

Current Concepts in the Management of the Patient with Status Asthmaticus

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Bronchial asthma continues to be a significantly distressing and frequently fatal disorder. In the general population, it is estimated that there are three million asthmatics with a fatality rate of 4000 to 7000 deaths annually.²³ The natural history of this disease continues to be a problem at the basic biological level and to the clinician. Present-day concepts in management of status asthmaticus will be reviewed in this article.

Definition

Precise definitions are variable, indicating the complex nature of the disease. In general, the syndrome of bronchial asthma is characterized by acute, recurrent, or chronic attacks of bronchial-bronchiolar obstruction, manifested by wheezing and dyspnea, variable in severity and usually of brief duration. Multiple factors such as allergy, air pollution, infection, stress, and psyche may initiate, interact, and intensify the process. Cough and sputum production may be an integral component. The definition of the American Thoracic Society is useful: "Asthma is a disease characterized by an increased responsiveness of the trachea and bronchi to various stimuli and manifested by wide-

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This study was supported in part by grants from the U.S. Public Health Service (National Institutes of Health Training Grant No. 5 TI HE 5654) and The Foundation for Research in Bronchial Asthma and Related Diseases.

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spread narrowing of the airways that changes in severity either spontaneously or as a result of the therapy."¹

Wheezing per se is not pathognomonic of bronchial asthma and the reader is reminded that cardiac failure, tracheobronchial neoplasia, laryngeal disease, foreign bodies, bronchitis, pulmonary emphysema, and pulmonary emboli³⁴ are the more common diseases to be considered in the diagnosis.

Clinical Classification

We find it useful to separate asthmatic patients according to their clinical state. That is, they may be in an acute or chronic state of varying severity. Either may be mild to moderate in intensity and manageable on an ambulatory basis. The extreme, intractable form, status asthmaticus, represents a medical emergency and requires hospitalization for full evaluation and the proper management. The diagnostic inclusion of any "bronchitic" element aids in the clinical understanding and management.

Extrinsic asthma occurs in genetically prone individuals, usually affects younger patients, and is characterized by acute paroxysms of short duration with intervening periods of a normal state. A physiological defect may be demonstrable with pulmonary function studies in the quiescent state.⁴ A family history of allergy is usually present in these patients and a personal history of allergy to drugs, foods, pollens, dusts, and molds can be elicited as well. Positive skin reactions to the offending allergens are frequently found and hyposensitization therapy may prove beneficial in the earliest stages. The overall outlook is good, unless a significant chronic bronchitis complicates the picture.

Intrinsic bronchial asthma occurs in patients having a much less well-defined allergic history and more commonly begins after the age of 35 to 40 years, but may be noted even earlier. Frequently nasal polyposis, sinusitis, and bronchitis may precede or initiate the asthma. These patients usually have a significant bronchitic component, viz., asthmatic bronchitis. Antiallergic therapy is apt to be less beneficial. Their intrinsic course may proceed with lung destruction and carries a graver prognosis. In many cases the intrinsic and extrinsic types of asthma merge, overlap, or remain undetermined.

PATHOPHYSIOLOGY

The basic functional disturbance in bronchial asthma is airway obstruction. The latter is primarily due to bronchospasm, bronchial mucosal edema, secretions, and expiratory ball valving from a redundant pseudopolypoid mucosa which may add further limitation. Allergen-antibody reactions are the stimuli for responses of the smooth muscles, glands and capillaries in such a direction. The release of pharmacologic mediators of bronchospasm such as histamine, acetylcholine, serotonin, or SRS-A (slow-reacting substance from antigen-antibody interaction), etc., further add to the changes in the target organ

augmenting the resistance to normal air flow. With such bronchial obstruction, resistance to air flow increases (dynamic compliance decreases) and a greater transpulmonary pressure is then required to generate a given tidal volume. In particular, the usual passive expiratory phase requires more effort to overcome the mechanical resistance to air flow. This results in a greater work or energy cost of breathing. In addition, under such stresses the respiratory pump itself demands an increased amount of oxygen which must be provided by additional ventilation.

When expiratory forces fail to expel all the inspired air, trapping of air occurs in the lungs and the midposition of the lung will rise. The diaphragm is displaced downward and becomes less efficient. In part, such overinflation (within limits) places the lung in a more advantageous mechanical position to perform work and also tends to increase the diameter of the airways, thus facilitating air flow.

Nevertheless, because of local bronchospasm, edema, and secretions, great variation in gas distribution with nonuniformity of alveolar ventilation will result in ineffective gas exchange. The same processes are responsible for observed decreases in ventilated lung volumes. Because of these pathological factors, the increased respiratory effort will attempt to overventilate relatively normal areas. However, overventilated alveolar units may not compensate for the underventilated alveoli. This will cause defective gas exchange with decreases in mean alveolar oxygen tension (PA_{O_2}) and blood oxygen saturation. Abnormalities in perfusion factors may be a consequence or cause of hypoxemia which in turn may increase pulmonary vascular resistance and decrease the cardiac output.² Carbon dioxide transfer is less affected because of its greater diffusibility, though when sufficient ventilation-perfusion (\dot{V}/\dot{Q}) imbalance occurs, hypercapnea will be seen.

