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PREVENTION OF CONGENITAL RUBELLA SYNDROME IN NEWFOUNDLAND

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ABSTRACT

The Newfoundland Department of Health administers several rubella vaccination programs for the prevention of congenital rubella syndrome (CRS). This study examined the effectiveness of these programs by reviewing rubella susceptibility in the population at risk for CRS, assessing the predictive value of a rubella vaccination record, and evaluating the effectiveness of the postnatal rubella vaccination program.

From 1989 to 1993, rubella susceptibility in women aged 15 to 44 averaged 4.6% overall, but was significantly higher in women aged 15 to 19 years, averaging 14%. The positive predictive value of a rubella vaccination record was 92% overall, but it differed by type of vaccine product and vaccine viral strain; 99% for any monovalent rubella vaccine, compared to 81% for recipients of HPV-77 DE-5 strain MR (measles rubella) or MMR (measles mumps rubella) vaccine. The postnatal rubella vaccination program failed to provide testing for 13% of pregnant women in the province in 1992, and 10% of susceptible women in 1992 were not subsequently vaccinated.

These results suggest that women of childbearing age in Newfoundland remain at risk of having children with CRS. The rubella vaccination record is not adequate proof of immunity for some of these women, and the postnatal vaccination program requires some improvement in order to prevent cases of CRS in the future.

RÉSUMÉ

Le Département de la Santé de Terre-Neuve gère plusieurs programmes de vaccination contre la rubéole dans le but de prévenir le syndrome de rubéole congénitale (SRC). Cette étude évalue l'efficacité réelle de ces programmes à réduire le nombre de femmes réceptives face à la rubéole. On y présente les taux de réceptivité rubéoleuse chez les femmes en âge de procréer, l'estimation de la valeur prédictive d'une preuve de vaccination contre la rubéole et l'efficacité réelle du programme de vaccination postnatal contre la rubéole.

Entre 1989 et 1993, la proportion moyenne de réceptivité à l'égard de la rubéole chez les femmes de 15 à 44 ans était de 4.6%; cette proportion était significativement plus élevée dans le groupe des 15 à 19 ans où elle s'établissait à 14%. La valeur prédictive positive d'une preuve de vaccination contre la rubéole étalt globalement de 92% mais variait selon le type de vaccin et la souche vaccinale, de 81% chez les récipiendaires d'un vaccin RR (rougeole-rubéole) ou RRO (rougeole, rubéole, oreillons) utilisant la souche HPV-77 DE-5 à 99% chez les femmes ayant reçu un vaccin antirubéoleux monovalent.

En ce qui concerne le programme de vaccination postnatal contre la rubéole, en 1992, 13% des femmes enceintes dans cette province n'ont pas subi d'épreuve de dépistage; par ailleurs, 10% des femmes réceptives n'ont pas été vaccinées après leur accouchement.

Ces résultats démontrent qu'à Terre-Neuve une proportion non négligeable de femmes en âge de procréer sont à risque de donner naissance à un enfant présentant un SRC. Une preuve de vaccination contre la rubéole ne constitue pas une preuve d'immunité pour plusieurs de ces femmes. Le programme de vaccination postnatal doit être amélioré afin de permettre la prévention de cas de SRC dans l'avenir.

DEDICATION

Ellen Sophie Stratton
February 17, 1931 - October 25, 1995
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TABLE OF CONTENTS

LIST OF TABLES

LIST OF TABLES (continued)

LIST OF FIGURES

CHAPTER I. INTRODUCTION

Infection with rubella virus in the postnatal period produces mild, self-limiting illness and long term immunity. However, rubella infection during pregnancy may result in fetal infection and subsequent miscarriage, stillbirth or congenital rubella syndrome (CRS). This syndrome includes a number of congenital abnormalities that can involve all body systems (1).

Rubella vaccination of women before pregnancy prevents CRS (2), and different strategies have been used to ensure that women are protected from infection. These strategies include vaccination of schoolgirls, universal infant vaccination, and postnatal vaccination of women found to be susceptible during pregnancy.

1.1 Rubella susceptibility in women of childbearing age

Rubella susceptibility in women of childbearing age has declined since the implementation of vaccination programs. In Canada, susceptibility in prenatally screened women now ranges from 4 to 10% (3). This continued susceptibility in vaccinated populations can be attributed in part to an expected vaccine failure rate of between 5 and 10%, and to a decrease in circulating wild virus that minimizes opportunities to acquire natural immunity (4).

1.2 The rubella vaccination record as a predictor of immunity

The rubella vaccines used to prevent CRS are highly efficacious and induce long-lasting protection; estimates of efficacy from field trials are as high as 90% over 15 to 20 years (5-9). A rubella vaccination record is therefore usually accepted as proof of rubella immunity, and serologic testing is recommended only for pregnant women (10). However, waning immunity may be a greater problem than these efficacy figures suggest, as previous studies of long term persistence of vaccine-induced immunity have been carried out in countries where the booster effect of wild virus is substantial (11).

The predictive value of a rubella vaccination record in areas with low incidence of disease has not been assessed, but based on efficacy figures, it is expected to be at least 90%. If the positive predictive value of a vaccination record is in fact lower than this, then more than 10% of the women assumed to be protected on the strength of a rubella vaccination record will be identified as susceptible when tested in pregnancy.

1.3 The postnatal rubella vaccination program

Postnatal rubella vaccination programs support infant vaccination programs by ensuring that women at direct risk for having children with CRS are protected from rubella infection. (Although these programs require both prenatal testing and postnatal vaccination components, they are referred to under the general term of

postnatal vaccination programs). All pregnant women are routinely and systematically tested for the presence of rubella antibodies, regardless of previous serology or vaccination. Those identified as susceptible are then offered vaccination in the postnatal period. The success of these programs depends on completeness of testing, and on completeness of follow-up.

1.4 Rationale for study

The 1994 Consensus Conference on Rubella identified the eradication of indigenous rubella infection in Canada by the year 2000 as a primary goal. Recommended activities to meet this goal include surveillance of rubella susceptibility in women of childbearing age, continued research into the issue of waning vaccine-induced immunity, and evaluation of postnatal rubella prevention programs (12).

This study was designed to evaluate these recommended activities when carried out in a highly vaccinated population that has had little exposure to wild virus in recent years. Specifically, the study will review rubella susceptibility among women aged 15 to 44 tested for rubella antibody from 1989-93, assess the predictive value of a rubella vaccination record, and evaluate the effectiveness of the postnatal rubella vaccination program in Newfoundland. Although the study population is restricted to Newfoundland residents, the findings are generalizable to similar populations in Canada.

CHAPTER 2. REVIEW OF THE LITERATURE

2.1 Rubella and congenital rubella syndrome

The congenital rubella syndrome (CRS) was first documented in 1941 by Gregg, an Australian opthamologist who recognized an association between infants with congenital defects, most notably bilateral cataracts, and rubella infection in their mothers during early pregnancy (13). As documentation of similar cases increased, the term CRS was used to describe any of a number of congenital abnormalities in the fetus associated with maternal rubella infection in pregnancy (14).

CRS is manifest in a number of conditions; the most common include sensorineural deafness, cataracts, microphthalmia, glaucoma, chorioretinitis, congenital heart disease and developmental delay (1,14-16). Less common are growth retardation, radiolucent bone disease, hepatosplenomegaly, thrombocytopenia and purpuric skin lesions. Some effects are progressive, including deafness, cataracts, diabetes mellitus, thyroid dysfunction and rubella encephalopathy (1).

The likelihood of fetal damage is greatest when rubella is contracted in the first trimester; up to 25% of children born to first trimester infected mothers will have CRS (1,4, 16-19). When the follow-up period for infants of mothers infected in the

first trimester is extended to two years, so that milder effects or conditions with delayed onset can be detected, the proportion of such infants affected may be as high as 85%. Rubella acquired after 20 weeks gestation rarely results in fetal damage (16). Following a rubella outbreak in British Columbia in 1985-86, 8 of 9 women (89%) infected in the first trimester delivered babies with CRS, compared to 1 of 6 women (17%) infected in the second trimester. No cases of CRS were found for the 4 women infected in the third trimester, although two babies had evidence of congenital rubella infection (Tingle, personal communication, 1995).

The impact of CRS depends upon the severity of disease; one third of a cohort of children born with CRS in the 1964-65 outbreak went on to lead relatively normal lives, one third lived semi-independently, and the remaining one third required institutional care (20). The 1983 cost of lifetime care for a person with congenital rubella syndrome has been estimated to be more than 200,000 American dollars (21). The American rubella epidemic of 1964-65 had an economic impact of 1.5 billion, in 1982 dollars (22).

Stillbirths, miscarriages and therapeutic abortions are also associated with rubella infection in pregnancy (23). In excess of 20,000 cases of CRS and 11,000 fetal deaths from abortion, miscarriage and stillbirths were estimated to have resulted from

the 1964-65 outbreak of rubella in the US (22). In the mid 1980s in the United Kingdom, terminations for rubella contact or infection in pregnancy ranged from 18 to 8 per 100,000 births (24). The 1985-86 British Columbia outbreak resulted in 14 terminations of pregnancy in a group of 35 women exposed to rubella either shortly before or during pregnancy (Tingle, personal communication, 1995).

Several maternal characteristics have been identified as risk factors for delivering a child with CRS. Parity, age and country of origin affect the risk for CRS (14,15,22,25,26), and are all related to the likelihood of not having been vaccinated against rubella.

Australian studies have shown that the risk for a CRS birth is lowest in mothers likely to have received rubella vaccine as schoolgirls (14,15). An American study found that younger primiparous women were at highest risk for a CRS birth (22). Parity can also be a significant risk factor, independent of age. In countries with established prenatal rubella prevention programs, primiparous women are more likely to deliver a child with CRS than are women who have given birth previously, as susceptibles in the latter group are more likely to have been identified in a previous pregnancy and vaccinated before their next pregnancy (25-27).

In the United States, Black and Hispanic women have been found to be at higher risk

for CRS births than white women of similar age and parity (22). In addition, recent immigrants from regions without vaccination programs, particularly South Asia, are more likely to deliver a child with CRS (14,18,27-31).

2.2 Incidence of rubella and congenital rubella syndrome

2.2.1 Rubella

In Canada, rubella has been a reportable disease since 1969 (4), and is part of the general passive surveillance system (32). It can be reported as a laboratory confirmed case or a clinical case. In clinical cases, symptoms must be present, as well as evidence of contact with a confirmed case or in conjunction with increased rubella activity in the reporting area (32). The current reporting definition of rubella is included in Appendix I.

Rubella is an under-reported disease. Clinical diagnosis of rubella is unreliable, as the symptoms of rubella are often subtle, and up to 30% of all cases are subclinical (1,16,33,34). Cases in women are reported more often than cases in men, probably because of the possibility of CRS (19,27).

Before vaccination programs began in 1969, rubella outbreaks in Canada occurred in three to ten year cycles (18,36-42). After 1970, there was a steady decline in

reported incidence, to a 1993 level of about 30 cases per 100,000 population per year (18).

This decline in incidence is typical of countries where vaccination programs have been introduced (1,4,10,16,19,21,43-48). However, rubella has not been completely eliminated, as outbreaks continue to occur in unvaccinated groups. In a 1989 British Columbia outbreak, 83% of reported cases were in persons over 15 years of age (39), and in a Newfoundland outbreak of 1986-87, more than half the cases occurred in adolescent males, a group who would not have been previously vaccinated (38,40). Outbreaks have also occurred in the adult and adolescent populations in schools, prisons, universities and in all age groups in some religious communities which refuse vaccination (16,49,50).

2.2.2 Congenital rubella syndrome

National notification of CRS in Canada began in 1979, through a passive general surveillance system. This was later supplemented by additional surveillance using birth records, hospital discharge data and laboratory data. The system has been further enhanced with specific case investigations and the Immunization Monitoring Program - Active (IMPACT) system (12). The current Canadian definition of reportable CRS includes laboratory confirmed and clinical cases (live and stillborn), where typical

defects are evident (32). The reporting definition for CRS is found in Appendix I.

CRS is probably under-reported, as the definition of clinical CRS is not consistently applied across the country, and is limited to cases occurring in the first year of life (12). Active surveillance in Quebec has revealed that four of nine cases of CRS occurring in the province from 1985-91 had not been detected by the national surveillance system (51).

The most severe cases of CRS (about 50%) can be identified at or shortly after birth (1), but milder cases and those with delayed onset of effects are often not reported, especially if there is no known history of rubella exposure during the pregnancy (2,4,23). CRS incidence is also underestimated because the number of rubella associated terminations, spontaneous abortions and stillbirths is unknown (3,4,12,15,23,27).

In Canada, an average of 3 cases of CRS have been reported each year from 1983 to 1993 (41,42).

2.3 Rubella susceptibility

Susceptibility to rubella infection is measured in levels of rubella-specific antibody. Screening tests detect rubella IgG resulting from vaccination or past infection (52).

