Status asthmaticus in children

A one-year study

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SUMMARY 50 children were admitted on 72 occasions during one year in status asthmaticus, defined as wheezing not relieved by two doses of bronchodilator 4 hours apart. At least one-third of children were hypercapnoeic on admission. They were managed with either oral prednisolone and nebulised salbutamol or IV aminophylline and hydrocortisone in addition to salbutamol. Those with peak expiratory flow rates of $>25\%$ expected for height were satisfactorily managed on the oral regimen. One child needed assisted ventilation. 73% were fit for discharge within 4 days and more than half of them needed a change in maintenance treatment.

About 40 children between ages one and 14 years die each year in England and Wales from acute asthma. This represents about 10% of all deaths due to diseases of the respiratory system in the same age group and is equal to about 8% of all deaths due to motor accidents (Office of Population Censuses and Surveys, 1977). In the mid-'sixties the death rate from asthma was even higher, particularly in the 10-14 age group (Speizer *et al.*, 1968a). In the subsequent analysis of events leading up to asthma deaths in young people (Speizer *et al.*, 1968b; Fraser *et al.*, 1971; Inman and Adelstein, 1969) 80% of such deaths were considered to have been 'sudden and unexpected'. In 39% the severity of the terminal attack had not been appreciated by doctors or relatives, and many children had not received corticosteroids during the attack. In a study of deaths from asthma outside hospital between 1963 and 1974 (Macdonald *et al.*, 1976) the associated factors were similar. In addition, several patients had died within a week of discharge from hospital after being treated for severe asthma, and it was suggested that physiological and blood-gas abnormalities had not resolved before their discharge.

In an examination of possible reasons for the recent increase in hospital admission rate for acute

asthma in children (Department of Health and Social Security, and Office of Population Censuses and Surveys), Anderson (1978) suggested that there might have been not only a change in morbidity but also a change in criteria for admission.

The purpose of the present study was to examine the factors leading up to the admission of children in status asthmaticus, to determine the severity of the attack, and to try to provide guidelines for management and admission policy.

Patients

During the period from 1 September 1976 to 31 August 1977, 50 children (29 boys and 21 girls) were admitted to this hospital on 72 occasions in status asthmaticus. This was defined as an acute wheezy episode not responding to two doses of bronchodilator 4 hours apart, given either at home or after arrival at hospital. 37 were admitted once, 9 on two occasions, 3 on three occasions, and 1 on eight occasions. This last child will be discussed separately. Therefore, 64 admissions will be considered.

As there is a specialist asthma clinic at the hospital to which children are referred from outside the district, the population from which the admissions were drawn may not have been representative of that served by the average district hospital. Table 1 gives the ages and treatment categories and locality of the children, both those attending the clinic and those admitted to hospital during the period of the study. The children in outpatients were managed as described by Godfrey (1977). For the clinic group, if a child had changed his treatment during the year he

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Table 1 *Percentage of children attending asthma clinic and percentage admitted in status asthmaticus during one year*

Patients	Clinic (n=289)	Admitted (n=50 on 72 occasions)
Male:female ratio	6:4	5.5:4
Ages (years)		
<1	1	4
1-4	15	22
5-9	50	36
10-14	31	34
15, 16	3	4
Treatment category		
Intermittent bronchodilators	32	32
Disodium cromoglycate	29	24
Theophylline	17	8
Beclomethasone	21	20
Corticosteroids on alternate days	1	4
No treatment	—	12
Local	74	68*
Not local	26	32†

*10 of these children did not attend the clinic. †3 of these children did not attend any hospital clinic and 5 were known severe asthmatics attending clinics outside the area.

was classified according to the treatment he was receiving at the end of the study. For the admission group, if a child was admitted more than once he was classified according to the treatment he was receiving before his first admission. Parents were advised to seek the help of their general practitioner, bring the child to casualty, or telephone the hospital if the child's wheezing did not respond to his usual bronchodilator.

