Asthma is a common medical emergency. Unfortunately, its assessment and management are not always appropriate to its potential fatal outcome. The potential for asthma to be fatal, and the cause for this, have recently been reviewed in detail.1,2 The significant factors contributing to avoidable deaths include failure by the physician and the patient to appreciate the severity of the attack and to delay in the adequate use of corticosteroids.

In this review we will focus on the emergency room assessment of patients with acute life-threatening asthma and outline an appropriate strategy for their management. History, physical examination, appropriate investigations and therapy will be considered.

**History of Symptoms**

In acute life-threatening asthma the patient may not be able to volunteer a history or, at best, his speech may be monosyllabic. This in itself is a marker of the severity of a particular attack. Where the attack is less severe, a number of pertinent features need to be assessed. The duration of the attack and specific triggering factors need to be elicited. The time frame over which the above symptoms develop, particularly if they have occurred over a prolonged period, will be an indication of the development of significant airway inflammation. This not only gives an indication of the severity of the current attack, but also highlights features of the patient’s management that need attention during the convalescent period.

The intensity of the symptoms can be gauged from their interruption of sleep, presence on waking and restriction of normal activities, as well as the overuse of \beta_2 agonists for symptomatic relief. Sometimes a prodromal upper respiratory tract infection will have precipitated an attack. Alternatively, exposure to an allergen or an agent to which the patient is intolerant, eg, acetylsalicylic acid, will be elicited.

Another feature which should be noted at this time is whether the patient and family physician responded appropriately to the acute deterioration: was beclomethasone increased or was prednisolone instituted or increased, and were these carried out early enough and in adequate doses? The appropriate attention to these matters at this time should prevent the future development of acute life-threatening episodes.

Asthmatic patients often have a better appreciation of the degree of airflow limitation than their physician,3 but considerable airflow limitation can be present when they are symptom-free. This poor perception of the presence of airflow limitation has been shown both in patients recovering from severe asthma in hospital where patients may be asymptomatic and still have an FEV<sub>1</sub> of 50 percent of predicted,4 and in experimental conditions where airflow obstruction has been induced by methacholine or histamine.5,6 These points stress that, while the history obtained is important, the use of objective measurements of airflow limitation by spirometer or a peak flow meter is more important. Unfortunately, most patients are still treated in the emergency room without these measurements being made.7,8

**Clinical Examination**

Although objective data are always required to document the severity of an asthmatic attack, the presence of certain clinical signs may be considered markers for a life-threatening attack.4 The physical signs normally associated with acute airflow limitation are tachycardia, tachypnea, hyperinflation, wheeze, accessory muscle use, pulsus paradoxicus, and diaphoresis. It should be stressed that the absence of these signs should not be taken as indicative that the episode in question is not life-threatening. The use of accessory muscles, pulsus paradoxicus, and diaphoresis are considered the most significant in terms of grading the severity of an attack. Apart from the presence of these signs, there is an added problem in the ability of the physician to detect the presence of an abnormality,9,10 and the high rate of inter- and intraobserver error in
evaluating clinical signs, again indicating the need for objective measurements.

In an attempt to overcome the problem of assessing the severity of an asthmatic attack, various attempts have been made to formulate a scoring index to assess the severity of an acute attack and the need for hospitalization. Fischl et al\textsuperscript{11} in 1981 reported one such index. An index score was formed using a combination of factors including pulse rate >120 per minute, respiratory rate >30 per minute, pulse paradoxus \( \geq \)18 mm Hg, peak expiratory flow rate \( \leq \)120 liters per minute, moderate to severe dyspnea, and use of accessory muscles and wheezing. Each of these signs was scored with one point. The authors calculated that a score \( \geq 4 \) was 95 percent accurate in predicting relapse and 96 percent accurate in predicting the need for hospitalization. Unfortunately, the clinical usefulness of the index was not borne out in two subsequent studies\textsuperscript{12,13} which failed to show such a useful predictive value. In fact, these studies indicated that decisions made on the basis of chance were just as likely to be correct.

Investigations

The primary investigation in assessing patients with acute life-threatening asthma involves measurement of their airflow rates. This can be achieved with a peak flow meter such as a Wright mini-peak flow meter or optimally with a spirometer. The difficulties in evaluating patients clinically and, in particular, their response to therapy make one of these investigations mandatory in the assessment of all asthmatic patients. These values are particularly helpful if one has, for comparison, the patient's prior best spirometry or peak flow meter readings.