Available methods include enzyme immunoassay (EIA), neutralization, and haemagglutination (HAI). For both EIA and HAI methods, susceptibility is defined as a rubella IgG titre value below a specified cutoff point (53).

The value corresponding to clinical protection has not been established (5,39,40,54) and Canada does not have a universally accepted laboratory standard to define rubella immunity at present (12). In the past, an EIA value of at least 15 IU/ml of rubella antibody defined immunity. However, vaccine-induced immunity produces a lower antibody titre than natural infection, and the minimum level of antibody for protection has been lowered to an EIA value of 10 IU/ml (46,52,53,55-57).

Laboratories that perform testing on a regular basis provide the most reliable results (16), with results reported as reactive (protected) or non-reactive (susceptible), rather than in absolute amount of antibody detected (53).

Most surveys of rubella susceptibility have been carried out among women of childbearing age. Rubella susceptibility is estimated to be 3% in the population tested prenatally in the United Kingdom (20,22,58,59). A 1988 estimate for Australian women showed a 9% susceptibility rate (6). In the United States, recent estimates of rubella susceptibility in women of childbearing age range from 6 to 25% (33,60,61).

Among studies conducted in other populations, an American study of male and female hospital employees indicated a birth cohort effect. Older employees (especially those born between 1960 and 1964) were less likely to be susceptible to rubella than those born after 1970 (62). In recent serosurveys of American military recruits, overall susceptibility ranged from 14 to 15%, with susceptibility highest in males and in younger age groups (63,64).

A 1988 serosurvey of prepubertal females in Prince Edward Island indicated that overall susceptibility was 12% (65). A 1992 Canadian serosurvey showed a rubella susceptibility of 10.8% in a population of 356 male and 36 female military recruits, with most of the susceptibles in the male recruits (66).

2.4 Rubella vaccine

Since 1969, several strains of rubella virus have been used to produce vaccine in North America, including HPV-77 DK-12, Cendehill, and HPV-77 DE-5. The RA 27/3 strain introduced in North America in 1979 has replaced these previously used strains (46,67). The vaccine has been administered as various products, including monovalent rubella vaccine, a measles-rubella vaccine (MR), and a measles-mumps-rubella combination (MMR) (68).

Vaccination produces a lower antibody response than does natural infection

(5,33,69,70). Efficacy differs between vaccine strains: HPV-77 DE-5 and Cendehill vaccines produced protection in 95% of recipients over a 16 year period (5,7,8,71), and efficacy for RA 27/3 vaccine ranged from 92% over 18 years (69,70), to 90% over 20 years (9). One study found that HPV-77 DE-5 vaccine was less immunogenic in the combination product than in the monovalent preparation. The specific product did not affect the vaccine efficacy with RA 27/3 (72).

Reported vaccine failure rates of between 5 and 10% may be due to primary vaccine failure (34) or secondary failure related to waning immunity (4,5). Failure to respond to vaccination may also be attributed to improper administration technique or impotent vaccine (28,58,73).

The side effects of rubella vaccination are similar to those for natural infection with the virus, but they occur less frequently (46,74). They include acute musculoskeletal symptoms, fever and rubella associated arthritis (16,20,75,76). The RA 27/3 vaccine that has been used in North America since 1979 results in fewer side effects and more resistance to infection than previously used HPV-77 vaccines (33,69,70).

Arthralgic reactions to vaccination occur most frequently with postpubertal females (76), with a small proportion of persons developing persistent or recurrent musculoskeletal symptoms (75). There have been case reports of chronic recurring

arthritis in recipients after postnatal vaccination with HPV-77 DE-5 or RA 27/3 vaccines (77). There may be a causal relationship between vaccination with RA 27/3 and later development of chronic arthritis, particularly in women vaccinated postnatally (8,78,79).

Although vaccination during pregnancy has not been shown to produce teratogenic effects (16,80), pregnancy remains a contra-indication for vaccination (8,23,46).

2.5 The rubella vaccination record as a predictor of immunity

Vaccine that is used to prevent CRS must produce an immune response that will last for decades, if it is to protect women vaccinated as infants throughout their childbearing years (21,71,81), and it is generally agreed that vaccines used in North America fulfill this criterion (8,54). However, although at least 90% of rubella vaccinees may have protection against disease for at least 15 years duration (5,7,8), the actual clinical efficacy of vaccine may be less than 90% over such a time period (28). Some people with documentation of rubella vaccination are susceptible on testing, (4,6,28,58), and there are also cases of previously vaccinated women delivering babies with CRS (14,29,34,82).

These findings have implications for Canada's current recommendations that serological confirmation of immunity is required only for prenatal clients and some

health care workers (10). If immunity does wane, the positive predictive value of a rubella vaccination record will be reduced, and it may not be sufficient proof of immunity for women of childbearing age, especially for those vaccinated as infants (83).

An Australian study found undocumented history of rubella vaccination to be an excellent predictor of serologically defined rubella immunity, yielding a positive predictive value of 99.8% (84). In an American study, the positive predictive value of an undocumented history of vaccination was 94.9% (85). Neither of these studies accounted for the length of time between vaccination and serological testing, and as they were both conducted in populations of health care workers, rubella vaccination may have been a fairly recent event.

2.6 Vaccination strategies

The objective of any rubella vaccination strategy is to prevent rubella infection in pregnant women and thereby prevent CRS. Selective vaccination strategies provide direct protection to women at risk by vaccinating women of childbearing age (16,18,85). This results in reduced disease incidence in the targeted groups (16,47), but has little effect on virus transmission in younger age groups (4,85). This strategy, used alone, allows wild virus to boost vaccine-induced immunity (4,33,86). Universal vaccination of all children at a young age provides more indirect protection of

pregnant women against rubella infection by interrupting transmission of the virus, and also protects vaccinees throughout their childbearing years (4,23,33,86). Universal vaccination may eventually eliminate the circulation of rubella, as successive cohorts of protected vaccinees reach childbearing age, but cases of CRS can occur during this elimination phase, as virus circulates amongst susceptible older age groups. Universal vaccination programs must therefore be supplemented with selective vaccination programs, such as postnatal rubella vaccination programs, in order to protect susceptible women (23,45,46).

Most countries with vaccination programs use a combination of approaches, and this has been the case in Canada (87). Most provinces implemented postnatal vaccination programs in the early 1970s, and by 1983, all of the provinces and territories had implemented universal infant vaccination programs and also had adopted the recommendations for vaccination of susceptible adolescents and adults (18).

Postnatal rubella vaccination programs target women at immediate risk for rubella in pregnancy (4), and they can prevent up to 50% of the cases of CRS, by identifying susceptible women in their first pregnancy and vaccinating them before the second (46,89). The remaining half of cases result from rubella infection in the first pregnancy, and cannot therefore be prevented by programs that provide vaccination after pregnancy.

2.7 Missed opportunities for postnatal rubella vaccination

Despite the existence of comprehensive rubella vaccination programs, CRS cases continue to be reported (17,22,89,90). In some instances, this may be related to vaccine failure; there are case reports of previously immunized women with laboratory evidence of immunity having contracted rubella in pregnancy, with and without resulting congenital damage (17,34,91). More commonly though, failure to vaccinate contributes to the continued risk for CRS births (22).

Several studies have documented missed opportunities for vaccination, including failure to vaccinate in school programs and failure to enforce school entry requirements for proof of immunity. With reference to postnatal rubella vaccination programs, missed opportunities occur when pregnant women are not tested, and when susceptible women are not vaccinated (58,62,85,89,90).

In one study of mothers who gave birth to CRS babies, more than fifty percent had not been screened for rubella antibody, although the opportunity had been there: during pregnancy, after an induced abortion, or as a premarital requirement (92). A utilization review in Australia showed that 49% of a sample of 10,000 women had not been tested for rubella antibody in pregnancy, despite the availability of testing at no cost to the patient (93).

Even when prenatal screening is done, results may not be linked to follow-up, and so susceptible women may enter the next pregnancy without having been vaccinated (3,86,94,95). A British study showed that although rubella screening was in place in 95% of health districts in England and Wales, follow-up vaccination rates ranged from 45 to 100%, and the women tested during pregnancy were the least likely to have been vaccinated, when compared with women who were screened for employment and other reasons (58). The opportunity to vaccinate postnatally is often missed when the pregnancy ends in a spontaneous or a therapeutic abortion (28,92).

Follow-up rates for postnatal rubella prevention programs invariably increase when vaccination is offered during the postnatal hospital stay (46,59,96). The current NACI statement on rubella prevention recommends that vaccination be offered during the postnatal hospital stay (12), and a recent review in Quebec recommended that postnatal vaccination of susceptible women become a hospital regulation (97). This type of approach is particularly effective in increasing vaccination rates among transient populations who may be difficult to trace after hospital discharge (72,92,95).

2.8 Rubella prevention in Newfoundland

Table 1 shows the chronology of rubella prevention programs in Newfoundland from 1971, when selective rubella vaccination of schoolgirls was first introduced, to the

present, where there is a postnatal rubella prevention program, MMR vaccination of all one year old children, and provision for the vaccination of others found to be rubella susceptible (98,99).

Vaccination rates in the province have been consistently high, exceeding 90% annually for the schoolgirl program, and since 1982, 98% or higher for MMR vaccination of school entrants (100). These programs have contributed to a decline in rubella incidence in the province, from 76.6 per 100,000 in 1972 to .02 per 100,000 in 1992 (101). Figure 1 shows the reported incidence of rubella in Newfoundland from 1960 to 1993. The last recorded outbreak of rubella in the province occurred in 1986-87(101).

CRS incidence has also declined, although during the 1960s and 1970s, it was not well reported in the province (102). Based on chart reviews and case investigations, at least 34 cases of CRS are known to have occurred in the province between 1963 and 1974, followed by two cases reported in 1987 (101,102). Cases of CRS in the province have occurred following rubella outbreaks, as seen in Figure 2 (101).

Rubella susceptibility in women of childbearing age has declined from 12% in 1976 to 8% in 1981 (101). Susceptibility remained stable at 4 to 5 % in the 15 to 19 year olds over this period, while it declined from 10 to 6% in women between 20 and 29

years of age, and remained highest in women 30-34 years of age, at 9 to 10 %. The decline in 20-29 year olds was attributed to the selective schoolgirl vaccination program (103).

Current age and sex specific susceptibility rates within the population at risk for CRS births are not known. Most women of childbearing age in the province are likely to have been vaccinated, either as schoolgirls or infants, and so susceptibility within this group is expected to be no higher than for the overall population tested (males and females), where it has remained at about 8% since 1984 (unpublished document, Newfoundland Department of Health).

Immigration of women to the province has probably had little effect on susceptibility; 96% of the population are Newfoundland born, 3.5% are from other regions of Canada, and the remaining 1.5% are immigrants. Sixty percent of immigrants to the province originate from the UK and the USA (104), countries where either selective or universal rubella vaccination programs are well established (16,19).

The postnatal rubella vaccination program in the province is designed to identify susceptible women who are at risk for CRS births. This program operates on the principal of universal screening, where all pregnant women are tested for rubella antibodies, regardless of previous test results. The program is centrally administered

by the Community Health Division of the Department of Health, with all testing done at the provincial Public Health Laboratory in St. John's. Test results are forwarded to the attending physician, and for women who are susceptible, duplicate reports are sent to the local health region, and to the Provincial Office of the Department of Health. The Provincial Office (Division of Disease Control and Epidemiology) enters the woman's identifying information as an individual record on the provincial Postnatal Rubella Vaccination Registry.

In the health region, the report is forwarded to a public health nurse who offers vaccination in the postnatal period. The result (vaccination or refusal) is documented in triplicate. One copy is sent to the woman's physician, one copy goes to the provincial office for updating of the woman's individual entry on the Postnatal Rubella Vaccination Registry, and one copy is kept in the region. When vaccination is provided in hospital, documentation of outcome is sent to the physician and the health region. The region then forwards the a copy to the provincial office for entry on the Registry. Figure 3 illustrates the information flow for the program.

The postnatal rubella vaccination program has been in place since 1972, but it has never been formally evaluated. This well-established and centralized program presents an opportunity to review both the completeness of testing and the completeness of follow-up vaccination achieved.

Table 1: History of rubella prevention programs in Newfoundland

YEAR	POLICY OR PROGRAM
1971	Rubella vaccination of all 10-11 year old schoolgirls.
1972	Postnatal rubella vaccination program introduced. Measles-rubella vaccine (MR) available for all 1 year olds.
1974	MR vaccine replaced by measles-mumps-rubella vaccine (MMR) for all 1 year olds.
1979	HPV-77 rubella virus vaccine strain replaced by RA 27/3 strain in MMR preparation.
1981-82	Final year for rubella vaccination of all 10-11 year old schoolgirls.
1983*-present	MMR vaccine for all one year olds. Postnatal rubella vaccination program. Vaccination of other persons found to be rubella susceptible.

