Survey to establish the incidence of minor side effects in infants following protective immunization

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SUMMARY. A study of the minor side effects from the immunization of children against diphtheria/pertussis/tetanus, diphtheria/tetanus, and measles is reported. The sample of 306 children received 1028 vaccinations. A secondary study of measles vaccine was made on 177 immunizations. A diary card was used to provide control data before injections and to measure the increase in incidence of minor symptoms after injection. The reported incidence of side effects after both diphtheria/tetanus and measles vaccinations was low and the patterns similar. The increase in side effects was greater after diphtheria/pertussis/tetanus injection, particularly when there was soreness at the injection site. The incidence of soreness was lower when the site of the injection was the buttock rather than the arm.

The diary card was found to be an effective method of providing control data and of monitoring any increase in the incidence of minor symptoms following immunizations. The information obtained should assist health care workers to provide accurate advice and to reassure parents who are concerned about their children's protection.

Introduction

MEDIA reports in the 1970s of serious side effects after pertussis vaccination were followed by a fall in the number of children presented for immunization.[1] This resulted not only from understandable parental anxiety but also doctors' uncertainty. When the senior tutors at St George's Hospital department of general practice discussed between them the advice they gave to parents about the side effects of vaccination, they realized it was based on subjective impressions rather than factual knowledge.

The purpose of this study was to determine the incidence and nature of the minor side effects of immunizations and a method was developed in which control data could be collected in addition to symptoms after immunization. This was made possible by diary cards used before and after immunization which allowed an assessment of the baseline level of symptoms and the increase in symptoms following injection.

Method

In 1982 three practices agreed to participate in the study, which was to last one year. Each practice had five partners and about 10 000 patients. One partner in each practice was a senior tutor in the department of general practice at St George's Hospital medical school. Practice A was in a health centre and practices B and C were group practices.

A register was kept of infants born into each practice and registered before any immunizations were undertaken. These children became the cases for the study. Some six weeks after the baby's birth a family profile form was completed and the course of immunization agreed with the parents. Parental choice or medical recommendation could lead to omission of pertussis vaccine.

Ten days before each immunization was due mothers were sent an appointment and diary card. During the week before immunization they were asked to record daily at the baby's bedtime whether or not 10 parameters were observed in the child: snuffles; vomiting; fever; rash; bowels — constipated, normal, diarrhoea; fretful; more sleepy than usual; and unwell and seen by doctor. The card was inspected before immunization and mothers were asked to continue recording on the day of immunization and for a further week. After immunization, an additional parameter was recorded: soreness or swelling at injection site. The card was then returned to the surgery. Efforts were made to recover cards that were not returned.

As the total number of children entered into the survey was relatively small the results of the diary cards from the three practices were amalgamated. The prevalence of side effects in the week after injection was compared with that in the week before injection (baseline level). The difference in the two prevalences was taken to represent the effects of injection. The significance of differences was assessed using the chi-squared test.

Immunization schedule

Practice C had always followed a policy of vaccinating against measles earlier than recommended and this was incorporated in the schedule: polio and diphtheria/tetanus or diphtheria/pertussis/tetanus at 12 weeks; polio at 16 weeks; diphtheria/tetanus or diphtheria/pertussis/tetanus at 20 weeks; measles (practice C) at 36 weeks; polio and diphtheria/tetanus or diphtheria/pertussis/tetanus at 44 weeks; measles (practices A and B) at 65 weeks.

Vaccines were those supplied by the health authority. They were adsorbed diphtheria and tetanus vaccine BP, or adsorbed diphtheria, tetanus and pertussis vaccine BP, oral poliomyelitis vaccine BP trivalent type, and Mevilin (Evans) for measles.

The doctors were allowed to choose their own site of injection. Practices A and B injected into the buttock and practice C into the arm.

Results

During the 12 months of the survey a total of 349 children were registered into the study: 25% from practice A; 25% from practice B; and 50% from practice C.

Before the first injection 20 children had moved or attended elsewhere leaving 329 for immunization. Three hundred and six children (93%) attended for their first injection — 233 received diphtheria/pertussis/tetanus plus polio, and the remaining 73 diphtheria/tetanus plus polio. Of the 306, 254 (83%) completed their course. Two hundred and ninety nine children were eligible for measles vaccination and 203 (68%) received it.

