Death in Status Asthmaticus:  
A Clinical Analysis of Eighteen Cases  

Jerome B. Shapiro, M.D.  
and  
Charles F. Tate, M.D., F.C.C.P.**  

Miami, Florida

Sudden death in status asthmaticus is not unusual, despite advances in management. This event has been the subject of several recent articles. Because of this continuing mortality, a review was made of recent records in a large municipal hospital to detect, if possible, any common features among fatal cases of bronchial asthma with the hope that their recognition might lead to improved treatment and prevention of death.

Method

The records of patients who died in status asthmaticus between May, 1958, and January, 1964, were reviewed. A patient was considered to have bronchial asthma if he had recurrent episodes of paroxysmal dyspnea with bilateral diffuse wheezing which could not be ascribed to other etiologies such as cardiac disease or chronic obstructive pulmonary emphysema. Between attacks, his physical findings were normal. He was considered to be in status asthmaticus if his present asthmatic episode lasted more than 24 hours and it could not be controlled either as an outpatient or in the hospital emergency room. Cases with pneumonia were excluded, as were those with any other disease which may have contributed to the death. There remained records on 18 patients who expired whose courses fulfilled the required criteria.

Results

Summarized in Table 1 are the clinical findings on the 18 patients who died as the result of status asthmaticus. Of the 18, 11 were female and seven were male. There were ten white and eight Negroes. These proportions parallel those in the hospital admissions in general at Jackson Memorial Hospital.

Age and length of attacks: One death occurred before the age of five and 13 after the age of 35 years. Fourteen had bronchial asthma for over ten years, with the longest for 40 years. Many had had recurrent hospitalization for asthmatic episodes.

Hospitalization time before death: Twelve expired within 48 hours of admission; nine of these within 24 hours. Those who expired after a longer period of hospital stay were usually admitted because of another medical condition and developed their status asthmaticus in the hospital.

Treatment: The treatment most often used was similar to that described recently by Sherman. It consisted usually of bronchodilators (aminophylline, epinephrine, and/or isoproterenol); sedation (a wide selection of drugs including paraldehyde, chloral hydrate, a phenothiazine, meperidine, and/or rectal ether); expectorants (mostly saturated solution of potassium iodide or sodium iodide in intravenous fluids); hydration (either orally or intravenously): antibiotics (mostly tetracycline); and adrenocortical steroids (mostly intravenous hydrocortisone or prednisone by mouth).

Since all 18 patients were in severe status asthmaticus, they all received a full range of treatment. Only four received meperidine. None received morphine. In four instances bronchoscopy was done. One had tracheostomy.

Clinical presentation: It was common for patients to relate a recent upper respiratory infection to recurrence of their asthma. All were treated as out-patients before being admitted for intensive treatment. By
the time of admission, all had had their present episode for over 24 hours and were already exhausted and becoming dehydrated. They had eaten and taken fluids poorly during this time.

The temperatures varied between normal and 102° F. All had the typical physical findings of bronchial asthma.

Laboratory data: In the 18 fatal cases, leukocytosis (greater than 10,000 per mm.³), with neutrophilia was present in 13. Eosinophilia occurred in only two.

In each of the four cases in whom serum electrolytes were done, serum potassium concentrations were below 4.0 mEq./L. (normal 4.0-5.5 mEq./L.). Electrocardiograms in two others were reported to show changes compatible with hypokalemia (depression of the T wave and exaggeration of the U wave). All of these patients had been treated with glucocorticoids and were receiving intravenous fluids without potassium supplements.

Modes of death: There appeared to be two modes of exitus. The most common was sudden unexpected death (13 of the 18 patients). In three, terminal electrocardiograms were taken and showed cardiac standstill with an occasional idioventricular beat. The other five expired gradually over a period of hours with shock, which would not respond to pressor agents, and cyanosis.

Pathologic findings: Ten patients had postmortem examinations performed; the typical lung changes found in patients who die in status asthmaticus were recorded:

"1. gross emphysema, 2. the bronchial tree plugged with sticky mucus, 3. the bronchial walls thickened by muscular hypertrophy, 4. widening of the bronchial walls by eosinophils, and 5. hyperactivity of the bronchial mucus glands." In none was any cardiac abnormality found.

Discussion

Bronchial asthma was long considered an innocuous disorder. Oliver Wendell Holmes is said to have stated that asthma "is the slight ailment that promotes longevity." Snapper found only seven necropsied cases of status asthmaticus recorded between 1886 and 1906. Yet by 1953, Earle was able to collect data on 160 fatal cases from the world literature and described 15 additional cases. More recently, Cardwell and Pearson reviewed 430 cases from the literature and added 68 new cases. And Messer and associates in 1960, described 35 cases from the Mayo Clinic.