MR - measles and rubella combined vaccine
MMR - measles mumps and rubella combined vaccine

*** In the school year 1982-1983, all Grade 5 girls lacking infant rubella vaccination records were given rubella vaccination.**

Figure 1: Rubella in Newfoundland 1960 - 1993. Reported cases per 100,000 population

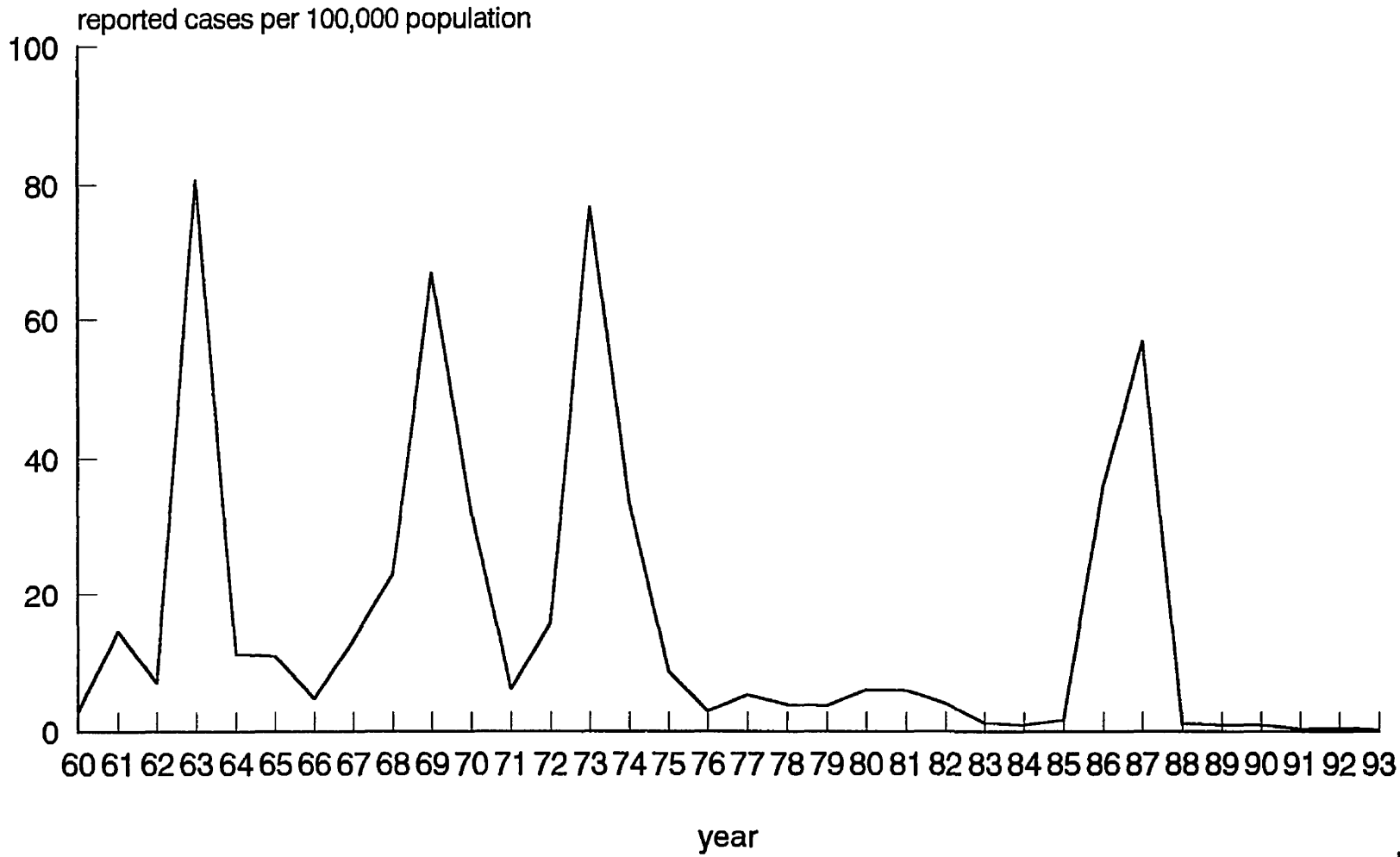
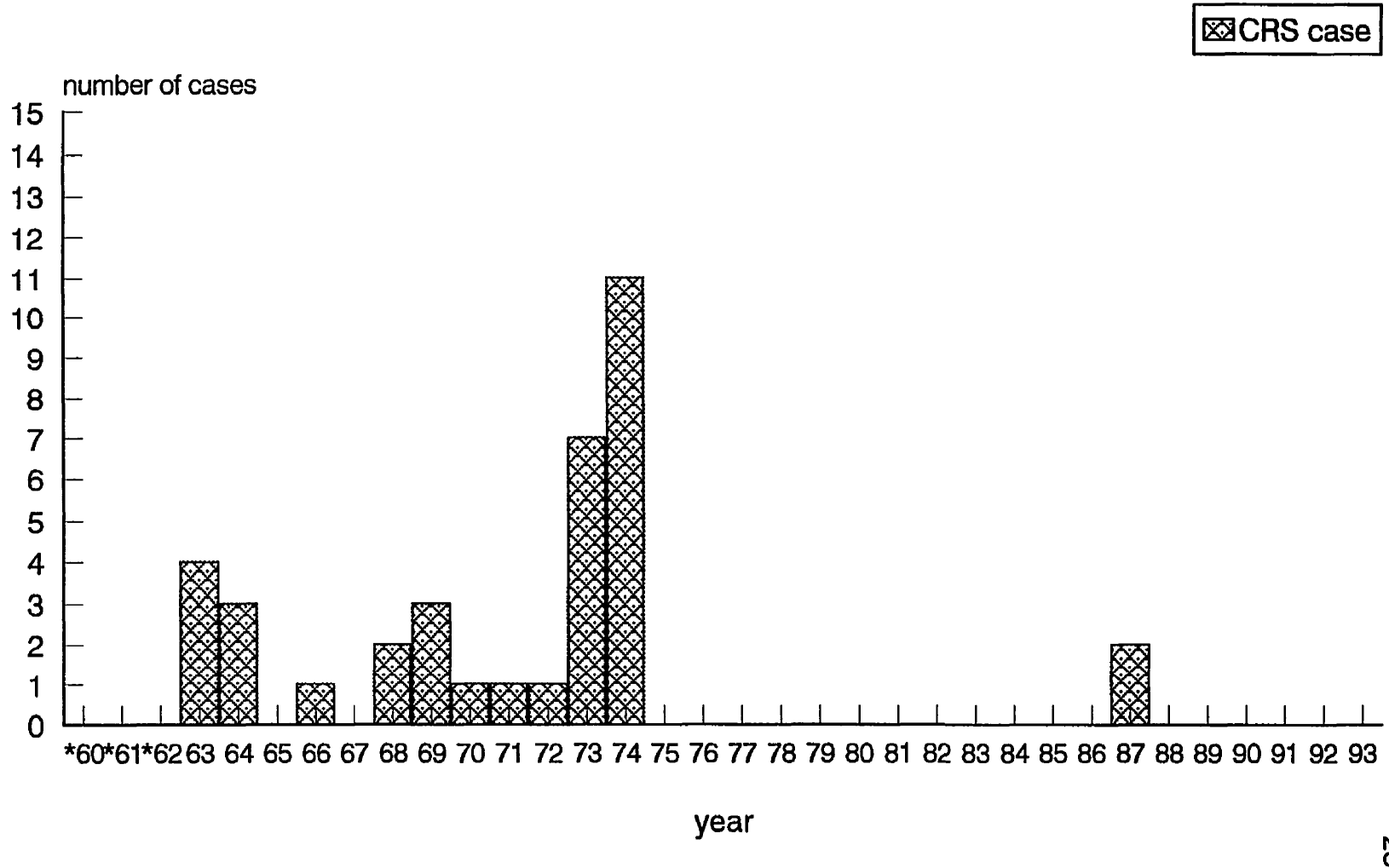
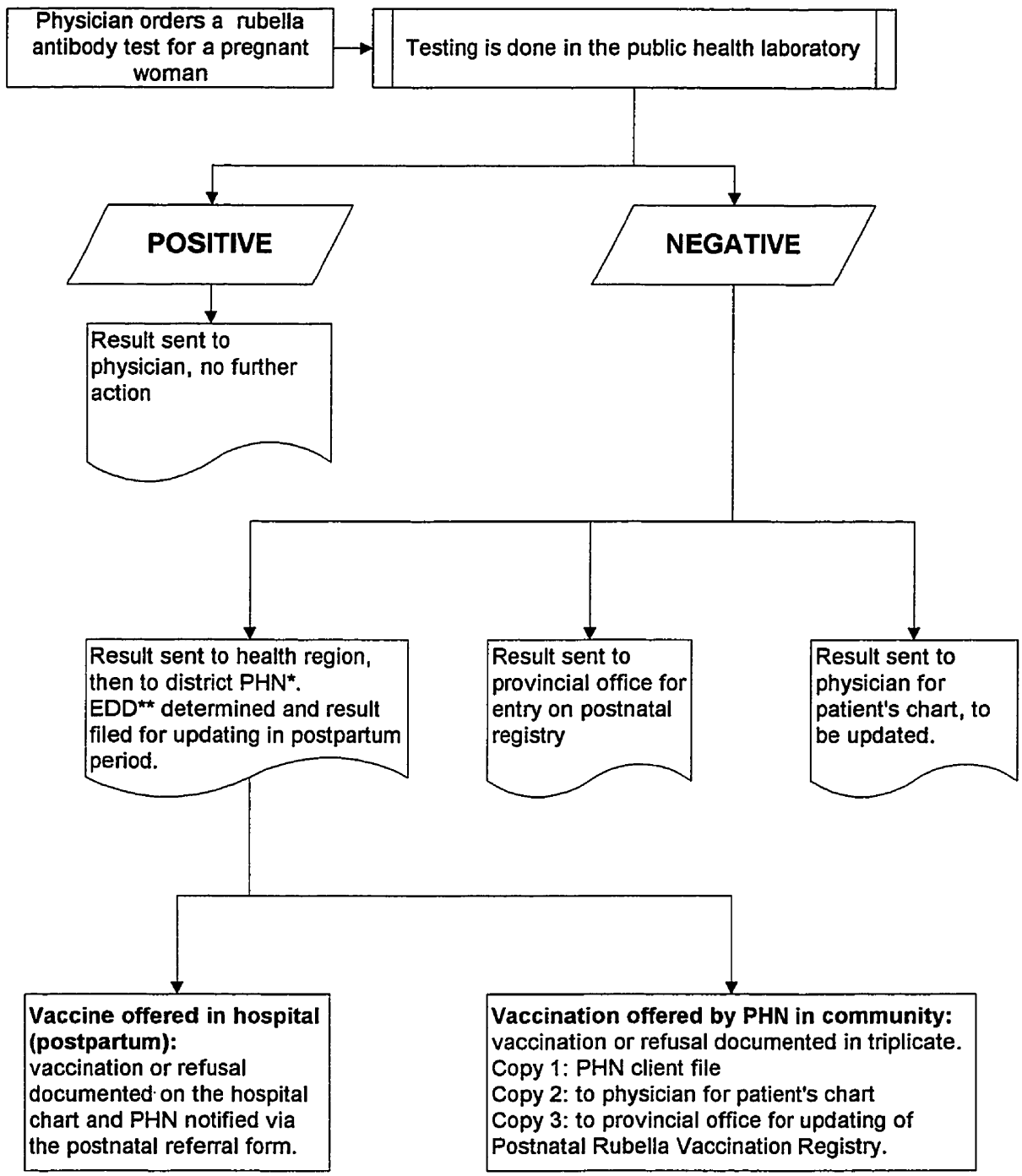


Figure 2: Congenital Rubella Syndrome in Newfoundland 1963-1993.
Recorded Cases



* no data available

Figure 3. Postnatal rubella vaccination program testing and reporting



* PHN: Public Health Nurse **EDD: expected date of delivery

2.9 Statement of purpose and objectives

CRS can only be prevented by preventing rubella infection in pregnancy. This study assessed the impact of vaccination programs on rubella susceptibility and evaluated some key components of existing programs.

Rubella susceptibility in the female population of childbearing age in Newfoundland was reviewed to identify age-specific or geographic pockets of rubella susceptibility. The positive predictive value of a rubella vaccination record was assessed to determine if assumptions of vaccine efficacy are valid in this population. Lastly, the effectiveness of the postnatal rubella vaccination program was evaluated to identify deficiencies in coverage and follow-up. Recommendations were made to improve existing programs to ensure protection from rubella before pregnancy occurs.

The specific objectives for the study were to:

1. Estimate rubella susceptibility among the female population of childbearing age in Newfoundland.

2. Determine the value of a vaccination record in predicting a positive rubella antibody test.

3. Evaluate the extent to which the postnatal rubella vaccination program identifies women at risk for a CRS outcome and ensures follow-up vaccination in the postnatal period.

