analysis of variance with the three variables (treatments) over the four times shown in the table showed a significant difference in drug effect ($0.05 > p > 0.01$), trial effect ($p < 0.0001$), and drug-trial interaction ($p < 0.0001$). The bronchodilatation effect was greater with nebulised salbutamol compared with the two other forms of administration but lasted longer with the oral treatment. Improvement in peak expiratory flow rate occurred rapidly after administration with all three methods. At 15 minutes the improvements in peak expiratory flow rate over baseline values achieved with the tablet and the powder were 61% and 75% respectively of the improvement achieved with the nebuliser.

Discussion

This study shows that the maximal bronchodilatation effect is obtained with nebulised salbutamol and confirms the effectiveness of this form of administration in asthmatic children.^{8,12} Unfortunately, nebulising systems are cumbersome and expensive and should probably be reserved for severely asthmatic patients.

The powder and tablet are easily administered and have a rapid onset of action. The powder is effective from at least the age of 3,⁹ and inhaled forms reliably block exercise-induced bronchoconstriction.^{13,14} Our study showed that the effect obtained with the powder was comparatively short, suggesting a need for frequent (three-hourly) administration. An increased dose might give a longer action. Powder forms are at least as good⁹ or better¹⁰ than metered-dose aerosols and avoid the risks, theoretical or otherwise, of using the aerosols.

The oral form, which is effective from at least the age of 3,¹ had a surprisingly rapid onset of action, and its bronchodilatation effect was superior to that of the other forms of administration after four and six hours. It is less effective in exercise-induced bronchoconstriction,^{13,14} but its longer-lasting action has implications for prominent nocturnal symptoms. A combination of oral and inhaled forms has an additive effect on bronchodilatation with minimal increase in side effects¹⁵; such combination treatment in childhood needs further evaluation. All the children in this study had been taking oral or nebulised salbutamol regularly for months or years, which might explain the absence of troublesome side effects¹⁶ apparently prevalent in adults taking large doses¹⁵; children generally tolerate sympathomimetics well.

A regimen in which the powder is given during the day when the patient is active and the oral form given last thing at night or as

baseline treatment may thus be optimal sympathomimetic treatment. Nebulised salbutamol should be reserved for patients with severe asthma.

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SHORT REPORTS

Hospital admissions for whooping cough in the Oxford Region, 1974-9

The number of statutory notifications for whooping cough in the United Kingdom increased substantially during 1977-9 compared with the previous few years. There has been speculation (a) about the extent to which this represented an increase in the proportion of cases notified as well as an increase in the incidence of the disease^{1,2}; (b) about the extent to which other respiratory illnesses may have been misdiagnosed and notified erroneously as whooping cough^{3,4}; and (c), because the increase in notification has not been paralleled by an increase in deaths from whooping cough, about whether any real increase in incidence has been one of relatively mild cases. We therefore studied statistics on hospital care for whooping cough in the Oxford Region.

Methods and results

Data on hospital discharges in the Oxford Region were obtained from Hospital Activity Analysis. This covers six of the seven health districts in

the region (total population of districts covered about 2 million). The existence of linkable hospital data in the Oxford Region enabled us to identify a few patients who were readmitted to or transferred between hospitals, and to exclude their second and subsequent hospital episodes from the results. The diagnosis in Hospital Activity Analysis is that given at the time of the patients' discharge from hospital, but, for comparison with notifications, the data were analysed according to the dates of admission. Notification statistics for whooping cough were obtained for patients resident in the same six districts.

The figure shows the number of hospital admissions and statutory notifications in the six districts, plotted logarithmically, in each quarter of the year from 1974 to 1979 inclusive. The size of the population in the relevant age groups did not vary appreciably during the period and the results for age-specific admission rates were similar to those shown in the figure. The number of hospital admissions in the quarters centred on the 1978 peak was significantly higher than that in the quarters centred on the 1974 peak (Wilcoxon's rank sum test: $p < 0.05$). Analysis by calculation of the correlation coefficient on the logarithmically transformed data showed a statistically significant association between the quarterly number of notifica-

tions and hospital admissions ($r=0.9$; $p<0.01$). There was a tendency throughout the period, when the figures for whooping cough increased, for the number of notifications to increase proportionately more than the number of admissions. In the peak quarters of 1974 and 1978 there were 25 and 58 admissions and 159 and 666 notifications respectively. We studied Hospital Activity Analysis statistics for a range of other respiratory and infective diseases in childhood during the period but found no disease other than whooping cough for which admissions corresponded with the quarter by quarter trends in whooping-cough notifications. There were three deaths—one in 1974, one in 1977, and one in 1979—asccribed to whooping cough in the region during the period.

