acetylators); further assessment is needed of this possibility in patients with exacerbations of chronic inflammatory bowel disease unresponsive to standard medical treatment.

Lishman and his colleagues[24] recently examined the range of antibiotic-associated diarrhoea and found that some patients remained clinically well despite high concentrations of faecal toxin. Ten of 53 patients with antibiotic-associated diarrhoea were excreting toxin (though only one patient had histological evidence of membranous colitis). A control group of 53 patients who had been given antibiotics but who did not develop diarrhoea were also tested; of these, four had faecal toxin. Titres of toxin in both groups were within the same range, suggesting that factors other than concentration of the toxin influence the response. Elderly patients, who are at greatest risk of severe antibiotic-associated colitis, may have low resistance to effects of the toxin. The disease has a wide variety of clinical manifestations, ranging from an asymptomatic carrier state to fatal—but fortunately rare—pseudomembranous colitis. The pathogenesis of antibiotic-associated diarrhoea in most patients, in whom faecal toxin cannot be identified, remains unexplained.

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Regular Review

Management of asthma in the child aged under 6 years

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Asthma presents specific problems of management under the age of 6 years. These have proved difficult to overcome, but recent progress has been made with better definition of the parts played by allergy and viral infection. The development of methods of measuring pulmonary function at this age has increased the effectiveness of treatment. These advances have improved our understanding of what lies beneath that cloak for diagnostic ignorance, wheezy bronchitis, and thereby have produced a more rational approach to treatment.

Under about 18 months of age most children with wheezy bronchitis do not respond to bronchodilator agents.[1-3] After this age most do respond to such drugs and, indeed, their response to exercise and drugs shows that there is excessive bronchial lability, as in the older child with asthma.[4 5] In both age groups viral infections are the most frequent precipitants of attacks under 6 years.[6-9] Similar viruses have been recovered from children with wheezy bronchitis and from those with other respiratory tract infections, which suggests that the difference between children who wheeze and those who do not in response to an infection is not determined by the infecting agent.[10 11]

Among those children with wheezy bronchitis whose symptoms start in the first year of life there are some who are not going to be asthmatics and will cease to have these attacks perhaps in the second year. Others, however, will become asthmatics but the proportions have not been determined. Bronchodilator agents are not likely to be effective in these children, though they may be worth trying. The persistence of attacks beyond the second year points strongly to asthma, and these children will benefit from bronchodilator agents.

In both groups antibiotics, which are so frequently prescribed, do not help.

Allergic aspects—A small group of asthmatics first develop sensitivity to allergens absorbed from the gut early in the first year of life. Foreign proteins in cows' milk, milk formulae, and egg may be absorbed and act as allergens, causing gut symptoms, failure to thrive, and, in a few children, asthma.[12 13] Skin-prick tests and the radioallergosorbent (RAS) test for specific IgE antibody help to identify the causal agents. Management should include the encouragement of breast feeding and elimination diets.[14] Negative test results do not exclude atopy, however; insufficient IgE may have been generated, so that the serum concentration of IgE may still be normal, and too little may have been deposited in the skin to produce a positive prick-test reaction.

The incidence of eczema and asthma may be greatly reduced by avoidance of offending protein.[15 16] Avoidance of allergens in the infants of allergic parents significantly reduces the incidence of eczema. Matthew, Brostoff, and Paganelli and colleagues[17–19] have shown that in adults disodium cromoglycate reduces the entry of antigens from the gut and diminishes the formation of immune complexes and the incidence of atopic symptoms. Its value in the first year of life, especially to protect the offspring of allergic parents, has still to be ascertained.

After the first year of life house dust and the dust mite, animals, and pollens become increasingly important. In the presence of atopy—proved on the basis of history or the skin-prick or RAS test to one or more of these groups—management should be based on avoidance. Animal contacts should be looked for not only in the child's home but in the homes of relatives and friends and in schools. Ideally, no allergic child should live in close contact with animals, and one should not be deterred from offering this advice by the comment that contact "doesn't seem to make him worse." Measures to eliminate the house-dust mite are easy to spell out but are likely to be ineffective unless vigorously applied. Even new bedding readily becomes infected.[20 21] At 5-6 years of age desensitisation is of value in a patient with proved sensitivity to dust mites or pollen.[22] The successful treatment of asthma depends on the avoidance of allergens, coupled with desensitisation when appropriate, combined with the use of prophylactic chemotherapeutic agents to combat the allergenic material which enters the body. Such treatment will fail if the input exceeds a critical threshold or the threshold has not been raised sufficiently by the prophylactic drugs.

Minor attacks of asthma may be treated with one of the many oral bronchodilators available when symptoms occur, or every four to six hours during the attack. The $beta_2$-selective drugs—salbutamol, orciprenaline, and terbutaline—are the most satisfactory, given as tablets or syrup. Pressurised canisters releasing single doses for inhalation are not suitable under 5 years of age, with the exception of terbutaline administered using the "spacer," which increases the efficiency of inhalation.[23] The chief prophylactic agent available at present is disodium cromoglycate, 20 mg four times a day. Children under the age of 5 years do not use the Spinhaler satisfactorily, however, and a mains-driven nebuliser delivering 1 ml (20 mg) of disodium cromoglycate four times daily is much more effective.[24] Though cromoglycate is an efficient bronchodilator, it is less effective than salbutamol during an attack.[25] At these times the cromoglycate may be reinforced by adding to the nebuliser salbutamol respirator solution or giving other bronchodilator agents by mouth.[26 27]

