Resuscitation of the moribund asthmatic

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THE asthmatic attack which fails to respond to adrenaline and aminophylline will, in most cases, settle with treatment which includes high doses of corticosteroids (above 60 mg of prednisolone) and antibiotics. Occasionally, in spite of these measures, remission is delayed, the condition of the patient deteriorates and, when the attack is prolonged, death may occur (Witts, 1936). Autopsy in such cases reveals a characteristic pathology (Huber & Koessler, 1922). There is widespread plugging of the bronchi

abnormal mucus production (Williams, 1953), while Houston, de Navasquez & Trounce (1953) suggested that constriction of the medium-sized bronchi is a causal factor in mucosal shedding. Whatever the basic fault, we believe that dehydration and drying of bronchial secretions are important factors in promoting the inspissation of mucus. Dehydration is the result of excessive water loss from sweating combined with the patient's inability to drink adequately due to the intense breathlessness. Drying

FIG. 1. A bronchus filled with a plug of mucus in which inflammatory and mucosal epithelial cells are enmeshed.

with inspissated bronchial secretions and shed mucosal epithelium (Fig. 1). The lungs are hyper-distended with air and may show areas of collapse. Sections of the lung show that the alveoli are distended but their walls are not thickened or destroyed (Fig. 2). Fig. 3 demonstrates patchy atelectasis.

The objective of early medical treatment should be to prevent the formation of widespread plugging. The mechanism of plug formation is unknown although infection has been cited as a cause of

of secretions is aided by mouth breathing and by the use of aerosols containing atropine. The benefits of humidifying the inspired atmosphere, and, in particular, the use of water and isoprenaline nebulized from a Bird ventilator, cannot be over-estimated.

When widespread plugging has developed, the prognosis is grave. The enormous work of breathing leads to exhaustion, coughing becomes more ineffective, further retention of secretions occurs and with increasing hypoxaemia and hypercarbia, the

FIG. 2. Emphysema with increase in the average diameter of the alveoli.

FIG. 3. Focal areas of collapse.

patient slips into coma and ultimately dies. This tragic progression of events may be hastened by uncontrolled oxygen therapy (Beale *et al.*, 1951) or sedation (Walton, Penner & Wilt, 1951). Another feature of this stage of the illness is acute cor pulmonale (Ambiavagar, Jones & Roberts, 1967b) and

a sudden unexpected cardiac arrest may occur (Sieker & Hickam, 1956).

During the period 1962–66, twenty-two adult patients, seventeen of whom were women, were treated by intermittent positive pressure ventilation (IPPV) in the Intensive Care Unit at Whiston

Hospital. Four patients were treated twice. Two patients were resuscitated from cardiac arrest and eight others were in coma. Two were drowsy and became unconscious after breathing pure oxygen for about 15 min. Systemic hypotension was present in

danger signs. Abdominal distension was a constant finding and paralytic ileus was present in a few. The gastric aspirate was copious and resembled that found in acute gastric dilatation. There was always a tachycardia of between 120 and 180 a minute, a

TABLE 1
Summary of arterial blood gas findings on admission and after 24 hr IPPV

Tension on admission			Tension after 24 hr IPPV	
Mean PCO ₂ (mmHg)	Mean PO ₂ (mmHg)		Mean PCO ₂ (mmHg)	Mean PO ₂ (mmHg)
	Air	Oxygen		
73	48	203	50	250
n = 14	n = 12	n = 7	n = 9	n = 9
R = 40-120	R = 35-70	R = 76-345	R = 35-80	R = 76-448

Hypoxaemia was corrected but hyperventilation was not produced.
n = Number of observations. R = Range.

FIG. 4. The ECG in acute asthma showing sinus tachycardia, P pulmonale, a mean frontal P wave axis of +140 degrees, S in leads 2 and 3, dominant R in aVR, and extreme clockwise rotation (rS pattern in lead V₆). (C.M., 20 April 1965.)

five, while in six the blood pressure was above 160/90. Cyanosis, sweating and ineffective cough were features in all cases. Decrease in wheeze with increase in breathlessness and reduction in tidal volume occurred in some and are to be regarded as

paradoxical radial pulse sometimes with complete obliteration during inspiration, visible and palpable epigastric pulsation and a triple cardiac rhythm. Analysis of arterial blood gases showed hypoxaemia, when the patients were breathing air, and

