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Status Asthmaticus in Adults

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Status asthmaticus is a severe, life-threatening exacerbation of bronchial asthma that fails to improve with "conventional" treatment. "Conventional" treatment has been defined as three subcutaneous injections of epinephrine given at 15-min intervals. The use of the term "status asthmaticus" has value in that it has simplified communication. However, it has the disadvantages that it is too restrictive. It draws attention away from other aspects of severe asthma; for example, that patients die at home[1,2] and, in some cases, within minutes of the onset of an attack.[1,3] It is probably more useful to talk of "severe acute asthma," rather than "status asthmaticus."[4]

Between 1959 and 1979, the overall mortality due to asthma in patients from 5 to 34 years of age ranged from 0.2 to 4.1 deaths per 100,000 persons. In the United States and Canada, mortality was fairly constant, being between 0.2 and 0.4 deaths per 100,000 persons.[5] The hospital mortality for severe acute asthma in adult patients is shown in Table 1. The mean mortality is 1.34%. Asthma remains a potentially lethal disease, and its mortality has not declined significantly over the last 20 years.

The Causes of Mortality in Asthma

Table 2 lists the commonly described factors associated with mortality in asthma. Underutilization of corticosteroids has been suggested as a significant factor in a number of reports.[1,2] Overmedication has also been incriminated. A new epidemic of deaths from asthma in New Zealand has been suggested to be due to the combination of oral theophylline with beta-agonists.[11]

Clinical Picture of Severe Acute Asthma

History

The history of the episode of asthma can provide important clues to the assessment of the severity of the attack and possibly its treatment. Drugs the patient has taken may precipitate an attack of asthma. These drugs include the beta-blocking agents propranolol and acebutalol[12,13] and nonsteroidal anti-inflammatory drugs such as aspirin, naproxen,[14] indomethacin, and zome-

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Table 1. Mortality for Adult Patients Hospitalized Because of Severe Acute Asthma

Year	Number of patients	Mortality (%)
1966–1968[6]	70	2.8
1972[7]	237	1.7
1974[8]	127	0.8
1967–1975[9]	811	1.0
1974–1976[10]	1345	0.4

pirac.[15] There is one report of asthma being improved by nonsteroidal antiinflammatory drugs, however.[16] The presence of an upper respiratory infection has been associated with an attack of asthma in 46%–64% of patients, but usually there is a viral, rather than bacterial, agent involved.[8,17] Severe bronchospasm has been reported as a complication of Legionnaires' disease.[18] Changes in bronchodilator therapy, or the failure of previously effective therapy, is important.[19] The speed of onset has been shown to have no relationship to hypoxemia,[20] hypercapnia,[20] or the severity of the attack.[21] On the other hand, a longer duration of the presenting asthma attack has been shown to be associated with a lessened effect of the subcutaneous injection of epinephrine[22] and a slower recovery.[23]

A history of previous hospitalizations for asthma should be sought, including information on whether tracheal intubation and mechanical ventilation had ever been necessary during such an admission.

Symptoms

The symptoms of severe acute asthma invariably include dyspnea,[24] which is moderate to severe.[25] Asking the patient to grade the severity of the dyspnea may be helpful,[19] but dyspnea does not correlate with the impairment of function[24] and there is a wide range.[25] Patients may become asymptomatic

Table 2. Causes of Mortality in Severe Acute Asthma

Progressive asthma, not responding to therapy
Inappropriate therapy
Too little (e.g., steroids)
Too much (e.g., isoproterenol)
Sedative or narcotic drugs
Associated pulmonary problems
Infection
Pneumothorax
Aspiration
Hemodynamic problems
Hypovolemia, shock
Pulmonary edema
Hypervolemia
Negative pleural pressure
Malfunction or accident during mechanical ventilation
Sudden cardiac arrest

when the overall mechanical function of their lungs ranges between 40% and 50% of predicted normal values.[24]

Subjective wheezing is common, but not invariable,[24] and as with dyspnea, it does not correlate with the severity of the attack.[24] Fatigue and inability to talk are commonly found.[19]

Signs

The signs of the severity of the asthma attack are also variable and lack correlation with the mechanical impairment. Objective wheezing is always present and is found even when symptoms have cleared.[24] Diminution of objective wheezing can be ominous in a patient who remains dyspneic, as it may indicate failure of gas movement.[19]

The use of the accessory muscles of ventilation was noted in 59% of patients with acute asthma[24] and correlated with the severity of impairment of pulmonary function.[24,26] It has been postulated that changes in retractions of sternomastoid muscle reflect changes in large airways obstruction, whereas alterations in objective wheezing and spirometry reflect changes in obstruction in more distal airways.[24] Clinically observable overinflation has been shown to indicate severity of disease; it was found in 81% of patients with an acute attack and in 100% when obstruction was very severe.

The respiratory rate is frequently increased in more severe attacks to levels of 24–30 breaths per minute.[20,25] Tidal volume usually diminishes.

The heart rate has been consistently reported to be elevated in patients with acute asthma and to correlate with severity. A rate equal to, or greater than, 115 beats per minute is indicative of severe obstruction.[10,17,19,21,25,27] Heart rate has been correlated with peak expiratory flow rate.[27] Systolic and diastolic hypertension is often present, with values of 140 over 90 indicating severe disease.[19,25]

Pulsus paradoxus is a greater than usual decline in pulse pressure during inspiration. Values ranging between 10 and 130 torr were found in one study[17] and were correlated with changes in forced expired volume in 1 sec.[17,26] The size of the paradoxical pulse also was correlated with severity of disease[10,21,25] and speed of recovery.[23] However, pulsus paradoxus may be present in mild, and absent in severe, attacks of acute asthma. Pulsus paradoxus is less marked during severe asthma in patients over 64 years of age, and the increase in pulse rate is less, even in the face of equivalent changes in pulmonary function tests, compared to younger patients.[28]

The mechanism of pulsus paradoxus has been shown to be a decrease in left ventricular stroke output, predominantly due to a decrease in left ventricular preload. This decline in preload is partly due to competition between the left and right sides of the heart for pericardial space, but more importantly, it is also due to an increase in impedance to right ventricular ejection.[29]

An interesting concept in severe acute asthma has been to emphasize the circulatory disturbances.[4] It was pointed out that the hallmarks of severe acute asthma are the circulatory disturbances, ranging from tachycardia through pulsus paradoxus to hypotension and circulatory collapse. It is claimed that these circulatory effects are part of the primary disturbance and are not secondary to hypoxemia.[4]