Theophylline preparations given by mouth may be used for prophylaxis as an alternative to or in addition to the treatment above. Choline theophyllinate and the micro-crystalline preparations must be given six-hourly to achieve a therapeutic blood concentration of 10-20 mg/l, though lower levels may be of some value.[28] Slow-release preparations of theophylline, aminophylline, and the liquid formulation, theophylline sodium glycinate, can be given 12-hourly. The drawback of theophylline preparations is the considerable variability of the concentrations achieved in the blood; both clinical effects and potential toxicity are unpredictable.[29–32]

Patterns of disease—These prophylactic measures do not influence the course of the disease. In severe asthma the aim should be to improve stability rather than to achieve normal pulmonary function. Prophylactic treatment may fail and the reasons may be baffling but may be understood by considering the interrelations between the clinical manifestations of asthma, the patient's allergic state, and viral infections. There are broadly three patterns. Some children get asthma with respiratory viral infections but are remarkably well between attacks. The asthma may be mild, yet the attacks may be severe if the child's resistance to infection is low. As resistance improves in the later years of childhood the asthma may become quite mild. Treatment with bronchodilator agents and avoidance of antibiotics are the main measures, but the addition of steroids for a few days early in the attack may also be valuable, especially if the attacks tend to be severe. Secondly, there are children who give a clear history of sensitivity to animals, dust or dust mite, or pollens and again are relatively well between exposures. These tend not to be the most severely affected asthmatics; they respond well to avoidance measures, prophylactic chemotherapy as outlined above, and desensitisation when skin-prick or RAS tests are positive.

The most difficult to treat, and clinically the most severely affected asthmatics, are those with persistent symptoms with impairment of pulmonary function between attacks. Often the relation between symptoms and viral infection or exposure to allergens is much less clear cut, though both may be important. A few have the characteristics of intrinsic asthma and the RAS test result may be negative. Avoidance of allergens is still indicated, coupled if necessary with air filtration or deionising filtration in the home and full prophylactic chemotherapy. Topical steroids may be used in the 4-6-year-old. Before the child inhales the steroid the bronchi should be dilated with a sympathomimetic amine and in addition physiotherapy should be given with postural coughing when there is significant secretion. Oral steroids are unsuitable at this age, but corticotrophin depot 10-20 units once or twice weekly may occasionally be of value during a difficult period.

The success of treatment depends on favourable parental attitudes and understanding, together with the continuous, active support of the family doctor and the hospital service. Successful parents are caring, try to understand the disease and the aims of treatment, take full advantage of advice from the family doctor and hospital, and thus learn to use drugs and to arrange the home and school environment to best advantage. Access to hospital on demand should be available, and the parents should be encouraged to use it unless there is an early response to the treatment of an attack in the home. In particular, parents should be cautioned against the repetitive administration of bronchodilators, especially sympatho-mimetics by inhalation. Death from asthma may occur at any age, but many workers emphasise the risks in severe asthma under the age of 5 years.[33–36] The chief cause of the failure of treatment in this group is a weak parental link, with

socioeconomic stress within the family. When this is irremediable residential treatment and special school arrangements may be required.

Admission to hospital in an attack should be considered when there is a poor response to bronchodilator agents given at home or in the admission room. Tachypnoea, obvious increase of respiratory effort with the use of accessory muscles, restlessness, interference with sleep and eating, any suggestion of cyanosis, and appreciably diminished breath sounds and wheeze are all points which favour admission. An attack prolonged beyond 24 hours will usually require admission.[35] Frequent blood-gas measurements may be required to monitor subsequent progress. A $Paco_2$ exceeding 7 kPa (53 mm Hg) and a Pao_2 below 7 kPa breathing air indicates respiratory failure and the possibility that assisted ventilation may be required.

Treatment may be started with subcutaneous adrenaline, intravenous salbutamol, or terbutaline by bolus or slow infusion,[35] but most patients will respond as well to the more convenient administration of nebulised salbutamol or terbutaline respirator solution.[37] This may be combined with intravenous aminophylline by bolus or slow infusion, provided that a check has been made that the drug has not been given already. Repeated measurements of the concentration of the drug in the blood are necessary. Severe attacks will require hydrocortisone intramuscularly or by slow infusion, but in a recent series of admissions to a large children's hospital steroids were required in no more than half the cases. Simpson *et al*[38] and McKenzie *et al*[27] should be consulted for dosage regimens.

In a severe attack the airway fills with mucoid secretion at a rate which exceeds the child's ability to remove it by coughing. Agents to aid removal by reducing viscosity have not been successful. Many physicians rely on humidification of air-oxygen mixtures, but the rationale of humidification is obscure. Much attention has been paid to the surface properties of the surfactant-containing film lining the alveoli, with emphasis on its importance for alveolar stability and compliance. The properties of the surface film of the secretion in the airway may be equally important but from the point of view at this site of airways resistance and removal mechanisms. The surface film of secretion seems likely to determine the stability and therefore persistence of bubbles formed on coughing and also of strands and webs of mucus across the airway, all of which contribute to obstruction of the airways. Sterile water administered via a nebuliser in the acute attack has a potent capacity to dilate the bronchi, and this effect may be due to modification of surface properties.[25] Humidification appears to reduce airways resistance, but whether it aids removal of secretion is unknown.

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