CHAPTER 3. METHODS

3.1 Data sources

The study was carried out in three sections: review of rubella susceptibility, assessment of the positive predictive value of a record of rubella vaccination, and evaluation of the postnatal rubella prevention program. The core data sources that were used to complete the three sections of the study were located in several divisions within the Department of Health, either in paper or electronic formats.

The specific databases for this study were built by linking the core data sources in various combinations, using some standard linkage procedures which are described below. In order to simplify the Methods section, the core data sources are described in Table 2, in terms of their format and contents. Their uses in building each dataset for the study are described in more detail in the appropriate sections.

Table 2: Data sources for study

source	format and contents
Public Health Laboratory computer database	**1. Aggregate rubella test results**: Rubella IgG antibody testing results, containing test date, result and health region. Results (reactive and non-reactive) aggregated by 5 year age group and health region for women 15-44 tested in 1989, 1991 & 1993. Printed output from the laboratory database, on ***dBASE*** software (Ashton Tate, Torrance CA 1989).
	2. Rubella antibody tests: Individual rubella IgG antibody test results containing identifying information, test date and result (reported as reactive or non-reactive). Individual reports from the laboratory database, on ***dBASE*** software, exported to an Epi-Info file.
Western Newfoundland Health Region files	**3. Postnatal referral forms**: Individual *Records of Livebirth Notification** issued for all hospital births for the region. Paper record containing mother's identifying information, obstetric history and birth record. Filed alphabetically by year of delivery.
Provincial Immunization Database	**4 . Vaccination record.** Individual *Immunization and Health Records**containing identifying information and documentation of all immunization received up until school leaving. Issued for every person born after 1954 and ever attending school in the province. Records from year of birth 1955 to 1971 on microfilm files, sorted alphabetically by year of birth. Records for year of birth 1972 and forward on paper files in the health region.
Provincial Birth Record Database	**5. Birth record file:** Individual records containing mother's identifying information, parity and birth record, stored by year. Stored on the Department of Health mainframe computer and down loaded onto ASCII files.
Postnatal Rubella Vaccination Registry	**6. Postnatal rubella vaccination record:** Individual *Rubella Immunization Consents**, completed for women identified as susceptible on prenatal testing, and then followed up. Contain identifying information, date of antibody test, date of vaccination or refusal. Epi-Info file.

* sample copies located in Appendix Two.

3.2 Laboratory tests

The Public Health Laboratory used the Rubella IgG assay (Abbott Laboratories, Diagnostics Division, Abbott Park, IL.), a micro particle enzyme immunoassay (MEIA) for measurement of IgG antibodies to rubella virus in serum. Rubella IgG antibody of at least 10 millilitre per IU was reported as reactive, and defined protection. Antibody of less than 10 ml/IU was reported as nonreactive, and defined susceptibility.

3.3 Linkage procedures

None of the files and records listed in Table 2 are routinely linked for any reason. Linked files were created specifically for this study by merging files, either manually or electronically.

Manual linkage was used to match paper and microfilm records, using full name and date of birth as matching fields. Because there are some small communities where a large proportion of residents have the same surname, both full name and birth date were used as matching fields. Where the given names varied on spelling, a birth date match was taken as proof of a true match.

Electronic linkage was used to match the computer-based records, via the Epi-Info (105) Merge File procedure. The medical ID number was used to link records, as this

unique identifier is the most efficient with an electronic system (106). For those records that remained unlinked after the merge procedure, a visual scan was performed and manual linkage by name and date of birth was used, as described above.

3.4 Rubella susceptibility in women of childbearing age

3.4.1 Objective and study design

An analysis of the existing province-wide laboratory database was used to estimate the rubella susceptibility of the female population of childbearing age in Newfoundland.

3.4.2 Study population

The study population consisted of all females between 15 and 45 years of age in Newfoundland who were tested for rubella antibody in 1989, 1991 and 1993. In 1988, the laboratory switched from a test cutoff standard of 15 IU/ml to one of 10 IU/ml, and so these years provided a five year span with a consistent test methodology. Alternate years were chosen to minimize the data retrieval costs.

3.4.3 Sample size

For each year selected there were between 7,000 and 10,000 subjects available.

Calculation of the sample size is based on the formula for the normal approximation to the binomial : $n=(z_{.99}/w)^2$ (107).

Using a 99% confidence interval and a p = 0.5, (the most conservative value requiring the largest sample size) with desired accuracy of plus or minus 2% to the true proportion, gives the following: $(2.56/.04)^2 = 4096$

To estimate the susceptibility in the sample population with a 99% confidence interval and a margin of error of 2%, a sample size of 4096 was required. For each year chosen, all of the available subjects were used, providing more than the required number at no extra cost.

3.4.4 Outcome measure

The outcome measure in this section was rubella susceptibility, defined as a nonreactive rubella IgG antibody test result.

3.4.5 Data source and analysis

This section used aggregate rubella test results from the provincial laboratory database (data source #1). The percent of women susceptible by year of test, and by standard age group and geographic region was calculated with confidence intervals for each year. Chi-square calculations were performed to compare susceptibility in

tested populations for each year, each region, and for each age group within each year.

3.5 The rubella vaccination record as a predictor of immunity

3.5.1 Objective and study design

The objective was to determine the utility of a rubella vaccination record for predicting a positive rubella antibody test over a period of years. A retrospective cohort design approach was used.

3.5.2 Study population

The study population consisted of all primiparous mothers from the Western Health region who delivered in 1992. This region provided ready access to the pertinent data sources, and 1992 was the most recent year for which all records had been forwarded from the districts to the regional office.

3.5.3 Sample size

The required sample size was calculated using the assumption of the normal approximation to the binomial (107). Published reports of rubella vaccine efficacy range from 90 to 98%, and so the most conservative value of the unknown p was set at 0.90 for this calculation (95% confidence interval), with a maximum absolute

difference of 3% for width, w = .06

$$n=(2z_{95}/w)^2 p^*(1-p^*) = (3.92/.06)^2 .9(.1) = 384.16 \text{ or } 385$$

As the two stage linkage procedures were used to build the final study file, the entire initial subject pool of all 517 primiparous mothers who delivered in Western Newfoundland was included, to allow some loss of subjects from non-linkage, without a substantial loss of accuracy in the estimate (108).

3.5.4 Exposure measure

The exposure measure was a rubella vaccination record, where both the vaccine product name and the date of vaccination were documented. Vaccination at any time before the date of the prenatal rubella antibody test was accepted as exposure.

3.5.5 Outcome measure

The outcome measure was a prenatal rubella IgG antibody test result, defined as either rubella antibody reactive or rubella antibody nonreactive.

3.5.6 Data sources, data handling and analysis

This section used postnatal referral forms (data source #3) and vaccination records (data source #4). Each postnatal referral form was manually linked with the corresponding vaccination record, using maiden name (if different from current

surname) and birth date as matching fields. The records were then entered onto an Epi-Info database, listing full name, maiden name, birth date, medical ID number, rubella vaccination date(s) and vaccination product(s). The Epi-Info database was then electronically linked by medical ID number to the rubella antibody tests (data source #2), adding rubella antibody status to each individual's record.

The proportion of persons with a record of vaccination who had subsequent positive serology reports was determined, with confidence intervals calculated for the proportion obtained. The same calculations were repeated, using the results stratified by vaccine product received, by interval between vaccination and rubella serology test, and by likely vaccine strain received. Confidence intervals for the differences between proportions were calculated as well.

All subjects with rubella vaccination records were considered to have the exposure of interest and were included in the original analysis. However, the current NACI guidelines stipulate vaccination on or after the first birthday as proof of immunity (10). Therefore, a repeat analysis was done excluding the subjects who were vaccinated before their first birthday.

3.6 Evaluation of the postnatal rubella vaccination program

3.6.1 Completeness of testing

3.6.1.1 Objective and study design

Analysis of the birth record database linked to the provincial laboratory database was used to estimate the proportion of women who had received rubella antibody testing in pregnancy.

3.6.1.2 Study population

The study population used to determine the testing coverage consisted of a 10% random sample of mothers who delivered in 1992. The year 1992 was the most recent year for which complete records were available for analysis.

3.6.1.3 Sample size

A ten percent sample of 1992 births yielded a sample size of 638 records. Specifying a 95% confidence interval, the width for an unknown proportion p as low as 0.5 was calculated as follows: $w = 2z_{1-\alpha}\sqrt{p(1-p)/n}$ (107).

$w = 2\ (1.96)\ \sqrt{.5(.5)/638} = .078$ 3.9%.

A sample size of 638 means that a 95% confidence interval would have a maximum width of 8% (plus or minus 4%), if the true proportion of women screened was as low as 50%.

3.6.1.4 Outcome measure

The outcome measure was the presence of a rubella IgG antibody test result, (reactive or nonreactive) for each subject, dated within 42 weeks before the date of delivery. The prenatal period was arbitrarily defined to include any time from the day of delivery to 42 weeks previous to delivery, and was calculated by subtracting the test date from the delivery date.

3.6.1.5 Data sources, data handling and analysis

This section used birth record files (data source #5), and rubella antibody tests (data source #2). The sample was initially generated from the birth record files, using a computerized random selection method that selected 10% of each health region's 1992 births.

The 10% sample file records were then electronically linked to the rubella antibody test files for 1991 and 1992. Both years were used to cover all possible prenatal periods for mothers who gave birth in 1992.

The proportion of those with a record of serology within 42 weeks previous to the delivery date was calculated with confidence intervals. The approximate number of

weeks gestation at which each subject was screened was calculated by the method described in Rushworth, Bell, Rob and Taylor (93) as follows:

date of test - date of delivery = X weeks.

40 weeks - X weeks = number of weeks gestation at time of test.

The approximate weeks gestation was calculated for each subject tested, and the mean weeks gestation was then calculated overall and for each region. Chi-square calculations were performed to compare the proportions who had prenatal testing for each of the health regions, and also to look for any differences in the proportion tested by age.

3.6.2 Completeness of follow-up

3.6.2.1 Objective and study design

Analysis of the Postnatal Rubella Vaccination Registry data for 1992 was used to determine the proportion women identified as rubella susceptible in pregnancy who were then given follow-up vaccination.

3.6.2.2 Study population

The study population used to determine the completeness of follow-up for susceptible women consisted of the 1992 provincial Postnatal Rubella Vaccination Registry entries. In regions A and C this included some women who were not prenatal clients,

as these particular regional procedures for follow-up of rubella susceptible clients did not differentiate between prenatal and other clients. Very few antibody tests would have been carried for non-prenatal clients; the Communicable Disease Nurses in these two regions indicated that this amounted to fewer than 10% of the entries. The registry entries were reviewed for documentation of vaccination or refusal, and the incomplete ones were traced back to the health regions for completion of information.

3.6.2.3 Sample size

All entries for 1992 were initially selected, but a staffing shortage in one of the regions at the time of the study meant that full information could not be retrieved to the same extent as in the other regions. This region was dropped from this portion of the study, leaving a sample size of 273.

3.6.2.4 Outcome measure

The outcome measure was the status of postnatal follow-up, as evidenced by a completed (date of vaccination or refusal recorded), or in the absence of this, notation of either "lost to follow-up" or a "pending documentation from family physician" on the region's copy of the prenatal antibody test result.

3.6.2.5 Data sources, data handling and analysis

The source of information was the postnatal rubella vaccination record (data source #6) as found on the Provincial Postnatal Rubella Vaccination Registry Epi-Info file. In some cases the report had not been completed on the Epi-Info file, and paper copies of the postnatal rubella vaccination record or the prenatal antibody test result were retrieved from the regions in these cases.

Each record was reviewed to determine the follow-up status, which was characterized into one of four categories:

Vaccinated - dated record of vaccination

Refused - documented refusal of vaccination

Lost to follow-up - no contact made with person

Pending - awaiting notification of vaccination or refusal

The overall proportion of follow-up completed was determined for the study population and for each of the four regions, and the proportions in each classification (vaccinated, refused, lost to follow-up and pending) were also calculated for each region.

These proportions in each region could not be directly compared for statistically significant differences, as in Regions A and C, the follow-up recording system did not distinguish between prenatal clients and other susceptible women.

3.7 Measures taken to ensure internal validity

In the various sections of this study, differential misclassification of subjects on rubella antibody status was possible, depending on the age of the subject. Vaccination produces a lower antibody response than natural infection (5,33,69,70), and it is likely that younger subjects would have been vaccinated and not naturally infected. Therefore, younger subjects would probably have lower antibody titres than older subjects, but still be immune. However, the laboratory used a test that favours a vaccinated population, so that subjects with "low positive" results were classified as reactive (immune).

Misclassification of subjects resulting from testing error was minimized; all rubella antibody testing in the province has been done in the Public Health Laboratory since 1971, and standard commercial test kits were used for all subjects in each year. It is therefore unlikely that testing error contributed to any misclassification of subjects by rubella antibody test results.