Pulmonary Function Tests

Alterations in pulmonary function tests are the most reliable methods of objective assessment of the severity of severe acute asthma. Peak expiratory flow rates (PEFR) below 20% predicted[21,24] or 100 L/min[10,24,25,27,30] are indicative of severe obstruction. One report indicated that a PEFR less than 16% predicted was more significant if accompanied by a failure to improve following the subcutaneous injection of epinephrine.[22] One report found no relationship among PEFR and pulsus paradoxus, arterial oxygen tension, or carbon dioxide arterial tension.[23] Diurnal variations in PEFR are thought to be related to severity of the asthma. One report, although it did not find a correlation between the diurnal swings and severity of obstruction, found variations of PEFR of greater than 50% during 24 hr in seven of eight patients prior to ventilatory arrest.[10] It was not found in the eighth because it was not measured. One report showed that diurnal variations were more prominent during the recovery phase.[27]

The volume exhaled in the first 1 sec of a forced vital capacity ($FEV_{1.0}$) is usually below 25% of predicted values[20,24] or below 1 L[17,24] in severe acute asthma. However, there is considerable overlap of values for $FEV_{1.0}$ between different categories of clinical severity in acute asthma. Severely distressed patients requiring immediate admission to hospital may have an $FEV_{1.0}$ that is three times the volume of that of a patient requiring an "elective" admission.[17]

A value of $FEV_{1.0}$ below 20% predicted may be associated with hypercapnia, although normal or low arterial carbon dioxide tensions are more usual.[20] A decrease in arterial oxygen tension is more common as $FEV_{1.0}$ decreases.[17,20] An increase in the size of pulsus paradoxus is also found with diminished $FEV_{1.0}$.[17] During recovery from acute asthma, $FEV_{1.0}$ has been shown to be reduced to 49% predicted when the patient is symptom free.[24]

Forced vital capacity (FVC) is reduced, although to a lesser extent than $FEV_{1.0}$, in patients with acute asthma.[17,28] The ratio of $FEV_{1.0}$ to FVC is usually reduced to approximately 0.5. In "emergency" situations requiring immediate hospitalization, this ratio was 0.45, compared to 0.57 in patients who were "electively" admitted.[17] Therefore, the ratio is not a good index to distinguish the severity of obstruction.

Airway resistance in a group of patients with acute attacks of asthma showed a mean value of 7.4 cm H_2O/L/sec and a mean specific conductance of 0.04 L/sec/cm H_2O/L.[24]

Total lung capacity (TLC) is usually increased. A mean value of 6.29 L (134% predicted) was found in one study.[24] Another study has suggested that the increase in TLC during acute bronchospasm results from the combination of loss of lung recoil, increased outward recoil of the chest wall, and increased strength of contraction of the inspiratory muscles.[31] Functional residual capacity (FRC) was markedly increased to 218% of predicted in one study of patients with acute asthma using a constant-volume body plethysmograph.[24] Even using the helium dilution technique, where falsely low values may be found, FRC was increased in acute asthma.[17] Residual volume is perhaps the

most affected of the static lung volumes and increases up to 379% of predicted have been reported during acute asthma.[24,31]

Arterial Oxygen Tension

Arterial oxygen tension (PaO_2) is invariably decreased during acute asthma.[10,17,20,25,27,28] The decrease correlates with $FEV_{1.0}$, such that at 17.6% of predicted values for $FEV_{1.0}$, arterial oxygen tension was 63 torr.[20] A correlation with PEFR has also been demonstrated.[25,27] Although PaO_2 correlates with these tests of pulmonary function, there is a wide scatter of data points.[17] The restoration of PaO_2 to a normal value is slow, and at the time of recovery of clinical signs and symptoms, it is usually still abnormal.[17,23] Cyanosis is an unreliable guide to the presence of hypoxemia.[17]

Hypoxemia found in acute asthma may be caused by alveolar hypoventilation. But, in addition, the alveolar-to-arterial oxygen tension gradient usually is greater than normal, and an increase in both the scatter of ventilation-perfusion ratios and shunting occurs.[20] Single breath carbon monoxide diffusion capacity is normal during acute asthma.[20]

Arterial Carbon Dioxide Tension

Arterial carbon dioxide tension ($PaCO_2$) is customarily normal or reduced.[17,20,23,25–28] In one study, $PaCO_2$ decreased to approximately 30 torr as $FEV_{1.0}$ declined to below 40% of predicted values. When $FEV_{1.0}$ fell below 20% of predicted, although $PaCO_2$ rose above normal levels in some patients, it remained normal or low in the majority of patients.[20] Values for $FEV_{1.0}$ below 1250 ml have also been related to hypercapnia.[17,26] Studies of PEFR in acute asthma have failed to show a correlation with $PaCO_2$.[23,27] The cause of the hyperventilation associated with acute asthma is not clear, but it may be related to the increase in end-expiratory lung volume.[32] Normocapnia or hypercapnia is usually considered to be a grave prognostic sign when associated with increasing dyspnea or falling $FEV_{1.0}$ or PEFR.[25] Hypercapnia may be exaggerated by the administration of added inspired oxygen.[17] With recovery, $PaCO_2$ returns to normal more quickly than PaO_2. One study reported a mean of 4.5 hr.[17]

The ratio of dead space to tidal volume (V_D/V_T) is increased to values above normal during acute asthma. Mean values of 0.55 and 0.43 have been reported and do not seem to be related to the severity of the asthma.[17,20] Minute ventilation is usually markedly increased, as is minute alveolar ventilation.[20]

Chest Radiograph

The chest radiographs in two studies of patients hospitalized with severe acute asthma showed hyperinflation in 55% and 39% of patients.[17,33] In the latter study, hyperinflation was defined as the presence of two of the following criteria: (1) lung height equal to or greater than lung width; (2) right hemidiaphragm at or below the sixth interspace anteriorly; (3) cardiac diameter

less than 11.5 cm; or (4) ratio of lung height to lung width reduced on follow-up radiograph as compared to admission. Patients with hyperinflation had significantly more severe pulsus paradoxus, faster heart rate, and lower $FEV_{1.0}$.[33] In the same study, consolidation or collapse was seen in 8% of patients, compared to 17% of patients in the report of Rebuck and Read.[17] Pneumomediastinum or pneumothorax was found in 4% and 1% of patients, respectively.[17,33] In the assessment of patients with acute asthma in the Emergency Room, the chest radiograph did not distinguish between those patients who required hospitalization and those who did not.[34,35]

Electrocardiogram

The electrocardiogram (EKG) is frequently abnormal in severe acute asthma.[17,36] An abnormal frontal plane P-wave axis has been correlated with the degree of airways obstruction and was thought to be due to alterations in the position of the heart caused by hyperinflation.[36] Cor pulmonale was believed to be present on EKG examination in 29% of patients in one study.[8]

