

Measles immunity in young Australian adults

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Abstract

Previous state-based serosurveys and recent outbreaks have indicated that young adults may be at risk of measles. To provide a national picture of immunity in adults, we tested 2126 sera from 19-49 year olds that had been opportunistically collected from laboratories across Australia, between July 1996 and November 1998. Sera were stratified into age groups based on expected levels of immunity. Sample numbers were proportional to the population size in each State and Territory. Immunity was determined using an anti-measles IgG enzyme immunoassay (EIA) according to the manufacturer's instructions. Results were compared with those on sera from 2 groups of 1-18 year olds; one group collected before the Measles Control Campaign (conducted in the second half of 1998) and the other group collected after the Campaign. Immunity was highest (98.3%) in subjects aged at least 30 years (born before 1968) reflecting greater exposure to the measles virus in these older subjects. Immunity was lowest in those aged 1-6 years (born in 1994-8; 83.6%) and 18-22 years (born in 1974-80; 88.9%). The relatively low level of immunity in 18-22 year olds is probably due to lower vaccination coverage in this group compared with younger cohorts (aged 6-17 years). These results indicate the ongoing need to improve vaccine uptake in infants and suggest that a vaccination campaign targeting young adults would be beneficial. *Commun Dis Intell* 2001;25:133-136.

Keywords: measles, immunisation, measles control campaign, young adults

Introduction

Recent outbreaks have indicated that young adults aged 18-30 years may be at risk of measles infection.¹⁻⁴ It is thought that they may have low levels of measles immunity as they are too old to have been part of the 2-dose measles-mumps-rubella (MMR) vaccination program (introduced in 1994) but have grown up in a period when exposure to wild measles virus was declining. Serological evidence to test this hypothesis is available from some jurisdictions;⁵⁻⁷ however, no national data are available. To obtain a national picture of adult immunity to measles in Australia we tested sera from 19-49-year-olds that were collected as part of the evaluation of the Measles Control Campaign (MCC), conducted in the second half of 1998.

Methods

Serum samples

All major public and private diagnostic laboratories throughout Australia were invited to contribute sera that had been submitted for diagnostic testing and would otherwise have been discarded; 45 of these 52 laboratories agreed to participate. Subjects who were known to be immuno-compromised, multiply transfused, or infected with human immunodeficiency virus, or to have possible recent measles infection were excluded. Only one sample from any subject was tested. The sera available from 19-49 year olds had collection dates between June 1996 and November 1998, but were classified as a pre-Campaign sample as most (99.7%) were collected prior to the MCC.

Antibody assays

De-identified sera were tested using the Enzygnost (Behring Diagnostics, Marburg, Germany) anti-measles IgG enzyme immunoassays (EIA), at the Institute of Clinical Pathology and Medical Research (ICPMR), Sydney, Australia. Methods and interpretation of results were according to the manufacturer's instructions. Equivocal results were re-tested. Those that remained equivocal were classified as non-immune, as past experience indicated that these sera were likely to have levels of immunity lower than those associated with protection from infection.⁸

Sample size estimation

The sera were stratified into age groups with similar expected levels of immunity based on past serosurveys and each cohort's likely exposure to measles and vaccination history (Table 1). For ages 19-30 years, we wanted to be able to detect a 5 per cent difference between the current and any future serosurvey using a level of significance of 5 per cent and a power of 80 per cent.⁹ For the 30-49 year age range, a precise estimate of immunity for this serosurvey for each 5-year age group was required (an absolute precision of ± 3 per cent of the true value with 95% confidence).¹⁰ The required sample size was distributed equally among years of age and sex within each age group and proportionally by the population sizes in each jurisdiction.

Statistical analysis

We determined the percentage of positive, negative and equivocal results for each age group. Ninety-five per cent

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confidence intervals (CI) were calculated for the percentage immune (positive) in each age group. The chi-square test was used to compare proportions and p values less than 0.05 were considered statistically significant. Statistical analyses were performed using Epi Info version 6.04b¹¹ and Confidence Interval Analysis (CIA).¹²

To provide a complete picture, we included the results of the national serosurveys previously conducted to evaluate the MCC. The sera used in these studies were from 1-18 year olds and were collected either in the 2 years before the MCC (2936 pre-Campaign sera), or the 5 months after the Campaign (2918 post-Campaign sera). A detailed report of these data can be found elsewhere.^{8,13} For this analysis, we incorporated the results of the pre-Campaign sample of 18 year-olds with those for the 19-22 year age group. Immunity for 18 year-olds was unaffected by the Campaign, unlike immunity in the 12-17 year age group, and was similar to immunity in the 19-22 year age group.

