Protection against pertussis by immunisation

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Summary and conclusions

Review of all 126 children admitted to the communicable diseases unit with whooping cough during the epidemic in 1978 showed that two had received two doses of triple vaccine and only one had had full primary immunisation against the disease. None of these three children suffered complications of the disease. Of the 123 children who had not been immunised against pertussis, however, 66 had had one or more complications. In Birmingham the dramatic decline in immunisation against pertussis has been accompanied by a fall in acceptance rates for diphtheria and tetanus immunisation. Nevertheless, of the 62 children aged over 1 year in this series, 41 had been so immunised.

These findings suggest that the apparently positive decision by parents to omit pertussis immunisation was misplaced, since immunisation does protect against the more serious complications of the disease. Furthermore, there is no firm evidence that pertussis immunisation of children without specific contraindications is associated with serious adverse reactions.

Introduction

Controversy surrounds both the safety and the efficacy of pertussis immunisation. The national epidemic of whooping cough in 1978 provided an opportunity to study a group of children admitted to hospital with pertussis. The aim was to see whether any children with disease severe enough to warrant admission to hospital had been immunised against whooping cough.

Patients and methods

One hundred and twenty-six consecutive children with pertussis who had been admitted to our communicable diseases department between January 1978 and March 1979 were studied retrospectively from their hospital records.

All 126 children had had paroxysmal cough, and pertussis was only diagnosed when the child also had (1) *Bordetella pertussis* cultured from a pernasal swab; (2) a lymphocytosis exceeding $9{\cdot}5 \times 10^9$/l (9500/mm^3) if aged under 1 year or exceeding $7{\cdot}5 \times 10^9$/l (7500 mm^3) if older; or (3) typical whoop. Details of the patients, time spent in hospital, and complications were taken from the case notes, the diagnosis of pneumonia in all cases being confirmed by chest radiography. Immunisation history was usually obtained from parents but in all instances was confirmed by the appropriate area health authority.

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Results

Of the 126 children, 115 were Caucasian, nine Asian, and two West Indian. The male to female ratio was 1·1:1. The table lists the complications and numbers satisfying each of the diagnostic criteria in the different age groups.

The median time spent in hospital for those aged under 1 year was 7·4 days (range 2-30 days), for older children 5·5 days (range 1-43 days). Two of the 126 children had received two doses of triple vaccine, and one three doses. No complications occurred in these three children. The remaining 123 children had not been immunised against pertussis.

Sixty-six children (52·4%) had had one or more complications (table). There were no deaths, and no child developed any permanent neurological sequelae. Of the 62 children aged 1 year and over, 41 (66%) had been immunised against diphtheria and tetanus.

Diagnostic criteria and complications in 126 children (percentages given in parentheses)

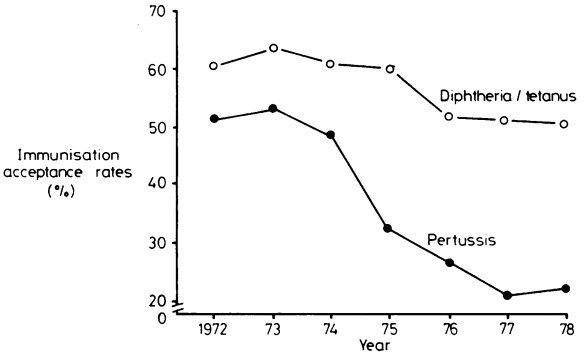
Age	No of children	Diagnostic criteria			Complications		
		Positive culture	Lympho-cytosis	Whoop	Cyanotic and apnoeic attacks	Pneumonia	Convulsions
<3 months	14	7	11	8	5	4	
3–5 „	27	9	25	18	6	8	1
6–11 „	23	9	20	15	1	6	
1–<2 years	38	14	27	26	4	22	6
2–<3 „	11	3	8	7		4	1
3–<4 „	4	1	3	4		2	1
4–9 „	9	2	5	8		5	
Total	126 (100)	45 (36)	99 (79)	86 (68)	16 (12·7)	51 (40)	9 (7·1)

Discussion

Assessing the efficacy of pertussis immunisation is difficult largely because of the problems in confirming the diagnosis retrospectively, and most reports rely on notification figures. Church[1] and Jenkinson[2] provided evidence of vaccine efficacy, and Pollard[3] showed a relation between the decline in immunisation and the increase in notifications of pertussis in different area health authorities. Miller and Fletcher,[4] who studied 8000 pertussis notifications in 1974-5, also thought that the disease was less severe in the immunised group, but commented that the most severe illness was often in children aged under 6 months, who may not have completed their primary immunisation. In our study, however, the complication rate of 51% in the 41 children aged under 6 months was similar to the 52% in the series as a whole. In contrast, Ditchburn,[5] in a Shetland practice, noted a similar incidence of infection among immunised and unimmunised children in the 1977-8 epidemic, though none in his practice had been immunised since July 1974.

