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A study of seroprevalence of rubella IgG in Maltese adolescents

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ABSTRACT: Objective - To determine the seroprevalence of rubella IgG antibodies in Maltese adolescents. Design - A cross-sectional study, with mailed questionnaire and blood sampling. Subjects - 172 individuals aged 14-15 years from Malta and Gozo. Outcome variables - Prevalence of vaccination and seropositivity (IgG) for rubella. Results - 85% were vaccinated; seropositivity was detected in 168 youths (97.7%). Conclusion - The study showed a high level of detectable humoral immunity to rubella. This could not be definitively attributed to vaccination alone.

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Background epidemiology

Rubella is a directly communicable condition of man caused by a Togavirus[1]. It is an exanthem of childhood, most disease is mild and up to 50% of infections are asymptomatic[2]. The public health significance of rubella lies mainly in its teratogenic potential, although the primary infection may rarely cause thrombocytopaenic purpura, encephalopathy and panencephalitis[3]. Up to 90% of all foetuses infected in utero during the first 8-10 weeks of pregnancy suffer damage, commonly involving multiple, vital functions[4]. Congenital rubella syndrome became notifiable in Malta in August 1990[5]. Since then two cases have been notified to the Department of Public Health, both in 1996.

Rubella became notifiable under Maltese law in 1978[6], and legal provisions for vaccination of female children aged 10 to 13 years were mandated in1989[7]. Figure 1 depicts a steady decline in incidence of notified rubella from the mid-80s, a trend which was sharply reversed in 1995 with a twentyfold increase (416 cases) over the previous year[8]. Table 1 presents the age and sex profile of notified cases from 1986-1995. The male to female ratio, as well as the mean age of cases, were all higher for the 1995 episode compared to the previous 9 years. The mean age (recorded in 84% of subjects) was 17.8 years (range 0.5-72). The cases originated from a wide geographic distribution in Malta. The episode was not virologically confirmed. It led, however, to concerns about the integrity of local herd immunity to rubella and it prompted the study being presented.

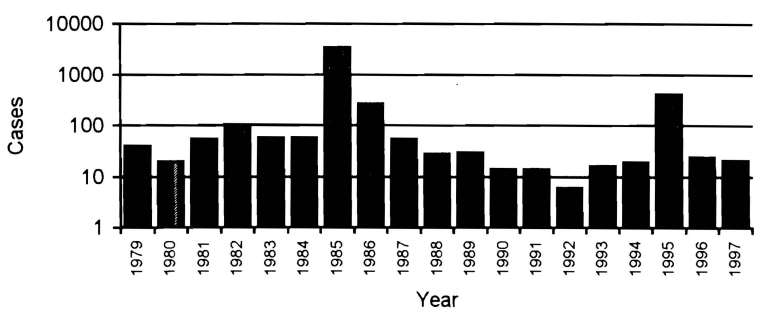

Fig. 1 - Notified rubella, Malta, 1979-1997. (NB Y-axis is on a Log10 scale)
Source: Department of Health Information, Malta.

Subjects and Methods

The aim of the study was to determine the proportion of Maltese adolescents who had detectable levels of rubella IgG in the blood.

The study was planned by the Department of Health and ethical approval was obtained from the Medical Council in 1996. It was decided to select study participants from Maltese and Gozitan youths aged 14-15 years. The sampling frame consisted of the national birth cohort of 1982 available on a database. 500 eligible individuals were selected from this list using a cumputerised random sampler (Epi Info 6.02). Selection was independent of sex, past history of rubella infection or vaccination.

Questionnaires were posted to all prospective candidates in December 1996. The questionnaire requested those identified to complete details of demography (name, date of birth, address) and status of vaccine and past infection. Parental consent was requested concomitantly. A reminder was sent to non-respondents in January 1997. By early February, 196 participants (39.2% response) had completed questionnaires. As the total 1982 birth cohort surviving to end December 1994 was estimated as 5871[9], the sample therefore approximated 3.3% of the persons at that age.