Pulmonary Artery Pressures

Pulmonary artery pressures related to atmospheric pressure in patients with severe acute asthma have been shown to be normal.[37] However, mean pleural pressure becomes markedly negative during acute asthma, and consequently, pulmonary artery and right ventricular pressures were increased.[37,38] Right ventricular afterload would also be increased.[38]

Measurement of the regional distribution of pulmonary arterial blood flow showed clear-cut focal abnormalities in 18 of 19 patients studied during an attack of acute asthma. Chest radiographs were normal.[39] The mechanism for the alterations in perfusion is not known, but focal hypoxia or air trapping have been postulated.[33]

Abnormalities Associated with Severe Acute Asthma

Alterations in Intravascular Volume

Hypovolemia, with mean blood volume reduced by 11%, was found in eight of nine patients with status asthmaticus, when compared to the asthma-free state.[40] The reduction in blood volume was accompanied by an increase in the hematocrit to 49% and an increase in serum protein to 7.5 g/dl. The reason for the apparent loss of plasma is not obvious, and the deficiency of intravascular volume may predispose to circulatory shock.[4]

Hypervolemia has also been described.[41] In seven patients with status asthmaticus, levels of antidiuretic hormone (ADH) ranged from 2 to 15.5 μU/ml plasma. The patient with the highest level retained more than 2000 ml of fluid in the first 24 hr of hospitalization.[42] The cause of the increase in ADH could be decreased left atrial filling, stress, or beta-adrenergic stimulation due

to drugs. It could also be due to low intravascular volume, although in the cases reported, none of the patients appeared clinically dehydrated.[42]

Pulmonary Edema

In a study of eight children with acute asthma, mean pleural pressure, assessed from measurement of esophageal pressure, ranged from −7.7 to −25.5 cm H_2O and correlated with the degree of impairment of vital capacity.[43] The more negative pleural pressure is analogous to an increase in left ventricular afterload, which has the effect of elevating the hydrostatic pressure in the pulmonary vasculature relative to pleural pressure.[43] A gradient favoring the development of pulmonary edema is therefore created.

Adrenal Failure

The intravenous administration of adrenocorticotropic hormone (ACTH) during an attack of severe acute asthma failed to increase plasma 17-OHCS in 3 of 17 patients studied.[44] All patients who have received long-term steroid therapy must be treated with systemic corticosteroids during an acute attack of asthma, as their adrenal response to stress may be diminished or absent.

Central Nervous System

As the acute episode of asthma progresses, patients frequently become irrational and confused. They may become obtunded and finally comatose. The cause of these changes is not clear. Hypoxemia or hypercapnia may be factors. Fatigue, the effect of medications, and possibly water intoxication may also contribute. A decrease in the level of consciousness is a grave sign, not only of increased disease, but also of loss of the patient's ability to cooperate with proposed therapies.

Metabolic Studies

Metabolic acidosis was not seen in a study of 101 patients with acute asthma.[20] However, in a study of more acutely ill patients, simple or combined metabolic acidosis was found in 37.9% of patients, accompanied by an increase in lactic and pyruvic acid.[45] Increased glycolysis and anaerobic respiratory muscle glycolysis were postulated as the causes. Previous hypocapnic hyperventilation may contribute.[45]

In patients with acute asthma, serum glutamic oxaloacetic transaminase, lactic dehydrogenase, and creatine phosphokinase activities are significantly increased. The mean serum value for 2,3-diphosphoglycerate was elevated to 17.5, compared to the upper limit of normal of 16 μmole/g hemoglobin, presumably a mechanism to enhance oxygen delivery at the tissues.[46]

Mean serum sodium levels are usually normal.[40,42,46] In one study of 23 patients, however, five of the patients had levels above 149 meq/L, perhaps reflecting dehydration.[46] Serum potassium levels are also characteristically normal.[40,46]

Lung Disruption

Lung disruption, with air found in the mediastinum, subcutaneous tissue, pleural space, or peritoneal cavity, is surprisingly rare in severe acute asthma.[7] In two series reporting 193 patients hospitalized for acute asthma, the incidence of pneumomediastinum or pneumothorax was 2.1%.[17,33] In 618 episodes of acute asthma examined in a further two studies, the incidence of lung disruption on chest radiograph was zero.[34,35] Subcutaneous emphysema can have serious consequences, and in one report, it necessitated tracheal intubation to prevent upper airway obstruction.[47] Pneumoperitoneum has also been caused by gastric rupture occurring during acute asthma.[48]

Differential Diagnosis

The patient's complaints of dyspnea and wheezing, together with the physical findings of expiratory rhonchi and retractions, make the diagnosis of an acute attack of asthma so obvious that they may unfortunately obscure the need to seek alternate explanations.

Upper Airway Obstruction

Intrathoracic tracheal obstruction will produce predominantly expiratory airway resistance. It may be difficult to distinguish this type of obstruction from asthma using only physical examination. Causes include a foreign body, tracheal stenosis, tracheomalacia, or an aberrant pulmonary artery. Diagnosis may be aided by the pattern of onset of the episode, but may only be confirmed by bronchoscopy.

Although extrathoracic airway obstruction characteristically produces inspiratory stridor, expiratory rhonchi may predominate. We have examined a patient who was being treated for the onset of severe acute asthma with intravenous aminophylline, but whose disease was cured by removing the large tablet that had lodged on the back of her tongue.

Pulmonary Embolism

Dyspnea and expiratory rhonchi are presenting symptoms in some patients with pulmonary embolism. Diagnosis may be difficult, as both acute asthma and pulmonary embolism may show focal filling defects on perfusion scan of the lungs.[39] If the usual clinical differentiating features are not clear, a pulmonary angiogram may be necessary.

Pulmonary Edema

Pulmonary edema is commonly associated with peribronchial cuffing and expiratory rhonchi. Edema caused by an elevated left-sided filling pressure can be diagnosed by means of pulmonary artery catheterization. Identification of the transmural pressure can be difficult in the presence of increased airway

resistance and lowered compliance caused by the pulmonary edema.[37,38,43] Pulmonary edema, in its early stage with normal filling pressures, may be difficult to distinguish from asthma. The clinical setting, and possible changes in the chest radiograph, may be helpful.

Pulmonary Infection

Acute bronchitis or bronchiolitis may mimic asthma. Examination of the sputum Gram stain will be helpful. Elevation of the white blood cell count is not a distinguishing feature, as it is often elevated in acute asthma without infection.