Methods

Assessment of severity and investigations. At the time of admission, the house officer recorded details of events leading to admission, including possible precipitating factors, number of previous hospital admissions, and current maintenance treatment. The length of the attack was taken from the time the child started to cough or wheeze until the time of admission. Details of physical examination including measurement of pulsus paradoxicus and investigations performed at the time of admission were also recorded. Each child was given a score for respiratory distress—the clinical score (Table 2). This is a modification of the pulmonary index score of Dabbous *et al.* (1966). The investigations, performed on admission whenever possible, were blood-gas analysis, peak expiratory flow rate (PEFR) measurement, and chest x-ray; nasopharyngeal swabs for viral culture and serum for respiratory viral titres were also collected. A specimen of convalescent serum was collected if possible 10–20 days later. Blood was taken for theophylline measurement if the child had received any theophylline compound.

Table 2 *Clinical score*

	Score			
	0	1	2	3
Wheeze	0	Expiratory	Inspiratory and expiratory	Audible without stethoscope or absent
Hyperinflation	0	+	++	+++
Use of accessory muscles	0	+	++	+++

Initial treatment. The patients were assigned one of two treatment regimens according to the severity of illness on admission. Children who met one criterion listed in Table 3 were given the intravenous regimen; otherwise they received the oral one.

Oral regimen

This consisted of prednisolone 2 mg/kg per day in two divided doses and salbutamol inhalations 2.5 mg of respirator solution in 3 ml saline every 4 hours. Salbutamol was given via a Wright's nebuliser with a flow of oxygen of 8 l/min from a wall supply. Those children who were already taking theophylline preparations continued to take them. If the symptoms or PEFR had not improved in 1–2 hours after admission, treatment with the intravenous regimen was started.

Intravenous regimen

The fluids and the intravenous drug dosages are given in Table 3.

All children received IV boluses and infusions of hydrocortisone and aminophylline. Salbutamol was given either intravenously or via a Wright's nebuliser every 4 hours. The order in which each child received

Table 3 *Intravenous regimen*

Criteria for treatment	Dehydration PaO ₂ <8 kPa PaCO ₂ >5 kPa PEFR unrecordable on Wright's peak flow meter
Fluids	Dextrose 4%, saline 0.18%, 70–120 ml/kg per 24 hours
Drug boluses	Hydrocortisone 2 mg/kg + Aminophylline 6* mg/kg over 5 minutes + either salbutamol 5 × 10 ⁻³ mg/kg over 5 minutes or nebulised salbutamol 2.5 mg respirator solution in 3 ml saline
Drug infusions	Hydrocortisone 1 mg/kg per hour + Aminophylline 1 mg/kg per hour + either salbutamol 5 × 10 ⁻³ mg/kg per hour or nebulised salbutamol 2.5 mg respirator solution in 3 ml every 4 hours

*At first aminophylline was given as a bolus of 4 mg/kg and an infusion of 0.7 mg/kg per hour. The dose was increased as serum theophylline concentration after 2 hours' treatment was consistently below the optimum therapeutic range (10–20 µg/ml).

the drugs and the route of administration of salbutamol was random as another trial was in progress to compare the effects of these drugs. This did not affect the results discussed in this paper and will be reported separately. The dose of aminophylline was modified in those children who had recently received a theophylline preparation (McKenzie *et al.*, 1978). Serum theophylline was measured 2 hours after the infusion was started and the rate of infusion was altered if this did not come between 10 and 20 $\mu\text{g/ml}$.

Antibiotics were given if the child had a fever and signs consistent with infection in the chest x-ray taken on admission. Oxygen was given by face mask to any child who was hypoxic and blood-gas analysis was repeated if there was no clinical improvement or improvement in PEFR after 4 hours of treatment.

Recovery phase. Once dehydration had been corrected and the PEFR had shown a sustained improvement to 30% of expected for height, IV treatment was replaced by oral prednisolone and nebulised salbutamol. Each child was considered fit for discharge when the PEFR was sustained at 75% or more of expected for height or, for children too young to use a peak flow meter, when wheezing, recession, and tachypnoea were absent. Prednisolone was then reduced over 3 or 4 days. Drug treatment was reviewed before discharge and altered if necessary and the children were regularly followed up in the outpatient clinic.

Statistics. The statistical method used for analysis of results was χ^2 test with Yates's correction for discontinuity.

Results

Age, sex, previous treatment. When compared with the overall population of children attending the outpatient asthma clinic (Table 1) there was no significant difference in the ages, sexes, or proportions of children admitted from the various treatment categories.

Month of admission. The admission rate each month was similar throughout the year. There were 33 admissions between April and September and 31 between October and March.

