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ORIGINAL ARTICLE

Hospitalisations due to pertussis in New Zealand in the pre-immunisation and mass immunisation eras

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Aim: Pertussis disease burden in New Zealand in recent decades has been large compared with other developed countries. However, these comparisons use data from relatively short time periods given the long epidemic cycle of pertussis. To better understand the current disease burden, this study examined pertussis hospitalisation data in New Zealand in both the pre-immunisation and mass immunisation eras.

Methods: Hospital discharge data and population data from 1873 to 2004 were used to estimate average pertussis hospital discharge rates per decade. Rates were compared using relative risks and 95% confidence intervals (CI).

Results: Average annual pertussis hospitalisation rates per 100 000 were less than two from 1873 to 1919, increased to 12 in the 1940s, decreased to less than four in the 1960s and have increased since then with the rate in the current decade being 5.8. Compared with the 1960s (3.8 per 100 000) the average annual rate has been significantly greater in the 1980s (RR = 1.11, 95% CI 1.03, 1.21), 1990s (RR = 1.33, 95% CI 1.23, 1.44) and 2000s (RR = 1.55, 95% CI 1.42, 1.68). Since 1960 hospitalisation rates have increased for those less than one year old, one to four years old and five years and older. The increases have been most marked for infants (RR 2000s vs. 1960s = 2.87, 95% CI 2.59, 3.18).

Conclusion: After an initial decline following mass immunisation, pertussis hospitalisation rates in New Zealand have subsequently increased steadily. To reduce pertussis disease burden improved immunisation coverage and timeliness is required and consideration given to spreading the pertussis vaccine schedule over a wider age range.

Key words: hospitalisation; immunisation; infant; New Zealand; whooping cough.

Pertussis vaccine has been available in New Zealand since 1945 and an immunisation schedule present since 1960.[1,2] Pertussis disease burden in New Zealand in recent decades has been large compared with other developed countries. Comparisons have been made using laboratory isolate, hospital discharge, and, since 1996 when it became a notifiable disease,[3] passive notification data. All three sources indicate a disease burden five to 10 times greater than that in the UK or the USA.

Key Points

1 Pertussis hospitalisation rates in New Zealand decreased following the introduction of mass immunisation, but have been increasing since the 1970s.
2 New Zealand has a pertussis hospitalisation rate five to 10 times higher than other developed countries.
3 Poor vaccine coverage is likely to be the dominant reason for the high rates with contributions also from an inadequate two-dose schedule from 1971 to 1984 and more recently from poverty and overcrowding.

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For example, from 1980 to 1989 the pertussis hospitalisation rate per 100 000 population per year was 3.75 in New Zealand and 0.37 in the USA.[4] The pertussis notification rate in New Zealand in 1996, an epidemic year, was 19.8 per 100 000.[5] This notification rate was more than seven times greater than that for the US epidemic in 1993.[6] The average annual pertussis hospitalisation rate in New Zealand during the 1995–1997 epidemic was 10.2 per 100 000. In comparison, the hospitalisation rate in the USA from 1990 to 1996 was 0.6 per 100 000 and in England in 1995 was 1.3 per 100 000.[7,8]

Unlike *Bordetella pertussis* infection, which is endemic, pertussis disease has a four yearly epidemic cycle with large fluctuations in incidence rates between epidemic and non-epidemic years.[9] Thus the use of data from one epidemic or even a decade does not allow trends over time to be determined.

The aims of this study were to describe the epidemiology of pertussis in New Zealand over a more extended period of time including both the pre-immunisation and mass immunisation eras. From this description we sought to determine whether there has been a sustained excess of pertussis disease burden in New Zealand as is suggested by the data reported from shorter time intervals.

Methods

Population, mortality and hospital discharge data were abstracted from official New Zealand publications from 1873 to

2004.[10–25] Epidemic years were defined as those in which the number of deaths and number of hospital discharges exceeded those in the previous and subsequent year.

Hospital discharge data were reported by five yearly age intervals from 1914 and by yearly intervals to age five from 1950.[11–22] Data were abstracted for those less than 5 years old from 1914 and less than 1 year old from 1950.