Lung Disruption

Air in the interstitium of the lung or in the mediastinum may compress airways, producing expiratory rhonchi and mimicking spasm and edema of airways. Pneumothorax may present with expiratory rhonchi. The detection of subcutaneous air and the findings on chest radiograph will be diagnostic.

Aspiration of Gastric Contents

Dyspnea and expiratory rhonchi may be produced following aspiration of gastric contents. Usually, the chest radiograph will be abnormal following aspiration. Often, however, the diagnosis of aspiration pneumonia is one of exclusion.

Drugs

A clinical picture identical to acute asthma may be produced by a hypersensitivity reaction or a direct effect of drugs.

Factitious Asthma

The characteristic findings of acute asthma can be readily mimicked by a patient.[49] A history or asthma can be provided, respiration can be labored, the accessory muscles used, and wheezing made audible. Symptomatic relief with therapy can be simulated. More objective signs of asthma will usually reveal this form of factitious illness. These include absence of hypoxemia and a normal alveolar-to-arterial oxygen tension gradient, lack of hyperinflation on chest radiograph, and normal small airway function soon after resolution of symptoms. Bronchial reactivity is absent.[49]

Drug Therapy in Severe Acute Asthma

The mainstay of the therapy of severe acute asthma is pharmacologic and attacks the problem from many directions.

Subcutaneous Beta-Receptor Agonists

The treatment of choice in the initial treatment of severe acute asthma is probably the subcutaneous injection of epinephrine.[25,26] In adult normal subjects, the effects of 0.5 mg epinephrine were[50]:

1. Onset of action within 15 min of injection
2. Maximum effect at 30 min
3. An increase in heart rate by 17.5 beats per minute
4. A 62% increase in cardiac output
5. Mean systemic blood pressure was unchanged; systolic pressure rose 23%, diastolic pressure declined 14%
6. Systemic vascular resistance decreased 39%
7. The effects persisted from 2 to 4 hr

The same dose (0.5 mg) of epinephrine given to 12 patients hospitalized with acute asthma produced an effect within 15 min and had a maximum effect at 45 min.[51] PEFR increased by 39% at that time. The effect persisted at least 3 hr.

When 0.3 mg epinephrine was given in three consecutive doses at 20-min intervals, the effect, 20 min after the third injection, was[52,53]:

1. $FEV_{1.0}$ increased 80%[52] and 50%[53]
2. Heart rate decreased by 5% of pretreatment values[52]
3. Systemic systolic, diastolic, and mean pressures were less than or equal to pretreatment values[52,53]

Different doses of subcutaneous epinephrine give a dose–effect relationship. In one study, single injections of 0.1 mg, 0.3 mg, or 0.5 mg produced, at 20 min, an increase of 58%, 88%, and 120%, respectively, in pretreatment PEFR.[54]

Therefore, subcutaneous epinephrine is an effective and relatively safe drug in the management of severe acute asthma.[55] It should be administered in doses of 0.3–0.5 mg of a 1 : 1000 solution, over 2–3 min.

Other agents have been proposed as being either more effective, less toxic, or longer-acting than epinephrine. In a comparison between 0.25 mg of terbutaline and 0.5 mg of epinephrine, both given by subcutaneous injection, the effects were[51]:

1. At 45 mins, PEFR was increased 34% with terbutaline and 39% with epinephrine, compared to pretreatment levels.
2. At 3 hr, PEFR was still increased by 33% of pretreatment levels following epinephrine, but by only 15% with terbutaline.
3. The cardiovascular effects were similar, except that terbutaline gave a slight increase in heart rate. Systemic systolic, diastolic, and mean pressures decreased after either drug.[51]

In normal adult volunteers, 0.25 mg of terbutaline produced similar qualitative and quantitative effects to those of 0.5 mg of epinephrine when given subcutaneously.[50] Heart rate increased by approximately 30%, cardiac output

by 50%, systolic pressure by 20%; systemic vascular resistance decreased by 40%. The length of action of these two drugs in the dosage stated was similar.

These studies do not present evidence that subcutaneous terbutaline, compared to epinephrine, has any advantage in terms of effect, toxicity, or duration of action.

There is no universal agreement that the use of either subcutaneous epinephrine or terbutaline is the initial treatment of choice. Published reports have first treated patients with severe acute asthma with inhaled salbutamol and intravenous aminophylline[23,28] or inhaled metaproterenol and aminophylline.[17] The latter report indicated that this treatment, combined with large doses of corticosteroids, was effective even for patients in the "danger" phase of acute asthma, where hypercapnia or obvious exhaustion was seen.[17]

In a randomized trial in the emergency treatment of acute asthma, inhaled isoproterenol (2.5 mg) was as effective as subcutaneously injected epinephrine (0.3 mg) when each was administered three times at 20-min intervals.[52] Although not shown to be statistically different, inhaled isoproterenol might have been more effective than subcutaneous epinephrine in improving $FEV_{1.0}$ in those patients in whom initial $FEV_{1.0}$ was below 1.0 L.[52]

Intravenous Aminophylline (Theophylline Ethylenediamine)

The intravenous administration of aminophylline has played a central role in the drug management of severe acute asthma. The addition of an intravenous infusion of aminophylline, when initial treatments such as subcutaneous epinephrine have failed to improve the patient's status, has been largely unchallenged.[8,17,22,23,25,26,28,30] Traditionally, aminophylline is considered to inhibit phosphodiesterase, mediating smooth muscle relaxation, and inhibits release of histamine by mast cells. The mechanism producing bronchodilatation, and even the hypothesis that bronchodilatation is the major benefit produced by aminophylline, has been challenged, however.[56]

There is no doubt that patients with acute asthma improve in both their pulmonary function tests and symptomatology following the administration of intravenous aminophylline. Using a loading dose of 5.6 mg/kg body weight and an infusion of 0.9 mg/kg/hr, $FEV_{1.0}$ increased by 25% at the end of 1 hr of therapy.[52] A loading dose of 4.3 mg/kg and an infusion of 0.84 mg/kg/hr has been associated, after 1 hr of treatment, with a 50% increase in PEFR.[57] Intravenous aminophylline has less than one half the effect of inhaled isoproterenol or subcutaneous epinephrine on $FEV_{1.0}$ when administered in clinically equivalent dosage to patients with acute asthma.[52]

Other facets of the pharmacologic properties of aminophylline that might contribute to the improvement in the patient's status are the diuretic effect, the central stimulation of ventilation, and the increased contractility of the diaphragm[58] caused by the drug. Aminophylline also increases right and left ventricular ejection fractions in patients with chronic obstructive pulmonary disease, whether or not ventricular function was depressed in the control state. Heart rate and systemic blood pressure increased slightly.[59]

Because aminophylline and the beta-adrenergic receptor-stimulating drugs act at different sites, an additive or even synergistic effect might be expected.

