

## Editorial

## Death from asthma

Thoracic physicians are rightly concerned that mortality from asthma fails to decline despite more widespread enthusiasm for modern management. The recorded mortality rate in England and Wales has remained roughly constant since the epidemic of the mid-1960s subsided.<sup>1</sup> There is no definite trend occurring generally or for any particular age group when corrections made necessary by the eighth and ninth revisions of the International Classification of Diseases coding in 1968 and 1979 are applied to mortality statistics obtained from the Office of Population Censuses and Surveys up to the end of 1982. About 1500 patients die annually in England and Wales despite improvements in modern pharmaceutical products and a wider understanding of the practicalities of their application in the management of a disorder now regarded as amenable to treatment.

These facts are particularly regrettable since avoidable factors were identified in the events leading up to 77 of 90 (82%) deaths reported in the most detailed prospectively planned study of deaths from asthma yet reported, which was carried out by the research committee of the British Thoracic Association (BTA) in 1979.<sup>2</sup> This emphasised the very serious deficiencies which occurred in the management of these asthmatic patients, selected for inclusion in the survey by their death. Of course, a description of shortcomings does not amount to an account of the reasons for the deaths and the discovery that there were avoidable factors cannot necessarily be taken to mean that the deaths were preventable.

The nature of deficiencies in the treatment of patients both at home, where most deaths occur, and in hospital has been described repeatedly.<sup>2-6</sup> None of the studies concerned was controlled, however, and it remains uncertain whether management is more deficient in those who die than it is in asthmatic patients in general. There is a need to test the relationship between deficient treatment and death scientifically, though this would require a large, carefully controlled epidemiological study and the

impracticability of finding a matched control patient from the same practice or unit would make such a study difficult. The lack of such a definitive study should not, however, cause further delay before implementation of all of the recommendations of the BTA asthma death survey.<sup>2</sup> When all the circumstances were considered retrospectively by the assessment panel of the BTA<sup>2</sup> death was considered to have been unavoidable in only a small proportion of cases (10 out of 90). This was either because the final attack was sudden in onset, severe, rapidly progressive, and fatal before emergency treatment could be administered; because of unavoidable delay in obtaining medical aid; or because of lack of response to appropriate treatment when it was given.

**Severe sudden attacks**

Those who have sudden severe attacks "out of a clear blue sky" will always be difficult to help. This problem is well illustrated by the case of the 27 year old woman whose asthma had apparently given no trouble for many months, who became faint and breathless while shopping in a supermarket. After using her inhaler she was taken to the manager's office, where she died 20 minutes later before an ambulance arrived. She might have survived if she had had a parenteral (subcutaneous) beta agonist available for self-administration. This would clearly not be practicable or even safe for all asthmatic patients, but it might help some with a history of near fatal attacks. At the moment we are unable to recognise all those at risk of such sudden death. In the BTA survey, however, 15 of 23 patients whose final attack lasted less than an hour had had rapidly progressive asthma on a previous occasion, whereas only 11 of 40 whose final episode was known to have lasted longer had previously had sudden attacks with rapid progression. Unfortunately data on these cases is not sufficiently certain for us to conclude that sudden, severe episodes are predictive of sudden death.

A confident diagnosis of asthma may be made from the necropsy findings, the condition being characterised by overinflated lungs protruding from

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the chest when it is opened and visible occlusion of bronchi by rubbery grey sputum plugs seen on the cut surface.<sup>7</sup> Histologically, mucosal oedema and shedding, a cellular infiltrate, and an inflammatory exudate are all present. Basement membrane thickening and bronchial smooth muscle hypertrophy is also present but "muscle spasm," the condition at which bronchodilator treatment is aimed, is not seen.

It is disturbing that the same appearances may be seen in the lungs of patients seen at necropsy after an accidental death even though they had apparently not been suffering from symptoms due to their asthma up to that time.<sup>7</sup> These rare fortuitously studied cases suggest that a subclinical state with bronchial occlusion and narrowing exists in some asthma sufferers, worsening in time of exacerbation and leading to the well known grosser postmortem appearances in the few who die from an attack. Most studies describe a small proportion of cases in which death occurs within a few minutes of the onset of symptoms of an attack, although it remains uncertain how many of them previously had subclinical asthma that might have been contributory. Whether any of these die as a result of bronchial muscle spasm alone without the usual histological features necessarily remains a matter for conjecture as such cases, of course, would not be recognised at necropsy. We should keep an open mind on the question of whether some of the sudden deaths in very rapidly progressive attacks are due to "pure bronchoconstriction" alone.

