

Characteristics of infants receiving prompt first diphtheria–tetanus–pertussis immunisation in an infant cohort

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Abstract: The Centers for Disease Control in the United States have stated that studies to determine factors associated with failure to receive the first recommended dose of diphtheria–tetanus–pertussis are required. We examined an infant cohort to identify family and infant characteristics predictive of prompt first immunisation, to document changes in prompt first immunisation rates over time and to identify reasons for immunisation delay. The study sample consisted of one-fifth of live births in Tasmania at risk of sudden infant death syndrome. From 1 January 1988 to 31 December 1994, families of 8011 infants (83 per cent of eligible infants) participated in a telephone interview when the infants were a median postnatal age of 11 weeks and 3 days. Prompt immunisation was defined as the report by parents of diphtheria–tetanus–pertussis vaccination before a postnatal age of 10 weeks. The proportion of cohort infants promptly immunised increased ($P < 0.0001$) over time from 1988 to 1994. Prompt immunisation was associated with various characteristics of the infant and family. The proportion of infants promptly immunised decreased as birth order increased and as the interpregnancy interval between the index child and his or her immediately elder sibling decreased. After exclusion of infants not promptly immunised because of illness, birth order and inter-birth interval remained significant predictors of prompt immunisation, suggesting that these factors are acting to increase immunisation delay through pathways unrelated to their potential effect on infant illness rates. (*Aust N Z J Public Health* 1997; 21: 489–94)

CHILDHOOD immunisation is an important part of public health. A target of 90 per cent of children with full immunisation by their second birthday has been set for the United States,¹ New Zealand² and Australia.³ For Australia, the most recent national survey, conducted by the Australian Bureau of Statistics in April 1995, found that the proportion of one-year-old children fully immunised was highest for diphtheria–tetanus (89 per cent) and lowest for *Haemophilus influenzae* type b vaccine (51 per cent).⁴ The low coverage rates for the latter vaccine may be because of the relatively recent (April 1993) addition of this vaccine to the standard schedule of the National Health and Medical Research Council.⁴ The proportions of children aged three months to six years who were fully immunised against diphtheria–tetanus, pertussis and polio were only 69 per cent, 60 per cent and 83 per cent respectively.⁴ Considerable work has been done on identifying the groups at risk of incomplete immunisation and the reasons for noncompliance.⁵ In a recent study among North Queensland preschool children attending child care, children who had not received any vaccines by three months of age were less likely to be fully immunised at two than children who started on time (odds ratio 10.3, 95 per cent confidence interval 5.2 to 20.9).⁶ A similar finding has been reported from several recent studies in the

United States.^{7,8} A delay in obtaining the first dose of either oral polio vaccine (OPV) or the diphtheria–tetanus–pertussis (DTP) vaccine was an important predictor of failure to be up to date with immunisation at the ages of one or two in studies in 11 United States cities and rural Nebraska.⁷ The United States Centers for Disease Control have reported that the reasons for failure of children to appear on time have not been well characterised, and consequently there is a need to understand the barriers to starting the immunisation schedule and to determine maternal, infant, social and vaccine-delivery factors associated with failure to receive a first dose of DTP as recommended.^{7,8} In Tasmania, a prospective cohort study was conducted from 1988 to 1995 to investigate the aetiology of sudden infant death syndrome and childhood disease. Here, the infant cohort born from 1988 to 1994 was examined to identify family and infant characteristics at birth which were predictive of prompt immunisation with the first triple antigen and to document changes over time and reasons given for delayed first immunisation.