The epidemic of pertussis in 1978 therefore provided an opportunity to try to resolve the controversy, which resulted in a dramatic decline in immunisation acceptance rates during the 1970s (see figure). (Acceptance rates are defined as the proportions of children aged under 4 years who had received a

full primary course of immunisation.) Normally a primary course of immunisation against pertussis would be completed by one year. In 1978, however, only 22% of children under 4 years of age in the City of Birmingham had received the full immunising course of three doses of vaccine. Only one of the 117 children under 4 years of age in our series was fully immunised. The difference between the Birmingham and hospital



Immunisation acceptance rates in Birmingham children during 1972-8.

figures is significant ($\chi^2=29{\cdot}376$; $p<0{\cdot}001$). This strongly suggests that immunisation does protect against the more serious complications of the disease, including cyanotic and apnoeic attacks and convulsions, which may cause brain damage, and pulmonary infections, which may lead to chronic lung disease.

The decline in the diphtheria and tetanus immunisation acceptance rate, which accompanied the fall in pertussis immunisation—though to a less degree—is also worrying. In 1978 only 50·3% of children under the age of 4 had received a full primary immunising course against diphtheria and tetanus. The unexpectedly high proportion of children in our series who had been immunised against diphtheria and tetanus suggests a positive decision by their parents to omit pertussis immunisation from the schedule.

Despite the considerable controversy about the safety of pertussis immunisation the National Childhood Encephalopathy Study Group found no statistically significant association between encephalopathy and recent immunisation.[6] We carried out a survey among paediatricians and physicians specialising in infectious diseases in the Birmingham area, and failed to discover any case of immunisation-associated encephalopathy seen by them during the past five years.

Our findings suggest that immunisation protects children against the more serious complications of whooping cough and is not associated with serious adverse reactions. We therefore strongly encourage the use of the pertussis component along with diphtheria and tetanus immunisation in all children who have no specific contraindications to its use.

Immunisation figures were obtained from Birmingham AHA(T) and the West Midlands Regional Health Authority. We thank Dr Anne Fellows and Dr A Penman for help in abstracting the information, and Dr S Green and the paediatricians of Birmingham for helping with the survey.

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SHORT REPORTS

Cold agglutinins accompanying Mycoplasma pneumoniae infection

Raised titres of cold agglutinins have been found in as many as half of cases of atypical pneumonia.[1] It has been suggested that these antibodies are produced in response to the I-like antigen on the infecting organism, *Mycoplasma pneumoniae*,[2 3] but direct evidence for this claim is lacking. Furthermore, although the occurrence of acute haemolysis in these cases is usually related to the thermal amplitude of the agglutinin, this correlation is not always observed.[4] We describe a patient with an *M pneumoniae* infection complicated by severe haemolysis and report some serological findings relevant to these questions.

Case report

The patient, a 57-year-old decorator, presented with a one-day history of jaundice, pallor, and dark urine. Two days before he had been discharged from our care after completing a course of benzyl penicillin for what had seemed a typical bacterial chest infection. He had improved symptomatically and was thought well enough to continue treatment at home with oral antibiotics. His symptoms worsened, however, and on this second admission chest radiography showed increased shadowing in both upper zones in addition to the new features of jaundice and frank haemoglobinuria. His haemoglobin concentration had fallen from 14·3 g/dl three days previously to 9·8 g/dl and a blood film showed red cell agglutination, spherocytosis, erythrophagocytosis, and some atypical lymphocytes. The direct antiglobulin test was positive with anti-C3 and -C3d. His blood urea concentration, previously normal, had risen to 19 mmol/l (114 mg/100 ml). An acute intravascular haemolysis complicating an *M pneumoniae* infection now seemed the most likely diagnosis, and this was later confirmed serologically. The patient was nursed in a heated room and was treated with erythromycin 500 mg six-hourly. Careful attention was given to fluid balance in view of his renal impairment. Nevertheless, massive haemoglobinuria persisted for another week, and 4 units of washed red cells were transfused to relieve the progressive anaemia. Thereafter he improved symptomatically, his blood urea concentration fell to normal, and he was discharged home three weeks after the onset of the haemolysis.

Specificities for cold agglutinin and mycoplasma antibody in serum of patient with mycoplasmal pneumonia

	Cold agglutinin titre (4°C)	Mycoplasma CF titre
Unabsorbed serum	640	20 480
Absorbed serum	Nil	20 480
Eluate	640	160

The cold agglutinin titre at 4°C was 1024 against adult (I) cells, and at room temperature a clear-cut anti-I specificity was demonstrable. Although agglutination was barely detectable at 32°C, it was possible to demonstrate C3 on red cells incubated with the patient's serum at strictly observed temperatures up to 37°C using an indirect antiglobulin test. In addition, the patient's serum was absorbed with group O red cells at 4°C and an eluate was prepared from the washed cells at 37°C. The unabsorbed serum, absorbed serum, and eluate were then tested for cold agglutinins and complement-fixing antibodies to mycoplasma. The results are shown in the table.