#### **Failure to diagnose asthma**

Failure to recognise asthma precludes any effective treatment. This failure may sometimes stem from a belief that a history of smoking and sputum production necessarily indicate chronic bronchitis rather than asthma, and the misapprehension that they are mutually exclusive. In children the failure to diagnose the condition may be due to an old fashioned reluctance of doctors to burden parents with an anxiety producing diagnosis, previously stigmatised by psychological overtones, when "bronchitis" may be easily substituted. Finally, failure to diagnose asthma may derive from plain failure to seek typical diurnal or day to day variation in symptoms or peak flow rate or to look for reversibility after use of a bronchodilator in all cases of undiagnosed cough, wheeze, or breathlessness. Unfortunately, in all of these situations a reluctance to "think asthma" may lead to reluctance on the part of the doctor to "think bronchodilator or corticosteroid" where appropriate.

Failure to recognise asthma and consequent fail-

ure to prescribe bronchodilators was well shown in a recent key study from Newcastle upon Tyne,<sup>8</sup> in which the diagnosis of asthma had been given to the parents of only 14 of 87 children who had had four to 12 or more episodes of wheezing a year; less than a third of the children received a bronchodilator, although half had lost more than 50 days from school because of wheeze in the last year. A similar failure to diagnose asthma occurred in the case of nine of the 90 deaths in the BTA survey.<sup>2</sup> In four of these cases the problem was never recognised in life and in the other five the doctor attending in the final illness had no knowledge that asthma had been a problem in the past. The "working diagnosis" at the time of death was chronic bronchitis in five patients, acute bronchitis in three, and hyperventilation in one. Shortcomings in making this easy diagnosis therefore seem to add considerably to the morbidity and probably add to the mortality.

#### **Risk factors for asthma deaths?**

If we cannot with certainty identify those who might die from asthma, whether it is suddenly or otherwise, can we at least say which individuals might merit special supervision? Data from studies on deaths<sup>2,5,6</sup> show that in a large proportion of cases asthma had started in childhood or adolescence and had lasted for over 20 years until middle age. Among these there was an unexplained predominance of women over 45 years of age.<sup>2</sup> Chronic and persistent symptoms were also a feature and in two thirds of all patients in the BTA inquiry<sup>2</sup> remissions, if any, had been of less than three months' duration in the last year of life.

Other risk factors that can be identified intuitively from ordinary clinical practice include previous sudden or severe attacks and unstable patterns with highly variable peak flow rates, particularly in those waking at night or in the early morning with symptoms.<sup>9</sup> Other patients at risk are those previously admitted to hospital, who are particularly in danger in the early weeks after discharge,<sup>6</sup> and those requiring emergency visits by their family practitioner or attendance at a hospital accident and emergency department, particularly if they have required parenteral or nebulised bronchodilator treatment.

#### **Shortcomings in supervision**

Whether the supervision of patients with asthma is carried out by the family practitioner or in the hospital outpatient clinic often depends on local factors but present concern about standards of care is rightly not restricted to the prevention of death.<sup>10</sup> In

the BTA survey<sup>2</sup> the assessment panel considered the deaths retrospectively and felt that supervision by the family practitioner had been in all respects satisfactory in only two of 90 patients; more frequent follow up had been indicated in 70; deterioration had not been fully appreciated in 57; and serial lung function tests had been indicated in 83. The panel also identified appreciable discontinuity in management in 19 cases arising from frequent changes of the practitioner seen. The family practitioners themselves considered that half of the patients had been fully compliant with recommended treatment; the remainder had been either reluctant to obtain medical help or unreliable in taking treatment, or they had defaulted from regular attendance. These difficulties in obtaining optimum supervision during the last year of life were all compounded by a lack of appreciation by patients, relatives, and family practitioners of the severity of asthma during what turned out to be the fatal attack. Significantly, 75% of patients were noted to be tolerant of breathlessness and this is hardly surprising in a condition from which they had always previously recovered with or without treatment.

