An outbreak of measles in a rural Queensland town in 1997; an opportunity to assess vaccine effectiveness

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Abstract

This report describes a measles outbreak in a rural town in south-east Queensland and presents the results of a vaccine effectiveness (VE) study performed during this outbreak. It is important to assess the effectiveness of a vaccine in an outbreak to determine if the outbreak is due to failure of the vaccine or failure to vaccinate. There were 44 cases of measles amongst local residents, which represents a notification rate of 396.7 per 100,000 population. Case investigations identified a group of people who had been exposed to measles at a seminar. The attack rate for the seminar cohort was 18% (11/61). This presented an opportunity to conduct a VE study using data about children aged less than 16 years who attended the seminar. In this cohort of 23 attendees, all 7 children who had not received any measles vaccinations became cases whilst the 6 who were fully vaccinated for their age according to NHMRC guidelines were protected from measles illness. Although there were insufficient fully vaccinated cohort members to reliably estimate VE for this group, the vaccine was 84.6% (95% CI: 15.0-99.7%) effective for those who had received at least one validated dose of vaccine. Despite the sample size limitations, the results support the view that failure to vaccinate rather than vaccine failure contributed to the high infection rate in the seminar cohort. *Commun Dis Intell* 1999;23:240-245.

Introduction

On 9 September 1997, a case of measles in a resident of a rural town in south-east Queensland was notified to Queensland Health. Serologically confirmed cases of measles had already been reported from a neighbouring town. By 15 September 7 measles notifications had been received. Investigation of these cases revealed that some had attended a local education seminar on 28 August.

Investigation of the education seminar cohort identified an opportunity to assess the effectiveness of the measles vaccine. Assessing the effectiveness of a vaccine in an outbreak is important to determine if the outbreak is due to failure of the vaccine or failure to vaccinate. Vaccine *efficacy* is usually determined under controlled conditions prior to licensing, however the *effectiveness* of a vaccine under normal (field) conditions may vary and should be assessed when the opportunity arises. Vaccines may fail due to incorrect storage and administration of the vaccine, drug interference or the age at vaccination. Vaccine effectiveness may vary in different populations.[1] Establishing that a vaccine is effective during an outbreak provides support for continuing efforts to improve vaccination coverage levels and may allow the appraisal of current vaccination strategies.

This report describes a measles outbreak in a rural town in south-east Queensland during 1997 and provides the results of a vaccine effectiveness (VE) study. The relationship of this outbreak to the state-wide outbreak is also discussed.

Methods

Case definitions

The NHMRC measles case definitions for national surveillance and a confirmed case[2] (Box) were used to define a case as being notifiable to the Queensland

Box. Measles case definitions for notification to the Queensland Notifiable Diseases Registry[2]

Measles case definition for national surveillance

An illness characterised by all of the following features:

(a) a generalised maculopapular rash lasting three or more days; and

(b) a fever exceeding 38.3°C; and

(c) cough or coryza or conjunctivitis or Koplik spots.

Measles confirmed case definition

A person with signs and symptoms consistent with measles and any one of the following:

(a) measles virus detected in an appropriate specimen; or

(b) the presence of measles specific IgM antibody; or

(c) a fourfold rise in measles antibody titre in sera obtained at least two weeks apart; or

(d) history of contact with a laboratory confirmed case.

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Notifiable Diseases Registry (NODS). A presumptive case was defined as having an illness characterised by a morbilliform rash, cough, and fever present at the time of rash onset.[2]

Notified cases with onset dates between 15 August and 31 December 1997 were considered part of the state-wide outbreak. This time period was chosen because 15 August was the onset date of the first notified case in 1997 from the town where this outbreak was first recognised, and the number of State notifications returned to pre-outbreak levels by 31 December. Cases considered part of the local outbreak were those with onset dates during the outbreak who resided in the rural Queensland town, or were linked to the education seminar.