Annual population statistics were obtained from five yearly censuses and intercensal estimates.[25,26] Statistics on the total population and total births were obtained from 1873, and on the population age 4 years and younger from 1914.

Hospital discharge rates were calculated for the total population and then by age group using the appropriate denominators. The annual number of births was used as the denominator for the estimation of infant hospital discharge rates.

In order to describe trends in rates over time average rates for decades were calculated.[27] These average rates minimised the effect of year to year fluctuations caused by epidemics. For these average rates, the number of hospitalisations in each year of the time period were combined as the numerator, and the number of people in the population for each year of the decade as the denominator. As an individual in the population could appear in the denominator more than once, the rates were reported in person-years.[28]

All pertussis hospital discharge rates were reported per 100 000 population or person-years. Infant hospital discharge rates were reported per 100 000 births or birth-years.

The average inter-epidemic time intervals prior to and since mass immunisation were compared using confidence intervals analysis software.[29] This same software was used to calculate 95% confidence intervals for rates. Average annual rates were compared between decades as relative risks with 95% confidence intervals using Epi-Info.[30] The significance of changes over time in the proportion of hospitalisations in different age groups were determined using the χ^2-test.

Results

Epidemic years occurred in 1874, 1878, 1880, 1884, 1888, 1892, 1895, 1900, 1904, 1908, 1911, 1914, 1917, 1921, 1926, 1932, 1936, 1941, 1944, 1946, 1949, 1952, 1955, 1959, 1961, 1964, 1967, 1971, 1974, 1978, 1982, 1986, 1991, 1996, 2000 and 2004. There were 35 inter-epidemic time periods. The mean ± SD interval between epidemic years was 3.71 ± 0.93 years. The inter-epidemic time periods prior to mass immunisation (1873–1944) and since immunisation (1945–2004) were not significantly different (3.89 ± 0.96 vs. 3.53 ± 0.87 years, $t = 1.15$, $P = 0.26$).

The pertussis mortality and hospital discharge rates (Fig. 1), and the average annual pertussis hospital discharge rate per decade (Fig. 2) are shown. Pertussis mortality rates were high and hospital discharge rates low (0.3–1.6 per 100 000) from the 1870s to 1910s. Hospital discharge rates (per 100 000 population) then increased from the 1910s (1.6) to the 1940s (11.9), decreased during the 1950s (7.6) and 1960s (3.8) and have then increased since the 1970s (3.8).

In Figure 2 the timing of changes to the national pertussis immunisation schedule are superimposed on the average hospital discharge rate per decade. The reduction in pertussis hospital discharge rates in the 1950s and 1960s coincided with the

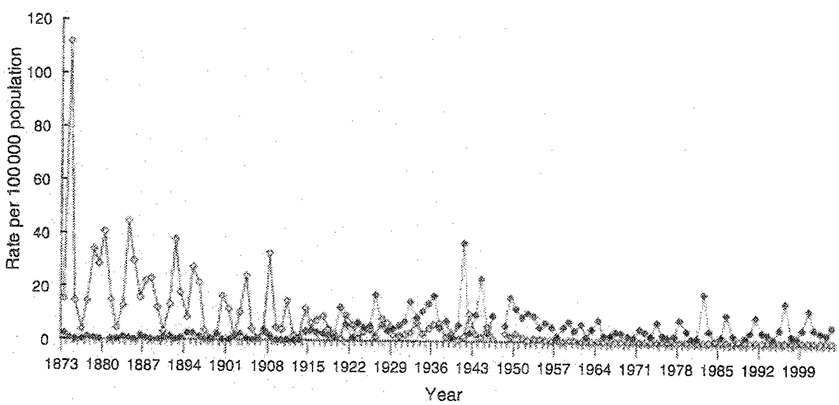

Fig. 1 Annual pertussis hospital discharge rate and death rate per 100 000 population in New Zealand 1873–2004. (–◇–) Mortality rate per 100 000; (–◆–) hospital discharge rate.