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Uptake of measles vaccine varied considerably between the practices. In practice C, where the vaccine was given at 36 weeks, there was an 82% uptake from eligible children and none had yet contracted the disease. In practices A and B, where measles vaccine was offered at 65 weeks, a 59% uptake was achieved: four of the children in these practices had already had measles.

Of the 1028 cards sent out 729 (71%) provided sufficient data for analysis. In addition 75 cards were collected after administration of polio vaccine alone but were not analysed. As diary cards were received following measles vaccination it became clear that some symptoms carried over into the second week, so a supplementary study was set up in 1984–85 to record the side effects for a two-week period. This produced 177 diary cards for analysis from 210 children.

Symptoms before and after immunization

Table 1 shows the percentage incidence of symptoms recorded on any day in the week before the first immunization and the measles immunization. In the measles group the incidence of vomiting was noticeably less, possibly because the children were older.

In order to identify the symptoms which increased after injection the total number reported for all injections for diphtheria/pertussis/tetanus or diphtheria/tetanus with or without polio, and measles were amalgamated and are also shown in Table 1. Five symptoms appeared with similar frequency before and after vaccination — snuffles, vomiting, rash, bowels constipated and unwell and seen by doctor.

Soreness or swelling where injected was the most frequently reported symptom after immunization. After diphtheria/tetanus or measles immunization it was reported in 12% and 13% of children, respectively, on the day of injection, rising to 18% on the first day after diphtheria/tetanus immunization then falling (Figure 1a). Following the first diphtheria/pertussis/tetanus immunization soreness or swelling where injected was reported in 28% of children on the day of immunization, but peaked to 40% on the first day after the second immunization and to 50% on the first day after the third immunization.

Fretfulness was reported frequently (Figure 1b). The incidence rose 15% above the baseline level after diphtheria/tetanus injection and 10% after measles vaccination. After the first diphtheria/pertussis/tetanus injection it rose by 27%, after the second 20% and after the third 22%.

Fever was not reported so often (Figure 1c). The incidence above the baseline was 4% on the first and second days after diphtheria/tetanus injection and 3% on the first day after measles vaccination. Following the three successive injections of diphtheria/pertussis/tetanus it was 5%, 6%, and 9% on the day of injection, and 5%, 13%, and 15% on the first day after immunization.

At the time of their first injection, 9% of children were reported as suffering from diarrhoea. In the week after diphtheria/tetanus immunization 5–8% more children were reported with this symptom (Figure 1d). After diphtheria/pertussis/tetanus vaccination the reported percentage rose with each injection to 13% above the baseline on the day of the third injection. After measles vaccination there was a 3–5% increase.

Six per cent more children were reported to be more sleepy than usual on the day of diphtheria/tetanus immunization, the figure peaking to 15% more on the first day after immunization (Figure 1e). After measles vaccination the figures were 5%, peaking to 8% on the second day after immunization. After the first diphtheria/pertussis/tetanus injection 19% more babies were more sleepy than usual on the day of injection, peaking to 20% on the first day after immunization. The figures for the second injection were 5%, peaking to 18% on the first day after injection and for the third 9%, peaking to 20% on the first day after injection.

The reported incidence of vomiting was minimal (Figure 1f). It peaked to 10% of children on day one following the first diphtheria/pertussis/tetanus immunization, but it was reported as being below the baseline rate in many instances.

Table 1. Symptoms reported on any day in the week before and after immunization.

	Percentage of cards reporting symptom			
	Before first immunization[a] ($n=208$)	Before measles immunization ($n=109$)	Before all immunizations ($n=729$)	After all immunizations ($n=729$)
Snuffles	25.0	28.0	24.0	21.7
Vomiting	16.0	2.0	7.7	6.9
Fever	1.1	3.5	2.2	3.3
Rash	6.5	2.5	4.4	4.3
Bowels:				
Constipated	8.0	4.7	5.7	4.5
Diarrhoea	9.0	6.2	5.5	10.0
Fretful	10.0	10.0	12.0	18.8
More sleepy than usual	6.0	3.4	3.4	7.8
Unwell and seen by doctor	1.2	1.0	1.5	1.7

[a]First polio and diphtheria/pertussis/tetanus or diphtheria/tetanus immunization. n = number of cards analysed.