Outbreak notification rates were calculated using the 1996 census population supplied by the Australian Bureau of Statistics. The distributions of local cases by age, sex, date of onset, statistical local area of residency, and method of diagnosis (clinical or laboratory confirmed) were determined.

Active case finding

All possible measles cases reported to the Central Queensland Public Health Unit outbreak investigation team were questioned about whether they had the symptoms and signs that defined a presumptive or notifiable case. Cases identified as being presumptive or notifiable were asked about their contact with other people during the period 1 day prior to developing signs of measles to 4 days after developing a rash. This period was defined as the infectious period of a case.[3] Individuals who had been in contact with an infectious case were interviewed to determine whether they had the symptoms and signs of measles. Presumptive or notifiable cases were also questioned about their contact with other people in the incubation period 7 to 18 days prior to developing signs of measles infection.[3] People identified as having had contact with a case during this period were then interviewed about whether they had the symptoms and signs of measles. Serological confirmation was recommended for presumptive cases that did not have incubation periods consistent with contact with an infectious case, or when clinical symptoms did not conform to those used to define a notifiable case. Notifiable cases identified by these active case finding methods were allocated to one of the case types described in Table 1.

Vaccine effectiveness study

The cohort

Interviews with presumptive and notifiable primary cases about their attendance at any gatherings during their defined infectious period identified 11 cases who had attended the education seminar. Investigation of these cases identified one person who had coryzal symptoms and conjunctivitis at the seminar and developed a rash the next day. This case was therefore defined as being the probable source case for the seminar cohort.

The education seminar was investigated further to identify a suitable cohort for performing a VE study. Details about the seminar were obtained from the seminar coordinator. The seminar was in a hall and there were two sessions with a tea break in between. The first session ran from 2 p.m. until approximately 5.30 p.m. and the second ran from 7 p.m. until 9 p.m. A list of people who attended the education seminar was constructed by the seminar coordinator and telephone interviews were conducted with available attendees. Seminar attendees, or a parent of an attendee, were questioned at least 18 days after the seminar (that is, after the defined incubation period for exposure to an infectious case at the seminar). Questions were asked about attendance at each of the seminar sessions, the attendees' age, their measles vaccination status, and whether they had the symptoms and signs that defined a presumptive or notifiable case. Attendees were also asked if they could provide the names of any other attendees in order to establish the completeness of the attendance list. The interviews established that the probable source case only attended the afternoon session

Table 1. Case definitions used during the investigation of a measles outbreak in a rural Queensland town, and at an education seminar in that town, 15 August - 31 December 1997

Type of case	Definition
Primary case	A presumptive or notifiable case.[+]
Secondary case	As for a primary case, *and* had an incubation period[#] consistent with exposure to an infectious* primary case.
Probable source case	As for a primary case, *and* whilst infectious,* they had contact with a primary case, *and* this contact was within the time frame for the incubation period[#] of the primary case.
Probable source case linked to the seminar	As for a primary case, *and* attended the seminar whilst infectious.*
Primary case linked to the seminar	As for a primary case, *and* attended the seminar, *and* had an incubation period between 7 and 18 days after the seminar.
Secondary case linked to the seminar	As for a secondary case, *and* their primary case attended the seminar.
Primary case indirectly linked to the seminar	As for a primary case linked to seminar, *except* a family member (not the case) attended the seminar.
Secondary case indirectly linked to the seminar	As for a primary case, *and* had an incubation period[#] consistent with exposure to an infectious* primary case indirectly linked to the seminar.

+ See Box for definitions.

[#] The incubation period was defined as between 7 and 18 days after contact with an infectious case.[3]

of the seminar and all primary cases linked to the seminar also attended this session. Therefore, attendees of the afternoon session of the seminar were a suitable cohort to perform a VE study.