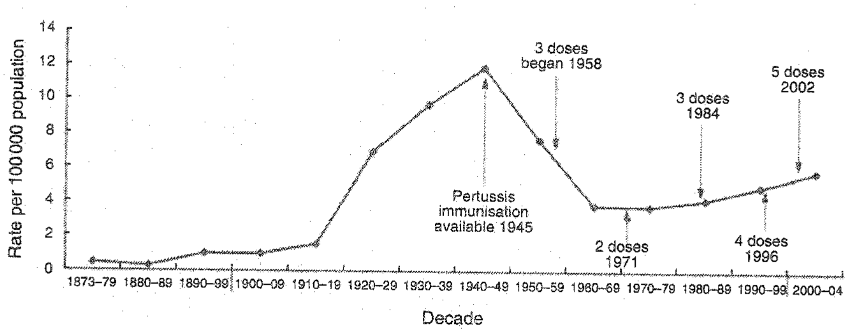

Fig. 2 Annual average pertussis hospital discharge rate per decade per 100 000 person-years 1873–2004. (–◆–) Hospital discharge rate.

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Table 1 Number of cases and average annual pertussis hospital discharge rates per 100 000 person-years per decade by age group

Decade	Age group							
	Less than 1 year		1–4 years		5 years and older		All ages	
	n	Rate	*n*	Rate	*n*	Rate	*n*	Rate
1950–1959	774	143.74	505	25.36	238	1.28	1517	7.64
1960–1969	638	101.87	253	10.55	76	0.33	967	3.82
1970–1979	780	132.32	268	11.53	96	0.35	1144	3.79
1980–1989	910	174.42	307	15.20	138	0.46	1355	4.17
1990–1999	1286	221.99	320	14.61	204	0.61	1810	4.98
2000–2004	821	292.55	147	13.67	172	0.94	1140	5.78

Table 2 Average annual hospitalisation rate per decade for 1970–2004 compared with 1960–1969

Decade	Relative risk (95% confidence interval) for each age group			
	Less than 1 year	1–4 years old	5 years and older	All ages
1960–1969	1.0	1.0	1.0	1.0
1970–1979	1.30 (1.17, 1.44)	1.09 (0.92, 1.30)	1.06 (0.78, 1.43)	1.01 (0.93, 1.10)
1980–1989	1.71 (1.55, 1.89)	1.44 (1.22, 1.70)	1.38 (1.05, 1.83)	1.11 (1.03, 1.21)
1990–1999	2.18 (1.98, 2.40)	1.38 (1.17, 1.63)	1.82 (1.40, 2.37)	1.33 (1.23, 1.44)
2000–2004	2.87 (2.59, 3.18)	1.30 (1.06, 1.59)	2.81 (2.15, 3.69)	1.55 (1.42, 1.68)

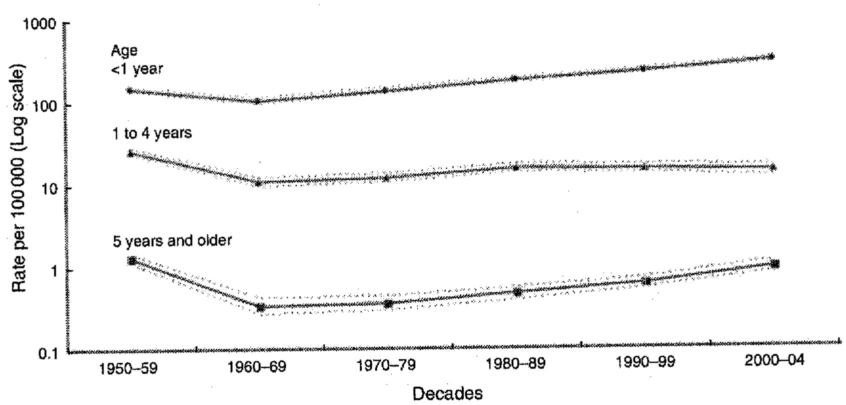

Fig. 3 Average pertussis hospital discharge rate by age group (with 95% confidence intervals) per decade per 100 000 person-years 1950–2004.