Clustering of symptoms following diphtheria/pertussis/tetanus injection

Additional symptoms were more commonly reported when associated with soreness at the injection site and soreness was most common following diphtheria/pertussis/tetanus injection. Thus, 422 cards were collected after diphtheria/pertussis/tetanus injections. Symptoms reported on the first day after injection were collated as this provided the highest reported number of symptoms.

Where soreness was reported (41% of the 422 cards) clustering of symptoms was apparent (Figure 2) and fever was almost always associated with fretfulness and sleepiness. Only 39% of the cards reported no additional symptoms. Where no soreness was reported 59% of cards reported no additional symptoms (Figure 2).

Site of injection

Following diphtheria/pertussis/tetanus injection soreness was reported in 46% of cases in practice C when given in the arm but in only 32% of cases when given in the buttock in practices A and B ($P<0.01$). The only other symptom showing a difference (but not significant) was fretful, which was reported for 38% of children in practice C but for only 29% in practices A and B.

Pertussis immunization as a predictor for measles vaccination

Parents choosing to have their child immunized against pertussis were more likely to have them immunized against measles as well. Of the 233 children given pertussis in their first immunization 75% of those eligible subsequently presented for measles vaccine. Among the 73 children in whom pertussis vaccine was omitted, only 47% of those eligible subsequently had the measles vaccine.