In patients with acute asthma, intravenous aminophylline, when used in conjunction with subcutaneous epinephrine, produced an improvement in $FEV_{1.0}$ of 130% over pretreatment levels, compared to a 50% increase with epinephrine alone.[53] Contrary to this result, a similar study, but with a slightly higher dose of epinephrine, showed no difference in the increase in PEFR whether epinephrine was used alone or in combination with intravenous aminophylline.[55] A similar conflict in results has been shown comparing the effectiveness of inhaled beta-adrenergic drugs when used with or without the addition of intravenous aminophylline.[53,62] The combination of intravenous aminophylline with intravenous salbutamol was shown to have no significantly greater effect on the recovery of PEFR or arterial blood gases than either drug given alone to patients with severe acute asthma.[57]

These studies, therefore, present conflicting data in regard to the question of whether or not aminophylline should be added to the therapeutic regimen when initial treatment with beta-receptor agonists has failed to produce improvement in patients with acute asthma. It is also possible that the dose or type of beta-receptor agonists should be altered. Salbutamol, a beta-2 receptor agonist, has been compared with aminophylline, when both were given by an intravenous infusion to patients with severe acute asthma. An infusion of approximately 4 μg/min of salbutamol in patients with severe acute asthma was significantly slower in onset (60 compared to 15 min) than 1 mg/min of aminophylline, and the degree of improvement was no greater.[57] A comparison of that same dose of aminophylline with more than double the infusion rate of salbutamol (10 μg/min) again showed a slower onset and less effect with salbutamol.[62] No loading dose of salbutamol was given in that study, however. Heart rate decreased during therapy with aminophylline, but stayed the same with salbutamol.[57,62] The authors of one of the studies speculated that in patients who respond poorly to initial intensive treatment, the subsequent infusions of a bronchodilator may not increase the rate of recovery from the rate that would occur naturally.[62]

There is no definite conclusion to be drawn from these data. In a patient who has failed to respond to initial treatment, it is probably prudent to treat the patient with an intravenous infusion of aminophylline. There is no proven advantage of intravenous salbutamol.

Dosage of Aminophylline. When aminophylline is administered intravenously, there is considerable variation in plasma theophylline levels between patients, and in the same patient, in different circumstances. The effect of theophylline on airway obstruction correlates with increasing plasma levels, such that a level of 5 mg/L increased $FEV_{1.0}$ by 29% compared to a level of 20 mg/L, when $FEV_{1.0}$ improved by 85%.[63] A study of patients treated with different levels of plasma theophylline, in addition to standard treatment with corticosteroids and inhaled beta-receptor agonists, showed that a plasma level of 10 mg/L was associated with an approximate 10% increase in $FEV_{1.0}$ and FVC, whereas a level of 20 mg/L caused an 80%–90% increase in pulmonary function tests.[61]

The optimal theophylline level is modulated by the toxicity of the drug. Gastrointestinal upsets, such as nausea and vomiting, occur at levels above

20 mg/L. At levels of 40 mg/L, cardiac arrhythmias are seen, and at 60 mg/L, central nervous system convulsions occur.[63] The usual therapeutic plasma level desired is from 10 to 20 mg/L.

The mean plasma half-life of theophylline in adult patients is 4.5 hr, with a range from 3.0 to 9.5 hr. The half-life is increased in patients with congestive heart failure, liver disease, pneumonia, or severe obstructive lung disease.[64] The half-life is also increased during acute respiratory viral illness,[65] following vaccination with influenza vaccine,[66] and during the oral administration of cimetidine.[67] The half-life is decreased in subjects who smoke,[64] in patients with chronic obstructive pulmonary disease with acidemia,[68] and in patients with cystic fibrosis.[69]

The dosage of intravenous aminophylline varies, therefore, with many factors. A loading dose of 6 mg/kg body weight should be given over 20 min. This should be reduced appropriately in patients who have been taking oral theophylline preparations. A standard maintenance infusion of 0.5 mg/kg/hr may then be started. This should be modified as follows:

1. In patients less than 19 yr of age, increase to 0.6 mg/kg/hr
2. With cigarette smokers, increase to 0.8 mg/kg/hr
3. Patients with congestive heart failure, liver disease, pneumonia, decrease to 0.2 mg/kg[p]
4. Patients receiving cimetidine, decrease to 0.3 mg/kg/hr

The rate of intravenous infusion of aminophylline should thereafter be regulated by measurement of serum theophylline levels.

Inhaled Beta-Receptor Agonists

Isoproterenol is a potent sympathomimetic agent that has both beta-one and beta-two effects in man. Administered by inhalation, it has little effect on heart rate or blood pressure in patients with acute asthma, while causing a significant increase in $FEV_{1.0}$, FVC, maximal expiratory flow rates, and maximal midexpiratory flow.[52] In patients with stable asthma, the inhalation of a metered dose of 0.3 mg is associated with the following effects[70,71]:

1. An increase in $FEV_{1.0}$ of 25%
2. A decrease in airway resistance of 40%
3. A decrease in FRC of 10%
4. Onset within 5 min
5. Maximum effect at 15 min
6. Duration of significant effect for 1–2 hr
7. Infrequently, a mild increase in heart rate
8. No significant change in systemic blood pressure

Arterial oxygen tension may decrease following the inhalation of isoproterenol. In a study of 16 patients with asthma, inhalation of 2.5 mg of isoproterenol was associated with a decrease in oxygen tension in 44% of patients. In the patients in whom PaO_2 fell, the alveolar-to-arterial oxygen tension gradient [$P(A\text{-}a)O_2$] increased.[72]

Selective beta-two receptor agonists have been developed. The inhalation of terbutaline has been shown to have the following effects[70,71]:

1. Onset within 5 min
2. Maximum effect at approximately 1 hr
3. Duration of significant effect for 6 hr

Other selective beta-two agonists include metaproterenol, salbutamol, and fenoterol. Apart from their more prolonged duration, there does not seem to be any documented clinical advantage of these agents over isoproterenol.