introduction of mass immunisation. The increase from a two-dose to a three-dose schedule in 1984, to a four-dose schedule in 1996 and a five-dose schedule in 2002 occurred during a time interval when pertussis hospital discharge rates increased.[31]

The average annual pertussis hospital discharge rates per decade from 1950 to 2004 for all ages and for the three age groups (less than 1 year, 1–4 years, 5 years and older) are shown in Table 1. Across all ages the hospital discharge rate decreased in the 1960s and 1970s compared with the 1950s and then increased in subsequent decades. A logarithmic plot of these data are shown in Figure 3. As demonstrated in the figure the hospital discharge rates in those less than one and in those 5 years and older increased while the rate in those aged 1–4 years increased until the 1980s, and has decreased slightly since.

In Table 2 the average annual hospitalisation rates per decade for the 1970s, 1980s, 1990s, and 2000–2004 are compared with the average annual rate for the 1960s. Across all ages the average annual rate has been significantly greater in all decades from 1970 onwards with the relative risk increasing in successive decades. Within age groups this same trend is apparent for infants from the 1970s and for those aged 1 year and older from the 1980s. For infants and those 5 years of age and older the relative risk of hospitalisation increased in successive decades, from the 1970s for infants and from the 1980s for those 5 years of age and older.

Table 3 Proportion of pertussis hospital discharges that were less than 5 years old (1914–2004) and less than 1 year old (1950–2004)

Decades	Proportion less than 5 years old	Proportion less than 1 year old†
1914–1919	0.72	–
1920–1929	0.70	–
1930–1939	0.71	–
1940–1949	0.80	–
1950–1959	0.84	0.51
1960–1969	0.92	0.66
1970–1979	0.92	0.68
1980–1989	0.90	0.67
1990–1999	0.89	0.71
2000–2004	0.85	0.72

†Data for this age group not available until 1950.

Table 4 Total number of deaths due to pertussis and mortality rate per 100 000 in 5-year intervals 1950–2004

Time interval	Number of deaths from pertussis	Pertussis mortality rate per 100 000
1950–1954	119	1.19
1955–1959	37	0.33
1960–1964	17	0.14
1965–1969	8	0.06
1970–1974	4	0.03
1975–1979	4	0.03
1980–1984	1	0.01
1985–1989	1	0.01
1990–1994	0	0.00
1995–1999	1	0.01
2000–2004	5	0.03

The proportions of pertussis hospital discharges in each decade for children who were less than 5 years old (from 1914 to 2004) or less than 1 year old (from 1950 to 2004) are shown in Table 3. The proportion who were less than 5 years old increased from 0.72 in 1914–1919 to 0.85 in 2000–2004 ($\chi^2_{trend} = 310.41$, $P < 0.001$). The increase in proportion who were less than 5 years was not constant over time. There was no increase from 1914 to 1939 ($\chi^2_{trend} = 0.010$, $P = 0.9194$). Over the next four decades the proportion increased from 0.71 in 1930–1939 to 0.92 in 1970–1979 ($\chi^2_{trend} = 258.12$, $P < 0.001$). The proportion less than 5 years old then decreased from 0.90 in the 1980s to 0.85 in 2000–2004 ($\chi^2_{trend} = 14.56$, $P < 0.001$).

The proportion of those hospitalised who were less than 1 year old increased from 0.51 in 1950–1959 to 0.72 in 2000–2004 ($\chi^2_{trend} = 144.35$, $P < 0.001$). As shown in Table 3 the increase in the proportion of hospitalisations in those less than 1 year old occurred mainly during the 1950s and 1960s (increase from 0.51 to 0.66, $\chi^2 = 41.92$, $P < 0.001$). Since then the proportion has increased to a lesser degree (from 0.66 to 0.72, $\chi^2_{trend} = 12.42$, $P < 0.001$).

The pertussis mortality rate in New Zealand has been less than 35 per 100 000 since 1900 and 10 per 100 000 or less since 1930. The number of deaths from pertussis in each 5 year interval since 1950 is shown in Table 4. The mortality rate was 0.01 per 100 000 or less from 1980 to 1999 but in the most recent 5 year time interval increased to 0.03 per 100 000.