Comment

Various interpretations of these figures are possible. Conceivably the controversy about whooping-cough vaccination led general practitioners both to notify and to refer for admission to hospital a higher proportion of incident cases in recent than in earlier quarters. It is also conceivable that epidemics of respiratory illnesses other than whooping cough had been misdiagnosed as whooping cough both by general practitioners and by hospital doctors. The simpler, and in our view more tenable, interpretation is as follows. Firstly, the figures for hospital admission corroborate the view that the "epidemic" of notifications represented an epidemic of whooping cough. Secondly, although the death rate from whooping cough remained low during the period, the epidemic included a rise in the number of patients whose illness was serious enough to need hospital care.⁵ None the less, as the incidence of the disease rose, either there was a proportionately greater rise in the number of mild than of severe cases or there was an increase in the proportion of incident cases which were notified.¹

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¹ Miller E, Jacobs B, Pollock TM. Whooping cough notifications. *Lancet* 1980;i:718.

² Anonymous. Whooping cough: how big a peak? *Lancet* 1980;i:725.

³ Stewart GT. Vaccination and notification rates for whooping cough. *Lancet* 1980;i:1299.

⁴ Stewart GT. Whooping cough in the United Kingdom 1977-8. *Br Med J* 1980;281:451.

⁵ Strachan RD. Return of whooping cough. *Br Med J* 1978;iii:1639.

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Post-transfusion non-A, non-B hepatitis in the Netherlands

To study the incidence of post-transfusion non-A, non-B hepatitis we have followed prospectively 380 recipients of HBsAg-negative blood for up to seven months.

Patients, methods, and results

Blood samples were taken from each patient before transfusion and at monthly intervals afterwards. Activity of alanine aminotransferase (ALT) in excess of 20 IU in two or more consecutive serum samples were taken as a sign of post-transfusion hepatitis. All patients had ALT activities below 21 IU before transfusion. Markers of hepatitis B virus infection were determined by radioimmunoassay (hepatitis B surface antigen (HBsAg), anti-HBs, and anti-HB core (HBc) antigen, Abbott Laboratories, USA) or enzyme immunoassay¹ (HBeAg and anti-HBe). The role of the following viruses in causing these episodes of hepatitis was examined by determining the presence of IgG and IgM antibodies to hepatitis A virus (radioimmunoassay, Abbott Laboratories, USA), cytomegalovirus (enzyme immunoassay, van Loon A M, and others, unpublished), and Epstein-Barr virus (immunofluorescence).²

Incidence of post-transfusion hepatitis in a group of 380 prospectively followed recipients of HBsAg-negative blood

No of recipients negative for markers of hepatitis B virus	No (%) transfused patients with:				
	ALT > 20 IU	Hepatitis A virus-IgM	Cyto-megalovirus	Epstein-Barr virus-IgM	Non-A, Non-B hepatitis
380 (100)	15 (4.0)	0	1* (0.3)	1† (0.3)	13 (3.4)

*Significant increase of antibody titre by enzyme-linked immunosorbent assay and complement fixation.

†One of the 7 donors of this recipient was also positive for IgM-Epstein-Barr virus.

The results, shown in table I, indicated that 15 of the 380 recipients developed hepatitis; all were asymptomatic. In the absence of a practicable test for non-A, non-B antigen(s) or antibody, 13 of these patients, in whom cytomegalovirus, hepatitis A, and Epstein-Barr viruses were not implicated, were considered to have post-transfusion non-A, non-B hepatitis. The number of units of blood they received varied from 1-10, with a mean of 3. The peak activities of ALT were mildly increased (28-100 IU, with a mean of 48 IU) in 11 patients, but in two patients they were 174 and 777; the former patient was the only one in our group in whom ALT activities remained raised for more than four months. The incubation period, defined as the interval between transfusion and the first significant increase in ALT activities, was five weeks in three patients, six to 11 weeks in eight (including the two with the highest levels), and over 11 weeks in two. These incubation periods agreed with those reported in the USA for patients with post-transfusion non-A, non-B hepatitis.³

Comment

There is a controversy in published reports about the value of increased ALT activities in donor blood in predicting the development of post-transfusion, non-A, non-B hepatitis. Some investigators found that the likelihood of developing such hepatitis increased greatly when the ALT activity in donor blood exceeded 45 IU,⁴ while others could not confirm these findings.⁵

In our group of 38 donors whose blood was implicated in post-transfusion non-A, non-B hepatitis the highest activity of ALT was 21 IU. This fact, together with the fact that only volunteer blood is used in the Netherlands, may explain the lower incidence of post-transfusion non-A, non-B hepatitis in our group (3.4%) than in the US (5.4-18.5%).⁴ Furthermore, because of our liberal criteria for diagnosing non-A, non-B hepatitis, its real incidence in our patients may have been even lower.

Nevertheless, the finding that 3.4% of a group of recipients of donor blood that had been screened for HBsAg developed non-A, non-B hepatitis emphasises the need for practicable methods of detecting non-A, non-B antigen(s). Furthermore, such methods are needed for studying the causal role of non-A, non-B agent in "auto-immune" chronic active hepatitis and in the serological diagnosis of acute hepatitis.