What form should supervision take? A minimum should be a preparedness on the part of doctors to see patients at risk regularly and at short notice if necessary in the family practitioner's surgery, outpatient clinic, or casualty department, when a basic clinical assessment should be carried out, including measurement of airflow obstruction, an explanation of drugs, and a reminder of how to take them. A patient with asthma which a family practitioner finds difficult to control should be referred to a specialist hospital physician, who should be willing, if necessary, to retain such patients for indefinite supervision.

### The role of treatment

For over 20 years, since the epidemic of deaths from asthma which occurred in England and Wales,<sup>11</sup> Australia,<sup>12</sup> and New Zealand<sup>13</sup> during the 1960s, there has been discussion of the possible role of treatment in bringing this about.<sup>14-16</sup> The isoprenaline inhaler emerged as the principal bogey, its reputation being confirmed as the rise and fall of sales in England and Wales closely paralleled the mortality rate from 1959 to 1969.<sup>14</sup> Overusage of this non-selective beta agonist in uncontrolled asthma was supposed to be causing fatal ventricular arrhythmias in the severely hypoxic myocardium and anecdotes concerning dead or dying patients found clutching an inhaler supported this. Indeed, in 1966 Tai and Read<sup>17</sup> showed that both isoprenaline and aminophylline may cause a fall in the arterial

oxygen tension and a rise in alveolar-arterial oxygen gradient in asthmatic patients. They concluded that this resulted from a reversal of pre-existing compensatory regional pulmonary vasoconstriction by the vasodilator action of both drugs in some patients. Concern about the potential dangers is therefore well founded. Possibly a small fall in the arterial oxygen tension due to these medications in a severe attack of asthma superimposed on an already low oxygen tension is the final straw which breaks the camel's back, inducing a fatal tachyarrhythmia.

Doubts were cast on the simple explanation that non-selective beta agonist inhalers were a direct cause of the excess of deaths by the finding in Australia, where there were also parallel increases in inhaler sales and deaths, that the reduction in mortality rate started before inhaler sales fell.<sup>18</sup> An impression has since arisen that an easing of hospital admission criteria for asthma and increased readiness to prescribe corticosteroids were both under way during the late 1960s, when the number of deaths in England and Wales was falling steeply.

Immense harm may have resulted from the poorly founded impression that the epidemic of the 1960s was largely due to overtreatment with beta agonist drugs because it has left a resistance to the use of all inhalers that is difficult to dispel. No definite evidence that excessive medication contributed to deaths from asthma was found by Fraser *et al.*,<sup>3</sup> MacDonald *et al.*,<sup>5</sup> or the BTA survey<sup>2</sup>—it appeared rather that undertreatment was the problem. MacDonald<sup>5</sup> showed that only 30 of 90 patients dying outside hospital in Cardiff were using bronchodilator inhalers and half only were taking corticosteroids at the time of their fatal episodes, some in suboptimal doses. The findings of the BTA survey<sup>2</sup> were similar: 32 of 62 patients receiving treatment with corticosteroids merited an increased dose and 28 patients who were not receiving this medication in the last year of life should have been. This study also showed that prophylactic drugs were underused and suggested that control might have been improved in half of the patients by treatment with inhaled steroids or sodium cromoglycate.

Against a background of studies which give a consistent impression of poor control due to undertreatment in general,<sup>8</sup> as well as in those who die,<sup>3,5,6</sup> we now hear of a new epidemic in New Zealand<sup>19</sup> with a real and steep rise in mortality from 1975 to 1979. Wilson and colleagues have suggested that combined oral theophyllines and beta<sub>2</sub> agonist drugs might be a cause,<sup>20</sup> but Grant<sup>21</sup> has noted that only two of the 16 "high risk" patients dying suddenly in their study were taking oral corticosteroids. His own impression of the New Zealand epidemic<sup>22</sup> was that sustained release theophyllines were probably not a

major factor, that too much was being expected of corticosteroid aerosols, and that oral corticosteroid treatment was being underused. His main concern, however, was the possible overuse of domiciliary compressor driven nebulisers, delivering a high dose of salbutamol without oxygen supplementation and without peak flow monitoring of the effects, which he thought might be contributing to the increase in mortality rate. The uncontrolled use of nebulisers in the home is becoming more widespread and it is clearly of great importance for us to learn the outcome of studies currently progressing in New Zealand and to apply any lessons learned. Until more information is available doctors and patients should be wary lest they become beguiled by the machinery itself—rather as they were with inhalers in the 1960s—to the detriment of other, more mundane aspects of control such as measurement of peak expiratory flow rate and consideration of whether oral corticosteroid treatment is indicated or whether the dose is adequate.