Discussion

As was seen in incidence reporting from other developed countries, pertussis hospital discharge rates increased from the 1920s to the 1940s before declining during the 1950s and 1960s in association with mass immunisation.[32–36] The large increase during the 1950s and 1960s in the proportion of cases in infants shows that the overall decrease in rates was secondary to immunisation. A similar concentration of disease in infants has been described in other countries in association with increased immunisation coverage. For example, in the UK as immunisation coverage increased from 30% in 1978 to 93% in 1993, pertussis incidence fell in all age groups but more markedly in those 6 months to 2 years old than in those less than 6 months old. As a result, the proportion of total cases who were less than 6 months old doubled.[37]

Since the 1970s pertussis hospital discharge rates have increased. These recent increases have been substantial with the hospital discharge rate in the current decade, approximately 1.5 times greater than in the 1960s although still less than half of the 1940s rate. In comparison with other developed countries the contemporary hospitalisation rates are excessive for both infants and the total population, being five to 10 times greater than those reported from the USA and England in the 1990s[7,8] Although the hospitalisation rates since 1970 have increased in all three age groups studied, the increases have been less marked in children 1–4 years of age than in younger or older children.

The mortality rate per 100 000 due to pertussis in New Zealand from 1995 to 1999 is the same as the reported mortality rate in England from 1994 to 1999 (0.01 per 100 000).[38] The mortality rate due to pertussis in New Zealand is higher than that in the USA, where the reported average annual mortality rates rate per 100 000 were 0.003 in the 1980s[39] and 0.004 in the 1990s[40] As in New Zealand, there has been an increase in mortality over the last two decades.[40]

It is important to acknowledge the limitations of the data. As this study used hospital discharge statistics it will have underestimated pertussis incidence. Diagnosis specific infant hospital discharge data were not reported until 1950, therefore we could only describe the discharge data for the entire study interval using the total population as the denominator. Data were collected over a long time interval and thus will have been affected by variability in a number of factors including changes in living conditions, diagnostic coding and hospital admission criteria. For example, the reduction in pertussis mortality and case fatality rates observed in both the UK and the USA in the early 20th century was thought to be due to 'an absolute and proportional reduction in physically substandard children.[35] Particularly with the absence of any laboratory diagnostic methods the accuracy of diagnosis of pertussis must have varied. This variability is

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likely to have been even greater than that which has been described in validation studies of the accuracy of death certificate diagnoses, where the recorded diagnosis varies from the autopsy diagnosis in up to 29% of cases.[41] However, none of these factors adequately explain the changes in hospitalisation rates that were seen over time, in particular the increase from the 1910s to the 1940s followed by the decrease until 1960s and the further increase since then.

As pertussis did not become a notifiable disease in New Zealand until 1996, hospital discharge data were the only type of incidence data available over a sufficiently long-time frame to enable temporal trends to be examined. A direct comparison between notifications and hospitalisations was performed shortly after the introduction of pertussis as a notifiable disease. This showed that during the 1995–1997 epidemic the hospitalisation rate for infants from 7 weeks to 2 months of age was twice as high as the notification rate.[5] The notification rate from 2000 to 2004 was 53.86 per 100 000 compared with 12.99 per 100 000 from 1995 to 1999, implying more complete notification in recent years, and thus now a complimentary measure of disease incidence.[42]

Improved laboratory diagnosis of *B. pertussis* infection is unlikely to explain the increase in hospital discharge rates in recent decades. Although culture for *B. pertussis* became available as a routine test in hospital laboratories during the 1980s, polymerase chain reaction did not become available in New Zealand until the late 1990s and is therefore likely to have made only a small contribution to the recent increase.