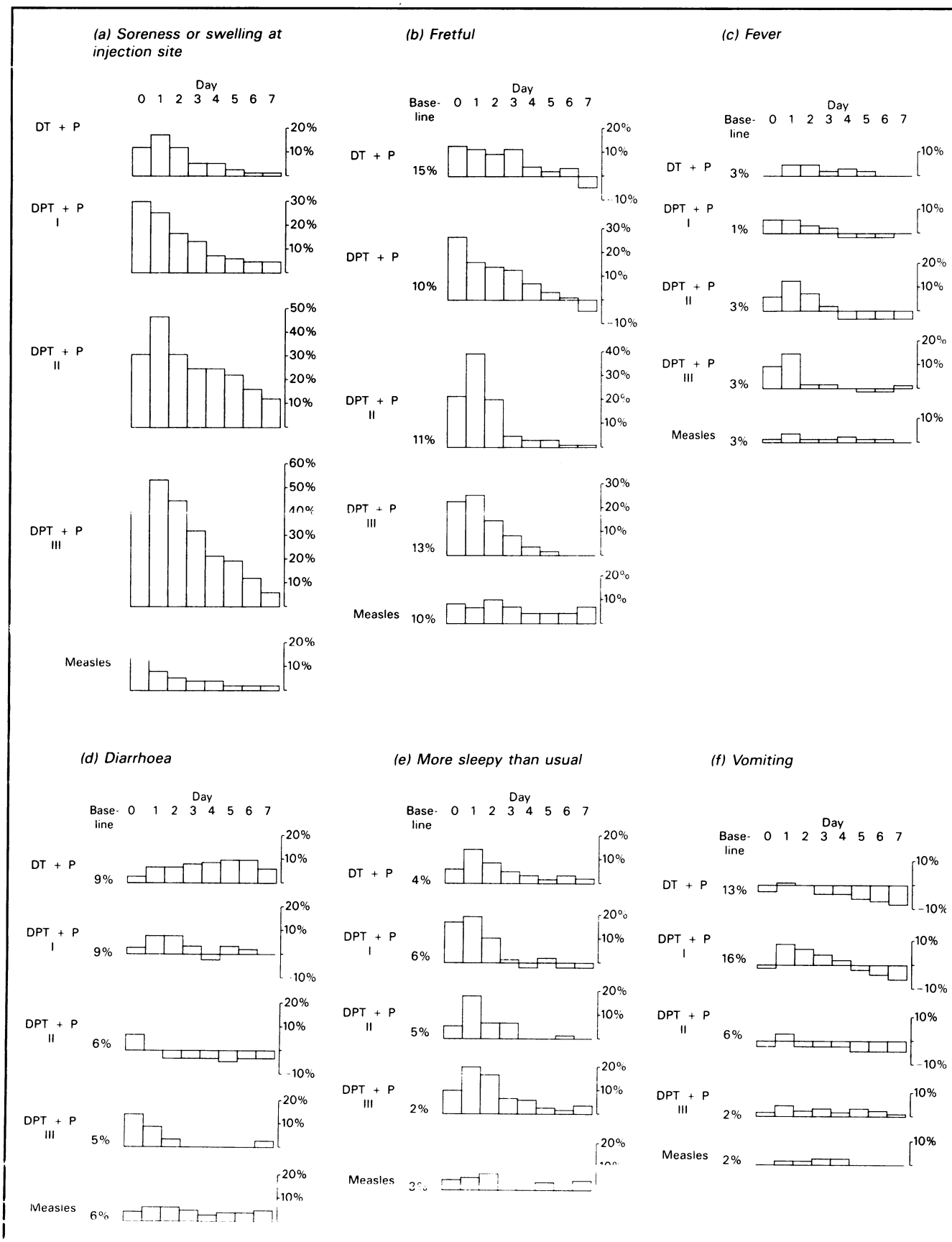

Figure 1. *Level of symptoms reported on the day of immunization (day 0) and in the following week compared with the baseline. For diphtheria/tetanus plus polio the results are a mean for the three injections.*

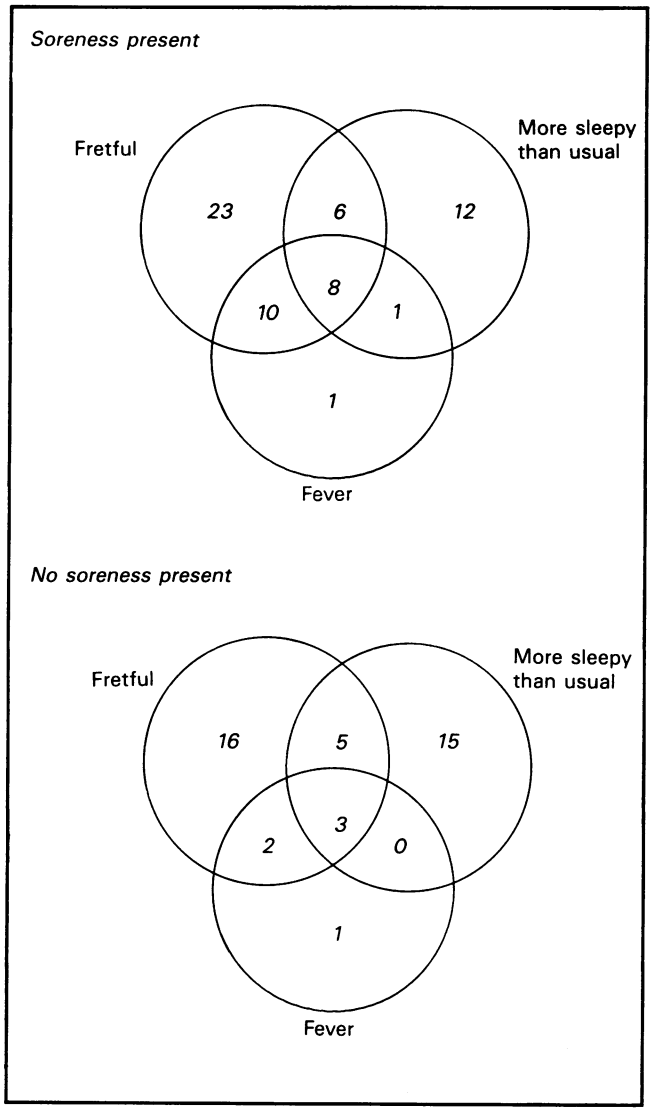

Figure 2. *Clustering of systems reported on 422 cards following diphtheria/pertussis/tetanus injection.*

Pertussis immunization as predictor for completion of course

Parents who opted for pertussis immunization were less likely to complete the child's immunizations than those who omitted it. Eighty three per cent of the children receiving diphtheria/pertussis/tetanus immunization completed the course compared with 92% who received diphtheria/tetanus only.