#### **Death from asthma—can we prevent it?**

At a recent symposium on this subject held at East Birmingham Hospital participants agreed that we were unlikely to be able to prevent all deaths from asthma but that there was good reason to believe that appropriate treatment could make death less likely for some sufferers. The pursuit of audit has revealed so many imperfections in our management that we should certainly be able to do a lot better. At the most basic level we must diagnose the asthma, recognising that it is most readily confused with other conditions at the extremes of age and that a peak flow gauge used with inhaled bronchodilator is an indispensable tool. The next requirement is that we must provide a level of supervision appropriate to the severity of the complaint, including at the very least serial measurements of airflow, analogous to blood pressure measurements in the management of hypertension.

Delay, present at every stage of care, was the most important and consistent theme in the BTA survey.<sup>2</sup> Failure to appreciate deterioration in the fatal attack by patients, relatives, and doctors led to delay in seeking medical aid or referral to hospital. There were difficulties in contacting the medical services and delays occurred before the arrival of some practitioners or their deputies or on occasion the ambulance service. On four occasions death occurred while the ambulance awaited permission to transfer the patient to hospital. Given a prompt response to deterioration by patients, a self-admission service for acute asthma, as run by Crompton and colleagues,<sup>23</sup> may reduce delay and prevent some

deaths. Such schemes deserve to be encouraged. Unfortunately factors related to local geography and the arrangement of local hospital services can pose difficulties. Furthermore, patients with undiagnosed asthma and those not thought to require special emergency arrangements cannot be helped in this way, and probably self-admission schemes can make only a small impact on the general mortality rate for these reasons.

The principal drugs available to treat asthma have not changed materially for 10 years, yet there remains a gap between their proper application and what actually happens in clinical practice. Most of the problems need to be tackled at the “mechanical interface” between doctor and patient. Here detailed, sympathetic education of sufferers about their condition and how to manipulate their own drug treatment are implicit in supervision. One essential is a detailed explanation of the purpose of each treatment—of which drug is for relief and which for prevention—and the doctor must emphasise the need to continue prophylactic treatment even when the patient is well. Teaching how to use inhalers of various kinds is best done by direct demonstration by a doctor or an experienced assistant and ideally it should not be left to a pharmacist, nor should the patient have to work it out for himself by reading the instructions with the product. There is nothing natural or easy about using inhalers and most patients will need repeated instruction. Any patient likely to need oral corticosteroid treatment will need a supply and lucid instructions about how and when to take a short, sharp self-tailored course. Each patient needs to be taught how to recognise deterioration sufficient to merit oral corticosteroid treatment. Failure to respond to the usual dose of bronchodilator inhaler is a most important symptom; others are broken nights due to asthma, persistent morning chest tightness, steady deterioration over several days, and any episode of immobilisation or asthma requiring an emergency injection. Finally, an explanation of when and how to obtain emergency help without delay may well be life saving if self-treatment measures fail.

Each practitioner will evolve his own way of imparting this information, whether by word of mouth, adding to it piecemeal at each visit, or with the help of written material. The need for the patient to manage the treatment of his own asthma has been emphasised.<sup>24</sup> Time spent in detailed explanation of treatment and its effects may be repaid later in shorter and more satisfactory consultations resulting from good control of the asthma.

The asthma societies also have an important role to play in the education of patients and relatives about the disorder. Several have been set up in Bri-



tain; they receive advice from physicians with an interest in asthma and support from the pharmaceutical industry.

The education of all professionals likely to come into contact with asthma is a formidable task. For doctors it needs to start in the medical schools, ideally with separate allocations of teaching time in thoracic medical units, including practical demonstrations. Thoracic physicians can do much themselves to teach, encourage, and disseminate knowledge of the disorder to colleagues, juniors in training, physiotherapists, and nurses. The pharmaceutical industry, through its responsible support for post-graduate education, has already done much in this area and may be able through its representatives to reach practitioners working far from the teaching centres, who may find meetings difficult to attend.

There remains a feeling that there is nothing radically new on the subject of death from asthma and that recent studies have only refined and extended the messages yielded by old ones. There is now, however, clear realisation that we need to direct our energies more towards the education of patients and all who come in contact with them about their condition. By this means we may actually be able to prevent some unnecessary deaths.