PATHOLOGY

Since the observations of Huber and Koessler in 1922,¹⁷ and more recently of Cardell and Pearson,¹¹ the basic morphological features found in patients with status asthmaticus have been described and include mucosal edema, hypersecretion of a viscous mucus by the bronchial mucous glands and epithelial goblet cells, and smooth muscle contraction.

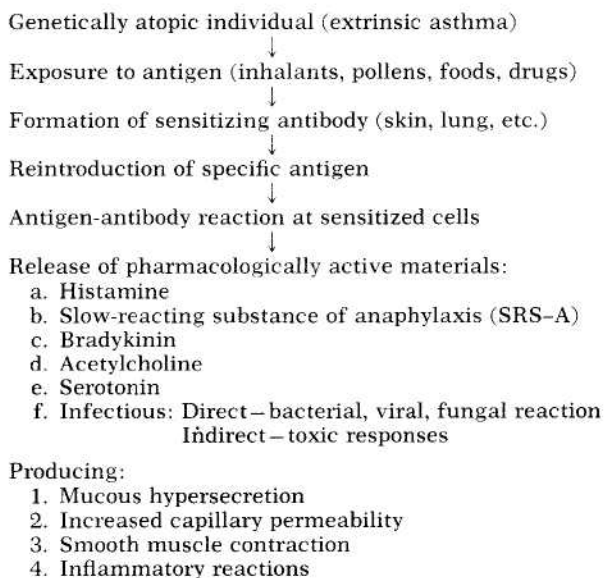
The lungs of patients dying in status asthmaticus at examination show gross overdilatation and do not deflate when the thorax is opened. Widespread tenacious mucous plugs in bronchi and bronchioles with local areas of overinflation and atelectasis are common.¹⁴ Such plugs are intrinsically viscous and adhesive to local structures. They contain PAS-positive material, eosinophils, and Charcot-Leyden crystals (degenerative crystalloids of the eosinophil). Broad detachment of bronchial epithelium has been observed in the sputum of such patients and appears to be lacking in the usual bronchitic patient.²⁴

Actual bronchospasm may be seen with folding of the internal sur-

face of the bronchioles. Often the smooth muscle layer is thickened. Thickening of the entire wall because of edema, inflammatory cell infiltrates (polymorphonuclears, eosinophils, and plasma cells) and prominence of mucous glands and goblet cells are common. Bronchial gland hypertrophy to the extent seen in chronic bronchitis is not described.²⁸ The basement membrane is usually widened and hyalinized. Despite such obstructive findings, the gross hyperinflation destructive features of emphysema due to breakdown of the alveolar septa are absent; however, the alveoli, alveolar ducts, and respiratory bronchioles are generally dilated.

Pulmonary vascular changes in status asthmaticus are difficult to determine. Exposure of asthmatic patients to histamine or specific antigen may cause increases in pulmonary artery pressure and tendency to increased pulmonary vascular resistance.¹⁶ Despite this, chronic cor pulmonale is not common, though electrocardiographic evidence of acute right heart strain may be observed.

It is generally accepted that a genetic predisposition exists but the evidence for a clear-cut immunologic mechanism is not convincing. The chemical basis for genetic and immune considerations has recently been reviewed by Middleton.²¹ A simplified scheme is presented below:



One may conclude that the exact nature of the sensitizing immunoglobulins, the target cells, and the pharmacological mediators of bronchial asthma in humans has not been firmly established.

TREATMENT OF STATUS ASTHMATICUS

Status asthmaticus may be defined as a state of continuous intractable asthma refractory to usual therapy. Presentation in a state of

extreme physiologic stress, including hypoxia, dehydration, anxiety, fear, and vascular alterations, makes the management of such patients a challenge to the physician.

Precipitating Factors

Successful management requires careful consideration of the various responsible factors and the patient's psychologic profile. Removal of the offending allergens and a trial with hyposensitization therapy should be instituted whenever indicated. Because search for the responsible agents is difficult and often completely unsuccessful, emphasis on the allergic approach to management should not exclude physiologic therapy.

The following precipitating factors may be responsible for the acute deterioration into the status state and should be evaluated and dealt with for therapy to be successful:

- | | |
|-------------------------------|---|
| 1. <i>Infection:</i> | Viruses, bacteria, fungi (bronchitis, pneumonia) |
| 2. <i>Allergic Factors:</i> | Pollens, animal danders, dusts, foods, drugs |
| 3. <i>Irritative Factors:</i> | Dusts, fumes, smoke (air pollutants) |
| 4. <i>Trigger Mechanisms:</i> | Sinobronchitic disease, nasal polypi, otitis media, weather changes |
| 5. <i>Emotional:</i> | Stress, fatigue |