There was one source of potential misclassification bias that was particular to the methodology for the assessment of the predictive value of a rubella vaccination record. Women vaccinated outside the school setting may have had no documentation of the event, and older women would have had more opportunity for such recent vaccinations: previous postnatal screening, job entry requirements, or travel

vaccinations. Thus differential misclassification of vaccination history by age might have occurred, with older women misclassified as having had only one rubella vaccination instead of several. This could falsely elevate the predictive value of the rubella vaccination record. This bias was minimized in two ways: primiparous mothers were selected for this portion of the study, as they would not have been recently vaccinated as a result of a previous negative prenatal antibody test result. In addition, the Western Health Region was chosen for this portion of the study because it has a history of well maintained records, with a long standing policy for documentation of any vaccinations given outside the school setting to be kept on auxiliary files in the region. The subjects were checked against these regional files to pick up any extra rubella vaccinations.

Possible ascertainment bias in this portion of the study was minimized by ensuring that the search for vaccination records was not influenced by a prior knowledge of serology results for the subject, whereby a positive result might prompt a more concentrated search for a record of rubella vaccination. For all subjects, vaccination history was determined before the serology status was obtained.

The linkage procedures used in this study made selection bias a possibility. For example, in the assessment of the positive predictive value of the rubella vaccination record, a two step linkage procedure was used. Subjects for whom a vaccination

record (exposure) could not be found and then linked to a rubella antibody test result (outcome) were dropped from the sample. If older subjects were systematically excluded, or if rubella laboratory results were missing for a particular geographic region, then the representativeness of the sample would be affected, making the results less generalizable. The possible systematic exclusion of subjects could not be prevented from occurring, but there was no *a priori* indication that this would be the case. However, all subjects excluded in all steps of linking were analysed by age and region to assess for selection bias.

The linkage procedures were somewhat vulnerable to other sources of error as well. Firstly, true matches might be missed if complete information was not available to link on, particularly with the electronic linkage, as a miscoded medical ID would result in a failure to link. However, the electronic linkage procedures was backed up with manual reviews of the files for subjects left unmatched, and this would reduce the likelihood of failure to link truly matched records. Secondly, there might be failure to reject false matches. This is less likely with the electronic linkage procedure than with the manual linkage using names. This possibility was minimized by using name and birth date to link manually. Both of these linkage errors could contribute to misclassification of subjects in the portion of the study that dealt with the completeness of testing, because subjects were classified as having had a prenatal rubella test if they could be linked to the Public Health Laboratory rubella antibody

test computer database. If true matches were missed, subjects would be misclassified as not having been tested. However, there was no reason to suspect that such misclassification would be differential.

3.8 Analysis software

All analysis of data was performed using the Epi-Info Version 6.02 software package (105).

3.9 Ethical considerations

Several of the data sources used in this study contained nominal information. Once linking procedures were completed, the nominal information was stripped from the study files and the raw data files were destroyed. The names of all rubella susceptible subjects were reported to the communicable disease nurses in the respective regions if there was no indication of rubella vaccination after the date of the test.

CHAPTER 4. RESULTS

4.1 Rubella susceptibility in women of childbearing age

In each of the years 1989, 1991 and 1993, between 8,000 and 10,000 women of childbearing age were tested for rubella antibody in Newfoundland. Overall rubella susceptibility was low, and did not vary significantly by year: 4.8% (99% ci: 4.2%-5.5%) in 1989, 4.2% (99% ci: 3.7%-4.7%) in 1991 and 5.3% (99% ci: 4.7%-6.0%) in 1993. When averaged over the three years reviewed, rubella susceptibility differed by health region (χ^2 =16.82, 4df, p=.002). Region E showed the highest overall susceptibility, averaging 6.7% over the three years reviewed (Table 3). Rubella vaccination rates in Region E are comparable to the other regions (100).

There were significant differences in susceptibility by age group (χ^2 =100.94, 10df $p < .001$). Women 15 to 19 years old had the highest proportion of susceptibles, ranging from 12.6% in 1989 to 17.2% in 1993. For each year reviewed, susceptibility in this age group was at least three times the level found in any other age group (Table 4). There was a trend of decreasing susceptibility as age increased towards the 25 to 29 year old group, then a slight increase in susceptibility again in the 30 to 44 year old women. This trend was consistent in each of the five health regions as well.

Susceptibility decreased over time in women from the 1970 to 1974 birth cohorts. In 1989, susceptibility was 12.6% in 15-19 year olds, and by 1993, in 20-24 year olds, susceptibility had dropped to 5.6% (χ^2 =60.0, 1df $p < .001$). This effect was evident in the 1965-1969 birth cohorts as well; 20-24 year olds in 1989 had a susceptibility of 3.7%, compared to 1.1% of the 25-29 year olds tested in 1993 (χ^2 =41.4, 1df $p < .001$).

Table 3: Rubella susceptibility in women of childbearing age.
Number susceptible/number tested, *% and (99% ci)* susceptible by health region.

year	health region					
	A	B	C	D	E	total
1989	122 /3057 *4.0 (3.1 - 5.0)*	79/1519 *5.2 (3.8 - 6.8)*	68/1338 *5.1 (3.7 - 6.8)*	55/1296 *4.2 (2.9 - 5.9)*	63/785 *8.0 (5.6 - 10.8)*	388/7998 * *4.8 (4.2 - 5.5)*
1991	130/4010 *3.2 (2.6 - 4.0)*	77/1919 *4.0 (2.9 - 5.3)*	78/1622 *4.8 (3.5 - 6.3)*	102/1689 *6.0 (4.6 - 7.7)*	38/887 *4.3 (2.7 - 6.3)*	425/10141* *4.2 (3.7 - 4.7)*
1993	142/3557 *4.0 (3.2 - 4.9)*	82/1744 *4.7 (3.5 - 6.2)*	83/1474 *5.6 (4.2 - 7.4)*	75/1379 *5.4 (4.0 - 7.2)*	57/729 *7.8 (5.5 - 10.7)*	440/8890* *4.9 (4.4 - 5.6)*
Tot.	394/10624 *3.7 (3.2 - 4.2)*	238/5182 *4.6 (3.9 - 5.4)*	229/4434 *5.1 (4.3 - 6.0)*	232/4364 *5.3 (4.5 - 6.2)*	158/2401 *6.6 (5.3 - 8.00)*	1253/27029* *4.6 (4.3 - 5.0)*

* includes some women tested without the region identified.

Table 4: Rubella susceptibility in women of childbearing age.
Number susceptible/number tested, *% and (99% ci)* by age group.

year	age group					
	15-19	**20-24**	**25-29**	**30-34**	**35-44**	**total**
1989	158/1258 *12.6 (10.3 -15.1)*	91/2438 *3.7 (2.8 -4.8)*	66/2438 *2.7 (1.9 -3.7)*	47/1254 *3.7 (2.5 - 5.3)*	26/610 *4.3 (2.4 -6.8)*	388/7998 *4.8 (4.2 - 5.5)*
1991	241/1886 *12.8 (10.9 - 14.9)*	94/3100 *3.0 (2.3 -3.9)*	43/3014 *1.4 (0.9 -2.1)*	30/1516 *2.0 (1.2 -3.1)*	17/625 *2.7 (1.3 - 4.9)*	425/10141 *4.2 (3.7 - 4.7)*
1993	233/1353 *17.2 (14.6 -20.0)*	148/2622 *5.6 (4.5 -6.9)*	29/2764 *1.1 (0.6 - 1.7)*	17/1600 *1.1 (0.5 - 1.9)*	13/551 *2.4 (1.0 - 4.6)*	440/8890 *4.9 (4.4 -5.6)*
Tot.	632/4497 *14.0 (12.7 - 15.4)*	333/8160 *4.1 (3.5 -4.7)*	138/8216 *1.7 (1.3 - 2.1)*	94/4370 *2.1 (1.6 -2.8)*	56/1786 *3.1 (2.2 - 4.4)*	1253/27029 *4.6 (4.3 - 5.0)*

4.2 The rubella vaccination record as a predictor of immunity

The object of this part of the study was to determine the positive predictive value (PPV) of a written rubella vaccination record for women in the childbearing years. The population originally selected for this study consisted of the 522 primiparous mothers who gave birth in the Western Health Region in 1992. In both the region and the province as a whole, 45% of births were to primiparous mothers.

Documented vaccination histories and prenatal rubella serology results were obtained for 399 of the original 522 subjects, for a failure-to-link loss of 123 subjects, or 24%. This final study population had an age distribution that was similar to the original group of 522 primiparous mothers and to the primiparous mothers in the province in 1992 ($\chi^2 = 8.47$, 2df, $p = .389$), as seen in Table 5.

Of the 399 women in the final study population, 350 (88%) had a rubella vaccination record. The 49 subjects who had no rubella vaccination noted on their immunization records differed from those with rubella vaccination by age; 50% of the group with no record of rubella vaccination were born in 1962 or earlier, compared to 10% of those with records. These older women would not have received schoolgirl or infant vaccination. Both groups were similar in the proportion rubella susceptible at the time of prenatal screening (8% and 12% respectively, with the 95% confidence interval for the difference in the proportion susceptible ranging from 0 to 13%).

Three different rubella vaccine combinations were used in this population: monovalent rubella vaccine, MR vaccine and MMR vaccine (Table 6). Specific product names were not noted on the vaccination records. The monovalent vaccine had been given to 186 women (53%), and the remaining 164 vaccinated women (47%) had received either the MR or the MMR combination.

The age at vaccination varied with the product given; of the 110 subjects vaccinated before the age of 5, 108 (98%) had received MR or MMR vaccine, and of the 48 vaccinated between five and nine years of age, 39 (81%) had also received one of these combination products. However, of the 179 women vaccinated at 10 to 14 years of age, only 5 (3%) had received MR or MMR vaccine. Only 13 (4%) of subjects had been vaccinated at age 15 or older, all with MMR vaccine.

The overall positive predictive value of a record of vaccination in the group of 350 women was 92% (Table 7). When the subjects were divided into those who had received monovalent vaccine and those who had received either MR or MMR, there was a significant difference in the positive predictive values, as monovalent rubella vaccine had a significantly higher positive predictive value than the MR or MMR vaccine (99% and 84% respectively, 95% confidence interval for the difference in the proportion susceptible ranging from 9.2 to 20.8%). It is noted that 174 (93%) monovalent vaccine recipients were vaccinated at 10 to 14 years of age.

Twelve subjects within the group of 350 (4%) had records that indicated more than one rubella vaccination had been received. In these cases, the most recent vaccination was used in the calculations. For 4 subjects the most recent vaccine was the monovalent product and for the remaining 8, MMR was recorded as the most recent vaccine. All 12 subjects had positive serology. After removing these 12 records, the overall PPV remained unchanged at 92%, the monovalent PPV remained at 99% and the PPV for the combination products did not differ significantly (84% and 83%, $\chi^2 = .04$, 1df, $p = .84$).

For the eleven subjects vaccinated at less than a year of age (all with MR or MMR), the PPV was 73%. For the additional 32 women vaccinated at 12 to 14 months of age, the PPV was 72%. This reduced PPV may have been due to interference from maternally-derived antibody. None of the women who had monovalent rubella records were vaccinated before four years of age.

Waning immunity might have contributed to the difference in the observed predictive values between the monovalent vaccine and the combination vaccines, as both MR and MMR were received at a younger age than the monovalent vaccine (Table 6). The results were therefore stratified by the time elapsed between vaccination and prenatal serology test. The median value for this interval was 15.5 years, and this was used as the cut point for stratification. Table 8a shows the results for subjects vaccinated

less than 15.5 years before their prenatal rubella test, and Table 8b shows the results for subjects with intervals of at least 15.5 years between these events. The overall PPV for any rubella vaccine (monovalent, MR or MMR) did not change when stratified (95% confidence interval for the difference in the PPV ranging from 0 to 12%). The PPV for the monovalent vaccine remained significantly higher than the PPV for the combination vaccines in those with less than 15.5 years between vaccination and serology (95% confidence interval for the difference in the PPV ranging from 3 to 21%). Similarly, the PPV for monovalent rubella was higher than the PPV for the MR and MMR vaccine in those vaccinated at least 15.5 years before rubella serology was done (95% confidence interval for the difference in the PPV ranging from 9 to 25%).

These results were then further stratified by year of birth, as those born before 1973 were more likely to have been exposed to wild virus. All recipients of monovalent rubella vaccine were born before 1973, and so were not considered in this step. The results for the recipients of the combination vaccines showed no difference in the PPV when stratified by length of time between vaccination and serology, and by year of birth, as noted in Tables 9a and 9b.

The RA 27/3 virus strain vaccine is more immunogenic than the HPV-77 DE-5 strain (33,69,70), and this may have had some effect on the PPVs. The HPV- 77 DE-5

strain was used in Canada until mid-1979, when it was replaced by the RA 27/3 strain (99). The results were stratified by vaccine strain, using vaccination dates as markers for the strain received (Tables 10a and 10b). Women vaccinated before 1979 were assigned to the HPV-77 DE-5 strain group and those vaccinated after 1979 to the RA 27/3 group. Those vaccinated in 1979 were excluded, as they may have received either strain. Women vaccinated before one year of age were also excluded from this step. For the women who received the HPV-77 DE-5 strain, the monovalent product PPV remained significantly higher than the combined product PPV (98% and 81% respectively, with the confidence interval for the difference in the PPVs ranging from 11 to 25%). With the RA 27/3 strain recipients, there was no difference in the PPV between monovalent and combination products (100% for monovalent product and 97% for the combination product). However, there were only 27 subjects in this group, and the wide confidence interval for the estimate (80% - 100%) limits the significance of the finding.