Methods

The prospective cohort study involved the six major obstetric hospitals in the state, representing approximately 93 per cent of live births in the state. Infants born within these hospitals were assessed using a scoring system to predict the infants at higher risk of sudden infant death syndrome. The development and performance of this model is described elsewhere.⁹ The infants were given a composite score based on maternal age, birthweight, season of birth,

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sex, duration of the second stage of labour and infant feeding. Infants with a score over a certain cut-off point were eligible to join the study. Infants with severe neonatal disease or a major congenital anomaly, infants who would not be resident in Tasmania at one month of age and infants for adoption were excluded from the study. Standard study measurements were collected by research assistants in three stages. First, a hospital interview was conducted with the mother (with the infant) when the infant was at four days postnatal age. Socio-demographic, obstetric and perinatal data, including information on maternal nutrition, alcohol and smoking patterns during pregnancy were obtained, as well as birthweight, height, head circumference and triceps and subscapular skinfold thickness measurements. Second, a home visit was conducted after the infant had reached four weeks of age: during the fifth postnatal week. Premature infants (36 weeks gestation or less) were seen at 40 weeks of postconceptional age. The home visit was deferred if the infant had not been discharged from hospital at least two weeks previously. A comprehensive questionnaire was administered. This is discussed in more detail elsewhere.¹⁰ Anthropometric and temperature measurements were made on the infant and a developmental assessment was conducted. The physical features of the house were noted. Readings were taken for humidity and 24-hour maximum and minimum infant bedroom temperatures on the day of the home visit were recorded. Third, a telephone interview was conducted after the infant was about 11 weeks of age, to review the infant's progress, illness history, feeding and immunisation. The interviewer asked the infant's parent at what age the infant received the first immunisation. If the immunisation was delayed beyond eight weeks, the parent was asked 'Why was it delayed?'. Over the period of the study, the National Health and Medical Research Council recommended that the first DTP immunisation should be administered to infants at a postnatal age of two months.^{11,12}

Study sample

From 1 January 1988 to 31 December 1994, 9692 infants were eligible for inclusion in the survey. This represents approximately one-fifth of all live births in the state over the period. Of these, 9280 infants and their mothers participated in the hospital interview, 8588 participated in both the hospital and home interviews, and 8011 (83 per cent) of eligible infants also participated in the telephone interview. The median postnatal age at telephone interview was 11 weeks and 3 days. By the end of the twelfth week, 61 per cent of telephone interviews had been conducted, and 91 per cent had been conducted by the end of the sixteenth week. Delay in completing the telephone interview was most often due to an inability to contact parents because they had no telephone, were unavailable, or had changed residence. Of these interviews, 320 were conducted in the form of a letter completed by the parents. Of those interviewed at home between 1 January 1988 and 31

December 1994, 20.6 per cent of infants were born to teenage mothers, 21.6 per cent were of low birthweight (under 2500 g), 68.9 per cent were male, 32.5 per cent were born in March or April and 65.2 per cent were bottle-fed (fully or partly). All multiple births were included in the study and 11.6 per cent of study infants were in this category. In 1989, 20.3 per cent of cohort infants were born to teenage mothers compared with 7 per cent of all Tasmanian live births, and 23 per cent weighed less than 2500 g at birth, compared with 6.7 per cent of all births in Tasmania.¹³

Statistical methods

Odds ratios and their 95 per cent confidence intervals were obtained from logistic regression with (log-odds of) immunisation status as the dependent variable. A chi-squared test for trend in proportions was applied to the annual immunisation rates.¹⁴ Stepwise logistic regression based on data available at birth was used to build models to predict immunisation status. Analyses used SAS version 6.09, except for the chi-squared test for trend in proportions.¹⁵ The latter was carried out using a custom-written GAUSS program.¹⁶

Results

Prompt immunisation was defined as the administration of the first triple-antigen vaccine before the tenth week of age in the subset of infants having the third interview at 10 weeks or later ($n = 7388$). Overall, 67.8 per cent (5007) were promptly immunised. The reasons given for immunisation delay were varied, but included: that the infant was unwell (28 per cent) and that the mother did not get around to it (29 per cent). For those responding that their infant was unwell, in most cases this was because the child had a cold.