The Airway

It is absolutely essential that a patent tracheobronchial airway be maintained at all times. Those patients capable of raising their own secretions can be managed as such. Those who are severely obstructed or poorly cooperative will have to be considered for supportive measures, endotracheal intubation, or tracheostomy. Bronchoscopy may be considered first in those patients who appear critically ill and unable to evacuate their own secretions. If done early and successfully, a tracheostomy may be avoided. Appropriate endoscopic lavage with warm isotonic saline, acetylcysteine (Mucomyst), or pancreatic dornase (Dornavac) may be lifesaving. Similarly, in any patient receiving full and appropriate inhalation therapy but deteriorating because of persistent and tenacious sputum, therapeutic bronchoscopy and lavage are indicated. The patient should always be well oxygenated during the procedure. Bronchoscopy with lavage facilitates the aspiration of trapped secretions, improves drainage, and may help restore an effective cough mechanism. A word of caution: in patients with underlying bronchospastic diseases, Mucomyst may prove irritating and actually produce bronchoconstriction. Its greatest effectiveness has been observed in the form of tracheobronchial lavage therapy through the bronchoscope or tracheostomy tube, though the percutaneous trans-tracheal route may be used. An endotracheal tube may be employed for short periods to maintain a patent airway for adequate ventilation and suctioning procedures. In some cases a tracheostomy will be required as an initial step or if a prolonged artificial airway is required.

Tracheostomy is frequently necessary and lifesaving to facilitate the removal of secretions, decrease the dead space, prevent further

hypoventilation, and provide a route for continuous ventilation as well as endoscopic therapy.³¹ It is best done in an unhurried manner in the operating room. Under emergency conditions, when performed at the bedside, the complication rate has been very high. Prior to tracheostomy, a cuffed endotracheal tube may be employed to insure ventilation and facilitate suctioning. This tube may be inserted nasally into the trachea and requires assiduous attention in order to prevent mucosal and laryngeal damage.

Once the tracheostomy is established an inflatable cuff should be fitted snugly around the end of the tube. It should be deflated for at least one minute every half hour in patients on continuous ventilation with an IPPB attachment. Frequent replacement of the tube, deflation of the balloon, cleansing of debris, and strict aseptic techniques are mandatory for the successful application of this technique. Local or tracheal infections may result quickly in the traumatized area, the organism varying with hospital environment. Isolation technique may be useful in halting the spread of offending staphylococci or gram-negative organisms.¹⁵ The presence of bacteria in tracheal secretions requires clinical evaluation as to the need for antimicrobial therapy. With proper use, prolonged endotracheal tubation alone has been employed for as long as one week without deleterious effects; however, it is not generally recommended for more than 24 to 48 hours. On the other hand, if mechanical ventilation is to continue for longer periods a tracheostomy should be performed and a cuffed tracheostomy tube inserted. It is essential that adequate humidification of the lower airway be provided at all times in these patients. Heated water aerosols should be nebulized in conjunction with IPPB, and bronchodilator aerosols (isoproterenol [Isuprel] or Vaponephrin) should be used intermittently when indicated. The patient receiving continuous ventilation must be checked frequently to see that no leaks are present, a patent airway exists, and adequate tidal volumes are maintained at all times.

SPECIFIC MEASURES

Tracheobronchial "Catharsis"

Whether the patient is being managed with or without an artificial upper airway, appropriate attention to secretions is necessary. There are two basic types of sputum, each requiring its own type of management. Muroid sputum is white, gelatinous, and adhesive due to mucopolysaccharide and mucoprotein gels. Clinical observation suggests that the more water the gel contains, the less viscid are the secretions; conversely, when water is lost through dehydration, its viscosity increases. Muroid sputum may be quite troublesome because of its greater viscosity and the fact that it cannot be altered by antibiotics. Mucomyst (N-acetylcysteine), by opening disulfide bonds in mucus, tends to lessen its viscosity and thereby facilitate removal.

On the other hand, purulent sputum consists of fibers of deoxyribonucleic acid (DNA) from necrotic parenchymal and inflammatory cell nuclei. Large volumes of such material with increased viscous and

adhesive properties may be generated by an infectious process. Pancreatic dornase (Dornavac), a pancreatic enzyme, may be employed for enzymatic degradation of DNA and assist removal of lodged and inspissated material. Finally, if both types of components are present, combination therapy should be employed. Mucomyst, in the form of a 20 per cent solution, may be directly instilled and aspirated through the tracheostomy tube or at the time of bronchoscopy. Dornavac (50,000 units, q.i.d.) may be directly instilled or aerosolized.

Adequate hydration by oral and/or intravenous routes is most essential in liquefying the secretions. Aerosols of saline (normal or slightly hypertonic) employing aerosol generators equipped with heating coils, such as the Puriton or Mistogen units, powered by air or oxygen, may be directed into the IPPB unit or into the tracheostomy. The detergent Alevaire seems to be effective only by virtue of its water content and is not generally recommended.

The use of iodides either orally or intravenously (1 to 2 grams NaI per liter) may help to raise trapped and thickened secretions, presumably by dilution and liquefaction of such retained materials. A disagreeable metallic, bitter taste is commonly experienced. Side effects include rashes, conjunctivitis, bronchorrhea, and adenopathy. A preliminary test for idiosyncrasy (0.1 cc. of saturated solution of potassium iodide by mouth) should be made on all asthmatic patients who are to receive iodides in any form. Glyceryl guaiacolate (Robitussin), in doses of 400 to 600 mg. q.i.d. (20 cc. of preparation), is also efficacious and particularly valuable in cases of iodide sensitivity. On occasion, the use of one of the "cough machines" (alternating positive-negative pressures) may dramatically help move trapped secretions outward. All of these measures improve bronchopulmonary drainage. However, suctioning techniques must be employed to evacuate the loosened secretions in patients who are unable to raise them because of loss of effective cough mechanisms. The patient may literally drown in his secretions if effective suctioning is not undertaken, particularly when debilitated or semi-conscious.