Table 5: **Proportionate age distributions for final study population, original study population (Western Region), and the referent population (province). Number and (%).**

age group subjects	15-19	20-24	25-29	30-34	35-44	Total
final study population	77 (19.3)	151 (37.8)	118 (29.6)	46 (11.5)	7 (1.8)	399 (100)
original study population	97 (18.6)	196 (37.5)	149 (28.5)	68 (13.0)	12 (2.3)	522 (100)
referent population	627 (20.2)	1021 (33.0)	984 (31.7)	382 (12.3)	78 (2.5)	3100* (100)

$\chi^2 = 08.47(8\ df)\ p = .389$ *includes 3 mothers less than 15 years of age

Table 6: **Study population by vaccine product noted on record and by age at vaccination. Number and (%).**

	Age at vaccination (years)				
vaccine	**0-4**	**5-9**	**10-14**	**15-19**	**all ages**
Rubella	2 (2)	10 (21)	174 (97)	-	186 (53)
MR or MMR	108 (98)	38 (79)	5 (3)	13 (100)	164 (47)
Total	110 (100)	48 (100)	179 (100)	13 (100)	350 (100)

Table 7: Positive predictive value of a record of rubella vaccination.

		Positive predictive value (PPV)	
vaccine product	**number with vaccination record**	**number & (%) rubella reactive**	**95% c.i.**
any product	350	322 (92.0)	88.6% - 94.6%
Rubella	186	184 (98.9)	96.2% - 99.9%
MR or MMR	164	138 (84.1)	77.6% - 89.4%

Table 8a: Positive predictive value of a rubella vaccination record for subjects vaccinated *less than* 15.5 years before rubella antibody testing.

		Positive predictive value (PPV)	
vaccine product	number with vaccination record	number & (%) rubella reactive	95% ci
any product	175	166 (94.9)	90.4% - 97.6%
Rubella	113	112 (99.1)	95.2% - 99.9%
MR or MMR	62	54 (87.1)	76.1% - 94.3%

Table 8b: Positive predictive value of a rubella vaccination record for subjects vaccinated *at least* 15.5 years before rubella antibody testing.

		Positive predictive value (PPV)	
vaccine product	number with vaccination record	number & (%) rubella reactive	95% c.i.
any product	175	156 (89.1)	83.6% - 93.3%
Rubella	74	73 (99.6)	92.7% - 99.9%
MR or MMR	102	84 (82.3)	73.5% - 89.2%

Table 9a: Positive predictive value of an MR or MMR vaccination record for subjects vaccinated *less than* 15.5 years before rubella antibody testing.

		Positive predictive value (PPV)	
year of birth	number with vaccination record	number & (%) rubella reactive	95% ci
before 1973	23	20 (86.9)	66.4% - 97.2%
1973 or later	39	34 (87.2)	72.6% - 95.7%

Table 9b: Positive predictive value of an MR or MMR vaccination record for subjects vaccinated *at least* 15.5 years before rubella antibody testing.

		Positive predictive value (PPV)	
year of birth	number with vaccination record	number & (%) rubella reactive	95% ci
before 1973	66	55 (83.3)	72.1% - 91.4%
1973 or later	36	29 (80.6)	64.0% - 91.8%

Table 10a: Positive predictive value of a rubella vaccination record for subjects vaccinated before 1979 - HPV-77 DE-5 strain recipients.

		Positive predictive value (PPV)	
vaccine product	number with vaccination record	number & (%) rubella reactive	95% ci
Rubella	146	144 (98.6)	95.1% - 99.8%
MR or MMR	119	97 (81.5)	73.4% - 88.0%

Table 10b: Positive predictive value of a rubella vaccination record for subjects vaccinated after 1979 - RA 27/3 strain recipients.

		Positive predictive value (PPV)	
vaccine product	number with vaccination record	number & (%) rubella reactive	95% ci
Rubella	27	27 (100)	87.2% - 100%
MR or MMR	29	28 (96.6)	82.2% - 99.9%

4.3 Evaluation of the postnatal rubella prevention program

4.3.1. Completeness of testing

Of the sample of 638 women tested for rubella antibody during pregnancy in Newfoundland in 1992, there were 557 who had a rubella antibody test within the 42 weeks preceding delivery, for an overall proportion of 87%. As seen in Table 11, there were no significant variations by health region in the proportion tested (χ^2= 11, 4df, p =.9987).

The time of testing ranged from within several days of delivery to 42 weeks before delivery. The mean time of test was 27 weeks before delivery, or 13 weeks gestation. Seventy-five percent of prenatal testing was done by the 16th week of pregnancy. The time of testing differed by region, as noted in Table 10 (F=2.53, p< .01), although every region except Region E had a mean testing time of 13 to 14 weeks gestation.

The sample group was representative of all mothers who gave birth in the province in 1992 by age at delivery (χ^2= 8.55, 5df, p =.128) and by parity (44% of the sample and of the total births in the province that year were to primiparous mothers).

The 557 mothers who had been tested prenatally did not differ in age from the 81 mothers who had no evidence of prenatal testing (χ^2= 0.09, 4df, p =.955). However, mothers tested in the prenatal period were significantly more likely to be primiparous

than mothers who were not tested in the prenatal period (44% versus 28%, 95% confidence interval for the difference in the proportions tested ranging from 5 to 27%).

Of the 81 women who were not tested within the prenatal period, 24 were tested either before the current pregnancy or during the postpartum. It is possible that the others may have been tested at sometime outside the two years selected for this review.

Table 11: Rubella antibody screening in pregnancy. Proportion screened and number of weeks gestation at testing, by health region.

	Proportion rubella screened during pregnancy				
region	**no.**	**no. and (%) screened**		**99% c.i.**	**mean weeks gestation at time of test**
A	206	176	(85.4)	78.1% - 91.1%	12.5
B	155	136	(87.7)	79.5% - 93.6%	12.2
C	110	96	(87.3)	77.0% - 94.1%	12.1
D	104	94	(90.4)	80.5% - 96.3%	13.3
E	63	55	(87.3)	72.9% - 95.8%	15.4
prov.	638	557	(87.3)	83.5% - 90.5%	12.8

4.3.2 Completeness of follow-up

The postnatal rubella prevention program in Newfoundland provides for postnatal vaccination of all women identified as susceptible on prenatal testing. This program is available in each region of the province, but as records were unavailable for one region, only four of the five regions were included in this section. These regions represent over 90% of the province's population.

The method for providing postnatal MMR vaccination varied by region. In Region A vaccination was provided either before discharge from the hospital or in the community from the public health nurse or family physician after discharge. In Region B, vaccination was provided primarily after discharge, by the public health nurse or family physician. However, some vaccination was provided in hospital, as some women from Region B give birth in a hospital located in Region A. In regions C and D, vaccination was done after discharge from hospital, by public health nurses.

The provincial postnatal registry identified 313 women susceptible to rubella. However, due to an error in notification of 34 individuals, only 279 records were available for review from the regions. This error had been corrected in early 1992, but when the study was conducted, some names supplied from the provincial registry were still missing from the regions. Follow-up was immediately initiated for these women, but they were not counted in this analysis of follow-up.

In total, 267 of 279 susceptible women (96%) were contacted and offered vaccination with MMR vaccine in the postnatal period. There were 12 women (4%) who could not be contacted at the address on file and who were considered lost to follow-up. Of the 267 who were offered vaccine, 250 (90%) accepted and 9 (3%) refused. The remaining 8 women (3%) chose to return to their family physician for vaccination or a repeat test. These women were classified as pending, as no results had yet been sent to the health unit from the physician.

The proportion of follow-up achieved varied from one region to another (Table 12). Overall follow-up achieved ranged from 100% in region D to 93% in region C. In terms of women who were actually vaccinated, the largest proportion of successful follow-up occurred in region D, where 98% of susceptibles were vaccinated. The other three regions had vaccination rates that were similar to each other, but somewhat lower than Region D (86 to 89%).

Refusals accounted for between 2 and 6% of the total subjects in each region, and the reasons for refusal included previous vaccination, sterilization, and concerns about the adverse effects of vaccination.

Regions A, B and C had between 3 and 5% of the susceptible women classified as pending, and an additional 4 to 7% were classified as being lost to follow-up. This

suggests that these three regions had between 8 and 10% of rubella-susceptible women left unvaccinated. Region D had no pending results and no clients in the lost to follow-up category.

In general, follow-up time was shorter in regions A and D than in regions B and C (Table 13). Since prenatal testing is done at about 13 weeks gestation (Table 11), suggests that regions A and D provide vaccine very early in the postnatal period.

Table 12: Follow-up for 1992 rubella susceptible females. Number and (%) followed-up by region.

	follow-up of susceptibles by region; number and (%)				
region and program	**vaccinated**	**refused**	**pending**	**lost to follow-up**	**total**
A:hospital/ PHN/physician	95 (89)	2 (2)	4 (4)	5 (5)	106 (100)
B:hospital/ PHN/physician	45 (86)	3 (6)	2 (4)	2 (4)	52 (100)
C:PHN	64 (86)	3 (4)	2 (3)	5 (7)	74 (100)
D:PHN	46 (98)	1 (2)	-	-	47 (100)
TOTAL	250 (90)	9 (3)	8 (3)	12 (4)	279 (100)

Table 13: Follow-up for 1992 rubella susceptible females. Range of follow-up time by region.

	Weeks between testing and follow up	
region and program	**mean interval(weeks)**	**range (weeks)**
A:hospital/ PHN/physician	24.9	<1 to 64
B:hospital/ PHN/physician	41.1	<1 to 142
C:PHN	41.8	2 to 91
D:PHN	27.5	1 to 42

CHAPTER 5. DISCUSSION

5.1 Rubella susceptibility in women of childbearing age

Rubella susceptibility for women of childbearing age in Newfoundland declined from 12% in 1971 (103) to a three year average of 4.6 % in 1989-1993. This current low level is what would be expected in a highly vaccinated population where the vaccine is between 90 and 95% efficacious (5,8,9). The rate is consistently low for all age groups, except for the 15 to 19 year olds, where the three year average is 14%. Other studies have also found the highest proportion of susceptibles in younger age groups (62,66). Past vaccination strategies in this population and the resulting declining rubella incidence in the province partially explain this finding, as older women were likely to have been vaccinated as schoolgirls, and are also much more likely to have been exposed to wild virus than younger women.

Women born before 1960 would almost certainly have acquired immunity through natural infection in childhood, as rubella outbreaks occurred in regular 3 to 6 year cycles in the province until the mid-1970s (101). Women born between 1960 and 1969 would have been vaccinated as schoolgirls, and would also have been exposed to circulating wild virus during childhood, allowing for infection-induced immunity or boosting of vaccine-induced immunity. Women in these age groups are also more

likely than the 15 to 19 year olds to have experienced at least one pregnancy, and susceptibles might also have been identified and vaccinated through the postnatal rubella vaccination program.

The 15 to 19 year olds were born between 1970 and 1978; most would not have been vaccinated as schoolgirls, as this program was phased out in the 1981-1982 school year. However, most should have been given MR or MMR in early childhood. This includes immigrant children, who should have received MMR vaccination if they had no documentation of previous vaccination (98). The 1980 provincial MMR vaccination rate for children born in 1975 was 90%, and it has continued to increase for each birth cohort since then (100). The high rate of susceptibility in this group cannot thus be completely explained by low vaccination rates.

There may have been some misclassification of women with low antibody titres into the susceptible group, but it is unlikely that the full 14% were misclassified; the 10 IU/ml cutoff in the laboratory test allowed for "low positive" results to be classified as immune.

Waning immunity might have contributed to the higher susceptibility in this age group. Most of these women were vaccinated in infancy or early childhood, and would not have benefitted from wild virus boosting of vaccine-induced immunity.

In addition, if these women were vaccinated as infants (that is, before 1979), the HPV-77 strain-product combination MR or MMR products would have been used. This strain-product combination has been shown to be less immunogenic than the RA27/3 strain combination product (72), and the findings from the second part of this study have shown similar results. This important hypothesis of waning immunity contributing to higher susceptibility in younger age groups could not be tested in this study, because no information was available on whether or not these women were actually vaccinated.

With reference to the decreased susceptibility in the 1970-74 birth cohorts, postnatal vaccination and vaccination following pre-employment and other screening are likely to have contributed to the overall decline in susceptibility in the women tested from these birth cohorts. It is unlikely that immunity was naturally acquired in these cohorts, as the most recent rubella outbreak occurred in 1986-87, and the decrease in susceptibility occurred between 1989 and 1993.

