephrine to patients less than 40 to 50 years of age. The subcutaneous dose of epinephrine is 0.1 to 0.5 mg in adults (0.01 mg per kg in children), usually given as 0.1 to 0.5 mL of a 1:1,000 solution every 20 minutes or longer. For convenience, adult patients may be given three 0.3-mg doses at 20-minute

## Acute Severe Asthma

### Perform an initial rapid assessment:

Brief history (to exclude diagnoses other than asthma)  
Focused physical examination—vital signs, lung sounds, accessory muscle use, alertness, color  
Objective testing—oxygen saturation, PEF or FEV<sub>1</sub> rate

### Improve airflow:

Inhaled beta<sub>2</sub> agonist  
Inhaled anticholinergic drug  
Intravenously administered magnesium sulfate (if patient's condition is severe)  
Consider use of leukotriene inhibitor.

### Decrease airway inflammation:

Systemic corticosteroid  
Consider low-dose aminophylline therapy.  
Consider use of leukotriene inhibitor.

### Provide supportive care:

Ensure that oxygen saturation is above 95%.  
Consider hydration.  
Monitor vital signs and cardiac rhythm.  
Consider use of heliox or noninvasive ventilation in cooperative patient.  
Plan for intubation if patient has impending respiratory arrest.

### Reassess patient:

Physical examination  
PEF or FEV<sub>1</sub> rate  
Oxygen saturation or ABG measurement  
Ancillary studies (chest radiograph, laboratory tests)

### Good response:

FEV<sub>1</sub> or PEF rate is ≥70% of predicted or personal best effort.  
Response is sustained for >60 minutes.  
Symptoms resolve.  
Physical examination is normal.

### Discharge patient:

Prescribe inhaled beta<sub>2</sub> agonist to be taken as needed.  
Prescribe systemic corticosteroid to be taken as needed.  
Continue or initiate inhaled corticosteroid therapy.  
Provide patient education.  
Create or update home action plan.  
Provide close follow-up.

### Incomplete response:

FEV<sub>1</sub> or PEF rate is ≥50% but <70% of predicted or personal best effort.  
Symptoms continue or improve slowly.

### Hospitalize patient:

Monitor oxygen saturation and PEF rate.  
Maintain oxygen saturation at >90%.  
Continue inhaled beta<sub>2</sub>-agonist therapy.  
Consider continued administration of inhaled anticholinergic drug therapy for 24 to 36 hours.  
Administer systemic corticosteroid therapy.  
Continue or initiate inhaled corticosteroid therapy.

### Poor response:

FEV<sub>1</sub> or PEF rate is <50% of predicted or personal best effort.  
Arterial carbon dioxide level is >42 mm Hg.  
Patient has signs of fatigue (e.g., confusion, obtundation).

### Hospitalize patient for intensive care:

Monitor oxygen saturation and cardiac rhythms.  
Obtain vital signs frequently.  
Maintain oxygen saturation at >95%.  
Administer inhaled beta<sub>2</sub> agonist by continuous nebulization.  
Administer intravenous corticosteroid therapy.  
Continue inhaled anticholinergic drug therapy for 24 to 36 hours.  
Consider use of heliox, ketamine, noninvasive ventilation, or intubation.

Improved

Improved

FIGURE 1. Overview of the initial management and disposition of patients with acute severe asthma. (PEF = peak expiratory flow; FEV<sub>1</sub> = forced expiratory volume in one second; ABG = arterial blood gas)

Adapted with permission from Hallstrand TS, Fahy JV. Practical management of acute asthma in adults. *Respir Care* 2002;47:178.

intervals (total dose: up to 1 mg).<sup>7</sup> Incremental doses of 1 to 5 mL of a 1:10,000 epinephrine solution can be given intravenously over five to 10 minutes. Rarely, epinephrine is infused at a rate of 1 to 4 mcg per minute.