Mode of admission. Most (60%) children were admitted after being brought to casualty by their parents, some (20%) first saw their general practitioners, and the rest came either directly from the asthma clinic (11%) or from other hospitals (9%). 70% of admissions were clinic attenders and two-thirds of these came directly to casualty.

Previous admissions. 18% of children had never been in hospital before, 36% had had no admissions in the previous year, 32% had had one or two admissions, and 14% had more than two admissions in the previous year.

Precipitating factors. Seven admissions followed an emotional upset at school or at home and 2 followed physical exercise. Three children had been participating in a drug trial and were admitted during the period they were receiving a placebo. One child had erythema multiforme. The precipitating factors for the rest of the admissions could not be defined at the time the children arrived at hospital.

Drugs in the 12 hours before admission. Seven children had had no drugs before admission. Six were undiagnosed asthmatics and one had run out of bronchodilators. The 6 children referred from other hospitals were receiving aminophylline and hydrocortisone, but the theophylline levels on admission in these children were without exception below the lower limit of the accepted therapeutic range (10–20 $\mu\text{g/ml}$). Either orciprenaline, subcutaneous adrenaline, terbutaline, or aminophylline by suppository had been given to each of 4 other children. The remaining children all had had 1–4 doses of salbutamol in addition to whatever other daily treatment they were receiving, either cromoglycate, beclomethasone, theophylline, or corticosteroids.

Severity of attack on admission. Arterial blood-gases were measured in 38 admissions, 9 of whom were breathing increased fractional inspired oxygen (FIO_2). PEFR measurements were made in 53 admissions. The relationships between the Pao_2 measurements breathing air, the Paco_2 measurements, the PEFR measurements, and the clinical score are shown in Table 4.

There was no correlation between the magnitude of Pao_2 breathing air and the clinical score. All children with Paco_2 measurements of >6.0 kPa (>45 mmHg) had clinical scores of at least 6 compared with 22 of 30 with Paco_2 measurements of <6.0 kPa ($\chi^2 = 4.5$; $P < 0.05$). 13 of 24 children under 5 years and 25 of those older than 5 years had blood-gas analyses ($\chi^2 = 0.43$; $P = \text{NS}$). Of those in whom measurements were taken, the younger group had higher Paco_2 values (Table 5). Children with pulsus paradoxicus of >25 mmHg tended to have Paco_2 values >5 kPa (>37.6 mmHg) (Table 6) although this did not reach significance. Ten of 11 children who had PEFR measurements of $>25\%$ expected for height had clinical scores of 5 or less compared with only 6 of 42 with PEFR measurements $<25\%$ expected ($\chi^2 = 20.8$; $P = <0.001$).

Table 4 Blood-gases, PEFR measurements, and clinical score on admission

	Clinical score		
	Good (<3)	Moderate (4-7)	Severe (>8)
PEFR (P/min)			
Unrecordable	0	18	6
<25% expected	0	14	4
>25% expected	4	7	0
Too young to blow	2	8	1
Pao ₂ in air			
<5.4	0	1	0
5.5-7.9	0	7	2
>8.0	1	15	3
Paco ₂ (kPa)			
>7.6		1	2
6.1-7.5		2	3
5.1-6.0		11	2
<5	1	14	2
Blood-gases not analysed	5	19	2

Conversion SI to traditional units—Pao₂ and Paco₂: 1 kPa ≈ 7.5 mmHg.

Table 5 Paco₂ and age

Paco ₂ (kPa)	Age (years)	
	<5	>5
5.0 or less	2	16
>5.0	11	9

$\chi^2 = 20.3$ P = <0.001

Table 6 Paco₂ and pulsus paradoxicus

Paco ₂ (kPa)	Pulsus paradoxicus (mmHg)	
	<25	>25
5.0 or less	6	1
>5.0	8	11

$\chi^2 = 2.36$ P = NS

There was no correlation between the length of symptoms before admission and Paco₂ or PEFR on admission.

Chest x-rays and viral studies. 53 admissions had chest x-rays taken and these were considered normal in 9. 28 had evidence of hyperinflation, 2 showed mediastinal emphysema, and 14 showed areas of abnormal shadowing. The presence of mediastinal emphysema did not influence the management and in neither child did it become worse although one child required intermittent positive pressure ventilation (IPPV).