There are several ancillary measures which may aid in tracheobronchial catharsis: (a) *Ipecac* may prove valuable by substituting effective retching for ineffective coughing. The syrup may be given in doses of 2 teaspoonfuls followed by a cup of lukewarm water. (b) *Postural drainage* may be of benefit to those patients whose sputum is liquefied, and who can cooperate—even those whose cough is somewhat depressed. With the patient properly positioned to utilize the forces of gravity, followed by chest tapping, trapped secretions may be liberated and effective bronchial catharsis may follow. (c) *Antitussives*. Coughing paroxysms in certain patients may be trigger mechanisms for inducing bronchospastic crises, expiratory ball valving and possible alveolar destruction. At no time should an effective, productive cough be eliminated. However, taking the edge off such an irritating cough may be beneficial, particularly at night when sleep is essential. Chlorphedianol hydrochloride (Ulo), codeine preparations, and pipazethate (Theratuss) are antitussive agents which may be prescribed.

Bronchodilators

Bronchodilator agents are an integral aspect of management. The following agents may be useful.

AMINOPHYLLINE. Preferably by intravenous route, 250 to 500 mg. may be given stat. This may be followed by continuous infusion of 500 to 750 mg./L. of 5 per cent dextrose and water preferably not to exceed 1.5 to 2.0 grams per day. Aminophylline may be given rectally, as a retention enema, in similar doses when the patient has improved sufficiently to omit the intravenous infusions. The oral route and suppositories are not recommended. Side effects include nausea, diaphoresis, hypotension, and palpitations.

ISOPROTERENOL. This preparation may be administered via commercial Freon propelled inhalers, nebulizer, or IPPB. With the latter, one employs 0.5 cc. of a 1:200 solution with 2 cc. saline in the nebulizer. Precautions as with epinephrine should be observed.

EPINEPHRINE. Subcutaneous injections of 0.3 cc. of a 1:1000 aqueous solution may be repeated at 30-minute intervals whenever indicated. Injections of subcutaneous Susphrine suspension (0.2 cc. to 1:200) are preferable and may last up to four hours. Precautions should be taken with cardiac, hypertensive, or cerebrovascular prone patients. The intravenous route should not be employed. Aerosols of Vaponephrine 2.25 per cent solution nebulized or administered via IPPB (0.2 to 0.5 cc. with 2 cc. saline) may be employed. Epinephrine refractoriness may be seen with repeated use and may possibly be related to a coexistent acidosis. The use of sodium bicarbonate may correct such an acidosis and relieve the reduced responses, as suggested by Mithoefer.²²

HEPARIN. Reports have indicated that heparin reduces airway resistance in asthma, but the exact mechanism remains unclear.⁸ Prompt relief by intravenous heparin has been observed in some cases of acute attacks of bronchial asthma. Some of these patients may have had pulmonary emboli, with wheezing as a manifestation. Further data are needed, but heparin could be considered in difficult clinical situations or when emboli are a possible contributory factor.

ATROPINE AND RELATED BELLADONNA ALKALOIDS. These preparations may be considered particularly in "wet" asthmatics if above agents fail. They are generally less potent than the sympathomimetic amines, act as bronchodilators, but also have a drying action on mucous membranes which should be avoided to prevent inspissation of residual secretions. Atropine sulfate 0.5 mg. may be given orally, subcutaneously, or preferably as an aerosol with Dylephrin (2.5 per cent racemic epinephrine and 0.5 gm. atropine sulfate).

IMMUNOSUPPRESSIVE DRUGS. Antimetabolic agents such as 6-mercaptopurine, nitrogen mustards, and azathioprine have been employed in the therapy of refractory asthma. Improvement has been noted in some cases, poor responses in others. Existing data indicate further study in order to place such an approach into proper perspective.^{3, 12}

Steroids

With seriously ill patients or those who are not responding to the

usual therapeutic measures, the use of adrenal corticosteroids is recommended. The reduction in mucosal edema, inflammatory reaction, epithelial desquamation, and mucous gland activity may produce a dramatic reduction in associated airway obstruction. In the critical status state, 100 to 200 mg. of hydrocortisone should be given immediately, intravenously, followed by approximately 300 mg. in 5 per cent dextrose in water or normal saline, employing flow rates of 30 drops per minute, with total volumes of 2 to 3 liters in 24 hours. Aminophylline in doses of 0.25 to 0.5 gm./L. may be added. With cardiac failure or other fluid retentive states, the volume of intravenous fluids should be appropriately reduced. When improvement is noted, the doses may be tapered. If more prolonged steroid therapy is required, the use of alternate day scheduling of oral prednisolone with the total dosage administered in the morning may reduce undesirable side effects, such as occult and overt peptic ulceration with gastrointestinal hemorrhage, intensification of underlying diabetes mellitus, hypocalcemia, progressive osteoporosis, psychosis, fluid retention, hypertension, risk of associated infections, spread of a tuberculous process, and other steroid stigmata.