The age distribution of attendees at the afternoon session of the seminar fell into two categories; children (aged between 2 and 15 years), and adults (aged at least 30 years). Vaccine effectiveness calculations were performed only for the children. Due to the measles vaccine not being widely available in Australia until 1970, adults aged at least 30 years are unlikely to be vaccinated against measles and most would be immune due to past exposure to the disease.[4] Since vaccination status and disease risk in the adult group are likely to depend on whether an individual has had past exposure to measles, VE calculations including this group would give spuriously low results.[1] The attendee thought to be the source of infection for the seminar cohort was excluded from the VE study as they were not at risk of infection at the seminar. Attendees with an unknown age, unknown vaccination status, or a history of measles were also excluded (as recommended by Orenstein, Bernier and Hinman[1]).

Determining the vaccination status

Measles vaccination dates were determined by asking parents of children who attended the seminar to read out the vaccination dates entered in childhood immunisation books. If a vaccination date could not be provided, consent to access the child's general practitioner and council records was requested. For the purposes of this study, a vaccination was considered to be 'validated' if the vaccination date could be obtained from any of the above sources. The vaccination status for children indicating they had a prior history of measles or who were not vaccinated was not confirmed. Children were defined to be 'fully vaccinated' if they had received all vaccinations recommended for their age[5] (that is, children aged between 1 and 9 years required one dose of measles vaccine and children aged 10 years or over required two doses to be defined as fully vaccinated).

Vaccine effectiveness (VE) was calculated using the following formula:[1]

VE(%)={(ARU-ARV)/ARU} x 100

where ARU=attack rate in the unvaccinated

and ARV=attack rate in the vaccinated

Exact 95% Confidence Intervals for the VE estimates were calculated using STATA.[6] All other analyses were performed using Epi Info 6.04b.[7]

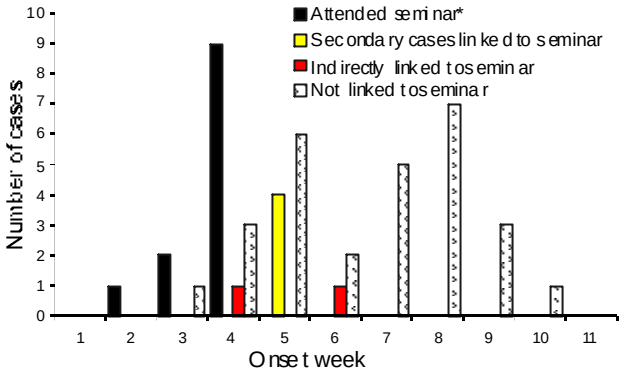
Results

The outbreak

Forty-six cases of measles were notified as part of the local outbreak (Figure 1). Two cases were visiting the area to attend the education seminar and 44 cases were local residents. This represents a notification rate for the area of 396.7 per 100,000 population (44/11,092). The local notification rate was 64 times the outbreak rate for Queensland (6.2/100,000 population).

During the outbreak period, more notifications were from this town than from any other area. Local cases accounted for 21% (44/208) of the State's outbreak notifications.

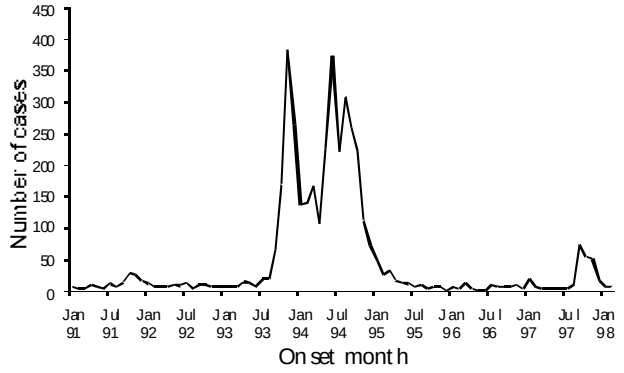
Figure 1. Measles notifications from a rural Queensland town and notifications linked to an education seminar in that town, by week of onset, 15 August-31 December 1997



*Probable source case for seminar cohort and primary cases linked to seminar

From this town, and a neighbouring town where the outbreak was first recognised, the outbreak appeared to spread across Queensland and interstate. This outbreak was the largest in Queensland since the epidemic of 1993 and 1994 (Figure 2).