The administration of the beta-receptor agonists by inhalation has been compared to the intravenous route. Studies of the effects of terbutaline suggest that when equivalent changes in $FEV_{1.0}$, FEV, and MMFR are produced, heart rate decreases with inhalation, but increases with the intravenous route.[73] Identical conclusions were shown in a comparision between inhaled and intravenous salbutamol.[74]

Corticosteroids

Corticosteroids have been used to treat patients with asthma for over two decades. In patients with severe acute asthma, the use of corticosteroids is standard therapy. The data establishing their benefit in acute asthma are conflicting, and the utility of corticosteroids has been challenged.[4] Results of studies of the effect of the addition of corticosteroids to treatment with standard therapy are shown in Table 3. The clinical score of adults and children

Table 3. The Effect of Administration of Corticosteroids to Patients with Acute Asthma

Ref.	Year	Age	Drug	Dose	Length of study (days)	Measurement	Effect of steroids[a]
75	1956	Adult	Cortisone	1.25 g orally over 9 days	14	Clinical score	+
76	1976	Adult	Hydrocortisone	250, 500, or 1000 mg i.v.	0.25	Clinical score $FEV_{1.0}$	0 0
77	1982	Adult	Hydrocortisone	100 mg i.v. every 2 hr	2	Clinical score PEFR	0 0
78	1982	Adult	Hydrocortisone	2 mg/kg then 0.5 mg/kg/hr	1	$FEV_{1.0}$ PaO_2	+ 0
79	1974	Child	Hydrocortisone	7 mg/kg then 7 mg/kg day	1	Clinical score $FEV_{1.0}$	0 0
			Dexamethasone	0.3 mg/kg then 0.3 mg/kg/day		PaO_2	+
			Betamethasone	0.3 mg/kg then 0.3 mg/kg/day			
80	1980	Child	Hydrocortisone	7 mg/kg i.v. every 6 hr	2	Clinical score PEFR	0 0

[a]0, no effect; +, improvement.

is shown to improve[75] or to be unaffected[76,77,79,80] by the addition of corticosteroids to the therapeutic regimen. Similar conflicting results have been demonstrated for pulmonary function tests[76–80] and arterial oxygen tension.[78,79] Confusion also exists in the literature as to the effects of different dosages of corticosteroids in patients with acute asthma. Increasing the dosage has been shown to produce a greater improvement in $FEV_{1.0}$.[81] However, other studies have shown no benefit from increasing dosage.[82–84]

Although the adverse effects of the administration of a short course of steroids are probably minimal, the single deaths reported in each of two series of patients with acute asthma were in patients treated with corticosteroids.[75,77] Death from aspergillosis has also been reported in this situation.[85]

The mode of action of corticosteroids is not known. A study of 14 patients who were acutely ill with asthma demonstrated that corticosteroids alone had no effect on $FEV_{1.0}$ unless beta-receptor agonists were added to the regimen.[86]

Any conclusions concerning the use of corticosteroids in acute asthma can be challenged, therefore. It is reasonable practice, however, to treat the patient with severe acute asthma with corticosteroids. The dosage and type are arbitrary. A regimen of hydrocortisone, 7 mg/kg as a loading dose followed by 7 mg/kg every 8 hr, or of dexamethasone, 0.3 mg/kg loading dose followed by 0.3 mg/kg every 24 hr, is reasonable.

Antimuscarinic Agents

Atropine is an alkaloid named after one of the Fates in Greek mythology, Atropos, the Inexorable, who carried the dread shears that cut the thread of life at the proper time.[87] The antimuscarinic drugs have been used for at least a century in the treatment of asthma.

In a study of 15 patients hospitalized with acute asthma, 1 mg of atropine sulfate dissolved in 2 ml of normal saline was given by inhalation. The patients were already receiving aggressive medical treatment with corticosteroids, sympathomimetic aerosols, intravenous aminophylline, and oral terbutaline. Sixty minutes after administration of atropine, there was a decrease by 19% in TLC and by 25% in FRC. Peak expiratory flow rate and forced vital capacity increased by 21% and 15%, respectively.[88]

Ipratropium bromide is a long-acting preparation that has a prolonged effect when given by aerosol and has low systemic toxicity. A dose of 500 μg of ipratropium was compared with 10 mg of salbutamol, with either being nebulized in normal saline.[89] Improvement in PEFR was similar with either drug. An additive effect was found when they were given consecutively.[89]

The role for antimuscarinic drugs in the management of severe acute asthma is not established. The customary therapeutic sequence at present is to initially administer a subcutaneous adrenergic agent, such as epinephrine. This would be repeated, and if improvement in the patient's status is not evident, an intravenous loading dose of aminophylline, followed by a continuous infusion, would be commenced. Inhaled beta-receptor agonists would also be administered. Corticosteroids would be added. Should the patient fail to improve, or even deteriorate, atropine or ipratropium should be given.

Other Therapies

Added Inspired Oxygen

Hypoxemia is a frequent accompaniment of severe acute asthma while the patient is breathing air.[10,17,20,25,27,28] Augmented inspired oxygen is always necessary. Arterial oxygen tension should be maintained above 60 torr by means of nasal prongs or a face mask. Arterial carbon dioxide tension may rarely be elevated by increasing PaO_2,[17] but the hazard of hypoxemia is greater than the potential fall in pH.

Humidity

The predominant pathologic finding in patients with severe acute asthma is obstruction of airways due to thick tenacious mucus. The addition of humidity to the inspired gas is probably of benefit to loosen secretions and allow productive coughing. Nebulized water may provoke bronchospasm, however, and the patient's response must be assessed. A theory has been postulated that asthma is a specific disease of increased permeability of the mucous membrane of the airways. The authors showed increased reactivity of the airways upon inhaling nebulized distilled water. No such reaction was found when a normal saline solution was nebulized.[90]

Intravenous Fluid Therapy

The infusion of intravenous fluids is governed by the same general principles as in any severely ill patient. Initial deficits should be replaced, as hypovolemia is common. Generous replacement has been advocated, with the intent to promote hydration of pulmonary secretions. There is, however, no evidence that intravenous fluid therapy aids lung clearance. In view of the potential development of pulmonary edema due to predominantly negative pleural pressures, the aim should be to maintain satisfactory intravascular volume without producing hypervolemia.

Antibiotics

The use of antibiotics in severe acute asthma is not warrented unless there is evidence of bacterial infection.[91,92] Although upper respiratory tract infections are frequently associated with acute asthma, they are usually viral, rather than bacterial, in origin.

Sodium Bicarbonate

Although uncommon, metabolic acidosis may occur in patients with severe acute asthma. Correction of this metabolic acidosis, or increasing partial compensation for respiratory acidosis, has been recommended in patients with severe acute asthma.[93,94] Correction of the underlying deficits is imperative,

but the immediate hemodynamic and pulmonary status may be improved if arterial pH is above 7.2.