Measurement of arterial blood gas levels (ABG) can be important in the assessment of an acute asthmatic attack, particularly regarding estimation of alveolar ventilation. Initially the \( PaCO_2 \) may be low; a "normal" \( PaCO_2 \) may indicate impending respiratory muscle fatigue; values above 40 mm Hg indicate a need for careful subsequent monitoring. The difficulty of assessing hypoxemia clinically is well documented. Raffin\textsuperscript{14} has recently reviewed the use of ABG measurements in the assessment of asthmatic patients, and noted the poor correlation of arterial blood gas tension with the severity of asthma, as measured by ventilatory function. A recent prospective study by Nowak et al\textsuperscript{15} showed that every patient with an FEV\textsubscript{1} >1 L or a peak expiratory flow rate >200 L per minute had a \( PaCO_2 \) >60 mm Hg and a \( PaCO_2 \) <42 mm Hg. They therefore suggested that ABGs were not warranted when flow rates were above these values, especially when the patient was responding appropriately to therapy. However, ABGs must be measured if ventilatory function is more impaired. Obviously, when a patient has an elevated \( PaCO_2 \) and is deteriorating objectively and clinically, close monitoring of ABG is indicated because mechanical ventilation may be required. However, the optimum frequency of arterial blood gas assessment is poorly defined\textsuperscript{16} and awaits appropriate prospective study.

A chest x-ray examination is often performed in the assessment of the acute asthmatic patient to examine for evidence of infection or the complications of hyperinflation (pneumothorax or pneumomediastinum); however, there are no objective data to support this routinely. Findley and Sahn\textsuperscript{17} reviewed 90 consecutive chest x-ray films in patients presenting with acute asthma. The results of this prospective study were that 55 (55 percent) films were reported as normal, 33 (37 percent) showed hyperinflation, and six (7 percent) showed minimal interstitial abnormalities unchanged from previous films. Although these data would support the policy of not routinely performing chest x-ray examinations in the assessment of acute asthma, x-ray should be considered in certain situations. For example, Reubuck and Read\textsuperscript{18} found two instances of unsuspected pneumothorax and one of pneumomediastinum in 58 patients during 80 hospital admissions. This suggests that a chest x-ray film is indicated in patients with attacks of such severity requiring hospital admission or where the patient is not responding appropriately to therapy.

Reubuck and Read also described the electrocardiographic changes, apart from sinus tachycardia, found in their patients. These abnormalities were present in 40 percent (35/88) of patients. The most common changes were those of right axis deviation (12.5 percent), clockwise rotation of the heart (10 percent) and, more rarely, evidence of right ventricular hypertrophy. These changes usually reverse completely within a few hours of the patient's response to initial therapy.

The sputum must be examined for color, yellow or green suggesting infection or eosinophilia. A Gram stain, culture and sensitivity are required only if there is lung consolidation or if the purulence does not respond to initial therapy. Other hematologic and biochemical investigations are not usually required with regard to decision making in the management of the acute asthmatic attack. The biochemical investigations which may have some importance in terms of monitoring patients during the acute phase are serum potassium (beta\textsubscript{2} agonists may cause hypokalemia) and serum glucose (corticosteroids may cause hyperglycemia).

Criteria for Hospital Admission

Criteria for hospital admission with severe asthma have recently been reviewed.\textsuperscript{19,20} Verbeek and Chapman\textsuperscript{19} have used FEV\textsubscript{1} of 2.0 L or less as a criterion for hospital admission. In addition, these
authors quote a number of features indicating the need for extra caution, as outlined above. It is difficult to support a recommendation of using an absolute value for the FEV<sub>1</sub>, but rather percent predicted FEV<sub>1</sub> is of more use. In their more comprehensive review of the currently available literature, Core and Rothstein<sup>20</sup> support this approach. McFadden and Lyons<sup>21</sup> have used a value of >51 percent of predicted FEV<sub>1</sub> as indicative of a mild attack. More recently, Nowak et al.<sup>13</sup> used 60 percent as a cutoff point while also mentioning an absolute value of 2 L. However, the same authors have previously used a value of ≤1.6 L.<sup>22</sup> Kelsen et al.<sup>23</sup> looked at improvement after treatment and found that where there was an increase in the FEV<sub>1</sub> ≤400 ml, these patients had a 67 percent relapse rate, while those with an improvement >400 ml had a relapse rate of only 29 percent.