Nasopharyngeal swabs for viral culture were collected from 37 admissions. Respiratory syncytial virus (RSV) was grown from one. Complement-fixation titres against respiratory viruses and *Mycoplasma pneumoniae* were measured in paired sera in 31 admissions. Three showed at least a 2-dilution rise

in titre to RSV (the positive culture was from one of these) and 2 children had a similar rise to *Mycoplasma pneumoniae*. All 5 children had abnormal shadows on chest x-rays.

Response to treatment. 18 admissions admitted received the oral regimen of prednisolone and nebulised salbutamol. They included all 11 in whom the admission PEFR was >25% expected for height and 2 others who had recordable PEFRs of 15 and 20% expected. Five other children in this group were too young to use the peak flow meter but 4 of them had clinical scores of <5 and the other had normal blood-gases.

The intravenous regimen was given to 46 admissions. This was continued for <12 hours in 12, 12-24 hours in 21, and >24 hours in 8. 14 children received either ampicillin or erythromycin. The time taken to be fit for discharge is shown in Table 7. Two children were discharged before their PEFR measurements were satisfactory and one returned 6 days later with continued wheezing. Most (73%) children were fit for discharge in 4 days or less.

There was no statistical correlation between either the length of symptoms before admission, the admission Paco₂ or the admission PEFR, and the time it took to be fit for discharge. 11 of 15 children with abnormal admission chest x-rays took at least 4 days to be fit for discharge compared with 7 of 37 with normal or hyperinflated chest x-rays ($\chi^2 = 11.7$; P = <0.001). (The other child who had an abnormal chest x-ray was discharged before his PEFR was satisfactory.)

One child required IPPV. He had been transferred from another hospital where he had had a rising Pco₂ over 24 hours. The main difference in treatment was that he had not received aminophylline until just before transfer. The Pco₂ on admission to this hospital was 9.6 kPa (72 mmHg). An initial fall in Pco₂ was not sustained and IPPV was necessary for 40 hours. He made an uneventful recovery. No other child was shown to have a rise in Paco₂ after admission.

The child who was admitted on 8 occasions was a 13-year-old boy who until the summer before the period of this study had been fairly well controlled at boarding school on beclomethasone. After the

Table 7 Time to be 'fit for discharge'

Days	*Peak flow reached 75% expected	Children too young to use peak flow meter
<4	42	5
5-7	9	4
>7		2

*Two children discharged before PEFR 75% expected.

holidays he did not want to return to school and remained at home. He was admitted on each occasion with a PCO_2 of >7 kPa (>52.6 mmHg) but he always responded rapidly to the intravenous regimen. It was, however, known that his early morning PEFR was often low in spite of receiving adequate doses of theophylline, corticosteroids every other day, and salbutamol. In spite of supervision this boy was never satisfactorily controlled and he did not return to boarding school. After the study had ended, he arrived dead in casualty one morning after an acute attack of about 9 hours' duration.

Complications of therapy. One child suffered tremulousness after nebulised salbutamol. Five children became nauseated for about 30 minutes after the bolus dose of aminophylline. Injection of salbutamol intravenously was in most cases followed by a sustained mean increase in heart rate above that measured at the time of admission of 5–10 beats/min.

Change of outpatient drug regimen. After reviewing management, the outpatient treatment was changed before discharge in 34 instances either from intermittent bronchodilator therapy to continuous theophylline or cromoglycate, or from theophylline or cromoglycate to beclomethasone.

Follow-up. Of the 50 children studied, 48 were available for review 6 months after their first admission during the period of the study. 34 had no further admissions and were well controlled. Seven children had had one further admission, 6 children had had 2 further admissions, and one child (the boy described above) had had 8 admissions during the year of the study. Of these 14 who were re-admitted, 5 were known to comply poorly with treatment at home and one was subsequently shown to have aspergillosis.

