EXPLORING THE IMPLICATIONS OF CHANGING PATTERNS OF RUBELLA IMMUNITY IN ANTENATAL WOMEN IN A SOUTH WALES VALLEY COMMUNITY

LINDA AMY MATTHEWS

A thesis submitted in partial fulfillment of the requirements of the University of the West of England for the award of Professional Doctorate in Biomedical Science

Faculty of Health and Applied Sciences

Cwm Taf Health Board

Submitted November 2013
Abstract

**Background/Aims:** Rubella can be devastating to a foetus if maternally acquired in early pregnancy. A single rubella vaccine (SRV), given to prepubertal girls was replaced by the MMR immunisation in infancy for both sexes in 1988. Women born before 1983 probably received the SRV and had contact with circulating rubella, whilst women born after 1982 probably received the MMR vaccine and had little contact with circulating rubella. When immunity levels fall, outbreaks can occur, as seen in the last 10 years. The rubella status of antenatal women in the Cwm Taf (South) Health Board area and post-partum vaccine uptake in the rubella susceptible women was explored.

**Method:** Data of 14,519 antenatal rubella tests (2005-2010) and questionnaire data from 111 rubella susceptible women (2009-2011) were analysed. Self-reported immunisation status and post-partum vaccine uptake were validated by examination of childhood immunisation records and medical records. Data for probable SRV recipients and probable MMR vaccine recipients were compared.

**Key Results:** The overall rubella susceptibility rate increased from 3.8% (88/2312) in 2005 to 4.6% (116/2536) in 2010. First pregnancy data showed a statistically significant increase in susceptibility from 6.4% (49/760) in 2005 to 8.9% (71/798) in 2010 \( (\chi^2=6.860, \text{ df}=1, \ p=0.009) \) and women born after 1982 were five times more likely to be rubella susceptible than those born earlier (odds ratio=5.05, 95% CI from 3.46 to 7.35). Those aged < 20 years had a mean susceptibility rate of 21.3% (236/1107) Average antibody titres for rubella immune women differed significantly by year of birth; those born earlier had a stable average of 58 IU/ml whilst those born later (following a period of steady decline) averaged 20 IU/ml. Of rubella susceptible women in the questionnaire study, 62.8% had received two or more doses of a rubella containing vaccine. Examination of medical records showed that over 36% (39/107) of rubella susceptible women in the study did not receive post-partum immunisation.

**Conclusion:** The results suggest that immunity is waning, and that a third dose of MMR vaccine in adolescence is required to ensure protection during pregnancy. The study also demonstrates that reliance on Child Health Records to assess need for immunisation is flawed. Post-partum MMR uptake also needs to be addressed if national targets are to be met.
Acknowledgements

Debbie Harding, Child Health Services Administrator, for allowing access to child immunisation records.

Nicola Ralph, Antenatal Screening Coordinator for help with gathering information re post-partum immunisations.

Matthew Smith, Clinical Audit Facilitator, for helping with retrieval of archived patients notes.

All pregnant women who completed the questionnaires.

Virology laboratory staff at the Royal Glamorgan Hospital who performed almost 15,000 rubella screening tests.

Emyr Adlam and Rhian Harris for Welsh translations.

Director of Studies Dr. Lynne Lawrance and tutors Professor Selena Gray and Dr. Debra Gray of the University of the West of England for help, advice and encouragement.

Dr Fiona Cramp for advice on the presentation of the Literature Search strategy.

Dr Paul White for advice on statistical analysis.
Overview

The Origins of this Study

This study arose out of my perception from laboratory practice, in the virology laboratory at the Royal Glamorgan Hospital (Cwm Taf Health Board) in South Wales, that the percentage of pregnant women who were rubella susceptible was increasing. Part of my substantive role was to supervise rubella antibody testing and to authorise the results. There seemed to be an increase in the number of samples with a rubella IgG antibody level of <10 IU/ml collected during antenatal screening. I decided to establish if this perception was supported by evidence and, if so, to explore the reasons why. The study was undertaken as part of a Professional Doctorate in Biomedical Sciences at the University of the West of England, Bristol.

The taught doctorate sessions guided the selection of data collection methods, the questionnaire design and the subsequent analysis. I was personally responsible for the ethical approval applications, collecting the data from booking blood forms, developing the questionnaire, extracting the relevant data and performing the appropriate analyses.

The results of this work have been disseminated in the form of seven oral presentations and six poster presentations at local, national and international events. Two journal publications were produced from data collected in this study. The first (Matthews et al, 2010) discussed the rubella susceptibility rates in the study area and subsequently has been cited in four other publications to date. The second (Matthews et al, 2013) discusses the uptake of post partum
MMR in the study area. A third paper entitled “Is vaccine induced rubella immunity waning in areas with no circulating rubella? A study of antenatal women in a South Wales Health Board” is ready for submission for publication to a relevant journal. I was the primary author in the preparation of all three papers, whilst the various co-authors had input into the final documents.