Intermittent Positive Pressure Breathing (IPPB)

Accepted by custom, intermittent positive pressure breathing is less well established in proven utility. Delivery of bronchodilating agents by IPPB has been shown to have no advantage over delivery by hand nebulizers.[95,96] Other studies have shown a marginal benefit to the delivery of bronchodilating agents with IPPB.[97,98] It should be noted that two quoted studies used inflating pressures between 11 and 20 cm H_2O, which might represent a restricted inflation volume[95,98] One study did not report the peak inflation pressure.[96] The essence of appropriate utilization of IPPB is to achieve a tidal volume greater than the patient's spontaneous breath. Therefore, failure to assess or measure the volume may disguise inadequate treatment.

IPPB in severe acute asthma is used mainly in patients who are not responding to other forms of therapy. It also has a place in the management of patients who are familiar with IPPB and believe that it is of value; that it may only be of psychologic support is not necessarily regrettable.

Chest Physiotherapy

Although the clear value of chest physiotherapy has not been proven in severe acute asthma, breathing exercises and assisted coughing are beneficial.

Progressive Airways Obstruction

Clinical recovery from severe acute asthma usually occurs within minutes or hours of initiation of the therapies outlined in the preceding sections of this article. Hypercapnia, pulsus paradoxus, and changes in the electrocardiogram disappear first, within hours. The $FEV_{1.0}$ and PEFR normalize more slowly, and may take more than 7 days.[23,24] Patient's symptoms may become normal when $FEV_{1.0}$ is still reduced to 30% predicted.[24] Functional residual capacity and residual volume remains elevated even when total lung capacity is normal.[24]

A percentage of patients, however, do not respond to the therapies already outlined. The differential diagnosis must be reexamined to ensure that a discrete identifiable factor has not been overlooked, such as tracheal stricture. Potentiating factors must also be sought—pulmonary embolism or edema, pneumomediastinum, pneumothorax, aspiration of gastric contents, or pneumonia.

Careful observation of the patient must be maintained, as sudden death, particularly in the early hours of the morning, is not uncommon. Danger signals in the patient's progress include:

1. Increase in pulsus paradoxus above 20 torr
2. Heart rate above 120 beats/min
3. Increasing $PaCO_2$, to levels above 65 torr

4. Progressive hypoxemia as inspired oxygen is increased
5. Increased use of accessory muscles
6. Inspiratory breath sounds diminished or absent
7. Increased hyperinflation on chest radiograph
8. PEFR below 100 L/min or $FEV_{1.0}$ less than 0.5 L, and failure to improve with bronchodilators

The use of an intravenous infusion of a beta-receptor agonist, such as isoproterenol, has been recommended in patients who have failed to improve inspite of the treatments already described.[99] However, inhalation of the beta-receptor agonists is as effective as the intravenous route, with less systemic toxicity.[73,74] Intravenous isoproterenol has been shown to increase theophylline clearance in children.[100]

Endotracheal Intubation and Mechanical Ventilation

Mechanical ventilation is instituted when continued increase in the severity of the patient's disease occurs in the face of optimal therapy with drugs. The benefits from mechanical ventilation are:

1. Minute ventilation is augmented or provided entirely by the ventilator. This spares the work of breathing by the patient, and maintains normal $PaCO_2$ and pH.
2. Arterial oxygen tension is maintained because the larger tidal volumes provided by the machine will help reverse airway closure and atelectasis.
3. The presence of an endotracheal tube allows improved pulmonary toilet in a patient who may be unable to cough effectively.
4. The patient is able to receive sedatives and narcotics and is allowed to rest.

However, the institution of mechanical ventilation is associated with high morbidity and mortality. If the data summarized in two studies on this subject are combined, published reports from 1964 to 1983 show a mortality of 15% of 265 patients mechanically ventilated for severe acute asthma.[9,101]

The indications for mechanical ventilation are not clearly identified or rigid, and each patient must be individually assessed. In published reports, 14% of 83 patients mechanically ventilated for severe acute asthma where intubated only following a cardiac arrest.[9,102,103] Thirty-four percent of 41 patients were ventilated because of respiratory depression due to sedative drugs.[9,102] The following are guidelines for the earlier institution of mechanical ventilation.

1. Possibly the most important are alterations in the patient's mental state. The onset of drowsiness, confusion, irritability, or coma are ominous because of their cause—possible cerebral hypoxia—and their consequence—lack of ability to cooperate with needed therapies.
2. Increasing fatigue, with use of the accessory muscles.
3. Acidemia (pH below 7.2) due to metabolic acidosis.
4. Increasingly elevated $PaCO_2$ in spite of treatment.

5. Persistent hypoxemia (PaO_2 less than 50 torr) in the face of increasing inspired oxygen fraction.
6. Diminished or absent breath sounds as tidal volume diminishes, with either decreased or increased expiratory rhonchi.

Endotracheal intubation is performed by insertion, preferably by the nasal route, of an inert polyvinyl cuffed endotracheal tube. This can usually be accomplished by means of topical anesthesia of the nasal passage with cocaine (4%) plus lidocaine (1%) to the pharynx and larnyx. If possible, a tube with at least an 8-mm internal diameter should be used to allow subsequent fiberoptic bronchoscopy if necessary. Small doses of diazepam can be given if the patient is agitated or restless. General anesthesia with halothane has been advocated as the technique of choice during tracheal intubation.[102] The position of the endotracheal tube is verified by chest radiograph and secured with adhesive tape.

The patient's spontaneous breathing is then gently assisted by means of a hand-ventilating device. Sedative or narcotic drugs should be administered. Choice of drugs are:

1. Morphine sulfate by intravenous injection. Increments of 2 or 3 mg may be given. Although releasing histamine and theoretically increasing airway resistance, it is commonly used in this situation.
2. Diazepam, 2 or 3 mg by intravenous injection can also be used.[9]
3. Ketamine hydrochloride has been advocated for use in patients with acute asthma. The drug has been shown to reduce airway resistance and increase compliance in patients with preexisting airways obstruction.[104]
4. If severe bronchospasm persists, inhalation of halothane can be employed. Halothane results in bronchial dilatation and has been reported to be effective therapy in patients with severe acute asthma.[105–107]
5. Blockade of the neuromuscular junction is rarely necessary in adult patients. If it becomes necessary, it has been suggested that the drug of choice is pancuronium bromide, which does not release histamine.[108]

Mechanical ventilation should be administered with a time- or volume-cycled machine. A tidal volume of 10–14 ml/kg body weight should be employed. The ventilatory rate should be sufficiently slow as to minimize air trapping. This can be judged by watching the patient's chest movement and by observing the filling of an expiratory spirometer if one is used. Restoration of a normal or low $PaCO_2$ should not be undertaken quickly, especially if there is a preexisting metabolic alkalosis. Seizures or cardiac arrhythmias may occur in this situation if hypocapnia is produced.