5.2 The rubella vaccination record as a predictor of immunity

Overall, the rubella vaccination record predicted positive serology in 92% of subjects, a result consistent with published reports of long term vaccine efficacy of between 90 and 95% (5-9). There were differences in the positive predictive value (PPV), depending on the vaccine product given; the monovalent rubella vaccination record

was an excellent predictor of immunity, at 98%, while the MR or MMR vaccine record predicted less well, at 84%.

It is most likely that the interaction of vaccine strain and specific vaccine product is responsible for the difference between the observed predictive values. Both HPV-77 DE-5 and RA 27/3 strains predicted immunity equally well, but the PPV for the monovalent product containing the HPV-77 DE-5 strain was 99%, compared to 81% for the combination product containing the same strain. This difference between products was not observed in the subjects with records of the RA 27/3 strain vaccine. This finding is consistent with that from a previous study showing that rubella HPV-77 DE-5 produces lower antibody titres when administered as a combination product than when administered as a monovalent product (72).

Waning immunity was considered as a possible factor, but it did not have an effect; the monovalent product PPV remained higher than the combined product PPV, regardless of the interval between vaccination and testing.

Although interference from maternally-derived antibody may lower the PPV of any vaccine given in infancy, when subjects vaccinated before one year of age were excluded, the original results were unchanged. The age at vaccination could not be further explored as an independent causal factor, as it was highly correlated with the

vaccine product received.

Previous exposure to wild virus did not affect the PPV of the combination products, since the PPV did not differ significantly for those born during an era of high exposure as compared to an era of lower exposure. Unfortunately, this comparison could not be made for the monovalent vaccine recipients, as they were all born before 1973, and even the youngest would have lived through at least two province-wide rubella outbreaks.

These findings have direct implications for the postnatal rubella vaccination program in the province. Despite having records of rubella vaccination, some women were not protected from infection during their first pregnancies, by the serological definition of protection (rubella antibody level of at least 10 IU/ml), although there is evidence that women with antibody levels lower than 10 IU/ml may be protected from infection, (56,57,73). Nevertheless, these women would still have required follow up vaccination in the postnatal period. Furthermore, more than half of the susceptible mothers were between 15 and 19 years old, an age group in which it is difficult to achieve a high rate of postnatal vaccination, and this places additional pressure on the existing postnatal rubella vaccination program.

5.3 Evaluation of the postnatal rubella vaccination program

The postnatal rubella vaccination program in the province is not completely effective. Not all pregnant women were tested for rubella antibody in pregnancy, and not all of the women identified as susceptible were vaccinated postnatally.

Despite the Department of Health's recommendation to provide rubella antibody screening for all pregnant women, coverage of the program remained incomplete in 1992. Thirteen percent of the women in this study sample had no evidence of rubella antibody screening in pregnancy.

There were no differences in screening rates by age, by health region of residence or by urban versus rural location. However, multiparous women were less likely to be screened than were primiparous women. This is probably due in part to physicians treating some multiparous women as 'known positives', based on positive test results from a previous pregnancy or on a history of rubella vaccination following a previous negative prenatal test. Seventeen percent of the women who were not tested prenatally had positive test results before the current pregnancy.

Repeating a rubella test in pregnancy when there is a recent positive test on a patient's chart may seem to be a duplication in service from the viewpoint of individual patient care. However, the postnatal rubella vaccination program is based on the principles

of population screening; the best way to identify all susceptible pregnant women is to apply the test to all pregnant women.

The postnatal rubella vaccination program failed to test between 10 and 17% of pregnant women in the province in any given year. Although this is a relatively small percentage compared to other studies, where up to 50% of pregnant women are not screened (92,93), it remains a concern, as each missed opportunity for identification of a susceptible woman leads to a missed opportunity for vaccination.

The completeness of screening can be improved by reminding physicians of the importance of universal screening, even with those clients that are 'known positives'. A requirement that every woman admitted to a hospital for delivery or abortion (therapeutic or spontaneous) must have a current prenatal antibody test result from the laboratory on the medical chart will pick up the women missed in routine prenatal care.

Follow-up vaccination was also incomplete. Ten percent of susceptible women did not receive follow-up rubella vaccination. This included mothers who were lost to follow up or who opted to defer vaccination (further testing or vaccination by a family physician), and a small proportion (3%) who were followed up but who refused vaccination. Fertile women who remained unvaccinated represent a continued

risk for rubella infection in future pregnancies.

Early contact in the immediate postpartum seems more important than the particular approach used to improve follow-up rates. Region A and Region D had the highest follow-up rates and the shortest delays of all four regions, although they used different approaches for postnatal vaccination. In fact, the highest rate was seen in a setting where postnatal vaccination is offered exclusively by public health nurses. At the time of the study, the public health nurses in Region D made at least one postnatal home visit to every mother, so that a strong link was made very early in the postnatal period. In areas where these early links are not made, the community-based postnatal vaccination approach may not achieve such high rates.

This study did not show that in-hospital vaccination programs improve vaccination rates. However, it must be noted that Regions A and B had just introduced the in-hospital vaccination program in 1992, in response to a problem with low postnatal vaccination rates. The rates in these regions may have improved substantially since that first year of the program.

Although the centralized testing program offers the advantages of single-source testing and reporting, certain problems in this system can hinder the early contact that is so important for maintaining high rates of postnatal rubella vaccination. For

example, occasional problems occur with the flow of information from the laboratory to the health region, and staffing shortages may sometimes delay contact between the susceptible mother and the vaccine provider. Periodic checks of the laboratory notification system, and extension of the in-hospital vaccination program to all regions in the province may shorten the delay between delivery and follow-up. An in-hospital vaccination program will also reach some transient mothers who may not be readily accessible after they are discharged from the hospital. In both in-hospital and community-based systems, there must be good record keeping, to prevent delayed notification and missed opportunities for vaccination.

The importance of eliminating any gaps in the postnatal rubella vaccination program is accentuated by the increased susceptibility to rubella found among younger women. The susceptibility rate found in this study was applied to the effectiveness figures for the postnatal rubella vaccination program to illustrate this problem:

Of the 700 women under 20 years of age who give birth in the province annually, up to 119 (17%) will not receive prenatal rubella screening tests. Out of these 119, up to 17 (14%) may be susceptible to rubella. Of the remaining 584 young women who are screened, 81 (14%) are likely to be susceptible, but 8 of them (10%) may not be given rubella vaccine. Therefore, in one year, there are as many as 25 rubella negative young women who will be missed by the current postnatal rubella

vaccination program.

5.4 Study limitations

The study methodology took into account possible sources of misclassification error, ascertainment bias and selection bias, but some limitations of the study remain.

The review of rubella susceptibility made only ecologic comparisons between susceptibility and probable vaccination status, and so no direct inference about the vaccination status of the particular individuals tested can be made for this section of the study. Given that the highest susceptibility was shown in subjects drawn from the birth cohorts who would have received the HPV-77 strain combined MR or MMR product, it would have been useful to link vaccination histories to individuals in these age groups, to determine if the increased susceptibility was related to the vaccine strain-product combination used.

Another limitation of the study was related to the linkage procedures. The two step linkage used in the assessment of the PPV of a vaccination record resulted in a high cumulative loss of subjects (24%). The dropped subjects did not appear different from the final study group by age, and were no more likely to be rubella susceptible, but as most were dropped because they lacked vaccination records, the possibility of a selection bias cannot be ruled out.

As previously noted, the methodology used for evaluating the completeness of testing in the postnatal rubella vaccination program might have produced some misclassification of subjects, by failing to recognize true matches or by making false matches. It is unlikely that they could account for the full 13% of subjects found to lack the prenatal screening test; a similar procedure used in another section of the study resulted in only a 3% loss from failure to link, but the possibility cannot be completely ruled out, as the methodology did not allow for assessment of the frequency of this kind of misclassification error, or for determination of a differential effect.

One region was not included in this review, and the reporting error noted in the results meant that 11% of the susceptible women identified in the remaining four regions were not included in the analysis, so the evaluation of the postnatal vaccination program may not be representative of the province as a whole. In addition, a small proportion of the women included in this analysis may not have been prenatal clients, and their experience of follow up vaccination does not reflect the efficiency of the postnatal vaccination program.

The generalizability of these results to the population of childbearing women in Canada is somewhat limited. The present population that the results were drawn from is a rather homogenous one, made up largely of Caucasian women and a small

proportion of aboriginal women, and this does not reflect the ethnic and cultural diversity of Canada's population as a whole. Although there is no reason to believe that this would affect the findings relating to the positive predictive value of the rubella vaccination record, the age-specific susceptibility rates may not be applicable to the rest of Canada, particularly in large urban centres. In addition, the success of the community-based vaccination program may not be applicable in any area where at home postnatal visits are not routinely made.

CHAPTER 6. CONCLUSION AND RECOMMENDATIONS

6.1 Conclusions

The review of rubella susceptibility in the female population of childbearing age in Newfoundland showed that there are age specific differences in susceptibility within this population. In women aged 15 to 19, susceptibility averaged 14% over a three year period, which is substantially higher than the 4.6% overall in the same period. This youngest age group represents the women now entering their childbearing years.

The assessment of the positive predictive value of a rubella vaccination record showed an acceptable overall value of 92%, a high predictive value of 99% for recipients of monovalent rubella vaccine, but an unacceptably low predictive value of 81% for recipients of HPV-77 DE-5 strain MR or MMR vaccine. These recipients were all aged 15 to 24 years at the time of prenatal testing, and this indicates that a vaccination record is not a reliable indicator of immunity for a specific group of women who are now in the childbearing years. However, this is likely to be a self-limiting problem. The RA 27/3 strain is more immunogenic and therefore the records of women vaccinated with MR or MMR after 1979 will most likely reliably predict serologic immunity. However, this needs to be tested with a larger group of subjects than were available in this study.

The evaluation of the postnatal rubella vaccination program identified deficiencies in the completeness of testing and the completeness of follow-up vaccination of susceptibles. Based on these findings, the following is a series of recommendations for improving existing programs and for conducting further research to strengthen CRS prevention programs in general.

6.2 Recommendations for practice

1 Promote serological assessment of immunity for all women of childbearing age so that susceptible women can be identified and vaccinated before pregnancy occurs.

2. Reinforce existing recommendations on prenatal rubella testing for all pregnant women, regardless of previous serology results.

3. Ensure that a current prenatal rubella antibody test result from the laboratory is on the medical chart for any woman admitted to a hospital or clinic for delivery or abortion.

4. In all health jurisdictions where postnatal rubella vaccination programs exist, conduct periodic evaluations that include:
   - reviews of rubella antibody testing rates for pregnant women
   - reviews of laboratory reporting procedures
   - assessment of postnatal vaccination rates

5. Offer rubella antibody testing and vaccination in abortion clinics.

6. Review strategies to ensure that postnatal vaccination is offered as soon as possible after delivery. In many jurisdictions, this is best achieved with in-hospital programs, where vaccination is a standing order for susceptible women. It can also be achieved in areas where community based public health nurse follow-up has been shown to be efficient.

6.3 Recommendations for further research

1. Monitor the trend for increasing rubella susceptibility in younger women by conducting periodic age specific serological surveillance of rubella susceptibility in women of childbearing age who are tested for rubella antibody.

2. Conduct specific serological surveillance of rubella susceptibility in women of childbearing age who are known to have received HPV-77 strain MR or MMR vaccines.

3. Conduct further studies into the persistence of vaccine-induced immunity in populations where the likelihood of wild vaccine boosting of vaccine induced immunity is low.

4. Review the effectiveness of postnatal rubella vaccination programs in other health jurisdictions in Canada, where the populations at risk for CRS include immigrant and native women.

REFERENCES

1. Freij BJ, South MA and Sever JL. Maternal rubella and the congenital rubella syndrome. *Clinics in Perinatology* 1988; 15:247-257.

2. Cochi SL, Edmonds LE, Dyer K, Greaves WL, Marks JS, Robira EZ, Preblud SR, Orenstein WA. Congenital rubella syndrome in the United States, 1970-1985: on the verge of elimination. *American Journal of Epidemiology* 1989;129:349-361.

3. Pelletier L and Duclos P. Surveillance of congenital rubella syndrome and other rubella-associated adverse pregnancy outcomes. *CCDR* 1996;22:35-37.

4. Arbuckle TE, and Sherman GJ. Is congenital rubella a vanishing disease? *Chronic Diseases in Canada* 1992; 13:24-27.

5. Christenson B and Böttiger M. Long-term follow-up study of rubella antibodies in naturally immune and vaccinated young adults. *Vaccine* 1994;12:41-45.

6. Yelland MJ. Rubella immune status in general practice. *Australian Family Physician* 1989;18:1279-1283.

7. Gillispie MA, Ebner, Johnson R. Rubella immunity in college-aged women. *Journal of American College Health* 1989;37:234-245.