FIG. 5. The chest X-ray: (a) At the start of IPPV showing hyperdistension of the thorax, depression of the diaphragm and a narrow cardiac silhouette, the superior vena cava shadow is absent. (b) After 36 hr of IPPV showing a reduction in thoracic distension and an increase in the transverse diameter of the heart, the SVC shadow is still not visible. In most cases the SVC shadow becomes visible during the 4th and 5th day.

hypercarbia in all but two cases (Table 1). The electrocardiograms showed changes of acute cor pulmonale (Fig. 4) and variation in voltage with

TABLE 2
Summary of the major ECG abnormalities

Common ECG abnormalities	On admission (%)	On recovery (%)
1. Tachycardia (120/min or more)	80	0
2. A P + 90° or more	66	0
3. Abnormal P waves		
(i) Pulmonale	46	0
(ii) Gothic	46	10
4. S waves in standard leads	60	20
5. Q in lead 3	26	20
6. S equal to or greater than R in V ₅	54	0
7. ST depression in standard leads 2 and 3	40	0
8. T wave flattening or inversion in standard leads	66	0
9. A QRS + 90° or more	53	0

respiration. Table 2 summarizes the major ECG abnormalities. X-rays of the chest showed marked hyperdistension of the thorax, increased trans-

radiancy of the lungs, depression and flattening of the diaphragms and a narrow cardiac silhouette which in some instances was only just wider than the vertebral column. The superior vena cava shadow was absent in over one-third (Fig. 5a).

Techniques of resuscitation

The patients who presented with coma, shock or cardiac arrest evidently needed immediate resuscitation. The decision on when to commence resuscitative measures in those who did not present with one of these features was largely a matter for clinical judgment and an understanding of the natural history of this condition. This may be aided by arterial blood gas estimations and respiratory pressure-volume loops obtained by a technique which we have described elsewhere (Ambiavagar & Roberts, 1966). Although a rising $Paco_2$ is always an indication for resuscitation (Bates *et al.*, 1965; Feldman, 1962), we have found that cardiac arrest may occur despite a normal $Paco_2$. The $Paco_2$ is therefore, in itself, an inadequate criterion.

Early in the series, patients were treated by tracheostomy and mechanical ventilation for periods of between 3 and 6 days. In many cases bronchoscopic aspiration had been performed initially but was

found to be of little value in removing the tenacious secretions which are situated beyond the reach of the instrument. This has been beautifully illustrated by Barach *et al.* (1952), who were unable to improve an asthmatic with bronchoscopy but produced a remarkable change with an exsufflator which enabled the patient to expectorate bronchial plugs by mechanically producing an artificial cough. Ventilation was difficult to manage in the first few patients we treated because high positive airway pressures produced severe hypotension, while lower pressures were inadequate to overcome the airways obstruction, and alveolar hypoventilation with increasing hypercarbia resulted. Muscle relaxants were used to control the restlessness resulting from the under-ventilation but did not improve alveolar ventilation. Furthermore, they prevented us from diagnosing a perforated duodenal ulcer in one patient and might have been responsible for 'total bronchospasm' that made IPPV impossible, in another. Increasing experience has shown that relaxants are not required except during bronchial lavage and, for this, we use gallamine.

Tracheostomies were abandoned when it was found that ventilation and bronchial toilet could be performed equally well through an endotracheal tube. Patients were more comfortable with a tracheostomy than with an endotracheal tube but the asthmatic who may require resuscitation more than once in a lifetime presents a different problem from acute short-term surgical disorders such as the crushed chest. Tracheostomies do not heal well in these steroid-treated subjects and the risk of pulmonary infection, which may develop from an infection of the tracheostomy wound, is greater than with an endotracheal tube.

The problem of systemic hypotension during IPPV was resolved by using rapid intravenous fluid therapy (Ambavagar & Riding, 1966), while the use of vigorous early bronchial lavage finally established our present technique which is now to be described.

As a first step, an intravenous drip is set up and in the first 4 hr, 3 litres of fluid are transfused to correct dehydration and 'shock'. In most cases the fluid is given as dextrose and saline but if severe hypotension is present 1 litre is given as plasma. A plastic Ryle's tube is passed and the stomach contents are aspirated. If the contents are considerable further aspirations are performed at hourly intervals until little or no aspirate is returned. The trachea is intubated with the aid of a short-acting muscle relaxant (suxamethonium, 40 mg i.v.) and topical analgesia of the vocal cords and larynx. The latter is effected by spraying with 4% lignocaine under direct vision and is used because in one patient the process of intubation resulted in a short period of 'total bronchospasm' and it was hoped that adequate

analgesia would reduce reflex irritability of the air passages. Patients who are in coma require no general anaesthesia prior to intubation; restless subjects are induced with a halothane-oxygen mixture and high concentrations (up to 8%) of halothane are required to produce sleep.