Certain historic features obtained from the patient are indications for a more cautious approach, but even in the absence of these, an FEV<sub>1</sub> of at least 60 percent of predicted has been suggested as the cutoff point between discharge or admission. Although this value seems high, there are no objective prospective data to support a lower value; however, anecdotally, with close supervision, we have been able to manage patients with lower levels as outpatients.

**Therapy**

While the above process of assessment is being carried out, therapy will have been initiated. Therapy should consist of aggressive use of bronchodilators, supplemental oxygen and, most importantly, corticosteroids.

**Beta<sub>2</sub> Agonists**

Studies have now shown that beta<sub>2</sub> sympathomimetic agents such as salbutamol are effective bronchodilators.<sup>24</sup> Traditionally, these agents have been given in the form of nebulized solutions in normal saline. However, successful delivery of therapy using a metered dose inhaler (MDI) alone has been reported.<sup>25,26</sup> Indeed, bronchodilator therapy can be administered successfully in this way even in the case of most severe asthma requiring hospital admission. The advantages of this system include cost, speed at which therapy can be commenced and equipotent bronchodilatation. One method is to routinely administer four puffs of salbutamol followed by further inhalations to a total of 12 puffs (or less if the patient is limited by tremor). This dose may be repeated at hourly intervals until subjective and objective improvement as measured by spirometry occurs, at which time dose requirements may be reduced to more orthodox levels. If one uses MDI therapy aggressively in this way, intravenous forms of beta<sub>2</sub> agonists are not needed. The use of the latter route adds considerably to systemic toxicity without appreciable gain in efficacy.

Another feature of the emergency room management of acute asthma is that many patients have pretreated themselves with salbutamol prior to arrival in the emergency room and therefore physicians assume they may not be responsive to further therapy. Rossing et al.<sup>27</sup> compared two groups of asthma patients presenting with acute exacerbations who were similar in all respects except that one group had had sympathomimetic therapy in the six hours prior to admission, and the other had received no such therapy. When data from both groups were analyzed, there was no significant difference in baseline FEV<sub>1</sub> and in response to beta<sub>2</sub> sympathomimetic therapy in the emergency room.

**Anticholinergic Agents**

A recent study<sup>28</sup> has indicated that the combination of an anticholinergic agent, ipratropium bromide, to fenoterol (another beta<sub>2</sub> agonist) is more effective than either agent alone. This additive effect is not surprising, as the anticholinergic agents differ in their mode of action from beta<sub>2</sub> agonists. Rebuck and coworkers<sup>29</sup> studied patients with asthma as well as a group with chronic airflow limitation who were treated in a randomized double blind control study with either fenoterol, ipratropium bromide or a combination of both administered in nebulized solutions. The greatest improvement followed treatment with the ipratropium-fenoterol combination (0.53 ± 0.40 L at 45 minutes; 0.57 ± 0.51 L at 90 minutes) and was significantly greater than following either ipratropium alone (p<0.001) or fenoterol alone in asthmatics but not patients with chronic obstructive lung disease (p<0.05).

**Corticosteroids**

Corticosteroids must be considered an essential part of the management of acute life-threatening attacks of asthma.<sup>20</sup> The rationale for their use is based on the fact that most attacks of this severity are associated with the cellular phase of airway inflammation which will not be influenced by bronchodilator therapy alone.<sup>30-32</sup> Unfortunately, in the emergency room setting, patients may be discharged without corticosteroid treatment, when they respond symptomatically to bronchodilator therapy. In all reviews of asthma mortality, failure to appreciate the severity of the attack by the physician or patient and failure to treat the condition with steroids have been important contributing factors.<sup>1</sup> Corticosteroids are believed to act in a number of ways to speed the resolution of an acute asthmatic attack.<sup>33</sup> These mechanisms include an anti-inflammatory effect by decreasing leukocyte accumulation, potentiation of beta<sub>2</sub> agonists, lysosomal membrane stabilization, reduction of capillary per-
meability, and inhibition of histamine release. Although the role of steroids in the acute asthmatic attack is not in doubt, there is some question as to the optimum dose, frequency and route of administration, as well as type of preparation used. Harrison et al reported a randomized controlled study in which 52 severely ill asthmatic patients, requiring hospitalization, were treated by conventional means with one group receiving intravenous hydrocortisone (3 mg/kg bolus and then six hourly as an infusion) or prednisolone orally (45 mg orally followed by 15 mg q8h po). At the end of 24 hours there was no difference in outcome between the two groups. This result is not surprising given that prednisolone is rapidly absorbed from the gut and peak plasma levels are obtained within 15 minutes of oral administration.