Because of the post-mortem findings, it is usually inferred that patients in status asthmaticus die from asphyxiation. However, certain features cannot be readily attributed to this, so additional mechanisms have been proposed.

Earle lists six possible causes contributing to death besides asphyxia: (1) drugs; (2) anaphylactic shock; (3) mediastinal emphysema and spontaneous pneumothorax; (4) psychologic factors with sudden death due to vagal inhibition of the heart; (5) acute cor pulmonale and (6) pulmonary infections.

From the eighteen cases reviewed herein, a common pattern of events appears to have transpired.

Pulmonary infection most likely played a prominent role in initiating the terminal episode of status asthmaticus.

Swineford states that true status asthmaticus has rarely been observed in his clinic in the absence of infection. Data from the cases reported here would tend to bear this out. Many of the patients had their fatal episode in the months between October and March when respiratory infections are greatest. Most gave a history of a recent cold or cough preceding the asthma. Fever was common and most patients had leukocytosis with neutrophilia. And as stated by Swineford, in the presence of infection "epinephrine and aminophylline are likely to produce incomplete and transient relief," as occurred in these patients.

The onset of a prolonged asthmatic attack led to the development of exhaustion, dehydration, electrolyte imbalance and hypoxemia.
During the initial days of the attack, the patients received standard therapy without relief. Most were unable to eat or take fluids well and developed vomiting. There was increasing anxiety, restlessness and insomnia. The stress which appeared clinically has also been demonstrated chemically: Israels and co-workers\textsuperscript{11} and Siegel and colleagues\textsuperscript{22} in two separate studies have shown an increase in adrenal steroid output during severe asthmatic attacks.

Dehydration and electrolyte imbalance, especially hypokalemia, developed. Sair and associates,\textsuperscript{23} who also quotes Hartmann,\textsuperscript{24} and Abramson\textsuperscript{25} all believe it is common to find hypokalemia in patients with severe asthma of any duration because of “negative potassium balance as a result of inadequate intake and the unusual losses incident to the stress of the illness.”

Hypoxemia also develops and has been shown to accompany prolonged asthmatic attacks.\textsuperscript{18,19}

The patient was hospitalized for intensive medical management.

The increased incidence of death in status asthmaticus seems to have occurred in the 20 to 30 years past. Snapper\textsuperscript{26} accounts for this because of the “dangerous drugs that have been added to the old-fashioned treatment.”

Epinephrine was introduced clinically in 1903, aminophylline in 1933 and isoproterenol about 1948. Under varying conditions they may produce cardiac arrhythmias.

Barbital was introduced in 1903 and this was followed in the subsequent years by many similar but more potent derivatives. The antihistamines followed in the late...


1940’s and the phenothiazine tranquilizers in the mid-1950’s. These latter drugs, besides producing sedation and respiratory depression in larger doses, may also have an atropine-like action and produce drying of secretions. The possible relationship of over-sedation and death in status asthmaticus was investigated by Neder and co-workers who found that most of their patients who expired had received too much sedation.

Glucocorticoids came into general clinical use in the 1950’s. Their use contributes to hypokalemia, especially in patients maintained on intravenous fluids with no potassium supplements. All fatal cases reported herein were receiving intravenous fluids with glucocorticoids, and none was given potassium supplements.

Expiration, usually suddenly and unexpectedly within 48 hours of admission.

When sudden and unexpected death occurs it is commonly ascribed to cardiac arrest. In the 18 cases reviewed, this seemed to have occurred in 13 with electrocardiograms taken on three in extremis showing cardiac standstills. Asthmatics may often die suddenly (Maxwell,* Walzer and Frost,¹ and Houston and colleagues). * 

The reason for cardiac arrest is not often clear, but certain factors present in susceptible patients may well contribute to its occurrence. These factors would be hypoxemia, electrolyte imbalance, and the use of drugs capable of inducing cardiac arrhythmias.

Also age appears to be a factor. Bellet* states that cardiac arrest is most likely to occur in the first decade of life and in older people. Patients who die in status asthmaticus most often occur before the age of five.

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and after the age of 35. This was true in the present series and in other series.  