Figure 2. Measles notifications for Queensland by month of onset, January 1991 to February 1998



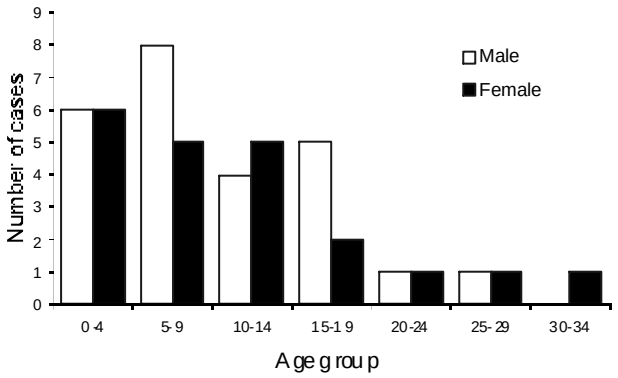
Eighteen measles notifications associated with the local outbreak were linked to the education seminar and 28 cases were local residents who were not linked to the seminar (Figure 1). Of the 18 cases linked to the seminar, one case was the defined probable source case for the seminar cohort, 11 were primary cases who had attended the seminar, 4 were secondary cases linked to the seminar, and 2 cases occurred in siblings whose well parents had attended the seminar. One of these siblings became ill 10 days after the seminar and was therefore a

primary case indirectly linked to the seminar. The other sibling was a secondary case indirectly linked to the seminar.

The probable source case for cases linked to the education seminar was an unvaccinated child who went to school in the town where the state-wide outbreak was first identified. Other cases had previously been identified who went to the same school. The source of infection for the 28 cases who were not linked to the education seminar is unknown.

The age range for notified cases associated with the local outbreak was 11 months to 34 years (median age 9 years). The number of notified cases generally decreased with increasing age (Figure 3). Only 3 cases were aged 1 year or younger. However, over half (54.3%) of the notified cases were aged less than 10 years. Thirty-nine out of the 44 local cases (88.6%) were aged less than 20 years. The notification rate for this age group was 1,090 per 100,000 population (39/3,579). There were slightly more male notifications (M:F ratio 1.2:1).

Figure 3. Measles notifications from a rural Queensland town and notifications linked with an education seminar in that town, by age and sex, 15 August-31 December 1997



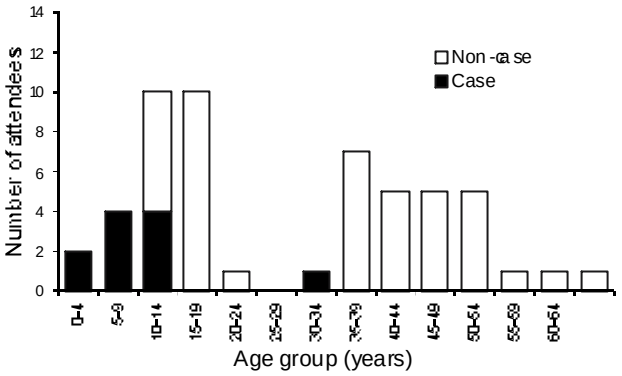
Ten of the 46 cases (21.7%) associated with the local outbreak were serologically confirmed, 2 of whom were primary cases linked to the education seminar. Two of the 3 children aged 1 year or younger were serologically confirmed.

The vaccine effectiveness study

The education seminar cohort

Sixty-two people were identified as having attended the afternoon session of the education seminar. The names of 57 attendees were on the list of attendees provided. Five extra attendees were identified by interviewing the listed attendees. Information was available to determine the disease status for all 62 seminar attendees. Excluding the probable source case for the seminar cohort, the measles attack rate was 18% (11/61). Of the 61 attendees exposed to the probable source case, 27 were defined as children and 26 as adults (Figure 4). Eight attendees (12.9%) refused to answer questions about their vaccination status and age.