The previously instituted therapies should be continued while mechanical ventilation is maintained. Endotracheal suctioning should be performed following instillation of 5–10 ml normal saline.

Complications of mechanical ventilation for severe acute asthma are not uncommon. Pneumothorax was found in 14% of patients.[9,101–103,109] Mechanical failure of the ventilator was reported in 6 of 43 patients ventilated.[6,9] Endo-

tracheal tube malfunction in 43% of 21 patients has also been reported.[9] Pneumonia was listed in 10% of patients.[9,101,103] Other complications include atelectasis, pneumomediastinum, pneumopericardium, hypoventilation, cardiac arrhythmias, and gastrointestinal bleeding.

The care and monitoring of the patient being mechanically ventilated must be meticulous:

1. Monitoring of the functions of the ventilator and endotracheal tube by alarms and careful observation
2. Daily chest radiograph
3. Daily Gram stain of sputum
4. Measurement of forced vital capacity at appropriate intervals
5. Monitoring of PaO_2, $PaCO_2$, and pH at intervals of not greater than every 6 hr; an indwelling arterial line is therefore advisable.
6. Positive end-expiratory pressure (PEEP) can be applied if oxygenation needs to be improved or inspired oxygen fraction reduced. The risk of hyperinflation and lung disruption would seem to be prominent in the patients, who may already be hyperinflated with gas trapping. It has been suggested, however, that PEEP may treat severe bronchospasm, reducing gas trapping and peak airway pressure during mechanical ventilation in patients with severe acute asthma.[110]

Spontaneous breathing with continuous positive airway pressure can be used as the recovery phase of the patient's disease begins. This mode of breathing is said to reduce the load on the inspiratory muscles, improving their efficiency and decreasing the energy cost of their action.[111]

Discontinuing Mechanical Ventilation

Although the criteria for weaning from mechanical ventilation have received considerable attention in the literature, no combination of factors has been shown to cover all aspects of the problem. Premature extubation can have a fatal outcome.[101,103] The following are some guidelines for successful weaning:

1. The mechanics of breathing are the major focus, and recovery of vital capacity is the most important variable. Vital capacity should exceed approximately 10 ml/kg body weight.
2. Expiratory rhonchi should be lessened and may be absent when extubation is finally accomplished
3. The patient is awake and cooperative
4. A period of spontaneous breathing is tolerated for 45 min, with $PaCO_2$ less than 50 torr

The period of mechanical ventilation in patients with severe acute asthma is usually brief. Mean duration in six published reports ranged from 20 to 113 hr, with an average of 61 hr.[6,9,102,103,109,112]

Mortality in Patients Mechanically Ventilated for Severe Acute Asthma

Mean mortality for patients mechanically ventilated for severe acute asthma was 15% of 265 patients. The mortality was 19% in results published in the decade from 1974 to 1983, compared to 12% in the preceding 10 years.[9,101] The failure to find a reduction in this mortality is unexpected, as the care of patients being mechanically ventilated has presumably improved over the past 20 years. It might be explained if fewer, and more sick, patients with severe acute asthma are requiring mechanical ventilation.

The causes of the deaths of 38 patients being mechanically ventilated for severe acute asthma is shown in Table 4. Hypoxic brain damage, usually associated with a previous cardiac or respiratory arrest, was seen in 32% of patients. Mechanical failure refers to the mechanical ventilator. Two patients who had been given curare died early in one series, when the ventilator became accidentally disconnected and remained undetected. "Steady deterioration" indicates that the patient's pulmonary function became progressively worse in spite of optimal therapy. Two deaths occurred shortly after extubation.

Failure of Patients to Improve During Mechanical Ventilation

Pulmonary Lavage. Instillation of large volumes of fluid into the airway has been used occasionally in patients with severe acute asthma who continue to deteriorate in spite of mechanical ventilation, bronchodilating drugs, and conventional pulmonary toilet. One such case was reported in a patient who had a known allergy to intravenous aminophylline. A solution of 250 ml normal saline, 30 ml of 20% *n*-acetyl cysteine, 0.5 ml Bronkosol, and 125 mg of Solu-Medrol was instilled via a fiberoptic bronchoscope. This was associated with improvement of arterial blood gases and was repeated in 24 hr.[113]

Extracorporeal Membrane Oxygenation. Support by extracorporeal membrane oxygenation can prevent immediate death, although it does not improve

Table 4. Causes of Death in Patients Being Mechanically Ventilated for Severe Acute Asthma*

Cause	Number of patients	(%)
Hypoxic cerebral damage	12	(32)
Pneumothorax	7	(18)
Mechanical failure	4	(11)
Septic shock	3	(8)
"Steady deterioration"	3	(8)
Cardiac arrhythmia	2	(5)
Following extubation	2	(5)
Other causes	5	(13)
Total	38	(100)

*From refs. 6, 9, 101–103, 109, and 112.

eventual survival in patients with adult respiratory distress syndrome. Its successful use has been reported in the management of a patient with severe acute asthma who was moribund in spite of bronchodilator drugs, mechanical ventilation, and pulmonary toilet with fiberoptic bronchoscopy. Extracorporeal support restored the patient's hemodynamic status and allowed pulmonary lavage. Recovery occurred even in the face of a sudden massive pulmonary hemorrhage and surgical drainage of empyema.[114]

Plasmapheresis. Apparent benefit has been reported in a patient with severe chronic asthma after plasmapheresis, although the documentation in that report has been criticized.[115] Plasmapheresis, if proven effective, is probably too slow in onset to be of value in severe acute asthma.

Long-term Survival following Mechanical Ventilation for Severe Acute Asthma

The necessity to employ mechanical ventilation to support the patient with severe acute asthma does not imply that the chronic course of the disease will involve more frequent or more severe acute attacks. In a study of 35 survivors of an episode of acute asthma requiring mechanical ventilation, 9 patients subsequently died. Death was attributed to asthma in eight of these nine patients, and occurred from 2 weeks to 6 years after the episode requiring ventilation. Still alive, from 9 months to 7 years after the episode of mechanical ventilation, were 23 patients who were available for follow-up. Fifty percent of these survivors had less clinically severe asthma in the period of time after mechanical ventilation as compared to the preventilation period. Six patients had improved, being asymptomatic or having mild asthma. Only three patients had worsened symptomatology when the follow-up period was compared to the period of time preceding the episode of severe acute asthma that required tracheal intubation and mechanical ventilation.[103]

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