Despite the above data, intravenous therapy continues to be used in current clinical practice. Haskell et al, in another randomized double blind study, compared three dosing schedules: 15 mg, 40 mg and 125 mg methylprednisolone q6h IV for three days. The best response was with the high dose; patients improved significantly within the first 24 hours. The medium dose improved in the middle of the second day, while the low-dose group failed to improve significantly over the three-day study period. There were no significant side effects at the different doses and the authors concluded that the 125 mg dose regimen was the most appropriate. In view of the data of Harrison et al, a logical compromise would seem to be to use the intravenous form for up to 24 hours and, if the patient is responding, substitute oral therapy.

Although intravenous steroids are routinely used in the hospitalized patient, there are fewer data available on patients discharged from the emergency room. The only well-controlled study addressing this issue has been published by Littenberg and Gluck. In this study, 97 acutely ill patients with bronchial asthma were enrolled in a double blind, placebo controlled trial of intravenous methylprednisolone (125 mg) given on presentation in the emergency room, in addition to standard emergency treatment for asthma. Subjective and objective assessment of airflow obstruction was similar in both groups at baseline. Subsequently, only nine of 48 patients (19 percent) treated with intravenous corticosteroids required hospital admission, as compared with 23 of 49 patients (47 percent) in the control group (p<0.003). When the decision was made to admit or discharge, all the admitted patients started IV steroids while the discharge group was placed on oral prednisolone. It is our policy to treat with prednisolone 30 to 40 mg daily for approximately five days at least or until symptoms are under optimum control. Once control has been achieved with the oral dose of prednisolone, the dose is rapidly discontinued or reduced to the minimum needed to maintain control. There were only three patients among the discharge patients who suffered relapse, one from the IV methylprednisolone group and two from the placebo group. This relapse rate is much lower than the rate reported in the literature which ranges as high as 26 percent. The low relapse rate is most likely related to the routine use of oral steroids in the discharge group.

In conclusion, corticosteroids are effective in the treatment of acute severe asthma. Despite the benefit with oral therapy shown in the study cited above, it continues to be our policy to give intravenous corticosteroids in the first 24 hours at least. Once there is objective evidence for improvement in airflow, a switch to oral corticosteroids can then be made. Further studies comparing oral vs intravenous route in the acute stage of life-threatening asthma may require this recommendation to be reviewed.

**Aminophylline**

Traditionally, aminophylline has been given for acute life-threatening episodes of asthma. However, Rossing et al have shown that the use of aminophylline confers no additional benefit to the use of beta agonists alone. A recent analysis of 13 adequately designed studies in patients with severe, acute asthma decided the evidence for its use was inconclusive. Not only does aminophylline have a low therapeutic ratio, it also has a marked potential for toxicity in the hypoxemic patient. In addition, obtaining a therapeutic dose is further hampered by the large number of variables affecting its metabolism, such as age, coincidental congestive cardiac failure, and concomitant therapy with such agents as erythromycin, cimetidine and also a history of smoking. Therefore, if optimal doses of beta agonists are being given, there appears to be no advantage and several disadvantages to using aminophylline.

**Adrenaline**

Adrenaline has been used in the management of acute life-threatening asthma since 1951. However, adrenaline is not needed when the other therapeutic modalities, as outlined here, are used to their optimal doses. A recent study compared the subcutaneous administration of terbutaline and adrenaline in the treatment of acute severe asthma. In this study there was no significant difference between the use of both these measures in patients who were otherwise treated the same. This therapy was given as an initial treatment and followed by more orthodox therapy with nebulized salbutamol, hydrocortisone and aminophylline. The authors comment on the fact that previous studies have reported significant side effects with adrenaline, but they relate this to inappropriate high dosage and also intravenous use, particularly in elderly patients.
In summary, despite this recent study, most authors agree that adrenaline is not required in the management of acute life-threatening asthma. However, it is reassuring in that this study indicates that adrenaline in a dose of 0.5 mg subcutaneously is well tolerated in this patient population without significant side effects and, therefore, can be considered if the other maneuvers outlined are ineffective.

**Mechanical Ventilation**

Occasionally, despite the above measures or before they can be implemented, the patient will progress to respiratory failure. In this instance, endotracheal intubation is a life-saving intervention. The approach to ventilating the asthmatic patient has undergone a change in recent years. The main problem with ventilation in these patients is the high peak airway pressures (PAP) and associated risk of barotrauma. A novel approach to overcome this problem has now been successfully reported by two groups of investigators. In these studies, a reduction in tidal volume, peak flow ventilatory rate, and paralysis with pancuronium bromide resulted in hypoventilation. Prolonged hypercapnia was successfully tolerated, once the PaCO₂ remained below 90 mm Hg. In contrast to other studies, where ventilated patients have a reported mortality from 9 to 35 percent related to pneumothorax, no patient died in these two quoted series.