For each age group we calculated the corresponding ranges for year of birth. For the pre-Campaign sample, it must be noted that the range of years in which subjects could have been born is wider than the corresponding age group as

these sera were collected over a 3-year period rather than at one point in time.

Ethics approval

The study was approved by appropriate institutional ethics committees and the state-wide Health Confidentiality and Ethics Committee of the New South Wales Health Department.

Results

Tests were performed on sera from 2126 individuals aged 19-49 years (Table 1). For each age group, except 19-22 and 23-25 years, proportions by State or Territory of residence were comparable with those of the 1997 Australian population (Australian Bureau of Statistics). For the ages 19-25 years, there were insufficient sera from Victoria and Western Australia so we over-sampled sera from New South Wales. (Note: the proportion of positive sera for 19-25 year olds was similar in Victoria, Western Australia and New South Wales — results not shown). In addition, there were fewer sera available from the 26-27 and 28-29 year age groups than required (Table 1). As the seroprevalence was similar for these 2 groups they were combined to achieve a higher level of precision for the seroprevalence estimate.

Table 1. Required number of sera to be tested and actual number tested, by age group

| Age group (ages in 1996-8) | Expected proportion immune | Sample size required | Sample size tested |
|----------------------------|----------------------------|----------------------|--------------------|
| 19-22 yrs | 0.87 | 600 | 596 |
| 23-25 yrs | 0.90 | 429 | 435 |
| 26-27 yrs | 0.94 | 207 | 130 |
| 28-29 yrs | 0.94 | 207 | 147 |
| 30-34 yrs | 0.95 | 203 | 205 |
| 35-39 yrs | 0.95 | 203 | 200 |
| 40-44 yrs | 0.95 | 203 | 203 |
| 45-49 yrs | 0.95 | 203 | 210 |

Measles immunity

In the pre-Campaign sample of sera from 1-49 year olds, measles immunity generally increased with age to be above 95 per cent in age groups over 29 years (Figure 1, Table 2). Following the MCC, immunity increased significantly in those age groups targeted by the Campaign, namely preschool (2-5 years), primary school children (6-11 years) and high school students (12-17 years). The level of immunity did not differ significantly between males and females either before (p=0.09) or after (p=0.9) the Campaign

When we examined the most recent data available (i.e. sera collected post-Campaign for 1-17 year olds and sera

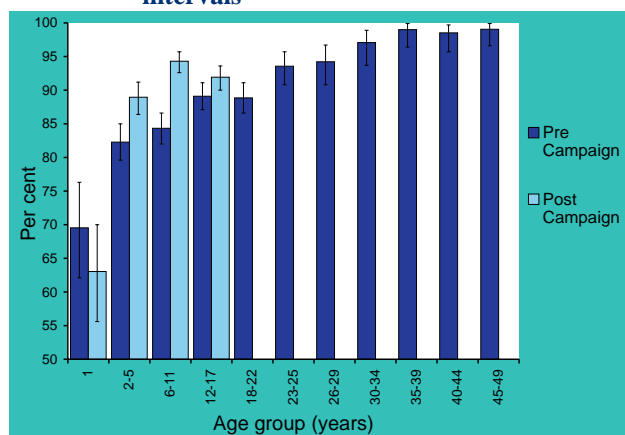
Table 2. Percentage of sera positive for measles IgG antibody before and after the Australian Measles Control Campaign, by age group

| Age group (years) | Pre-campaign | | Post-campaign | | p value* |
|-------------------|--------------|--------------------------------------|---------------|--------------------------------------|----------|
| | No. tested | % Seropositive (95% CI) [†] | No. tested | % Seropositive (95% CI) [†] | |
| 1 | 174 | 69.5 (62.1-76.3) | 184 | 63.0 (55.6-70.0) | 0.2 |
| 2-5 | 756 | 82.3 (79.6-85.0) | 715 | 89.0 (86.4-91.2) | <0.001 |
| 6-11 | 958 | 84.3 (82.0-86.6) | 965 | 94.3 (92.6-95.7) | <0.001 |
| 12-17 | 899 | 89.1 (87.1-91.1) | 904 | 91.9 (90.0-93.6) | 0.04 |
| 18-22 | 745 | 88.9 (86.6-91.1) | | | |
| 23-25 | 435 | 93.6 (90.8-95.7) | | | |
| 26-29 | 277 | 94.2 (90.8-96.7) | | | |
| 30-34 | 205 | 97.1 (93.7-98.9) | | | |
| 35-39 | 200 | 99.0 (96.4-99.9) | | | |
| 40-44 | 203 | 98.5 (95.7-99.7) | | | |
| 45-49 | 210 | 99.0 (96.6-99.9) | | | |