Immunisation pattern by year of birth

The proportion of infants promptly immunised by year of birth was: 1988, 66.5 per cent; 1989, 62.5 per cent; 1990, 64.0 per cent; 1991, 63.0 per cent; 1992, 68.3 per cent; 1993, 75.9 per cent and 1994, 74.5 per cent. There was a trend of increasing prompt immunisation rates over time (chi-squared test for trend, $P < 0.0001$).

Family and infant characteristics associated with prompt immunisation

The proportion of infants promptly immunised varied according to the characteristics of the infant and his or her family (Table 1). The proportion of infants promptly immunised according to the marital relationship between the infant's parents was: for parents who were married and living together, 58.5 per cent; parents unmarried and living together, 59 per cent; parents unmarried and not living together, 58.6 per cent; and divorced, separated or other, 42.7 per cent. The proportion of babies promptly immunised was lowest (52.2 per cent) for mothers with less than 10 years of schooling. Prompt immunisa-

Table 1: Family and infant characteristics associated with prompt first diphtheria–pertussis–tetanus immunisation for infants at high risk of sudden infant death syndrome: Tasmania, 1988–1994

Characteristic	Data collection stage	Proportion promptly immunised		Univariate analysis		Multivariate analysis ^a	
		<i>n</i>	%	OR ^b	CI ^c	OR ^b	CI ^c
Six-week infant check conducted	Telephone	4142/6922	59.8	2.52	2.08 to 3.06	2.47	2.01 to 3.02
Check not conducted		173/466	37.1	1.00		1.00	
Mother satisfied with motherhood, no reservation	Home	3850/6486	59.4	1.36	1.18 to 1.56	1.33	1.15 to 1.54
Other replies		461/889	51.9	1.00		1.00	
>1 child health clinic contact	Home	2792/4566	61.2	1.33	1.21 to 1.47	1.57	1.11 to 1.74
≤1 child health clinic contacts		1530/2827	54.1	1.00		1.00	
Private health insurance	Hospital	1440/2317	62.2	1.26	1.14 to 1.39	1.21	1.06 to 1.38
No private health insurance		2762/4879	56.6	1.00		1.00	
Male infant	Hospital	3053/5138	59.4	1.14	1.03 to 1.26	1.00	0.90 to 1.11
Female infant		1280/2278	56.2	1.00		1.00	
Maternal age <20 years	Hospital	829/1379	60.1	1.09	0.97 to 1.23	0.97	0.85 to 1.11
Maternal age ≥20 years		3503/6036	58.0	1.00		1.00	
Placid temperament (1 or 2) ^d	Home	1779/3028	58.8	1.03	0.93 to 1.13	0.99	0.88 to 1.10
Nonplacid temperament (3, 4 or 5) ^d		2163/3726	58.1	1.00		1.00	
Maternal education ≤12 years	Hospital	3200/5475	58.4	0.97	0.85 to 1.10	1.00	0.87 to 1.15
Maternal education >12 years		714/1205	59.3	1.00		1.00	
Intention to bottle-feed	Hospital	1749/3004	58.2	0.99	0.90 to 1.08	0.92	0.83 to 1.02
Intention to breast-feed only		2583/4410	58.6	1.00		1.00	
Multiple birth	Hospital	517/938	55.1	0.86	0.75 to 0.98	0.89	0.76 to 1.04
Single birth		3816/6478	58.9	1.00		1.00	
Fully or partly bottle-fed	Home	2707/4742	57.1	0.86	0.78 to 0.94	0.83	0.72 to 0.92
Fully breast-fed		1624/2669	60.9	1.00		1.00	
Father unemployed	Hospital	932/1706	54.6	0.82	0.74 to 0.92	0.82	0.72 to 0.92
Father employed		3261/5490	59.4	1.00		1.00	
Mother smoked during pregnancy	Hospital	2011/3624	55.5	0.79	0.72 to 0.86	0.79	0.72 to 0.88
Mother did not smoke during pregnancy		2311/3770	61.3	1.00		1.00	
Usual sleeping position: prone	Home	625/1192	52.4	0.75	0.66 to 0.85	0.83	0.72 to 0.95
Usual sleeping position: not prone		3703/6214	59.6	1.00		1.00	
Antenatal care from ≥15 weeks of pregnancy	Hospital	668/1274	52.4	0.74	0.65 to 0.83	0.76	0.67 to 0.86
Antenatal care from <15 weeks of pregnancy		3596/6000	59.9	1.00		1.00	
Mother smoked after birth	Home	1793/3310	54.2	0.73	0.66 to 0.80	0.74	0.67 to 0.82
Mother did not smoke after birth		2530/4087	61.9	1.00		1.00	
Low birthweight (<2500 g)	Hospital	812/1670	48.6	0.60	0.54 to 0.67	0.59	0.52 to 0.67
Not low birthweight (≥2500 g)		3521/5746	61.3	1.00		1.00	
Very premature (<28 weeks' gestation)	Hospital	18/64	28.1	0.25	0.15 to 0.44	0.36	0.20 to 0.64
Premature (29 to 36 weeks' gestation)		666/1358	49.0	0.62	0.55 to 0.70	0.74	0.63 to 0.87
Not premature (>36 weeks' gestation)		3634/5973	60.8	1.00		1.00	
Gap between index birth and previous birth:	Hospital						
<27 months		954/1868	51.1	0.55	0.49 to 0.61	0.47	0.41 to 0.54
28 to 34 months		296/579	51.1	0.55	0.50 to 0.66	0.49	0.40 to 0.59
35 to 60 months		631/1150	54.9	0.64	0.56 to 0.73	0.58	0.49 to 0.68
>60 months		264/474	55.7	0.66	0.54 to 0.80	0.64	0.52 to 0.80
Not applicable (no previous birth)		2178/3320	65.6	1.00		1.00	
Birth order:	Hospital						
2		1368/2401	57.0	0.70	0.62 to 0.78	0.60	0.53 to 0.69
3		590/1182	49.9	0.52	0.46 to 0.60	0.45	0.38 to 0.53
4		201/446	45.1	0.43	0.35 to 0.53	0.37	0.29 to 0.46
≥5		80/193	41.5	0.37	0.28 to 0.50	0.33	0.24 to 0.45
first-born child		2089/3186	65.6	1.00		1.00	