Therefore this study has contributed to the knowledge of rubella status in pregnant women in the early 21st Century. Information from the first published paper, documenting rubella susceptibility rates from early data produced by this study (Matthews et al, 2010), was used (along with other information) in discussions about policy change (Tookey, P.A. 2012; Department of Health, 2011). In the Cwm Taf study the rubella susceptible women had their immunisation status checked against Child Health records, which also produced new data that have implications for the proposed changes in antenatal screening. The most important finding in this study arises from the examination of rubella IgG antibody levels in those pregnant women who are classed as immune. These data demonstrate waning immunity in the absence of circulating rubella, which has long term implications. These data will have implications for future decisions of the Joint Committee on Vaccination and Immunisation.

Presentations:


L.A. Matthews, L. M. Lawrance, D. Gray, S. Gray. 27th September 2011 “Rubella immunity in pregnancy – are we asking too much of the MMR?” Biomedical Science Congress (IBMS), Birmingham. (Appendix 4).

Linda Matthews 25th-26th November 2011a.”Rubella Susceptibility in Pregnancy - are we asking too much of the MMR?” Welsh Microbiological Association Winter Meeting, Oswestry. (Appendix 5).

Linda Matthews 7th December 2011b “MMR vaccination in antenatal care”. Bristol Microbiology Forum, Bristol. (Appendix 6).


Posters:


Publications:


Citations (Matthews et al, 2010):


[Accessed February 2012]. This document is now no longer available but the outcomes can be accessed in Rubella Susceptibility Screening in Pregnancy Policy Position Statement UK NATIONAL SCREENING COMMITTEE 25 April 2012. [http://www.screening.nhs.uk/rubellasusceptibility](http://www.screening.nhs.uk/rubellasusceptibility)


[Accessed September 2012].


S. SKIDMORE, E. BOXALL and S. LORD. Is the MMR vaccination programme failing to protect women against rubella infection?. Epidemiology and Infection, available on CJO2013. doi:10.1017/S0950268813002045. Published online: 18 August 2013

[http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=8976995&fulltextType=BT&fileId=S0950268813002045](http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=8976995&fulltextType=BT&fileId=S0950268813002045)
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<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<td>CDSC</td>
<td>Communicable Disease Surveillance Centre</td>
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<tr>
<td>COVER</td>
<td>Cover of Vaccination Evaluated Rapidly</td>
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<td>CRS</td>
<td>Congenital rubella syndrome</td>
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<tr>
<td>ECDC</td>
<td>European Centre for Disease Prevention and Control</td>
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<tr>
<td>EEA</td>
<td>European Economic Area</td>
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<td>EFTA</td>
<td>European Free Trade Association</td>
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<td>EIA</td>
<td>Enzyme immunoassay</td>
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<td>ELFA</td>
<td>Enzyme-linked fluorescent assay</td>
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<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
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<td>EU</td>
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<td>HA</td>
<td>Haemagglutination</td>
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<td>HAI</td>
<td>Haemagglutination inhibition</td>
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<td>IDPSP</td>
<td>Infectious diseases in Pregnancy Screening Programme</td>
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<td>JCVI</td>
<td>Joint Committee for Vaccination and Immunisation</td>
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<tr>
<td>MEIA</td>
<td>Microparticle immunoassay</td>
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<tr>
<td>MMR</td>
<td>Measles, mumps and rubella vaccine</td>
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<td>MR</td>
<td>Measles and rubella vaccine</td>
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<td>NEQAS</td>
<td>National External Quality Assessment Service</td>
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<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
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<tr>
<td>NPHS</td>
<td>National Public Health Service</td>
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<td>ONS</td>
<td>Office for National Statistics</td>
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<td>POST</td>
<td>Parliamentary Office for Science and Technology</td>
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<tr>
<td>SRH</td>
<td>Serial radial haemolysis</td>
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<td>WHO</td>
<td>World Health Organisation</td>
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Trust Changes

Please note that during the period of the study:

- Llwynypia hospital closed and services were transferred to the new Ysbyty Cwm Rhondda.
- Pontypridd and Rhondda NHS Trust merged with North Glamorgan Trust to become Cwm Taf NHS Trust north and south.
- Cwm Taf NHS Trust became Cwm Taf Local Health board using the operating name of Cwm Taf Health Board
- The National Public Health Service (Wales) (NPHS) was renamed Public Health Wales (PHW)
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