* p value for comparison of the percentage of seropositive results pre and post-Campaign

[†]CI Confidence Interval

Figure 1. Percentage of sera positive for measles IgG antibody, before and after the Australian Measles Control Campaign, by age group and including 95 per cent confidence intervals



collected pre-Campaign for 18-49 year olds) the key findings were: (a) the proportion of immune subjects was high (98.3%; 95%CI: 97.2-99.1) in those 30 years of age or older (born before 1968); and (b) subjects aged 18-22 years (born in 1974-80) had a significantly lower level of immunity than an older cohort aged 23-25 years (born in 1971-5, $p=0.008$); and younger cohorts aged 12-17 years (born in 1982-7, $p=0.04$) and 6-11 years (born in 1988-93, $p<0.001$, Figure 2).

Equivocal results

The proportion of equivocal results varied by age, but not by gender or period of collection. In the pre-Campaign sample there was an increasing proportion of equivocal results up to

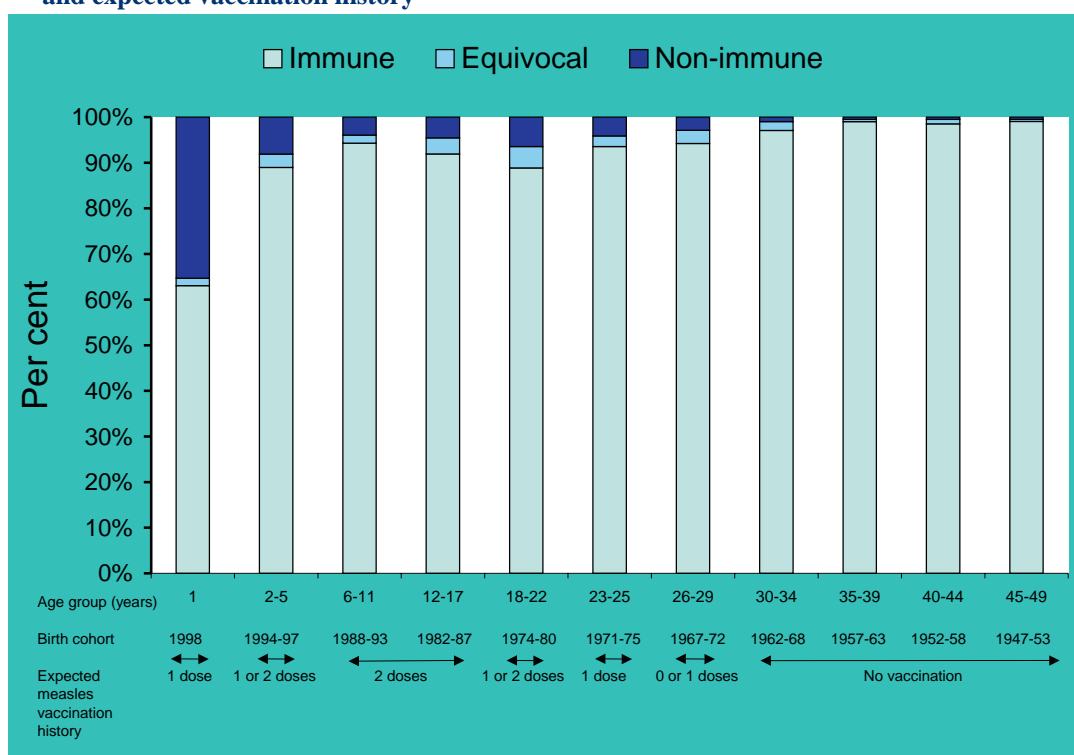
the age of 19 years, then a progressive decrease for older ages to below 1 per cent in the 5-year age groups over 34 years. A similar trend for 1-18 year olds was seen in the post-Campaign sample. Using the most recent data available for each age cohort, both the 12-17 and 18-22 year age groups had significantly higher levels of equivocal results than the younger and older age groups respectively ($p=0.02$, for comparison of 6-11 and 12-17 year age groups; $p=0.04$, for comparison of 18-22 and 23-25 year age groups), (Figures 2 & 3).

