

Management of Severe Asthma*

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In this summary of therapy for severe asthma there is no mention of etiologic factors. The author presumes that if infection is the primary factor in the progression to severe asthma that this will be recognized and appropriately treated. A chest x-ray must be an initial laboratory study for the recognition of pneumonia or complicating pneumothorax. However, unlike respiratory failure due to emphysema, here the specific therapy of the altered pulmonary physiology is of paramount importance. Attention to the inciting factors is of minimal therapeutic benefit once infection can be ruled out. After the patient can breathe comfortably again the role of allergy can be investigated. Premature investigation of emotional factors can be a lethal therapeutic error in the ill asthmatic.

The treatment of asthma at the University of Virginia Hospital can be divided into three rather specific periods (Table 1).

Mystery Period. Until 1962 arterial blood gas and pH measurement were not routinely available as a clinical tool in our laboratories. Most patients with severe asthma did well with our routine management. Other patients who looked the same might die suddenly with no major change in their clinical course. The mystery revolved around our inability to judge precisely who had life threatening asthma and who did not.

Measurement and Aggression 1962-1968. (Table 2). As soon as arterial puncture became a routine procedure the mystery cleared somewhat. Many patients with severe asthma were found to our surprise to have severe hypoxemia and hypercarbia. It is presumed that the prior mystery deaths were most likely due to respiratory failure with CO₂ narcosis or hypoxemia-induced fatal ar-

rhythmias. These patients were recognized usually late in their disease. Immediate tracheostomy was done; many were hyperventilated with a volume controlled ventilator into frightening states of alkalosis, and the hospitalization was prolonged for two to three weeks. The patients did not die from asthma, however, and survived their respiratory care (3).

Measurement and Intensive Care. Employing the lessons learned from our middle period, since 1968 our management of severe asthma has changed (Table 3). In the period 1965-1967, 10 patients with severe asthma were ventilated following tracheostomy and all survived. From 1968 to 1971 there were 299 admissions of asthmatics to the University of Virginia Hospital. Of these patients, 50 were judged to be in status asthma, and 36 had a P_{CO₂} greater than 45 mm Hg. Despite the serious nature of their disease, only 8 patients were intubated, 6 were briefly ventilated, and only 1 patient needed a tracheostomy. No deaths occurred (4).

Common Errors in Management. (Table 4). A review of patients previously reported with tracheostomy and our current series since 1968 revealed the same errors in management with the difference being one of degree.

Steroids. In the prior series, two patients received no steroids at all prior to tracheostomy. In our current patient group, several who were intubated received steroids late in their clinical course and in small amounts.

Sedation. The use of sedation continues to be an identifiable factor probably responsible for the deterioration and intubation in at least half of the patients intubated since 1968. Valium® and other tranquilizers are replacing the barbiturates as major offenders. Sedatives have no place in the management of severe asthma.

* Presented by Dr. Hunt at the Symposium on Respiratory Failure, May 26, 1972, at Richmond, Virginia.

TABLE 1.
MANAGEMENT OF SEVERE ASTHMA
University of Virginia Hospital

Mystery Period—Until 1962
Measurement and Aggression 1962–1968
Measurement and Intensive Care 1968–Present

Oxygen. The indiscriminate use of high flow oxygen is not as devastating to the asthmatic in acute respiratory failure as to the patient with chronic bronchitis and emphysema. An attempt should be made to keep the arterial oxygen in the physiologic range (70–110 mm Hg) which generally means the use of no more than 28–35% oxygen.

Nursing Position. Classically, the patient with asthma is immediately put flat in bed, and, to make sure he stays there, intravenous fluids are begun apparently to facilitate rapid drug administration. Like the patient with emphysema, the asthmatic is much more comfortable breathing in a chair. IV fluids should be replaced with oral medication usually within 24–48 hours except in unusual circumstances. This can be of immense psychological benefit as well as prevent painful phlebitis.

Tracheostomy. From our current experience and that of others (2), tracheostomy should rarely be necessary in the management of asthma. The morbidity associated with the procedure itself and the prolongation of hospital care, coupled with the short clinical course of aggressively treated asthma, all make nasotracheal tube intubation the procedure of choice when respiratory failure supervenes.

Patients at Risk. Who are the patients who are in the most danger of progression to respiratory failure? The same group (Table 5) appears in every series.