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## References

- <sup>1</sup> Anonymous. Saving asthmatics. *Br Med J* 1979;i:1520.
- <sup>2</sup> Research Committee of the British Thoracic Association. Death from asthma in two regions of England. *Br Med J* 1982;285:1251-5.
- <sup>3</sup> Fraser PM, Speizer FE, Waters SDM, Doll R, Mann NM. The circumstances preceding death from asthma in young people in 1968 to 1969. *Br J Dis Chest* 1971;65:71-84.
- <sup>4</sup> Cochrane GM, Clarke TJH. A survey of asthma mortality in patients between ages 35 and 64 in Greater London hospitals in 1971. *Thorax* 1975;30:300-5.
- <sup>5</sup> MacDonald JB, Seaton A, Williams DA. Asthma deaths in Cardiff—1963 to 1974. *Br Med J* 1976;ii:1493-5.
- <sup>6</sup> Ormerod LP, Stableforth DE. Asthma mortality in Birmingham 1975 to 1977—53 deaths. *Br Med J* 1980;280:687-90.
- <sup>7</sup> Dunnill M. *Pulmonary pathology*. Edinburgh: Churchill Livingstone, 1982:50-66.
- <sup>8</sup> Speight ANP, Lee DA, Hey EN. Underdiagnosis and undertreatment of asthma in childhood. *Br Med J* 1983;286:1253-6.
- <sup>9</sup> Hetzel M, Clark TJH, Branthwaite M. Asthma—analysis of sudden death and ventilatory arrest in hospital. *Br Med J* 1977;1:808-11.
- <sup>10</sup> Anderson HR, Cooper JS, Bailey PA, Palmer JC. Influence of morbidity, illness label, and social, family and Health Service factors on drug treatment of childhood asthma. *Lancet* 1981;ii:1030-2.
- <sup>11</sup> Speizer FE, Doll R. A century of asthma deaths in young people. *Br Med J* 1968;iii:245-6.
- <sup>12</sup> Commonwealth Bureau of Census and Statistics. Causes of death, Australia 1968-1979. Canberra: CBCS, annual reports.
- <sup>13</sup> National Health Statistics Centre. New Zealand health statistics report—mortality and demographic data, 1959-79. Wellington: National Health Statistics Centre, Department of Health, annual reports.
- <sup>14</sup> Inman WHW, Adelstein AM. Rise and fall of asthma mortality in England and Wales in relation to use of pressurised aerosols. *Lancet* 1969;ii:279-85.
- <sup>15</sup> Stolley PD, Schinnar R. Association between asthma mortality and isoprotenerol aerosols: a review. *Prev Med* 1978;7:319-38.
- <sup>16</sup> Speizer FE, Doll R, Heaf P. Observations on recent increases in mortality from asthma. *Br Med J* 1968;i:335-9.
- <sup>17</sup> Tai E, Read J. Response of blood gas tensions to aminophylline and isoprenaline in patients with asthma. *Thorax* 1967;22:543-9.
- <sup>18</sup> Gandevia B. Pressurised sympathomimetic aerosols and their lack of relationship to asthma mortality in Australia. *Med J Aust* 1973;i:273-7.
- <sup>19</sup> Jackson RT, Beaglehole R, Rea HH, Sutherland DC. Mortality from asthma: a new epidemic in New Zealand. *Br Med J* 1982;285:771-4.
- <sup>20</sup> Wilson JD, Sutherland DC, Thomas AC. Has the change to beta-agonists combined with oral theophylline increased cases of fatal asthma? *Lancet* 1981;i:1235-7.
- <sup>21</sup> Grant IWB. Has the change to beta-agonists combined with oral theophylline increased cases of fatal asthma? *Lancet* 1981;ii:36-7.
- <sup>22</sup> Grant IWB. Asthma in New Zealand. *Br Med J* 1983;286:374-7.
- <sup>23</sup> Crompton GK, Grant IWB, Bloomfield P. Edinburgh emergency asthma admission service: report on 10 years' experience. *Br Med J* 1979;iv:1199-201.
- <sup>24</sup> Brewis RAL. Asthma. In: Wilkes E, ed. *Long term drug prescribing*. London: Faber and Faber, 1982: 50-60.