Notes:

(a) Full model included characteristic and year of birth, teenage motherhood, low birthweight, multiple birth, sex, season of birth, duration of second stage of labour, intention to bottle-feed at time of hospital interview, hospital of birth and interviewer.

(b) OR = odds ratio.

(c) CI = 95% confidence interval.

(d) Parents were asked to circle the number of best fit on a five-point scale, where 1 = 'never cries/inactive' and 5 = 'irritable/restless'.

tion was positively associated with a completed six-week check, attendance at a child health clinic, private health insurance and maternal satisfaction with motherhood. Prompt immunisation was less likely among infants who were bottle-fed. The clear association between decreasing prompt immunisation rates with increasing birth order is shown in Table 1. In addition, the interval between the birth of the infant and his or her immediately elder sibling's birth appears to be important (Table 1). When infants whose immunisation delay was because of illness were excluded, birth order and birth interval remained as predictors of delayed immunisation.

At-birth models to predict prompt immunisation

Multiple logistic regression models were constructed for the purpose of trying to predict which babies were likely to be immunised promptly. Information used in these models was restricted to that available at the time of birth, as this information could be used to target babies at risk of not being immunised promptly. In each case, the logistic regression models were developed on some of the infants (the training set) and then tested on the remaining infants (the test set). The infants were divided in two ways: 1. infants born in 1988 to 1992 (5330 infants) were used as the training set, and the model was tested on those born in 1993 and 1994 (2086 infants); and 2. 5330 infants were randomly selected from the whole period to form the training set and then the model was tested on the remaining study sample. To investigate further whether the time trend in immunisation affected associations with other factors, the models were used with and without a term for year of birth.