Figure 4. Seminar attendees by measles status and age group



Of the 12 cases that had attended the seminar, only 7 had been notified. The other 5 (41.7%) were identified by the case investigation methods. Similarly, of the 6 secondary cases linked to the seminar, 5 (83.3%) were identified by the case investigation methods.

The vaccine effectiveness study cohort

Of the 27 seminar attendees who were known to be children and could have been exposed to measles at the seminar, 3 gave a history of past infection with measles and 1 child's vaccination status was unknown (Table 2).

Table 2. Vaccination status of children who attended the education seminar by age group

Age group	1-9 years	10-15 years
Not vaccinated	5	2
History of measles	0	3
1 dose of measles vaccine (% validated[#])	5 (100%)	10 (70%)
2 doses of measles vaccine	0	1*
Unknown vaccination status	1	0
Total	11	16

[#]Validated = vaccination date provided by parent, doctor or council

The VE study cohort consisted of 23 attendees excluding the 4 cases noted above. Of these attendees, 15 had received one dose of measles vaccine and one had received two doses. Thirteen of these 17 doses (76.5%) were supported by the report of a vaccination date. The date of vaccination was provided by the parent (8/13), doctor (2/13) or the council (3/13).

In this cohort, all children who had not received any vaccinations against measles (n=7) became cases, whilst those who were fully vaccinated (n=6) were protected from disease. However, the small sample size of this

Table 3. Measles vaccine effectiveness for children who attended the education seminar

Comparison	Attack rate in vaccinated	Attack rate in unvaccinated	Vaccine effectiveness % (95% CI[+])
Received at least one dose vs never vaccinated	3/16	7/7	81.3 (17.0-98.8)
Received at least one validated dose* vs never vaccinated	2/13	7/7	84.6 (15.0-99.7)

* Validated = vaccination date provided by parent, doctor or council

[+] CI = Confidence Interval

comparison meant that the VE could not be estimated with any precision. For children who had received at least one dose of measles vaccine, the point estimate VE was 81.3% (Table 3). When considering only validated doses, the VE was 84.6%. There were insufficient cohort members to stratify VE calculations by age.

Discussion

The outbreak

The outbreak notification rate in this town was high, especially compared to rates for the rest of Queensland. The rate is still likely to be an underestimate of the true incidence. A large proportion of cases associated with the education seminar were only identified by active case finding during the investigation. Reasons for the high rates in this town compared to the rest of Queensland are unclear. Data recorded on the Queensland vaccination register does not suggest that vaccination coverage levels for local children are lower than for the rest of the State (assuming the completeness of the vaccination register is consistent across Queensland). However, the vaccination register only provides vaccination coverage levels for children up to the age of 2 years at present, therefore population coverage levels cannot be determined. For children aged 2 years or younger, the available vaccination coverage levels do indicate a degree of protection which is consistent with there being few local cases in this age group. Prior to the outbreak, only one measles notification had been received from this town since notifications were first recorded on the NODS data base in 1991. If notifications are equated to the disease incidence and hence to exposure, past exposure is likely to be minimal, which may explain the high local rates during this outbreak.

Local cases were distributed evenly among children aged less than 10 years. This is unlike the age distribution of national notifications for 1996[8] and State notifications during the outbreak, where the most susceptible age group was infants too young to be vaccinated. Locally, infants may have been under-represented as contacts with the virus, especially at the education seminar which was for school aged children and their parents. The seminar was the most likely source of measles infection for a significant proportion (23.9%) of the local outbreak cases.