The use of supplemental potassium, regulation of sodium intake, adequate protein intake, antacid therapy, monitoring of blood sugar, electrolytes, and bone films will aid in the appropriate management, particularly with continuous steroid therapy. Specific recommendations for withdrawal of steroids have recently been reviewed by Thorn.³³ There has been some suspicion that corticosteroids may contribute to therapeutic failures in asthma.¹⁸ Such impressions may be valid; however, conditions of analysis were poorly defined and it does not appear that severe cases are more at risk when treated with corticosteroids.²⁶ The importance of such observations at least is to stress the necessary care during such therapy and avoidance of adrenal hypofunction during withdrawal.

Oxygen

Normal oxygen tensions should be maintained in a case of status asthmaticus. Hypoxia may cause increased pulmonary vascular resistance with pulmonary hypertension and contribute indirectly to cardiac decompensation or directly by influencing normal myocardial metabolism. In addition, anoxic encephalopathy with mental impairment, metabolic effects upon oxygen-dependent enzyme systems, and reduced respiratory responses to increase in CO_2 tensions which may contribute to ventilatory failure, all may be the result of hypoxemia. Significant in management is that irreversible changes in the brain follow 3 to 5 minutes of complete anoxia.

For routine use the double-pronged, plastic nasal cannula may deliver oxygen concentrations up to 35 per cent in the inspired air at valve outlet with flow rates of 6 to 8 L./min.; the Eliot open-face tent will provide concentrations of 35 to 50 per cent with 6 to 10 L./min. flow rates. If higher concentrations are required, one may employ a comfortably fitting but well-sealed rubber face mask with a nonrebreathing valve to eliminate CO_2 . With the endotracheal tube or tracheostomy, an IPPB unit may be attached with appropriate adjustment of oxygen

Table 1. *Comparison of Oxygen Administration*¹⁹

	Approximate Per Cent O ₂ at Alveolar Level	L./min. Flow of O ₂ Required	CO ₂ Accumulation (at 8 L. O ₂ Flow)
Rubber oronasal mask (BLB)	40	4	Yes
(OEM)	50	6	
	55	8	
	60	10	
Plastic face mask	30	4	No
Nasal catheter	40	5	
Face tent	45	8	
Nasal cannula	50	10	
O ₂ tent	25	6	No
	35	10	
	43	15	

input. A soft plastic tracheostomy box should be used in the tracheostomy patient not requiring IPPB with oxygen flowing through a water aerosol chamber warmed to body temperature (Puritan Unit). It is mandatory in oxygen therapy that the gas be adequately humidified at all times to prevent drying of secretions or irritative bronchitis. Table 1 provides comparison of O₂ administration.

In the patient with chronic hypercapnea, oxygen depression of the carotid-aortic chemoreflex centers must be avoided. However, such patients are usually severely hypoxic and desperately in need of oxygen. Low concentrations of oxygen, 2 to 4 L./min., employing the plastic nasal cannula may be initiated and the patient observed. It should be emphasized that oxygen must be given in states of advanced hypoxia and, if depression of respiration ensues, adequate ventilation along with oxygen therapy must be provided by the physician.

Helium-Oxygen Mixtures

The rationale for such therapy is based on the lower specific gravity of helium which allows for less flow resistance through compromised orifices, at about 50 per cent less effort compared with air. For clinical use, mixtures of 70 to 75 per cent helium balanced with oxygen may be administered with the closed metered expiratory positive pressure mask (O.E.M.) or Hood devices with expiratory positive pressure breathing, IPPB unit or directly into the endotracheal tube or tracheostomy tube.²⁹ Reduction in the work of breathing, lessening of cyanosis, dyspnea, and wheezing, and restoration of confidence of the critically ill patient may be observed with this technique. Unfortunately, it is too costly for routine use.

Adequate Alveolar Ventilation

In addition to careful physical evaluation of the status asthmaticus patient, it is necessary to find whether alveolar ventilation (\dot{V}_A) is ade-

quate. This means that the patient is well oxygenated and carbon dioxide is properly eliminated. Estimation of V_A based on actual tidal volumes and body weight may be in serious error, as may be the use of nomograms (Radford, Ohio) to determine the advisable tidal volumes necessary to maintain adequate alveolar volume. This is because compliance-resistance factors, variable metabolic demands, alterations in perfusion, and increased physiologic dead space ventilation may be present and offset such predictions.²⁷

While alveolar ventilation can be measured more accurately by expired and alveolar P_{CO_2} values, this time-consuming procedure is generally unnecessary. The use of an end-tidal sampler or rebreathing apparatus can provide data on alveolar, and thereby arterial, CO_2 tensions. "Arterialized" hand venous blood, obtained by warming the hand or arm for ten minutes, may be used for P_{O_2} and P_{CO_2} tensions as an index of ventilatory adequacy. In practice, the direct measurement of arterial blood for P_{CO_2} , P_{O_2} and pH is the simplest method of assessing alveolar ventilation. In this manner, while the above-mentioned variables tending to influence alveolar ventilation may not be absolutely clarified, the end result of the ventilatory process may be established by these blood-gas measurements. In general, Pa_{O_2} of 60 mm.Hg or less, a Pa_{CO_2} of 60 mm.Hg or more, and a pH of 7.25 to 7.30 should be considered conclusive of ventilatory failure at the alveolar level, unless previously established data indicate that such values were present during a chronic stable phase.