Major side effects

This study was not designed to study the major side effects of immunization although three were reported during the investigation. Two children had fits — one was reported as a febrile convulsion and the other as epilepsy. The third child had swollen knee joints after the pertussis injection.

Supplementary study of measles vaccination

During the 14 days after measles vaccination on which symptoms were recorded, two or fewer symptoms were reported in 38% of the children vaccinated. A preponderance of symptoms occurred around days eight, nine and 10. Overall a 4% increase in vomiting occurred around days two, four, and six and a 2–5% increase in feverishness from days five to 11, centred around days seven and 10. The incidence of diarrhoea was raised by 5% from day one to day 13. Rash, fretfulness, and sleepiness were raised by up to 10% after the injection. For rash the increase started on day three and the incidence was maximal on days nine, 10, 11 and 12. Fretfulness was reported from the day of injection to day 13 with a peak on day nine when it was reported in 20% of the children. Being more sleepy than usual was reported from the day of injection to day 13, peaking on days nine and 10.

Discussion

Parents are increasingly likely to question their doctor's or health visitor's recommendation about immunization. The purpose of this study was to describe the incidence and nature of the minor side effects of immunizations so that health professionals can provide parents with evidence of the likely occurrence of these symptoms, and hopefully increase the uptake of immunizations. The use of a diary card was shown to be an effective way of gathering control data in order to assess the development of symptoms following injections.

Few studies have been published concerning minor side effects of infant immunization and those that have lack control data. Haire and colleagues reported a study of two double blind trials of quadruple vaccine.[2] A health visitor called unannounced to the homes of vaccinated children. If the child had had no reaction she paid a final visit one week later. Where major reactions were reported one of the researchers made a more detailed assessment.

In Pollock and colleagues' study nurses followed up each child immunized by telephone, home visit or clinic visit not more than two days after immunization.[3] A total of 10 028 children were studied but collection of control data was not reported.

The department of paediatrics in Los Angeles gave parents a questionnaire and asked them to record their child's temperature three, six, 24 and 48 hours after immunization.[4] Side effects were also reported. Home visits, telephone calls and postal questionnaires were used. Waight and colleagues studied pyrexia after diphtheria and tetanus vaccines with and without pertussis.[5] They took the temperature of 808 children before and after immunization but no control data was reported.

In this survey there was a rise in the incidence of fretfulness, fever, diarrhoea and sleepiness after the injection, particularly when pertussis was given and when there was soreness at the site of injection. Although the incidence of symptoms increased with succeeding diphtheria/pertussis/tetanus injections the findings of this study do not confirm Pollock and colleagues' results[3] which suggested an increased incidence of soreness at subsequent injections. The finding that injections in the buttock result in soreness in 32% of children compared with 46% for injections in the arm suggests that the buttock should be used for routine immunization.

The higher uptake of measles vaccine when given at the age of 36 weeks instead of the recommended 65 weeks, raises the question of the appropriate timing. In this study four children had already had measles when the vaccine was offered at 65 weeks and presumably some of these episodes would have been avoided if the children had been given protection earlier. In a small survey undertaken by a trainee and his trainer in schools in Croydon during a measles outbreak, no difference could be found in loss of induced immunity between children aged eight to 11 years given vaccine at 36 weeks and 65 weeks (Opie P. Unpublished report).

Conclusions

In this study the reported minor side effects were real but not excessive in number, and we feel that the vaccines used can be

given with a high degree of confidence. Parental anxiety can be allayed by warning parents what to expect based on the evidence presented here.

1. Not all the symptoms a child gets after immunization are due to the vaccine.
2. The child is more likely to have side effects lasting no more than seven days if pertussis vaccination is included with diphtheria and tetanus and this needs to be balanced against the benefits of receiving that vaccine.
3. After measles, symptoms may occur at any time over 14 days but frequently during days 9–12 after injection, and may include rash, fretfulness, fever, more sleepy, diarrhoea, and vomiting.

Knowledge of the pattern and relatively low incidence of minor side effects may prevent inadvisable reassurance on the rare occasions when minor episodes ensue.

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