The models did not perform well enough to be of practical use for identifying infants at risk of not being promptly immunised. For example, the model derived from randomly selected infants with terms for maternal smoking during pregnancy, late start to antenatal care (15 weeks gestation), birth order, birth interval, low birthweight, prematurity, multiple birth, intention to bottle-feed, paternal occupation, marital status and private health insurance had a sensitivity of 30.4 per cent and specificity of 84.3 per cent for predicting delayed immunisation. For both ways in which the infants were divided and irrespective of whether year of birth was included in the model, three variables consistently remained statistically significant when used on the test data: the indicators of birth order being one or two (both positively associated with prompt immunisation) compared with three or higher, and maternal smoking during pregnancy (negatively associated with prompt immunisation). When the 1988-to-1992 births were used as the training set, private medical insurance (positively associated) and premature birth (negatively associated) also remained significant when the model was applied to the test data. For the random-selection model, a gap of less than 27 months since the previous birth was still significantly negatively associated with prompt immunisation when the corresponding model was applied to the test data.

Discussion

Prompt first DTP immunisation improved over time from 1988 to 1994. Important independent positive predictors were being first or second in the birth order and private health insurance. Negative independent predictors of prompt immunisation were prematurity, low birthweight, a late start to antenatal care, marital status, a birth interval of less than 27 months between the infant and elder sibling's birth and maternal smoking during pregnancy.

Cohort studies have not often been conducted in research on immunisation, owing to cost, difficulty in obtaining satisfactory follow-up rates and bias introduced by excluding children with an incomplete home immunisation record.¹ This cohort study has the following advantages and disadvantages. An advantage is that the study had a good follow-up rate, with 83 per cent of eligible families completing all three interviews for their infants. Selection bias can be a serious problem in immunisation studies with low response rates, particularly if the characteristics of the nonresponders and those who participate in the study differ, and these characteristics are also associated with immunisation failure. The high response rate in this study lessens concerns about such selection bias. The cohort consisted of the one-fifth of live births in Tasmania over the study period who were at risk of sudden infant death syndrome. Possible confounding by the component variables of the scoring system were controlled for (Table 1). The characteristics of the study sample have been described to allow the readers to consider whether their target population is similar. An advantage is that the sampling strategy provides an overrepresentation of infants born to families of lower socioeconomic status. The barriers to prompt immunisation are important to understand in this group to ensure that essential care is available to the poor.¹ A disadvantage of the study is that the outcome definition—delayed first DTP and polio immunisation—was based on parental report only. This approach has been used in other studies. For example, in a recent cohort study in New Zealand, factors associated with incomplete immunisation were based on a structured questionnaire administered by child health nurses.² However, parental report has been found to have limitations, with discrepancies being found between parents' and doctors' report in New Zealand.¹⁷ Also, in a study of 128 children attending 24-hour medical centres in Western Sydney, 108 children (mean age 23 months) were reported by their parents as having been immunised, but of these, only 84 per cent (91) had serological immunity. Of the remaining 16 per cent (17), in only 12, at maximum, could this be attributed to possible seroconversion failure, leaving at least five children whose failure to be serologically immune was because of either incorrect parental report or vaccine mishandling.¹⁸ In this study, it is likely that incorrect parental report was less, because the interview was conducted soon after the first immunisation was due, minimising inaccurate recall. Second, the parents were asked the age of the infant at first immunisation so that they would not be placed in a

position of having to provide a *yes* or *no* response. Third, the parents of the infant had had an opportunity to build a relationship with the infant health survey interviewer in the previous two interviews. There is some evidence for this possibility, in that 37 per cent of mothers interviewed by the time their baby was 12 weeks old admitted that their child had started solid food, although the current recommendations are for solid diet commencement at a post-natal age of four months or later.¹⁹ However, we acknowledge that the outcome measurement still remains a deficiency in the study, and therefore consider the cohort findings are not definitive but a guide to future work in this area.