If the only abnormality is a decrease in Pa_{O_2} and the patient can tolerate oxygen administration without respiratory depression, this is all that is required. If respiratory depression occurs on such therapy or if advanced hypercapnea is present which is not responding to supportive measures (aminophylline, bronchodilators, removal of secretions, etc.) then adequate alveolar ventilation must be provided by other means.

Providing Adequate Alveolar Ventilation

This may be accomplished in numerous ways: by manual compression of a rebreathing bag in a closed or open circuit system; by use of a tank respirator; by the use of complicated, electromechanical devices that supply variable amplitudes and frequencies of respiration automatically responding to signals from servo mechanisms (activated by the arterial blood gases and pH and the circulation-pulse rate, arterial and venous pressures); by use of volume-cycled instruments (Engstrom) or by the use of pressure-cycled (IPPB) units. Commonly, long-term ventilation with IPPB is employed to provide ventilatory assistance in maintaining adequate alveolar ventilation. No attempts should be made to ventilate a patient continuously for long periods by face mask or mouthpiece. The endotracheal tube or tracheostomy techniques must be employed in these patients as described above.

Once a patient is connected to the ventilator, appropriate tidal volumes (450 to 600 cc.) should be established. The effectiveness of the selected minute volume must be checked by P_{O_2} and P_{CO_2} determinations

to prevent either hyperventilation or hypoventilation. Hyperventilation in patients with respiratory acidosis may cause respiratory alkalosis which may lead to seizures or circulatory collapse.

The usual type of IPPB ventilation is that triggered by the patient's inspiratory effort and is called *assisted ventilation*. The latter may be run periodically or continuously, depending upon the clinical status and the ability of the patient to cooperate. Intermittent positive pressure breathing therapy, with bronchodilator aerosols, is most effective for periodic-assisted breathing for periods of 15 to 20 minutes, four to six times a day. The effect of hyperventilation with IPPB therapy is transient, and sustained lowering of elevated carbon dioxide levels cannot be accomplished by brief periodic treatments. Some improvement in the patient being treated with IPPB may be due to an effective delivery of a bronchodilator aerosol that relieves bronchoconstriction and improves expectoration. It is not uncommon in comatose patients to lower the P_{CO_2} , and correct the pH, and still observe the coma state.³⁰

In general, *assisted mechanical breathing* is employed in the moderately ill patient, whereas *controlled mechanical breathing* with IPPB is employed in the critically ill patient.²⁵ Patients who cannot maintain effective ventilation or acid-base balance by means of assisted ventilation or those who are uncooperative should be placed on controlled ventilation until a more compensated phase of the disease occurs which is responsive to assisted breathing. Controlled mechanical breathing may be performed with the endotracheal tube technique for brief periods, or with the tracheostomy for longer periods, and may require the use of meperidine (Demerol), morphine, or curare derivatives (e.g., succinylcholine) to slow or completely suppress spontaneous respiration. The latter procedure must be undertaken with constant control, established airway, and monitoring of serial blood-gas data.

An example of drug control of respiration is given in the following case report:

A 35-year-old white man was admitted to the Boston City Hospital with a history of chronic asthmatic bronchitis and a recent increase in productive cough, wheeze, and dyspnea. The deterioration was due to bronchopulmonary infection and related airway obstruction. Initial therapy consisted of intravenous fluids, aminophylline, iodides, penicillin (on basis of sputum Gram stain), Methylprednisolone sodium succinate (Solu-Medrol) and IPPB via assisted (mask) ventilation with nebulized isoproterenol (Isuprel) and 40 per cent oxygen. Blood gases at admission are noted (Table 2). Early the next day, progressive bronchospasm and retention of secretions were associated with severe agitation, confusion and poor cooperation for IPPB. Tracheostomy was performed and assisted ventilation with a Bird Respirator was begun. Blood gases under these conditions are recorded in the table.

Consultation with the Lung Station (Tufts) group was called because of obvious clinical deterioration and blood-gas evidence of inadequate ventilatory support by assisted ventilation. This was limited because of severe motor agitation and extreme uncooperation, even with high pressures and flow rates on the IPPB. Ten milligrams of morphine sulfate was then given intravenously with only moderate respiratory depression and persistence of motor agitation. Because of this, 40 mg. of succinylcholine was given intravenously, resulting in complete apnea. Controlled machine ventilation with a preset tidal volume,

pressure, and rate was begun. The findings from blood-gas monitoring over the next few hours are recorded in the table. With continued careful management of bronchospasm and secretions, clinical improvement was noted. When semi-awake 6 hours later, the patient was able to cooperate fully on an assisted-ventilatory schedule. Complete recovery was noted thereafter.