TABLE 2.
MEASUREMENT AND AGGRESSION 1962–1968

Arterial Gas Measurements Begun in 1962
Usually Obtained Late in Course
Serious Nature of Disease Recognized
Usually Immediate Tracheostomy
Frequently Hyperventilated
Two to Three Week Hospitalization

TABLE 3.
MEASUREMENT AND INTENSIVE CARE 1968–PRESENT

Arterial Gas Measurement Early in Suspicious Cases
Review of Prior Medication Imperative
Uncomplicated Asthma—Low P_{O_2} —LOW P_{CO_2}
Severe Asthma—Normal P_{CO_2} , a Grave Prognostic Sign

How to Evaluate Severity of Asthma.

Prior Medications. A patient who is in marked respiratory distress with asthma, and who has taken only a few tablets in the prior 24 hours, is in a different prognostic category than the patient with the same degree of airway obstruction who has tried Tedral®, aminophylline suppositories, and 20 mg of prednisone two hours before. An assessment of prior therapy then enables you to plan current therapy and escalate from theophylline, ephedrine and adrenaline, to high dose steroid therapy and hopefully avoid respiratory failure and intubation.

Arterial Blood Gases. The major initial defect in asthma is hypoxemia, as large areas of the lung that have excellent perfusion get progressively less ventilation, shunting poorly oxygenated blood into the arterial circulation. Initially, the asthmatic in respiratory distress can easily overventilate the uninvolved areas of the lung lowering arterial CO_2 (Pa_{CO_2}). The classical arterial gases of the dyspneic, but non-fatigued asthmatic, are a low Pa_{O_2} (50–60 mm Hg) and a low Pa_{CO_2} (20–30 mm Hg). As the patient tires, is sedated, gets worse, and is restrained in bed, he will begin to move less air, and underventilation will begin with the Pa_{CO_2} approaching normal. This is a *grave* prognostic sign.

If the arterial oxygen rises as the P_{CO_2} rises and the patient is more comfortable, all is well. If the arterial oxygen falls and the P_{CO_2} approaches normal, you should immediately escalate your therapy (Table 6).

TABLE 4.
COMMON ERRORS IN MANAGEMENT

Too Little Steroids Too Late
Sedation
High Flow Oxygen
Patient Put in Bed
Tracheostomy

TABLE 5.
PATIENTS AT RISK

Tired
Old
Fat
Chronic Bronchitis and Emphysema
Heart Disease

Escalation of Drug Therapy.

Combination Tablets and Isuprel®. Most patients with asthma who present to the physician with a severe episode have already tried regular therapy with one of the phenobarbital, theophylline, or ephedrine combinations such as Tedral® or Quadrinal®. They have generally used, and at times have overused, an Isuprel® preparation. These drugs then have little place in the management of the severe asthmatic. It is important, however, to obtain specific historical facts about their use in planning therapy. A patient who has had little or no prior medication can be expected to respond more rapidly to less medication.

One investigator has found that patients with severe asthma are specifically unresponsive to Isuprel®, so that response to Isuprel® was a measure not only of the severity of the disease, but also an index of the patient's response to other therapy, primarily steroids. More and more Isuprel® is then used by the worsening patient with less and less results. At times the Isuprel® has been shown to have been responsible for increasing the asthma and may actually cause hypoxemia.

Epinephrine and Aminophyllin. The response to 0.3 cc of epinephrine subcutaneously can at times be magical and should always be tried. The effect occurs within minutes and may last an hour. If no results are obtained after three doses

repeated at 15 minute intervals, a response will usually not be obtained. The response to IV aminophyllin may be equally as rapid and last for hours, frequently as long as six. The dose must be large—500 mg for an adult—and must be given over 15–45 minutes, not over hours in a large bottle of fluids. Two methods are equally acceptable:

1. 500 mg (a 20 cc ampule) given intravenously by syringe, over a 10 minute period. This is excellent if you have the time.
2. 500 mg in 250 cc glucose and water given by IV drip over a 30–60 minute period may be equally effective.

Decisions. Only the consultant the next morning has the benefit of the clearly outlined flow sheet documenting blood gases, clinical state, and time of the therapeutic maneuvers. In actual practice, the patient arrives in respiratory distress, arterial gases are obtained, and the above medications are given—epinephrine X2 followed by 500 mg of IV aminophyllin. This takes approximately one or one and one-half hours. The initial blood gases become known to the physician about half way through this therapy. He usually waits until 15–20 minutes after the aminophyllin is given and repeats the arterial gases and pH.

Initial Gases. If the Pa_{CO₂} is below 50 mm Hg, supplemental oxygen is begun (24 or 28% ventimask). If the Pa_{CO₂} is greater than 40 mm Hg and the patient has not obtained evident clinical improvement from his initial therapy, 250 mg of hydrocortisone is given intravenously in addition to the other drugs previously described.