**Other Measures**

Other approaches which have been reported anecdotally in the literature, in patients resistant to orthodox therapy, have included general anesthesia. Problems encountered with this approach include hypotension and arrhythmias, presumably exacerbated by the hypoxemia experienced by these patients. Other dramatic interventions which have been reported have included selective whole lung lavage to relieve inspissated secretions. The use of extracorporeal membrane oxygenator support has been also described. There are no control data to support the use of these interventions, but their use may be required if the measures outlined previously fail to improve the patient.

**Prevention of Future Life-threatening Exacerbations**

Most emergency visits, hospital admissions and life-threatening exacerbations are preventable because severe asthma usually develops over days and there is time to increase treatment to reverse them before they become severe. Occasionally, a severe attack is of sudden onset after the accidental ingestion of a food, non-steroid anti-inflammatory drug, sulfite preservatives or monosodium glutamate to which the patient is hypersensitive or intolerant. Occasionally, a severe attack can develop over hours after over-exposure to an allergen or occupational chemical sensitizer (isocyanate) to which the patient is hypersensitive. These sudden attacks, however, are in a minority and avoidance strategies plus the use of drugs prophylactically should prevent them in future.

Symptoms should be reduced to a minimum and FEV₁ or PEFR after bronchodilator therapy should be normal or at a maximum for that patient. Current beliefs regard any exacerbation as due to airway inflammation triggered by respiratory infections, allergens or occupational chemical sensitizers or inadequate maintenance treatment with anti-inflammatory drugs. Any exacerbation should be treated at the earliest indication by the addition of or an increase in anti-inflammatory treatment, of which corticosteroids are the most effective. The patient needs an individualized plan to treat exacerbations.

The life-threatening exacerbation must be taken as an opportunity to identify why the exacerbation was allowed to become so severe and to discuss future management to prevent a recurrence. Did the patient know when to increase treatment? Did the patient know how to increase treatment? Did the patient know that they should have phoned early for advice if they did not know how to treat the exacerbation or if the increased treatment was not successful? Was there an exacerbating factor which could be avoided in the future?

Occasionally, the history will not identify how the exacerbation could have been prevented. In this instance especially, the possibility of poor perception of airflow limitation should be considered. This is identified by the absence of symptoms when the PEFR or FEV₁ are reduced. Such patients will not detect symptoms, or will not be bothered by them, until the FEV₁ is severely reduced when there may be little or no time to prevent a severe exacerbation. These patients, in particular, must own a peak flow meter to measure their PEFR before and after administration of an inhaled bronchodilator at least once daily until the best values are determined, minimum medication requirements are established, and it is determined whether regular measurements are required to detect an exacerbation. The use of a peak flow meter should also be considered by other adults and children to help detect the severity of exacerbations and to start appropriate treatment early.

**Conclusion**

Acute life-threatening asthma is a common medical emergency. It requires careful assessment with an appropriate history focusing on current symptoms, requirement for beta₂ agonist therapy, previous or concurrent history of steroid use, as well as a history of previous hospitalization, in particular requirement.
for mechanical ventilation. Appropriate physical examination assessing respiratory rate, pulse rate, the presence of pulsilus paradoxicus as well as signs of fatigue and the level of consciousness of the patient are indicated. The most valuable form of assessment is the measurement of airflow limitation ideally with a spirometer but, at the very least, with a peak flow meter. These measurements allow comparison with the patient’s previous best, as well as objectively establishing the severity of the current attack. In addition, they can be used subsequently to monitor the patient’s response to therapy. Therapy for the acute attack should proceed with optimum bronchodilator therapy using a combination of beta₂-sympathomimetic agents as well as one of the newer atropine derivatives, (ipratropium bromide). In addition, the majority of patients requiring assessment in the emergency room, whether admitted or discharged, will require steroid therapy for control of airway inflammation. If the patient is discharged, he or she must be reviewed by their family physician or referred to an appropriate specialist. Life-threatening asthma is usually preventable and the opportunity must be taken to determine why the severe exacerbation occurred so that the patient can be given an individualized plan to prevent a recurrence in the future.

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