Table 2. *An Example of Drug Control of Respiration*

ADMISSION — ASSISTED IPPB		NEXT DAY — ASSISTED ON TRACHEOSTOMY		CONTROLLED VENTILATION (hours after No. 2)					
		No. 1	No. 2 (one hour later)	1.45	2.50	4.00	5.50	next day	
P_{aCO_2} mm.Hg	41	57	87	71	71	58	46	46	
pH	7.40	7.31	7.15	7.18	7.19	7.27	7.26	7.46	
P_{aO_2} mm.Hg	56	38	173	250	168	245	101	—	
Tidal Volume (cc.)	220	—	350	500	550	450	400	400	
Respir- atory rate (per min.)	30		34	18	18	16	16	14	

It is advisable to have brief alternate rest periods during assisted IPPB therapy. Repeated overdistention of the lungs may depress the Herring-Breuer reflex and reduce the effective ventilatory drive. Again, with continuous assisted or controlled IPPB therapy, tidal volume should be measured periodically through the exhalation port with a Wright respirometer or a similar device so that adequate minute ventilation is provided. However, an arterial blood sample for P_{CO_2} , and P_{O_2} , and pH should be obtained to provide a more reliable index of artificial ventilatory support. For example, a patient with an initial tidal volume of 500 cc. at 15 cm. H_2O pressure on the IPPB unit might, as secretions collect and pulmonary compliance changes (stiffer lung) after a few hours, have a tidal volume of 200 cc. and yet the pressure setting on the IPPB unit would still remain at 15 cm. of water. The IPPB pressure setting should be the minimum that will provide adequate ventilation. This may require adjustment of flow and rate valves to achieve good tidal volumes. Leaks may develop around the tracheostomy tube and machine, compensation may not follow (unless the machine is fitted with flow accelerative adaptors or volume-cycled instruments) and hence, inadequate tidal volumes will be delivered. This requires immediate attention. Assiduous nursing care and careful monitoring of equipment throughout are mandatory.

Finally, patients with long-term hypoxia and severe carbon dioxide retention may have respiratory depression when on assisted or continuous IPPB when high concentrations of oxygen are employed. In these patients, concentrations of 30 to 40 per cent are usually adequate. If respiratory depression does occur, controlled ventilation with an automatic cycle will be necessary.

Therapy of Associated Acidosis

On occasion seriously ill patients with status asthmaticus have respiratory acidosis as a complicating aspect. When this is present and severe, therapy should be directed to improving alveolar ventilation and thereby reducing P_{aCO_2} . Generally, if the pH is less than 7.20, one is justified in employing $NaHCO_3$, titrating to end point pH by serial blood determinations. Both improvement in myocardial function and enhanced catecholamine responsiveness may be anticipated.⁶

The extent to which complicating metabolic acidosis or alkalosis may be playing a role in such disorders needs clarification for intelligent management, e.g., a respiratory acidosis plus a metabolic acidosis. To evaluate properly the degree and origin of complicating abnormality, one must know how much pH change to expect for a given increment of P_{CO_2} . The work of Schwartz^{9, 32} has defined the acute titration curve for man and this may be useful in interpreting changes in a previously normal patient. Similar chronic "predicted" responses in dogs and in man may be used to make similar assessments of associated metabolic disorders in patients with chronic lung disease.¹³ Often, however, the clinical reconstruction of the metabolic state is the only available method to derive a working concept of the acid-base disorder in a given case in conjunction with measurement of P_{CO_2} , pH, bicarbonate, and other pertinent electrolyte-renal parameters.

The above can be best illustrated by reference to the previously discussed patient in Table 2.

The pH and equivalent nanomoles (nM) and the P_{CO_2} data of this case of asthmatic bronchitis in ventilatory failure are shown in Figure 1. Note that in the initial decompensation phase, P_{CO_2} + pH relationships fall within the predicted band established by Schwartz. This would

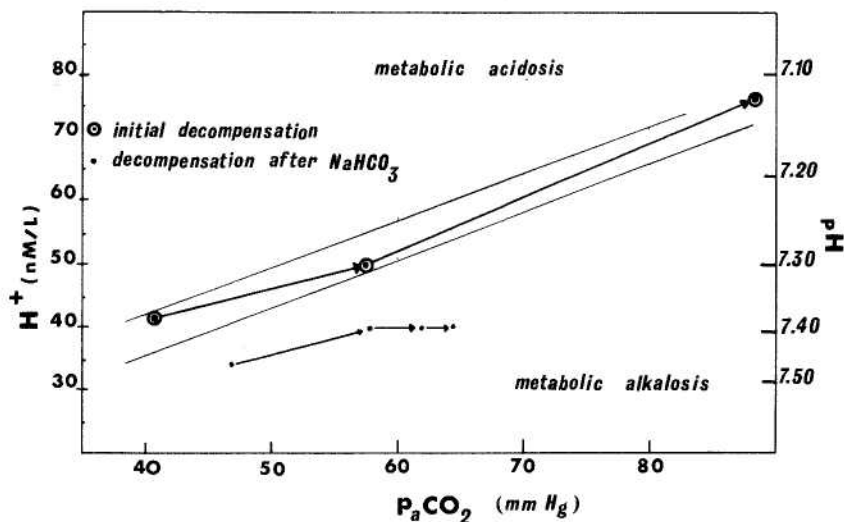


Figure 1. Pertinent acid-base data in a case of asthmatic bronchitis in ventilatory failure (see text).