Following intubation, manual IPPV with 100% oxygen and carbon dioxide absorption is performed by compressing the reservoir bag of a Boyle's circle absorber system. After 5 min, IPPV is stopped and between 10 and 20 ml of sterile isotonic saline, warmed to body temperature, is poured down the endotracheal tube and the trachea and main bronchi are then cleared with a Pinkerton catheter attached to a mechanical suction unit. IPPV is then recommenced and by this time the effects of the relaxant used for intubation are beginning to wear off. Ventilation is, therefore, manually assisted for about 5 min and then bronchial lavage and aspiration are repeated. This often produces prolonged spasms of coughing that make IPPV impossible and when this happens the patient is paralysed with gallamine. IPPV and bronchial lavage are alternated for about 1 hr and we have found that high arterial oxygen tensions can be maintained without much rise in arterial carbon dioxide tensions. At the end of this period of vigorous lavage, the effects of the gallamine are diminishing, more than 2 litres of fluid have been infused and, if the patient does not resist manual IPPV, mechanical ventilation is commenced using a Cape ventilator. When the patient fights the machine, manually assisted ventilation is continued until control is again obtained. This manoeuvre is necessary because these patients have an inflexible breathing pattern and are unable to coordinate their respiratory excursions with a different pattern such as is imposed by a mechanical ventilator (Ambavagar & Jones, 1967). During manual IPPV, respiratory rates, inflation pressures and inspiratory flow rates can be rapidly and finely adjusted by the response of the patient and the feel of the bag. Airway pressures of up to +70 cm and -20 cmH₂O are required initially to move tidal volumes of less than 300 ml. Cournand *et al.* (1948) have shown that inflation pressures of above 20 cm may result in interference with venous return, cardiac output and blood pressure. In the asthmatic patient, however, the high pressures are dissipated in overcoming the airways obstruction and are not transmitted to the mediastinum. Systemic hypotension, when it occurred, was corrected by rapid intravenous fluid replacement. It has been suggested that the use of a negative phase during expiration in obstructive airways disease may result in air trapping with an increase in residual capacity (Jones, MacNamara & Gaensler, 1960) but this was not seen in our patients. The size of the chest, in fact, diminished and this change can be demonstrated radiographically (Fig. 5b).

In setting the ventilator, a tidal volume of 500 ml is initially chosen, quite arbitrarily, and the rate of the ventilator is determined by auscultation of the chest. The rate at which expiratory wheeze ends before the next inspiratory cycle commences is chosen. The patient is then observed for signs of systemic hypotension and a tendency to fight the machine; the latter is to be regarded as a sign of underventilation. Following establishment on the machine, the patient is managed and monitored by specially trained staff who employ routines described elsewhere (Ambiavagar *et al.*, 1966) and perform

may be taught the controls of the ventilator and allowed to alter the machine settings to suit his requirements. This is desirable because improvement to complete recovery is usually rapid at this stage. Termination of assisted ventilation and extubation can normally be accomplished during the following 12 hr even though some degree of bronchospasm remains. Using this technique, the total period of ventilation has averaged about 48 hr.

During resuscitation, hydrocortisone (100 mg) is given intravenously at 4-hr intervals for 24 hr and then every 6 hr; ampicillin or tetracycline are given

FIG. 6. ECG recorded after 24 hr IPPV. Record shows a reduction in heart rate and disappearance of S in leads 2 and 3, dominant R in aVR and clockwise rotation. The P waves are smaller but remain peaked. (C.M., 21 April 1965.)

tracheobronchial lavage with 5 ml of warm saline at hourly intervals.

Mechanical ventilation is terminated when bronchial obstruction and spasm have been sufficiently relieved for the patient to breathe without severe distress. This can be determined at the bedside because the patient looks well, the pulse rate is reduced, wheezing is less and the pressures on the ventilator's manometer have fallen to less than half the original values. At this juncture the patient is placed on a Bird (Mark 8) ventilator which is set to assist and not control ventilation. The patient

intramuscularly. Parenteral therapy is considered important because absorption from the intestines may be defective. Oral administration of drugs is commenced after 48 hr; prednisolone is substituted for the hydrocortisone and is then gradually reduced and stopped after 2–3 weeks.

