Deaths from asthma in children on aerosol corticosteroids

Between 1961 and 1966 the number of deaths from bronchial asthma rose alarmingly, particularly in children. This alerted the medical profession for the first time to the potential dangers of drug treatment in that disease.[1] The simplistic view that this "epidemic" of asthma deaths was wholly due to the overuse of bronchodilator aerosols, particularly those containing isoprenaline, is no longer widely held,[2] but the deaths and their investigation did have the valuable effect of directing attention to the possible hazards of every new treatment for asthma.

Aerosol corticosteroids were introduced in 1968 and proved effective in many patients who would otherwise have been exposed to the considerable risks of systemic treatment. Candidiasis affecting the oropharynx and occasionally the larynx is a fairly common side effect,[3] but there is no evidence that it ever extends to the bronchi or lungs. Anxiety that the prolonged administration of a corticosteroid aerosol could cause epithelial atrophy and damage collagen and elastic tissue in the respiratory tract has not yet been justified. A recent study of biopsy specimens[4] found no such changes in the bronchial epithelium or submucosa. So far this form of treatment seems unlikely to prove a specific cause of mortality or serious morbidity in patients with bronchial asthma. Corticosteroid aerosols are, however, often used to replace systemic corticosteroids partially or completely, so that the suggestion made by Mellis and Phelan[5] that weaning from long-term systemic treatment in these circumstances may increase the risk of sudden death in children with severe chronic asthma clearly warrants critical attention.

Mellis and Phelan reported the deaths of five such children over a 12-month period. Two of the children had not been treated with a corticosteroid aerosol, and the necropsy findings were typical of bronchial asthma, with extensive mucus plugging of the smaller bronchi. In contrast, the other three had been treated with a beclomethasone dipropionate aerosol while systemic corticosteroid treatment was being withdrawn. All had acute inflammatory changes in the lungs at necropsy, with no mucus plugging. Those observations imply that an infective process (presumably viral, since there was no convincing pathological evidence of bacterial infection) was responsible for the death of these three children and that the corticosteroid aerosol may have contributed in some way.

Children with severe chronic asthma who have been treated with systemic corticosteroids for long periods are always in a precarious state. Even a slight increase in hypoxia, such as could be produced by viral infection, can result in sudden death; and this is all the more likely if the pituitary-adrenal response to stress has been impaired by the prolonged administration of corticosteroids. The risk is even greater if infection occurs shortly after this treatment is withdrawn or even when the maintenance dose has been substantially reduced. Perhaps, then, the main reason why these children die is that they are being given an inadequate dose of systemic corticosteroid. If that is so, Mellis and Phelan's only real justification for their suggestion that aerosol corticosteroid treatment may have contributed to the deaths they reported is that the dose of systemic corticosteroid might have been reduced less rapidly, if at all, in three of their five cases had aerosol therapy not been available. Some doctors stop systemic treatment abruptly after aerosol therapy is introduced,[6] but recovery of a normal pituitary-adrenal response to stress may take as long as a year,[7] and throughout that period the life of a child with severe chronic asthma is constantly at risk.

Rapid withdrawal of systemic treatment is therefore both unwise and unnecessary, and if prednisolone is the drug being used the daily dose should be reduced at a rate not exceeding 1 mg per month. Such a policy will give the pituitary-adrenal axis more time to recover; but it cannot protect every child from the consequences of an acute respiratory infection or a severe attack of asthma. In that event the urgent need is treatment with massive doses of systemic corticosteroids and immediate admission to a respiratory intensive therapy unit. Nevertheless, in some cases, unfortunately, the child may die suddenly before these measures can be implemented. Caution in withdrawing systemic corticosteroids and a more realistic appreciation of the limitations of aerosol corticosteroids might prevent some at least of these fatalities.

[1] Speizer, F E, Doll, R, and Heaf, P, *British Medical Journal*, 1968, **1**, 335.
[2] *British Medical Journal*, 1972, **1**, 459.
[3] Willey, R F, *et al*, *British Journal of Diseases of the Chest*, 1976, **70**, 32.
[4] Anderson, E, *et al*, *British Journal of Diseases of the Chest*, 1977, **71**, 35.
[5] Mellis, C M, and Phelan, P D, *Thorax*, 1977, **32**, 29.
[6] Brown, H M, Storey, G, and George, W H S, *British Medical Journal*, 1972, **1**, 585.
[7] Malone, D N S, *et al*, *British Medical Journal*, 1972, **3**, 202.

The Mahler revolution

Under the direction of Dr Halfdan Mahler the activities of the World Health Organisation have undergone a quiet revolution in the past few years. In keeping with other organisations of the United Nations, WHO channels its activities through the governments of the countries in which it operates. The former emphasis on universities and their medical schools has now swung towards primary health care and basic health services—a change spelt out in the resolutions of the 1975 World Health Assembly, which stated that all other echelons of the health services should support the needs of their peripheral activities. This is a great contrast from recent policies in most developing countries, where the financial commitments—and the interest of politicians—have been to teaching hospitals and other services, mainly in the cities.

The change is not easy, as our own Ministry of Overseas Development has discovered. While priority is now to be given to aid to the poorest countries—and the least privileged people in those countries—it may prove more difficult to use money effectively in this way than in building "disease palaces." The new emphasis on basic health services means, for example, that money needs to be spent on an adequate supply of vaccines and low cost drugs to prevent or treat common conditions, making less money available for rarer diseases requiring expensive facilities. Governments may pay lip service to such a programme, but change will be difficult to achieve; for these new policies will soon lead to the cutting back of services to the politically vocal city-dweller, at times supported by those senior medical men to whom the politician turns for his own personal health care.

In any health service the cost of employing health workers and their supporters is the largest single expenditure. But unfortunately, when we examine how many doctors in the underdeveloped countries spend their time—preferring to live in towns rather than in the rural areas—we find that much