Second Arterial Gases. These results have usually been obtained at a time when full therapeutic benefits will have occurred from epinephrine and aminophyllin therapy. A lack of clinical response by the patient and a lack of significant reduction in Pa_{CO₂} dictates that *aggressive steroid therapy should be begun.* If the Pa_{CO₂} has dropped into the 30 mm Hg range, therapy with aminophyllin and epinephrine can be continued and a maintenance drug such as Tedral® SA begun at an appropriate time.

Steroid Therapy.

General Considerations. There is no reason to give hydrocortisone except for the initial dosage. There is theoretical evidence that the therapeutic effect of hydrocortisone should be more rapid

TABLE 6.

BOTH STATES MAY BE ASSOCIATED WITH REDUCTION
IN WHEEZING AND A QUIET PATIENT

P _{O₂} —60 P _{CO₂} —30 pH—7.48	→	P _{O₂} —50 P _{CO₂} —40 pH—7.4	WORRY! ACT!
↓			
P _{O₂} —70 P _{CO₂} —40 pH—7.40		REJOICE!	

than prednisolone, but there is little data. I am in agreement with Sheehy *et al.* that airway resistance is reduced by steroids "in several hours" (4). This has been shown to be true by the studies of Pinkerton and Van Meter (1).

This brings up the practical consideration that by the time one decides to escalate to steroid therapy one must wait one to two hours for therapeutic effect. One must then give steroids *one or two hours before they are needed*. This is why 250 mg of hydrocortisone is given if the initial gases indicate even slight CO₂ retention instead of awaiting the second set two hours later. Pinkerton and Van Meter (1) could show little difference in the dose response curves of oral and IV steroids. However, in a seriously ill patient who may vomit, the intravenous method is preferable.

Dosage Schedule. As long as the patient is in respiratory distress and the Pa_{CO₂} is 44 mm Hg or above, prednisolone 50 mg should be given every two hours. If the Pa_{CO₂} continues to rise, the dosage should be increased to 100 mg every one to two hours.

Pediatric Dosage. In severe asthma (as defined under "Initial Gases") 7 mg/kg of hydrocortisone should be given as an initial stat dose. Another 7 mg/kg of hydrocortisone may be given during the next 24 hours in divided doses. As is true in adults, there is little specific data to direct prednisone therapy in children within narrow dosage guidelines.

Mucolytic Agents. Hydration with appropriate intravenous fluids and aggressive therapy of asthma are the only two mucolytic techniques of proven benefit. Glyceryl guacolate (Robitussin®) is of proven uselessness and acetylcysteine (Mucomyst®) will provoke asthma. Humidified air can be added to the ventimask if the patient is a mouth breather, but humidity and heat are usually no problem as long as the nose is still in the circuit.

Intubation and Ventilation.

Indications for Intubation. A rising Pa_{CO₂}, above 60 mm Hg, a pH below 7.2, increasing fatigue, increasing somnolence with inability to cough despite the therapy as outlined above are indications for intubation and ventilation.

General Considerations. The use of the cuffed nasotracheal tube has revolutionized the respiratory care of severe asthma. Only in unusual circumstances should tracheostomy have to be done

for asthma. Once nasotracheal intubation is accomplished and the patient is being artificially ventilated, *aggressive therapy must be continued*. Unlike the patient with chronic bronchitis and emphysema, the patient with asthma responds quickly and fairly predictably to therapy (primarily corticosteroids) and can be weaned from the ventilator in 24 to 72 hours. The unfortunate tendency is for the physician to relax following intubation of the patient. Unless the appropriate therapy is continued, weaning from the ventilator can be prolonged by a relapse which increases the possibility that tracheostomy will need to be done.

Plan of Action. The physician should presume that with appropriate therapy and barring serious complications, the patient can be extubated within 48 hours. The first twelve hours that the patient is on the ventilator should *not* be complicated by premature weaning procedures. The fatigued patient should be allowed to rest. His ability to cycle with the ventilator should be enhanced with diazepam (Valium®) or if this is not immediately effective, with 5 to 10 mg of intravenous morphine (given every one to four hours as needed). Obviously the patient cannot be simultaneously sedated for control of ventilation and weaned from the ventilator, although this is frequently tried with disastrous results. Prednisone 100 mg every two hours should be continued during this most important phase of therapy.