indicate that the developing acidosis was entirely respiratory in basis. Several days later the patient was given sodium bicarbonate; a milder second ventilatory decompensation then occurred. The relationships are shifted toward the alkalotic side of the normal band indicating, as was known, the presence of a complicating metabolic alkalosis. In practice, then, complicating metabolic factors may be evaluated by the use of such a nomogram.

Sedation

Moderate sedation has always been considered an important aspect of treatment, since fear, anxiety, and agitation may contribute to the therapeutic problems. Most patients with acidosis and pH 7.20 will be poorly responsive or comatose and no sedative is required. The use of barbiturates, tranquilizers, and even opiates may be beneficial, though the degree to which such agents may depress respirations may not be fully realized, particularly in the patient with ventilatory insufficiency. The quiet patient is not always a better patient and, while auscultation may show much less wheezing, the concomitant decrease in breath sounds may indicate poor ventilation and significant lodging of secretions. The absence of obvious respiratory distress under sedation may be *misinterpreted* by the physician as the patient actually deteriorates. Therefore, potential respiratory depression and ineffective alveolar ventilation should be checked by clinical and arterial blood-gas analysis whenever these agents are employed. In addition, any drug which suppresses a "useful" cough or dries up secretions should be avoided.

Ether by rectum²⁰ or general anesthesia⁷ may be considered in those patients who become progressively unresponsive. Ether anesthesia by inhalation or by rectum and cyclopropane anesthesia have been reported to provide relief of persistent attacks, by mechanisms not entirely clear other than general relaxation. Concomitant bronchoscopic lavage may be performed at the time of anesthesia. Adequate ventilation should be insured to prevent atelectasis and blood-gas alterations. Cyclopropane may occasionally precipitate a ventricular arrhythmia (possibly potentiated by prior use of epinephrine) and must be used with great caution in hypoxic patients. Ether used to the stage of light anesthesia is preferred by many physicians. It may be administered rectally in doses of 60 to 90 cc. dissolved in equal amount of olive oil. This may be repeated after several hours.

Paraldehyde may be used rectally as an amnestic or hypnotic agent in doses of 20 to 30 cc. mixed with an equal volume of olive oil. It may also stimulate cough and loosen secretions, and may be repeated in 12 hours. It is generally poorly tolerated orally and should not be administered intravenously or intramuscularly.

Therapy of Infections

Viral or bacterial infections of the respiratory tract may precipitate or aggravate status asthmaticus. Since such bacterial complications may be present, one is justified in giving an antibiotic when clinically indicated. In practice a Gram stain of the sputum is used to ascertain

the types of organisms present. Antibiotic choice is based initially on such findings with necessary modifications once culture and sensitivities are repeated. Follow-up evaluation of the sputum is necessary in the event of significant changes in flora. It is important that this initial decision be based upon an adequate sputum specimen. We decide this by use of a crystal violet stain in which the presence of bronchial epithelial cells, macrophages (particularly dust-containing cells with a minimum of oral squamous cells) suggests a representative bronchial specimen. The presence of tuberculous or fungal lesions as precipitating causes must be kept in mind, though their exact role is not well defined. Each patient should be screened for sensitivity to the selected antibiotic, as hypersensitivity to such an agent may be responsible for unyielding bronchospasm. The possibility that extrapulmonary infections such as paranasal sinusitis are responsible for the asthmatic state should always prompt a search for associated paranasal sinus infections, etc.

The Antihistamines

On theoretical grounds, the antihistamine drugs with chemical structures similar to histamine that allow for competitive inhibition at receptor sites should thereby inhibit bronchial smooth muscle contraction induced by the offending antigen. Experimentally such inhibitions are usually slight¹⁰ and in practice these drugs are generally inefficient. However, in certain cases, they seem of value and are worth a trial. Beneficial side effects include sedation and possible potentiation of epinephrine; detrimental effects include atropine-like effect with drying of secretions. Chlorpheniramine (Chlor-Trimeton) 4.0 mg., t.i.d., diphenhydramine (Benadryl) in divided doses up to 200 mg., q.d., or promethazine (Phenergan) 12.5 mg., b.i.d. or t.i.d., may be employed as initial doses and may be increased as indicated.

SUMMARY

Status asthmaticus is a medical emergency requiring an intensive multidisciplinary approach by the physician. Evaluation of background disease, precipitating factors, and extent of physiological impairment is necessary for appropriate management. The importance of establishing an airway, removing secretions, providing adequate ventilatory exchange, and use of pharmacologic agents has been stressed. Didactic, defined approaches are difficult to establish and each physician aware of the complexity of the disease and therapeutic modalities must learn his own approach. While basic measures should be observed, each particular case will require a personalized program to obtain the optimum result.

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