Discussion

After the epidemic of deaths from asthma during the 'sixties (Speizer *et al.*, 1968a, b; Inman and Adelstein, 1969; Fraser *et al.*, 1971) there was an acute awareness of the need for earlier recognition and more aggressive treatment of acute severe asthma. Crompton and Grant (1975) emphasised the need for prompt admission to hospital for asthmatics, and an emergency service was set up in Edinburgh for this. The Hammersmith Hospital has operated an open admission policy for asthmatic children for several years. Parents are advised to seek medical help early if their child becomes acutely wheezy. Most children in this study were clinic attenders and many either had come straight to casualty, often after a

phone-call to the hospital, or had made an emergency appointment at the clinic from where they were admitted. The criterion for admission to hospital was the failure to respond to two doses of bronchodilator 4 hours apart, and this may seem to be a low threshold. Nevertheless at least one-third of the 64 children had admission PCO_2 measurements of >5 kPa and in 24 of 53 admissions who could use a peak flow meter the measurement was unrecordably low. We think that our criterion for the diagnosis of 'status asthmaticus', and hence admission to hospital, was reasonable.

There was no seasonal variation in admission rate and children belonging to different treatment categories were just as likely to have an acute episode. Most admissions were within the first 48 hours of the start of cough or wheeze but there were a significant number who waited longer before seeking help. The deaths of young asthmatics are thought to be 'sudden and unexpected' (Speizer *et al.*, 1968b). This study shows that the blood-gas analyses and PEFR measurements on children admitted early in their attack are not much different from those admitted later. It may be argued that had an open admission policy not been in operation the early admissions may have stayed longer at home with a less favourable outcome.

The precipitating factor for each admission was difficult to evaluate. Only 16% of children investigated were shown to have an associated viral or mycoplasmal infection. Mitchell *et al.* (1976) found a similar incidence of serological evidence of viral infection in a group of children with wheezy bronchitis and asthma but had more success in isolating the viruses. The methods for collecting and transporting swabs in this study may not always have been satisfactory.

The relationship between the clinical score and the admission PCO_2 was barely significant and neither was the presence of pulsus paradoxus helpful in predicting hypercapnoea. We suggest therefore that, in all but the slightest attacks, the measurement of arterial blood-gases is the only satisfactory method to assess the severity of physiological disturbance in status asthmaticus. Commey and Levison (1976) suggested that sternocleidomastoid contraction and supraclavicular recession are useful signs of severity but their absence does not mean that severe airways obstruction is not present. Similarly, although Galant *et al.* (1978) were able to relate the magnitude of pulsus paradoxus to other parameters of respiratory function, such as PEFR, the absence of large paradox did not mean that severe airways obstruction did not exist.

Young children were much more severely ill on admission as judged by blood-gas analysis than

older ones. Six of 8 deaths reported by Buranakul *et al.* (1974) were in children aged 3 years or less and 6 of 13 children in respiratory failure reported by Simons *et al.* (1977) were under age 3 years. Particular attention should therefore be paid to the evaluation of status asthmaticus in young children.

PEFR measurements are useful in following progress after admission to hospital and, in this study, the admission PEFR was also useful in predicting those children who were likely to respond favourably to oral corticosteroids and nebulised salbutamol alone. It may be that those children who can record a PEFR of $>25\%$ expected for height could be satisfactorily managed at home either after nebulised salbutamol given in casualty or IM salbutamol given at home together with a short course of prednisolone.

The treatment outlined in this paper resulted in a rapid and sustained improvement in PEFR and was relatively free from side effects. Most children were fit for discharge and return to school within 4 days. Only one child needed IPPV. No other child had a rise in P_{CO_2} , not even those receiving increased $F_{I_{O_2}}$. Children with abnormal chest x-rays took longer to recover and all five with proved viral or mycoplasma infection took over 4 days to recover. We suggest that if an antibiotic is to be used in asthmatic children, erythromycin is a suitable choice as it will treat *Mycoplasma pneumoniae* and many of the bacteria pathogenic to the respiratory tract.

Gregg (1975) stated that 'Every attack of severe asthma should be regarded as a failure in (his) previous medical care . . .'. In this study over half the children required a change in treatment after their outpatient control had been reviewed. This emphasises the need for regular follow-up of all childhood asthmatics and the need to educate parents to seek help if their children's symptoms increase in frequency.

We suggest that all children presenting in status asthmaticus with a PEFR of $<25\%$ expected for height should be admitted to hospital and should be treated with IV aminophylline and hydrocortisone in addition to nebulised salbutamol. They should be considered fit for discharge when PEFR measurements are sustained at 75% expected for height. Young children should, of course, be accompanied by an adult. This practice may not only reduce the mortality due to asthma but also the need for IPPV and will ensure a rapid return to school and normal activity.

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