**Conclusions**  

From the foregoing the following recommendations are made for the treatment of status asthmaticus:

1. The use of a broad spectrum antibiotic such as tetracycline should be started as early as possible.  
2. Hydration should be maintained, with intravenous fluids if necessary.  
3. Serum electrolytes should be monitored, especially to prevent hypokalemia.  
4. Bronchodilators should be used intelligently, so that pharmacologically similar preparations are not given too often and in too large a quantity. Abramson points out that many of these drugs may have synergistic side effects. Also it should be remembered that acidosis may cause fastness to epinephrine and may need correction with sodium lactate solution if epinephrine is to be effective.  
5. Facilitate expectoration with agents such as warm fluids, saturated solution potassium iodide and bronchoscopy if necessary.  
6. Cautiously use light sedation, with the drug probably being ether and olive oil per rectum or phenobarbital in small doses. Antihistamines are contraindicated due to their drying action and phenothiazine tranquilizers should probably not be used. Narcotics such as morphine produce too much respiratory depression and bronchoconstriction. Meperidine has an atropine-like effect and should be used only with extreme caution.  
7. Glucocorticoids are beneficial and should be used regularly.  
8. Oxygen should be given only for evidence of hypoxemia since it may act as a drying agent. If there is evidence of carbon dioxide narcosis, oxygen should be administered with caution by an intermittent positive pressure breathing apparatus.  
9. Tracheostomy may be indicated to facilitate aspiration of secretions and to improve air exchange.  

Arterial pH, carbon dioxide tension and oxygen saturation may be helpful in deciding when this procedure is indicated.

The above outline method of treatment is aimed at maintaining the patient in the best possible condition until the bronchial plugging and hypoxemia have responded to treatment. It is hoped by these methods to avert the possibility of cardiac arrest.

**Summary**  

The charts of 18 cases of status asthmaticus who expired in the hospital were reviewed. A fairly similar clinical course was observed. Most of the cases were less than five and above 35 years of age. They had evidence of pulmonary infection. Physical evidence of dehydration, exhaustion and hypoxemia was present. Treatment was aggressive and consisted of a wide variety of the usual drugs. Hypokalemia was observed in four cases where electrolytes were done. Death occurred usually within 24 to 48 hours after admission and was usually sudden and unexpected; most likely due to cardiac arrest. The significance of this clinical course is discussed and a program of treatment outlined.

**Resumen**  

La revisión de las hojas clínicas de 18 casos de status asthmaticus fallecidos en el hospital ha permitido comprobar que todos presentan una evolución clínica análoga. La mayor parte eran menores de cinco o mayores de treinta y cinco años. A mas de los indicios de infección pulmonar se pudo comprobar la presencia de hipoxemia, deshidratación y agotamiento. El tratamiento fue de tipo agresivo, basado en el empleo de una amplia variedad de los medicamentos usuales. En los casos en que se investigó el balance electrolítico se comprobó la presencia de hipokalemia. La muerte sobrevino en forma repentina e inesperada, generalmente dentro de las 24 o 48 horas subsiguientes al ingreso en el hospital y fue debida, con toda probabilidad, al paro cardiaco.

La significación de estas comprobaciones para el replanteo de un plan terapéutico efectivo es objeto de análisis.

**Resumé**  

L'auteur examine les observations de 18 cas de mal asthmatic qui moururent à l'hôpital. Il observe une évolution clinique pratiquement similaire. La plupart des cas étaient âgés de moins de cinq ans ou plus de 35 ans. Ils firent la preuve physique de déshydratation, d'épuisement et d'hypoxémie. Le traitement avait été très actif et avait consisté en une grande variété des produits habituels. Une hypokälémie fut observée dans quatre cas, lorsque le dosage des électrolytes fut fait. La mort survint habituellement en 24 ou
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OBSURCTIVE EMPHYSEMA

Preservation of functional lung tissue is the hallmark of excellence in the surgical technique of obliteration or removal of emphysematous bullae. Unroofing and oversewing of a large bulla is the treatment of choice. This may or may not be augmented by a resection of the pulmonary pleura. Lobectomy will be necessary in less than 10 per cent of the patients. It is not unusual after obliteration or resection of bullae to have a space differential between the remaining lung tissue and the hemithorax. This situation may be remedied by a "tailoring thoracoplasty" or a dropping down of

the apical pleura in a so-called pleural tent procedure. The author prefers the latter, since it is less time-consuming and because the tent can sometimes be pushed back up as the residual lung becomes more expansile. By mechanically irritating the parietal pleura with a gauze sponge (pleurodesis) the two pleural layers form an early symphysis. This facilitates quicker removal of chest tubes and enables the patient to have a more productive cough.