Choice of ventilator

The Bird (Mark 8), East Radcliffe, Cyclator, Barnet and Cape ventilators have been tried. It was found that during constant-volume-ventilation fluctuations in inflation pressures occurred from moment to

moment, probably due to changes in the degree of bronchospasm present. It was noticed that pressure-preset machines, i.e. Bird, Radcliffe, Barnet and Cyclator, required frequent readjustment to maintain a steady level of alveolar ventilation. When such readjustment was not adequately performed, periods of underventilation occurred and the arterial carbon dioxide level rose. The Cape was the instrument of choice in our experience. The production model of this volume-preset machine was modified to allow inspiratory pressures of up to 70 cmH₂O and expiratory pressures of -20 cm. It was quiet,

masked by the use of muscle relaxants. Case 12 became severely hypotensive during IPPV with the Cyclator; lower positive pressures were used and under-ventilation occurred. Shortly after an intravenous injection of D-tubocurarine, an urticarial skin eruption appeared and this was followed by a period of 'total bronchospasm' and cardiac arrest. At post-mortem there was widespread plugging of the bronchi, overdistension of the lungs and an acutely dilated right ventricle. The patient had received D-tubocurarine several times during a previous admission and also earlier in the day of his

FIG. 7. ECG during convalescence. Normal record with mean frontal P wave axis of $+60^\circ$. (C.M., 5 May 1965.)

reliable, easy to understand, required a minimum of readjustment and produced the desired result.

There were four deaths in the twenty-six ventilator episodes. All occurred early in the series, before our present technique had been fully established, i.e. before rapid intravenous fluid therapy and bronchial lavage. Cases 2 and 4 became hypotensive and remained cyanosed during IPPV with the Bird and Cyclator, and cardiac arrest occurred within a few hours of the start of resuscitation. Autopsy in each case revealed bronchial plugging and gross overdistension of the lungs. Case 10 died from a perforated duodenal ulcer, the signs of which had been

death, without apparent side-effects. It is, however, tempting to postulate that the sudden deterioration was due to histamine release which is known to occur with this drug (Goodman & Gilman, 1965).

IPPV as a means of resuscitating the desperately ill asthmatic who has failed to improve with medical treatment was first reported by Hugh Jones (1958) and its use has subsequently been acclaimed by other workers (Table 3). Why is IPPV effective? It rapidly corrects hypoxaemia and, at the same time, reduces the grossly abnormal intrathoracic pressure fluctuations which occur in the asthmatic during spontaneous breathing (Ambiavagar *et al.*, 1967a, b). Acute

cor pulmonale is relieved after some hours (Figs. 6 and 7), while hypercarbia is more gradually reduced (Fig. 8). We believe that in addition to correcting

TABLE 3

Summary of the results of treatment of moribund asthmatics with IPPV

Reference	Patients treated	
	No. treated	No. survived
Hugh Jones	1	1
Broom (1960)	2	2
Leonhardt (1961)	2	2
Feldman (1962)	1	1
Copeman (1963)	3	3
Bradley, Spencer & Semple (1964)	1	1
Marchand & van Hasselt (1965)	14	11
Drew & Sando (1965)	3	3
Bates <i>et al.</i> (1965)	9	9
Holmdahl (1965)	16	?
Ambiavagar & Riding (1966)	15	11

FIG. 8. Details of changes in PaCO_2 : (a) before IPPV, and (b) after 24 hr IPPV.

hypoxaemia, IPPV has immediate beneficial effects on the circulation which are brought about by mechanical means and which play an important role in sustaining life until such time as the airways obstruction can be relieved by bronchial lavage.

References

- AMBIAVAGAR, M. & JONES, E.S. (1967) Resuscitation of the moribund asthmatic. Use of intravenous infusions, bronchial lavage and intermittent positive pressure respiration. *Anaesthesia* (In press).
- AMBIAVAGAR, M. JONES, E.S. & ROBERTS, D.V. (1967a) Intermediate positive pressure ventilation in severe asthma.