Respondents were given appointments to

Table 1 - Age and Sex profile of Notified Rubella cases in Malta, 1986-1995

Year	Cases	M:F Ratio	C. incidence (per 104 pop)	Mean Age (y)	Range (y)
1986	270	1.37:1	7.86	7.5	0.3-38
1987	56	1.43:1	1.62	9.0	0.6-42
1988	28	0.87:1	0.80	4.4	0.5-20
1989	30	0.76:1	0.85	6.6	0.4-60
1990	14	0.27:1	0.39	8.0	0.4-45
1991	14	1.33:1	0.39	9.0	0.6-23
1992	6	0.2:1	0.17	4.4	0.5-10
1993	17	0.89:1	0.46	9.8	0.8-38
1994	20	1.5:1	0.54	14.0	1-30
1995	416	1:0.29	11.18	17.8	0.5-72

Source: Department of Health Information, Central Office of Statistics, Malta.

attend health centres at Paola, Mosta, Rabat or Gzira for completion of the questionnaire and for blood sampling. These encounters were organised on two Saturdays to avoid interference with schooling. A 'mop-up' session was held on one evening for those who could not make it otherwise. Gozo participants (nine) were called up to Victoria Health Office[10]. Data was entered and analysed using Epi Info Ver 6.02 (CDC/WHO, October 1994), and MS Excel Ver 4.0. Venous blood (5 ml) was collected from each participant by the first two authors and another doctor in Gozo and processed at the Virology Laboratory at St Luke's Hospital, G'Mangia. The serology was performed using Abbott IMx R Rubella IgG 2.0 Antibody assay based on the Microparticle Enzyme Immunoassay (MEIA) to rubella. The breakpoint for seropositivity using this quantitative analysis is 10 IU/ml, which is the accepted cut-off for immune status[11]. Participants were informed of their sero-status by letter and those testing negative were offered vaccination.

Findings

A total of 172 participants were tested for the presence of rubella specific antibodies. The male to female ratio was 1:0.91. Out of these, 147 (85%) were vaccinated, mostly (75%) at school, but also by their GP (10%) and at health centres (15%). Of the 143 in whom the date of vaccination was established, 78% were vaccinated in 1995. 109 of vaccinees gave no previous history of rubella. Twenty-six were vaccinated despite a previous history of rubella-like disease.

Out of the 172 tested, 168 (97.7%) had antibodies for rubella. Table 2 gives the results by sex. No statistically significant difference between the sexes could be shown. Only 4 participants tested negative, all of whom reported no history of rubella or rubella vaccination (Table 3).

Conclusions

1. The study showed a high prevalence of humoral immunity against rubella (0.97, 90% CI 0.95-0.99) amongst Maltese females in the pre-childbearing age-group.

2. The study could not differentiate between vaccine induced immunity or that imparted by disease.

3. Those who gave a history of rubella or vaccination or both had a statistically significant increased chance of being seropositive in contrast to those whose exposure was negative or unestablished (Table 3). The basic assumption here is that infection, vaccination or both together are equivalent opportunities for developing antibodies, and that no history or an unestablished history signifies no opportunity for development of antibody.

Table 2 - Detection of rubella IgG by sex, Malta, 1997 (n=172).

Serology result	Females	Males	Total
Negative	3	1	4
Positive	79	89	168
Total	82	90	172

Proportion seronegative = 0.023; 95% CI 0.006-0.059 (after Zar)

Fisher exact 1-tailed P-value = 0.276

Table 3 - Serology results by vaccination status and history of rubella, Malta, 1997 (n=172).