#### MAGNESIUM SULFATE

Magnesium sulfate is a calcium antagonist that induces smooth muscle relaxation. In three randomized controlled trials, magnesium sulfate improved symptoms in patients with severe asthma who had not responded to other treatments.<sup>23</sup> A dose of 30 to 70 mg per kg (1 to 3 g) is given intravenously over 20 to 30 minutes.<sup>7</sup> The safety and potential benefits of magnesium sulfate justify its use in nonresponding patients. This agent may be particularly beneficial in patients who are prone to hypomagnesemia because of prolonged, heavy use of inhaled beta<sub>2</sub> agonists.

#### METHYLXANTHINES

At one time, aminophylline and theophylline were the mainstays of asthma treatment. Currently, these agents are second-line bronchodilators because they are only about one third as effective as beta<sub>2</sub> agonists. Treatment with aminophylline has been shown to improve oxygenation and reduce the incidence of intubation in children with severe status asthmaticus.<sup>24</sup> Unfortunately, the therapeutic level of this agent (approximately 10 mg per L) is close to the toxic level. Signs of toxicity include cardiac dysrhythmias, nausea, tremor, and headache. A prudent aminophylline regimen is a loading dose of 5 to 6 mg per kg administered intravenously over 30 minutes, then 0.5 mg per kg per hour.<sup>12</sup>

#### LEUKOTRIENE INHIBITORS

Some patients with severe asthma seem to respond to leukotriene inhibitors, which are anti-inflammatory drugs. In the acute setting, zafirlukast (Accolate) may be given orally twice daily; the dose for adults is 20 mg, and the dose for children up to 12 years of age is 10 mg. Zileuton (Zyflo), in a dosage of 600 mg four times daily, may be given to patients older than 12 years.<sup>4</sup>

#### NONINVASIVE VENTILATION

Continuous positive airway pressure or bi-level positive airway pressure machines use tight-fitting face masks to assist ventilation and reduce the work of breathing without intubation. Noninvasive ventilation is indicated in cooperative patients who may have impending respiratory failure

but do not need immediate intubation. Noninvasive ventilation may avoid the possible complications of sedation, paralysis, and intubation, but it should only be used in alert patients who have an intact airway.<sup>7,25</sup>

#### HELIOX

Heliox is a helium-oxygen mixture that decreases turbulent airflow. Benefits include decreases in the work of breathing, muscle fatigue, and carbon dioxide production.<sup>26</sup> No significant adverse effects have been reported; however, this treatment is not available in most hospitals.

#### Intubation and Mechanical Ventilation

When possible, intubation should be avoided. Tracheal intubation may aggravate bronchospasm, induce laryngospasm, increase barotrauma, and depress circulatory function.<sup>16</sup> In addition, intubation is associated with a mortality rate of 10 to 13 percent.<sup>6,12</sup> Indications for intubation include cardiac or respiratory arrest, severe hypoxia, exhaustion, or deterioration of mental status.<sup>3</sup> To prevent complications, it is recommended that rapid normalization of the carbon dioxide level be avoided, and that mild hypercapnia be tolerated until lung function improves.<sup>3,12,16</sup> In particular, high per-minute ventilation rates should not be used, because they lead to air trapping and decreased venous return, which may impair cardiopulmonary function.<sup>27</sup>

*The author indicates that he does not have any conflicts of interest. Sources of funding: none reported.*

*The opinions and assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the U.S. Naval Medical Department or the U.S. Naval Service at large.*

#### REFERENCES

1. McFadden ER Jr, Warren EL. Observations on asthma mortality. *Ann Intern Med* 1997;127:142-7.
2. Higgins JC, Kiser WR, McClenathan S, Tynan NL. Influence of an interventional program on resource use and cost in pediatric asthma. *Am J Manag Care* 1998;4:1465-9.
3. Werner HA. Status asthmaticus in children: a review. *Chest* 2001; 119:1913-29.
4. Ayres JG, Miles JF, Barnes PJ. Brittle asthma. *Thorax* 1998;53:315-21.
5. Del Prete G. Difficult asthma [Book review]. *N Engl J Med* 2000; 342:363-4.
6. O'Donnell WJ, Drazen JM. Life-threatening asthma. In: Grenvik A, Ayres SM, Holbrook PR, Shoemaker WC, et al., eds. *Textbook of critical care*. 4th ed. Philadelphia: Saunders, 2000:1451-8.
7. Guidelines 2000 for cardiopulmonary resuscitation and emer-