- Mechanical effects on the circulation. *Anaesthesia*, **22**, 134.
- AMBIAVAGAR, M., JONES, E.S. & ROBERTS, D.V. (1967b) Mechanical effects of intermittent positive pressure ventilation on the circulation in status asthmaticus. *Anaesthesia* (In press).
- AMBIAVAGAR, M. & RIDING, W.D. (1966) Treatment of status asthmaticus. *Lancet*, **i**, 363.
- AMBIAVAGAR, M. & ROBERTS, D.V. (1966). A method of recording respiratory pressure volume relations in acute illness. *Anaesthesia*, **21**, 184.
- AMBIAVAGAR, M., ROBINSON, J.S., MORRISON, I.M. & JONES, E.S. (1966) Intermittent positive pressure ventilation in the treatment of severe crushing injuries of the chest. *Thorax*, **21**, 359.
- BARACH, A.L., BECK, G.J., BICKERMAN, H.A. & SEANOR, H.E. (1952) Physical methods simulating cough mechanisms. *J. Amer. med. Ass.*, **150**, 1380.
- BATES, D.V., KLASSEN, G.A., BROADHURST, C.A., PERETZ, D.I., ANTHONISEN, N.R. & SMITH, H.J. (1965) Management of respiratory failure. *Ann. N. Y. Acad. Sci.* **121**, 781.
- BEALE, H.D., SCHILLER, I.W., HALPERIN, M.H., FRANKLIN, W. & LOWELL, F.C. (1951) Delirium and coma precipitated by oxygen in bronchial asthma complicated by respiratory acidosis. *New Engl. J. Med.* **244**, 710.
- BRADLEY, R.D., SPENCER, G.T. & SEMPLE, S.J.G. (1964) Tracheostomy and artificial ventilation in the treatment of acute exacerbations of chronic lung disease. *Lancet*, **i**, 854.
- BROOM, B. (1960) Intermittent positive pressure respiration and therapeutic bronchial lavage in intractable status asthmaticus. *Lancet*, **i**, 899.
- COPEMAN, P.W.M. (1963) Artificial ventilation in acute respiratory failure. *Practitioner*, **190**, 110.
- COURNAND, A., MOTLEY, H.L., WERKO, L. & RICHARDS, E.W. (1948) Physiological studies of the effects of intermittent positive pressure breathing on cardiac output in man. *Amer. J. Physiol.* **152**, 162.
- DREW, M.J.R. & SANDO, M.J.W. (1965) Resuscitation of the moribund asthmatic patient. *Med. J. Aust.* **7**, 242.
- FELDMAN, R. (1962). Recognition and treatment of potentially fatal asthma. *Ann. intern. Med.* **57**, 29.
- GOODMAN, L.G. & GILMAN, A. (1965) *The Pharmacological Basis of Therapeutics*. New York.
- HOLMDAHL, M.H. (1965) The use of buffers in the management of respiratory failure. *Ann. N. Y. Acad. Sci.* **121**, 882.
- HOUSTON, J.C., DE NAVASQUEZ, S. & TROUNCE, J.R. (1953) A clinical and pathological study of fatal cases of status asthmaticus. *Thorax*, **8**, 207.
- HUBER, H.L. & KOESSLER, K.K. (1922) Pathology of asthma. *Arch. intern. Med.* **30**, 689.
- HUGH JONES, P. (1958) Oligopnoea. *Proc. roy. Soc. Med.* **57**, 104.
- JONES, R.H., MACNAMARA, J. & GAENSLER, E. (1960) The effects of intermittent positive pressure breathing in simulated pulmonary obstruction. *Amer. Rev. resp. Dis.* **82**, 164.
- LEONHARDT, K.O. (1961) Resuscitation of moribund asthmatic and emphysematous patients. *New Engl. J. Med.* **264**, 785.
- MARCHAND, P. & VAN HASSELT, H. (1966) Last resort treatment of status asthmaticus. *Lancet*, **i**, 227.
- RIDING, W.D. (1966) The management of the severe asthmatic attack. *Practitioner*, **197**, 659.
- SIEKER, H.O. & HICKAM, J.B. (1956) CO₂ intoxication Clinical syndrome: its etiology and management with particular reference to the use of mechanical respirators. *Medicine (Baltimore)*, **35**, 389.
- WALTON, C.H.A., PENNER, D.W. & WILT, J.C. (1951) Sudden death from asthma. *Can. med. Ass. J.* **64**, 95.
- WILLIAMS, D.A. (1953) Deaths from asthma in England and Wales. *Thorax*, **8**, 137.
- WITTS, L.J. (1936) Prognosis in asthma. *Lancet*, **i**, 273.