Serology	History of Rubella and Vaccination			
	Rubella + Vaccine	Rubella Only	Vaccine Only	None
Positive	26	7*	121**	14***
Negative	0	0	0	4

* 2 had vaccine status unknown
** 12 had past rubella history unknown
*** history of rubella or vaccine negative or not established

Proportion seronegative in unexposed group = 0.222; 95% CI 0.064-0.476 (after Zar)
Fisher exact P (1st 3 clms vs last clm) = 0.0001

Discussion

Active immunity after natural infection and vaccination is usually permanent. However, the immunity developing post vaccination is less robust. Where vaccination coverage in childhood is high, rubella outbreaks are seen in older persons[12].

In Maltese state health services, Measles-Mumps-Rubella vaccine is given at 15 months and at 11-13 years of age[13]. Up to May 1989, vaccination was offered to girls in their last year of primary school or the first year of secondary school and to women before marriage. A wider and more comprehensive strategy, which also included boys, was adopted from May 1989[14].

Rubella in children is unlikely to occur in the early years following vaccination. In the 1995 episode the average age of those affected was relatively high. This is probably due to high vaccination coverage in childhood. In fact, the group studied had an 85% coverage of at least one dose of rubella vaccine. In contrast, 70% of the 1993 national birth cohort were covered for their 15-month dose of MMR by July 1997[15]. The difference between the groups may be

attributed to:

- increased public awareness of rubella-associated congenital defects in children born to non-immune mothers;
- better opportunity for vaccination in schools rather than a separate encounter at a young age;
- more complete notification of vaccination in this group in contrast to the 15-month group;
- bias from the sample in this study which may have over-represented the motivated (read protected) fraction of the population.

Recommendations

Although the study design precludes direct correlation of immune status to degree of vaccine cover, it is reasonable to conclude that a good proportion of protection is directly attributed to vaccination. Hence, the authors stress that there is no place for complacency with continued vaccination. Vaccination is still recommended for children with previous history of rubelliform illness.

The study as performed may be repeated in the future either to follow up the same birth cohort to assess any variation in immune status, or else in subjects of the same age group to measure variations over years in similar populations. The authors also feel that this study should be complemented by at least one other study investigating antibody protection in females at different stages of the childbearing period - the ultimate target population for anti-rubella measures. Given the high level of seroprevalence found in young people in this study, the determination of short-term efficacy of vaccination in this age-group may be technically difficult.

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References

1. Edmond BTD, Bradley JM, Galbraith NS. Infection. Blackwell Scientific Publications, London, 1991; p241.
2. Chernesky MA, Mahony JB. Rubella virus. In Murray PR et al. Manual of Clinical Microbiology 6th ed. ASM Press 1995; p.968.
3. White DO, Fenner FJ. Medical virology 4th ed. Academic Press, California, USA 1994; p.427.
4. Joint Committee on Vaccination and Immunisation. Immunisation against infectious disease. HMSO, London 1996; p132:22.1.17.
5. Legal Notice 110/90. Infectious or Contagious Disease (Extension) Order. Cap 36 of the Laws of Malta.
6. Government notice No. 10 of 1978. Cap 36 of the Laws of Malta.
7. Legal Notice 50/89. Rubella (Vaccination) Regulations. Cap 36 of the Laws of Malta.
8. Health Division, Malta. Notifiable infectious diseases in the Maltese Islands. Annual Report 1995.
9. Central Office of Statistics, Malta. Demographic Review of the Maltese Islands - 1994; p.8.
10. Muscat P. Medical Officer for Health, Gozo. Personal communication. 1997.
11. Abbot Laboratories, IL, USA. IMx® System Rubella IgG 2.0. Test kit insert, July 1996; p8.
12. Benenson AS. Control of Communicable Diseases in Man. APHA. 15th edition 1990; p378.
13. Department of Primary Health Care. A guide to the vaccination schedule. Malta. December 1995.
14. Sciberras M. Nursing Officer. Immunisation Services, Floriana Health Centre. Personal communication. 1997.
15. Department of Primary Health Care. Quarterly Report on Immunisation Uptake, Malta, 18 July 1997. Unpublished data, DH File 78/91.