This study confirms observations by others that mass immunisation has had no significant effect on the pertussis epidemic periodicity.[9,32,43] Previous research from New Zealand had suggested a lengthening of the epidemic cycle following the introduction of immunisation.[44] These conclusions were based upon a study interval commencing in 1948 and hence did not include sufficient data from the pre-immunisation era. The lack of effect of immunisation on the epidemic periodicity is central to our understanding of pertussis as an endemic disease in adolescents and adults and hence to future immunisation strategies aimed at improving pertussis control.[45]

The two principal reasons for pertussis hospitalisation rates to increase in developed countries have been decreased vaccine efficacy (e.g. Canada in late 1980s and the 1990s) and decreased immunisation coverage (e.g. UK in late 1970s and the 1980s).[37,46–48]

Pertussis vaccines used in New Zealand have been shown to be efficacious in other countries.[49–54] Pertussis vaccine efficacy estimates performed in New Zealand have been consistent with the international efficacy data.[55,56] Therefore, neither the high hospitalisation rates nor the recent increases are likely to be due to poor vaccine efficacy.

Since first measured in the 1970s vaccine coverage in New Zealand has been mediocre. The most reliable estimates are from a birth cohort in 1978, and from national and regional immunisation surveys performed in 1992 and 1996 that used WHO recommended methods.[57–60] The complete infant series was received by 89% in 1978, 81% in 1992 and 86% in 1996. In 1992 and 1996 approximately 20% of children were delayed for the 6-week, 30% for the 3-month and 45% for the 5-month pertussis immunisations.[59,60] During the 1996 pertussis epidemic delayed receipt of any of the three first year vaccine doses was associated with a fivefold increased risk of hospitalisation with pertussis.[61] Thus, low immunisation coverage and even lower on time coverage is likely to be the dominant reason for high pertussis hospitalisation rates in New Zealand, particularly so for infants who currently account for approximately 70% of all children hospitalised with pertussis (Table 3).

Two other factors may also have contributed. First, the increase in pertussis hospitalisation rates over the past four decades are likely a reflection of the increasing proportion of New Zealand's children whose lives are adversely affected by poverty. Income inequalities have increased in New Zealand over the past 20 years.[62] The average after tax household income in New Zealand has declined since 1980 with the decline being greatest in single parent, Maori and Pacific households.[63] In 1981, 12% of children under 15 years old lived in one parent families. By 2001 this had increased to 29% of all children.[64] A larger proportion of Maori and Pacific children compared with European children live in single parent families.[63,65]

The increase in single parent families has been paralleled by an increase in multi-family and extended family households, leading to increased household crowding. Given the central role that household transmission plays in pertussis spread, it is likely that such crowding is a driving force for the increase in pertussis hospitalisation rates in recent decades.[35,66–68] This is consistent with the dominant role that household crowding has played as a disease risk factor during the recent national meningococcal epidemic.[66]

In addition to facilitating disease spread poverty also creates powerful barriers to immunisation.[69] From an immunisation delivery perspective the National Health Committee has identified children living in poverty as one of the key groups for whom immunisation services are currently inadequate. It estimates that 55% of Maori children, over 40% of Pacific children and nearly 30% of European/other children fall into this 'hard to reach' category.[70] If vaccine preventable disease morbidity is to be reduced then New Zealand must find a way to deliver immunisation on time to these children.

Second, from 1971 to 1984 New Zealand had an inadequate two-dose (age 3 months, 5 months) pertussis vaccination schedule. Thus, children immunised during these years, who will now be of child-bearing age, will have had poorer vaccine-induced immunity to pertussis.[31] Therefore, they are likely to have experienced more severe disease and to have been effective spreaders of *B. pertussis* to younger vulnerable children.

How can pertussis disease burden in New Zealand be decreased? First, immunisation coverage and timeliness must improve. Infant hospitalisation rates will not decrease unless the infant immunisations are given early in infancy. Second, a reliable and accessible record of each child's immunisation history that enables frequent and accurate measurement of coverage must be developed. A national immunisation register is currently being created and will potentially solve this problem.[71] Third, in order to both protect infants and reduce pertussis hospitalisations the pertussis immunisation schedule must be spread over a much broader age range than the schedule which in 2005 delivered the first dose at age 6 weeks and the fifth and last dose at age 4 years.[31] Changes to the immunisation schedule from 2006, with the booster doses given at ages 4 and 11 years, rather than 15 months and 4 years, will start to address this issue.[72]

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