Discussion

The pattern of immunity found here is due to a complex mixture of interacting factors. However, the major determinants of each cohort's immunity levels are their vaccination history and past exposure to measles virus. Older aged cohorts have obviously lived longer and therefore had more time to come in contact with the measles virus, but they are also more likely to be immune due to the higher incidence of disease in the past. The high levels of immunity in those older than 28 years of age in 1996 or 30 years in 1998 are to be expected as the incidence of measles was high^{14,15} prior to the approval of the measles vaccine in 1968. Before this, epidemics occurred every 2-3 years and eventually 95 per cent of the population was infected.¹⁶

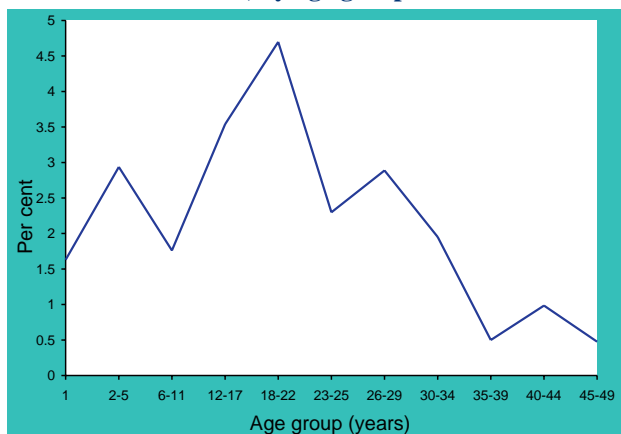
Cohorts born since measles vaccine became available have differing levels of immunity due to variations in their risk of infection and vaccination coverage. With each new birth cohort there was a reduction in risk of infection (due to a decrease in the circulation of measles virus) and an increase in vaccination coverage with one dose of measles vaccine at one year of age.¹⁷⁻¹⁹

Figure 2. Most recent* national data available for immunity to measles, Australia, by age group/year of birth and expected vaccination history



* Sera from 1-17 year olds collected in January-May, 1999 (after the Measles Control Campaign). Sera from 18-49 year olds collected in June 1996-November 1998.

Figure 3. Equivocal measles IgG results using the most recent* national data available, Australia, by age group



* Sera from 1-17 year olds collected in January to May, 1999 (after the Measles Control Campaign). Sera from 18-49 year olds collected in June 1996 to November 1998.

Those aged 18-22 years (born in 1974-80) had the lowest level of immunity of any adult age group and the highest proportion of equivocal results. This cohort has lived in a period when the incidence of measles was substantially lower than for older cohorts,* but the uptake of the first dose of measles vaccine at one year of age was still below 50 per cent.¹⁶ In addition, most of this cohort would not have been eligible for the adolescent MMR dose given to 10-16 year olds between 1994 and 1999, unlike younger cohorts (aged 6-17 years, born in 1982-1993) who would have been eligible for 2 doses of MMR vaccine either as part of the MCC or the routine schedule for adolescents.²⁰ The high proportion of equivocal results compared with other ages may be due to reduced opportunities to boost immunity naturally via contact with the measles virus (compared with older ages) and a longer time since vaccination in infancy (compared with younger cohorts).

Our results appear to reflect historical changes in immunisation policies and disease incidence. Little is known however, about whether opportunistically collected sera are representative of the true level of immunity in the Australian population. Our convenience sample of sera was obtained from most major laboratories around Australia. Any selection biases are likely to be limited because these laboratories offer a wide range of diagnostic services, therefore reasons for which the sera were submitted are unlikely to differ between laboratories or over time.^{8,21}

Conclusion

Based on the most recent national serosurvey data available, there are 2 cohorts with levels of immunity below 90 per cent — those aged under 6 years in 1999 (born in 1994-1999) and those aged 18-22 years in 1996-98 (born in 1974-1980). Only persons aged 30 years and over in 1996-98 (ie born before measles vaccine was available) had immunity levels above 95 per cent.

These results indicate the ongoing need to improve vaccine uptake in infants and suggest that a vaccination campaign targeting young adults would be beneficial.

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* Although there were no national notification data for measles between 1948 and the mid 1980s, data about measles admissions and cases of encephalitis in Victoria¹⁵ and national notifications since 1991¹⁷ suggest that the incidence of measles declined during this period.