Choice of Ventilator. The tendency of a nasotracheal tube to leak, coupled with the extremely high airway pressures (30–60 cm H₂O) necessary to ventilate asthmatics, makes pressure cycled ventilators (Bird or Bennett) poor choices. A volume controlled ventilator such as the Bennett MA-1 or the Emerson postoperative ventilator is usually necessary for effective ventilation of these noncompliant lungs. The MA-1 enables the respiratory care personnel to easily monitor tidal volumes and oxygen percentage of inspired air (FI_{O₂}). Both machines will intermittently and automatically hyperinflate the patient's lungs to reduce atelectasis. Both are dependable machines.

Complications. All of the legion of complications incident to intubation and mechanical ventilation of course can occur. The excellent prognosis for return to normal in these patients should make their recognition and reversal all the more important. Several complications however are more peculiar to the asthmatic.

Pneumothorax. In the pediatric patient, the

extremely high airway pressures needed for ventilation make this a common complication. Insertion of a chest tube with adequate seal is imperative to prevent a tension pneumothorax. This is a rare complication in adults.

Overventilation with Alkalosis. The very nature of the disease makes this complication potentially common and severe. The patient with severe, reversible airway obstruction is connected to an efficient ventilator, and aggressive appropriate therapy is given. Success in therapy will almost always result in hyperventilation, unless blood gases are monitored frequently as the patient improves and the minute ventilation reduced.

Cardiovascular Collapse as Mechanical Ventilation is Begun. This is more common in the patient with emphysema since the high airway pressures are transmitted more readily to the heart through abnormal lung tissue hindering right heart filling. The asthmatic has some protection due to the normal lung parenchyma. However, the combination of high inspiratory airway pressures, hypovolemia, and a short expiration time may rapidly reduce cardiac output even in the asthmatic. The physician must prolong expiration as much as possible relative to inspiratory time, reduce tidal volumes even if CO_2 cannot be lowered initially, and immediately correct the hypovolemic state.

Weaning. Improvement can be judged by a return of the Pa_{CO_2} to normal (30–40 mm Hg) and a reduction in the percentage of oxygen necessary to maintain Pa_{O_2} within a physiologic range (70–100 mm Hg). Reduction in airway obstruction can be monitored by following the “effective compliance” (tidal volume divided by airway pressure expressed as liters/cm H_2O).

If at the end of 12 hours, blood gases and pH are normal and the effective compliance has doubled, sedation should be discontinued and the patient's ventilatory capabilities measured, using a Wright Respirometer. If it can be determined that the tidal volume is greater than 5 cc/kg and the vital capacity greater than 10 cc/kg, a period of time off the ventilator should be monitored with blood gas measurements (arterial puncture 15–30 minutes off ventilator with patient receiving humidified 28–30% O_2 by means of a Briggs T-piece). If the patient is able to maintain a normal or reduced Pa_{CO_2} , extubation should be considered. Alternately this procedure

is repeated every 12 hours or at even shorter intervals depending upon the observed rate of improvement.

Preparing for Discharge. The exciting part of the therapy is now over, and the tendency toward management errors increases. If the reason for the onset of the severe episode of asthma is known and has been corrected (infection, exposure to irritant fumes, resolved psychic trauma) then the steroid dosage can be quickly reduced to 100–200 mg of prednisone given as a single daily dose, then every other day, and finally discharge of the patient on 10 or 20 mg of prednisone every other day. If the cause of the asthma remains unknown, caution will have to be exercised in the rapid reduction of steroids.

Two major facts should be borne in mind: 1) Even large amounts of prednisone (50–100 mg) given as a single early morning dose may be taken by the patient for up to 30 days without significant adrenal suppression. 2) Alternate day prednisone therapy, again a single early morning dose, can be given with little danger of side effects and may be continued for months.

Summary. The successful management of severe asthma involves recognition and aggressive appropriate therapy, with rapid escalation to steroid therapy as soon as indicated. Intubation with a nasotracheal tube and ventilation with a volume controlled mechanical ventilator should be an available option in therapy. Tracheostomy need rarely be done since most patients can be extubated within 72 hours.

REFERENCES

1. PINKERTON, HERMAN H., JR. AND VANMETER, THOMAS E., JR. Immediate therapy for the acute attack of asthma. *New Eng. J. Med.* 258:363–366, 1958.
2. SHEEHY, A. F., DiBENEDETTO, R., LEFFAK, S., AND LYONS, H. A. Treatment of status asthmaticus. *Arch. Int. Med.* 130:37–42, 1972.
3. TABB, W. C. AND GUERRANT, J. L. Life-threatening asthma. *J. Allergy* 42:249–260, 1968.
4. VIA, C. AND HUNT, W. B., JR. The management of severe asthma. (To be published.)

(A more complete bibliography may be obtained by writing Dr. William Hunt.)