Transmission of measles at the seminar was probably by airborne droplet nuclei.[9] As the measles virus is known to be viable for several hours in droplet form,[9] people who attend the same room within 2 hours of an infectious patient are considered 'at risk' of infection.[2] Therefore the high attack rate amongst afternoon seminar attendees is not unexpected. Transmission also occurred indirectly to one child whose well parents had attended the seminar. This child may have been infected via contact with articles freshly soiled with nasal or throat secretions containing the measles virus.[3]

Vaccine effectiveness

The results of this study support the view that the measles vaccine was effective in preventing infection in the study cohort. All children who attended the education seminar and were fully vaccinated were protected against disease. In addition, the point estimates of VE for children having received at least one dose of vaccine are consistent with the findings of other VE studies[10,11] that indicate that the vaccine was effective in other settings. However, the outbreak investigation could only identify a small cohort to determine the VE, hence the VE estimates have wide confidence intervals due to sample size limitations. The inability to obtain precise VE estimates highlights one of the difficulties encountered when trying to estimate VE during an outbreak. Despite these limitations, it was important to have performed the study as the results do not suggest the vaccine failed and provide support for ongoing efforts to improve vaccination coverage.

Selection and misclassification biases can affect VE estimates. Problems with the sensitivity and specificity of the case definition, case ascertainment, validity of vaccination and disease histories, comparability of vaccinated and unvaccinated cohort members, and non participation can bias the VE estimate. Vaccine effectiveness calculations using the seminar cohort minimise many of the biases that can be encountered when estimating VE.

The definitions used to define a notifiable case were applied to all cohort members equally by asking each attendee, or their parent, whether they had the symptoms and signs that defined a presumptive or notifiable measles case. Two primary cases linked to the seminar were serologically confirmed. These two measures should have minimised misclassification of the disease status of cohort members. All known seminar attendees were followed for a time that would have identified the cases in this group. Therefore unequal case ascertainment is unlikely to affect the VE estimates. It is possible that not all attendees were identified, and the effect this would have on the VE estimates is unknown. This possibility was minimised by obtaining a list of attendees and asking identified attendees if they knew anyone else who attended. Only one VE cohort member had an unknown vaccination

status, further minimising the possibility of non participation bias. Eight attendees were excluded because they refused to provide information about their age and vaccination status. Orenstein, Bernier and Hinman recommend these unknowns be excluded as it is difficult to predict how they would distribute themselves with regard to vaccination status.[1]

The VE estimates are unlikely to be affected by differences in past exposure to measles between vaccinated and unvaccinated cohort members. Firstly, cohort members with a stated history of measles were excluded regardless of vaccination status. Secondly, as previously discussed, past exposure is likely to be minimal in the age groups used for the calculations (assuming most children have been long term residents of the area). Exposure during the current outbreak is also relatively uniform as all attendees were in the same hall as the source case for a similar amount of time.

A high proportion of vaccinations could be validated by report of a vaccination date. Council and general practitioner records are likely to be accurate, and would not be biased by a knowledge of the attendee's disease status. Parental recall has been found to be an unreliable method of determining vaccination status.[12] To minimise recall bias, parents were asked to read out the dates of vaccination from written records. Similar methods have been used in previous Australian studies[10,11] and it is unlikely that parents would fabricate a vaccination date. However the validity of this method remains unproven. No attempt was made to validate a history of measles or vaccination records for VE cohort members stating they had not been vaccinated. Therefore the results of this study need to be interpreted with caution. Some members who stated they were unvaccinated may have been vaccinated, and this would lead to a biased estimate of VE if their reported vaccination status was biased by whether they were a case.

Conclusion

This outbreak investigation identified an opportunity to assess the effectiveness of the measles vaccine under field conditions. There is an ongoing need to assess vaccine effectiveness in order to establish that a vaccine is effective in a given situation, and to provide support for efforts to improve vaccination coverage levels. This vaccine effectiveness study supports the view that failure to vaccinate rather than vaccine failure contributed to the high infection rate in the education seminar cohort.

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