The trend of increasing rates of prompt first immunisation among cohort infants is encouraging. The largest increase in prompt immunisation rates between years occurred between 1992 and 1993. In May 1993, a comprehensive personal health record system was released to replace the smaller child health clinic book.²⁰ Both booklets have sections for a written immunisation record. In addition, in 1993, a discussion paper outlining a new immunisation strategy was distributed for public comment and among health care providers.²⁰ Parent-held immunisation records are thought to increase the parent's awareness of the need for immunisation and encourage parents to take responsibility for their child's health.²¹

Some of the characteristics identified in this cohort to be associated with delayed immunisation have been reported previously. For example, being high in the birth order has been associated with incomplete immunisation^{2,22,23} and delayed immunisation,²³ with birth order being found to be more important than family size in one study.²⁴ Associations with single parenthood and unemployment have also been reported.⁴ The New Zealand cohort study found older mothers were more likely to have babies who were incompletely immunised,² but other studies have found the infants of younger mothers to be less likely to be immunised.⁵ Similarly, mothers of both high^{2,22} and low^{2,23} education have been reported to be less likely to have a completely immunised infant. In this study, we found maternal age was not related to prompt immunisation. An interesting finding from this study was that the birth interval between the index infant and his or her next oldest sibling was a significant predictor of prompt immunisation status, even after adjustment for birth order and other factors in the multivariate analysis. This indicates that information on birth interval should be sought in future immunisation health research, as it is a potentially important characteristic to be considered in health care planning. Birth order and birth interval remained as predictors of delayed immunisation, even when infants with delay because of illness were excluded, indicating that these two variables act to increase immunisation delay, in part, through pathways unrelated to their potential effect on increasing the risk of infant illness.

An at-birth model to predict prompt first immunisation was developed because it is thought that activ-

ity aimed at high-risk groups could more effectively increase population immunisation coverage. The identification of children at risk for missing their first dose of DTP would enable them to be targeted for intensive follow-up to minimise the delay in receiving appropriate vaccinations.⁸ However, our model did not have a high sensitivity and would not be useful as a screening test for delayed immunisation. The low sensitivity of the model may be due to the omission of vaccine delivery factors (such as ease of access to immunisation services) which may also lead to failure to start the immunisation schedule.⁸

In this study, as in others, minor illness was a major reason why infants did not receive prompt first immunisation.^{1,2,5} Minor temporary intercurrent illness is not a contraindication to the first DTP immunisation,²⁵ and therefore a greater effort to improve the knowledge of parents and providers with regard to contraindications for immunisation should be made. Another situation that is often unclear is the timing of the first immunisation for premature infants. The National Health and Medical Research Council recommends that premature infants be immunised at a postnatal age of two months and that corrections not be made for prematurity.¹² However, this recommendation is sometimes not followed and immunisation for preterm infants is sometimes delayed.^{26,27} This appears to have occurred in this cohort, as prematurity was found to be a significant predictor of future immunisation delay. This may not necessarily have been the result of medical advice, because although 19.2 per cent of cohort infants were premature, only 1 per cent of the delayed immunisations in 1994 were attributed to a delay based on medical instructions. In the recent 1995 national immunisation survey, the major reason given for nonvaccination in relation to diphtheria, tetanus, pertussis or polio was that the baby was too young, although all subjects were over the required age for first dose of these vaccines.⁴

In conclusion, in this prospective cohort study, various characteristics of the infant and his or her family were found to be associated with a higher risk of first DTP immunisation delay. Interbirth interval was a significant predictor of delayed immunisation. Further research on the determinants of delayed immunisation should assist in the design of new interventions to improve immunisation coverage in Australia.

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