- gency cardiovascular care. Part 8: advanced challenges in resuscitation: section 3: special challenges in ECC. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. *Circulation* 2000;102 (8 suppl):1229-52.
8. Expert Panel report 2: guidelines for the diagnosis and management of asthma. Bethesda, Md.: National Institutes of Health, National Heart, Lung, and Blood Institute, 1997; NIH publication no. 97-4051.
  9. Busse WW. A 47-year-old woman with severe asthma. *JAMA* 2000;284:2225-33.
  10. Caruana-Montaldo B, Gleeson K, Zwillich CW. The control of breathing in clinical practice. *Chest* 2000;117:205-25.
  11. Kolbe J, Vamos M, Fergusson W, Elkind G. Determinants of management errors in acute severe asthma. *Thorax* 1998;53:14-20.
  12. Bone RC. Status asthmaticus. In: Parrillo JE, Bone RC, eds. *Critical care medicine: principles of diagnosis and management*. St. Louis: Mosby, 1995:627-36.
  13. Polgar G, Promadhat V. *Pulmonary function testing in children: techniques and standards*. Philadelphia: Saunders, 1971.
  14. Knudson RJ, Lebowitz MD, Holberg CJ, Burrows B. Changes in the normal maximal expiratory flow-volume curve with growth and aging. *Am Rev Respir Dis* 1983;127:725-34.
  15. Guidelines on the management of asthma. Statement by the British Thoracic Society, the British Paediatric Association, the Research Unit of the Royal College of Physicians of London, the King's Fund Centre, the National Asthma Campaign, the Royal College of General Practitioners, the General Practitioners in Asthma Group, the British Association of Accident and Emergency Medicine, and the British Paediatric Respiratory Group. *Thorax* 1993;48(2 suppl):S1-24.
  16. Boulet LP, Becker A, Berube D, Beveridge R, Ernst P. Canadian Asthma Consensus Report, 1999. Canadian Asthma Consensus Group. *CMAJ* 1999;161(11 suppl):S53-9.
  17. Rossing TH, Fanta CH, Goldstein DH, Snapper JR, McFadden ER Jr. Emergency therapy of asthma: comparison of the acute effects of parenteral and inhaled sympathomimetics and infused aminophylline. *Am Rev Respir Dis* 1980;122:365-71.
  18. Ackerman AD. Continuous nebulization of inhaled beta-agonists for status asthmaticus in children: a cost-effective therapeutic advance? *Crit Care Med* 1993;21:1422-4.
  19. Lanes SF, Garrett JE, Wentworth CE III, Fitzgerald JM, Karpel JP. The effect of adding ipratropium bromide to salbutamol in the treatment of acute asthma: a pooled analysis of three trials. *Chest* 1998;114:365-72.
  20. Hallstrand TS, Fahy JV. Practical management of acute asthma in adults. *Respir Care* 2002;47:171-82.
  21. Rowe BH, Spooner CH, Ducharme FM, Bretzlaff JA, Bota GW. Corticosteroids for preventing relapse following acute exacerbations of asthma. *Cochrane Database Syst Rev* 2002;(4):CD000195.
  22. Rowe BH, Keller JL, Oxman AD. Effectiveness of steroid therapy in acute exacerbations of asthma: a meta-analysis. *Am J Emerg Med* 1992;10:301-10.
  23. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev* 2002;(4):CD001490.
  24. Yung M, South M. Randomised controlled trial of aminophylline for severe acute asthma. *Arch Dis Child* 1998;79:405-10.
  25. Kass JE, Terregino CA. The effect of heliox in acute severe asthma: a randomized controlled trial. *Chest* 1999;116:296-300.
  26. Antonelli M, Conti G, Rocco M, Bui M, De Blasi RA, Vivino G, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. *N Engl J Med* 1998;339:429-35.
  27. Bellomo R, McLaughlin P, Tai E, Parkin G. Asthma requiring mechanical ventilation. A low morbidity approach. *Chest* 1994;105:891-6.