8. Preblud SR. Some current issues relating to rubella vaccine. *JAMA* 1985;254: 253-256.

9. O'Shea S, Woodward S, Best JM, Hozel H, Dudgeon JA. Rubella vaccination: persistence of antibodies for 10-21 years. *Lancet* 1988;ii:909.

10. National Advisory Committee on Immunization. *Canadian Immunization Guide*. Ottawa, Ontario: Health Canada (Supply and Services Canada, Cat. No. H49-8/1993E).

11. Just M, Just V, Berger R, Burkhardt F, Schilt U. Duration of immunity after rubella vaccination: a longterm study in Switzerland. *Reviews of Infectious Diseases* 1985;7:S91-S94.

12. Laboratory Centre for Disease Control. Mumps and Rubella Concensus Conference. *CCDR* 1994;20:165-176.

13. Gregg, NM. Congenital cataract following german measles in the mother. *Transactions of the Opthalmological Society of Australia* 1941; 3:35-46.

14. Condon RJ and Bower C. Rubella vaccination and congenital rubella syndrome in Western Australia. *Medical Journal of Australia* 1993;158:379-382.

15. Stanley FJ, Sim M, Wilson G, Worthington S. The decline in congenital rubella syndrome in Western Australia: an impact of the school girl vaccination program? *American Journal of Public Health* 1986;76:35-37.

16. CDC. Rubella Prevention. Recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR* 1990;39(RR-15):1-18.

17. Das BD, Lakhani P, Kurtz JB, Hunter N, Watson BE, Cartwright KA,Caul EO and Roome AP. Congenital rubella after previous maternal immunity. *Archives of Diseases in Children* 1990; 65:545-546.

18. Furesz J, Varughese P, Acres SE and Davies JW. Rubella immunization strategies in Canada. *Reviews of Infectious Diseases* 1985; 7: S191-S193.

19. Miller E. Rubella in the United Kingdom. *Epidemiology and Infection* 1991;107: 31-35.

20. Ellis M. Rubella. *Practitioner* 1990;234:906, 908-10.

21. White CC, Koplan JP, Orenstein WA. Benefits, risks and costs of immunization for measles, mumps and rubella. *American Journal of Public Health* 1985;75:739-744.

22. Kaplan KM, Cochi SL, Edmonds LD, Zell ER, Preblud SR. A profile of mothers giving birth to infants with congenital rubella syndrome:an assessment of risk factors. *American Journal of Diseases of Children* 1990;144:118-123.

23. Dales L, Kizer KW and Elliott GV. Joint California Department of Health Services - California Medical Association Campaign to eliminate congenital rubella syndrome. *Public Health and Preventative Medicine* 1988;148:355-57.

24. Miller E, Waight PE, Vurdien JE, White JM, Jones G, Miller BHR, Tookey PA, Peckham CS. Rubella surveillance to December 1990: A joint report from the PHLS and National Congenital Rubella Surveillance Programme. *CDR* 1991;1:R33-R37.

25. Dalton R. Rubella prevention. *Journal of The Royal College of General Practitioners* 1988:38:277.

26. Knox, EG. Theoretical aspects of rubella vaccination strategies. *Reviews of Infectious Diseases* 1985;7:S194-S197.

27. Miller E, Tookey P, Morgan-Capner P, Hesketh L, Brown D, Waight P, Vurdien J, Jones G, Peckham C. Rubella surveillance to June 1994: third joint report from the PHLS and the National Congenital Rubella Surveillance Program. *CDR* 1994;4:R146-R152.

28. Lawman S, Morton K, Best JM . Reasons for rubella susceptibility among pregnant women in West Lambeth. *Journal of the Royal Society of Medicine* 1994;87: 263-264.

29. Maisach CR, Alsop CL, Kurinczuk JJ, Bower C. Prepregnancy counselling for the primary prevention of birth defects: rubella vaccination and folate intake. *Medical Journal of Australia* 1995;162:403-406.

30. Sekla L, Stackiw W, Du J, Besant D, Ronald A, Wilt JC. Congenital rubella syndrome in infant born to an Indochinese refugee - Manitoba. *CDWR* 1980;6:233.

31. Miller E, Nicoll A, Rousseau SA, Sequeira PJR, Hambling MH, Smithells RW, Holzel H. Congenital rubella in babies of South Asian women in England and Wales: an excess and its causes. *BMJ* 1987;294:737-739.

32. LCDC. Canadian communicable disease surveillance system: disease-specific case definitions and surveillance methods. *CDWR* 1991;17S3:1-34.

33. Herrmann KL. Rubella in the United States: toward a strategy for disease control and elimination. *Epidemiology and Infection* 1991; 107:55-61.

34. Robinson J, Lemay M, Vaudry WL. Congenital rubella after anticipated maternal immunity: two cases and a review of the literature. *Pediatric Infectious Diseases Journal* 1994;13:812-815.

35. Lavigne PM. Congenital rubella syndrome. *CDWR* 1985;11:93.

36. Mahoney JB, Smailly F, Chernesky MA. Sequential rubella outbreaks in Hamilton, Ontario. *CDWR* 1987;13:131-134.

37. Izumi T. Laboratory confirmations of cases of epidemic measles and rubella, Saskatchewan, 1986. *CDWR* 1987;13:83-86.

38. Bokhout M. Rubella outbreak among immunized male high school students in Wabush/Labrador City - Newfoundland. *CDWR* 1987;13:199-202.

39. Ng T, Farley JD, Middleton PJ, Nicoll J, Millar J. Rubella activity 1989 - British Columbia. *CDWR* 1989;15:97-99.

40. Ratnam S and Stratton F. An ongoing epidemic of rubella in Newfoundland and Labrador. *CDWR* 1987;13:119-121.

41. LCDC. Notifiable Diseases Annual Summary 1992. *CCDR* 1994;20S:81

42. LCDC. Notifiable Diseases Annual Summary 1993. *CCDR* 1995;21S:41-42.

43. Bart KJ, Orenstein WA, Preblud SR, Hinman AR. Universal immunization to interrupt rubella. *Reviews of Infectious Diseases* 1985;7:S177-S184.

44. Galzaka A. Rubella in Europe. *Epidemiology and Infection* 1991;107:43-54.

45. Peltola H, Heinonen OP, Valle M, Paunio M, Virtanen M, Karanko V, Cantell K. The elimination of indigenous measles mumps and rubella from Finland by a 12 year two-dose vaccination program. *New England Journal of Medicine* 1994;331: 1397-1402.

46. Orenstein WA, Bart KJ, Hinman AR, Preblud SR, Greaves WL, Doster SW, Stetler HC, Sirotkin B. The opportunity and obligation to eliminate rubella from the United States. *JAMA* 1984;251:1988-1994.

47. Cote TR, Silverston D, Horan JM, Lindegren ML and Dwyer DM. Evaluation of a two dose measles mumps and rubella vaccination schedule in a cohort of college athletes. *Public Health Reports* 1993;108:431-435.

48. Williams WW, Hickson MA, Kane MA et al. Immunization policies and vaccine coverage among adults. *Annals of Internal Medicine* 1988;108:616-625.

49. Briss PA, Fehrs LJ, Hutcheson RH, Schaffner W. Rubella among the Amish: resurgent disease in a highly susceptible community. *Pediatric Infectious Diseases Journal* 1992;11:955-959.

50. Jackson BM, Payton T, Horst G, Halpin TJ, Mortensen BK. An epidemiologic investigation of a rubella outbreak among the Amish of northeastern Ohio. *Public Health Reports* 1993;108:436-439.

51. Valiquete L, Saintonge F, Carsley J, Charbonneau S, Bédard L, Tremblay M, Perron L, Guérard L. Survey of congenitall rubbella syndrome, Montréal, Laval, and Montérégie, Quebec, 1985-1991. *CCDR* 1996;22:33-35.

52. Herrmann KL. Available rubella serologic tests. *Reviews of Infectious Diseases* 1985;7:108-112.

53. Dimech W, Bettoli A, Eckert D et al. Multicenter evaluation of five commercial rubella virus immunoglobulin g kits which report in international units per milliliter. *Journal of Clinical Microbiology* 1992;30: 633-641.

54. Hermann KL, Halstead SB, Branding-Bennett AD, Witte JJ, Wiebenga NH, Eddins DL. Rubella immunization. Persistence of antibody four years after a large scale field trial. *JAMA* 1976;235:2201-2204.

55. National Committee for Clinical Laboratory Standards. Evaluation and performance criteria for multiple component test products intended for the detection and quantitation of rubella ISG antibody; tentative guidelines. Approved Standard I/LA6-T (I5SN1-S-6238-158-X)ed. Villanova, PA: National Committee for Clinical Laboratory Standards, 1992:1-2.

56. O'Shea S, Best JM, Banatvala JE. Viremia, virus excretion and antibody responses after challenge in volunteers with low levels of antibody to rubella virus. *Journal of Infectious Diseases* 1983; 148:639-647.

57. Stehr-Green PA, Cochi SL Preblud SR, Orenstein WA. Evidence against increasing rubella seronegativity among adolescent girls. *American Journal of Public Health* 1990;80:88.

58. Berkeley MIKB, Moffat MAJ and Russell D. Surveillance of antibody to rubella virus in Grampian: closing the immunity gap. *BMJ* 1991;303:1174-1176.

59. Gay NJ, Valambia S, Galasko D and Miller E. Selective rubella vaccination programs: a survey of districts in England and Wales. *CDR Review* 1994;4:R77-R79.

60. CDC. Increase in rubella and congenital rubella syndrome - United States, 1988-1990. *MMWR* 1991;40:93-99.

61. CDC. Rubella and congenital rubella syndrome - United States, January 1, 1991-May 7, 1994. *MMWR* 1994;43:391-400.

62. Fraser V, Spitznagel E, Medoff G and Dunagen WC. Results of a rubella screening program for hospital employees: a five year review (1986-1990). *American Journal of Epidemiology* 1993;138:756-764.

63. Clardy, WF. Susceptibility in USAF recruits to vaccine-preventable diseases. *Vaccine* 1993; 11:573-575.

64. Smoak BL, Novakoski WL, Mason CJ, Erickson RL. Evidence for a recent decrease in measles susceptibility among young American adults. *Journal of Infectious Diseases* 1994; 170:216-219.

65. Hockin JC, MacLeod EB, MacPhail M, Weber J, Wells G. Immunity to rubella in prepubertal girls in Prince Edward Island. *CMAJ* 1988;139:308-310.

66. Duclos P, Tepper ML, Weber J and Marusyk RG. Seroprevalence of measles and rubella specific antibodies among military recruits, Canada, 1991. *Canadian Journal of Public Health* 1994;85:278-281.

67. Plotkin SA and Mortimer EA. *Vaccines*, 1st edition. Philadelphia:WB Saunders Company, 1988.

68. Best JM. Rubella vaccines: past, present and future. *Epidemiology and Infection* 1991;107:17-30.

69. Horstmann DM, Schluederberg A, Emmons JE, Evans BK, Randolph MF, Andiman WA. Persistence of vaccine-induced immune responses to rubella: comparison with natural infection. *Reviews of Infectious Diseases* 1985;7:S80-S85.

70. Cusi MG, Valensin PE, Cellesi C. Possibility of reinfection after immunisation with 27/3 RA live attenuated rubella virus. *Archives of Virology.* 1993;129:337-340.

71. Chu SY, Bernier RH, Stewart JA Herrmann KL, Greenspan JR, Henderson AK, Liang AP. Rubella antibody persistence after immunization: sixteen-year follow-up in the Hawaiian islands. *JAMA* 1988;259:3133-6.

72. Lerman SJ, Bollinger M, Bruken JM. Clinical and serologic evaluation of measles, mumps and rubella (HPV-77:DE-5 and RA 27/3) virus vaccines, singly and in combination. *Pediatrics* 1981;68:18-22.

73. Serdula MK, Halstead SB, Wiebenger NH, Herrmann KL. Serological response to rubella revaccination. *JAMA* 1984;25:1974-1977.

74. Seager C, Moriarity J, Ngai A, Staehle BO, Nolin DR. Low incidence of adverse experiences after measles or measles-rubella mass vaccination at a college campus. *Vaccine* 1994;12:1018-1020.

75. Mitchell LJ, Tingle AJ, Shuken R, Sanreorzan JA, McCune J, Braun DK. Chronic rubella vaccine associated arthropathy. *Archives of Internal Medicine* 1993; 153:2268-2274.

76. Petty RE and Tingle AJ.Arthritis and viral infection. *Journal of Pediatrics* 1988;113:948-949.

77. Tingle AJ, Chantler JK, Pot KH, Paty DW, Ford DK. Postpartum rubella immunization: association with development of prolonged arthritis, neurological sequelae and chronic rubella viremia. *Journal of Infectious Diseases* 1985;152: 606-612.

78. Howson CP, Katz M, Johnstn RB Jr, Fineberg HV. Chronic arthritis after rubella vaccination. *Clinical Infectious Diseases* 1992;15:307-312.

79. Chantler JK, Ford DK, and Tingle AJ. Persistent rubella infection and rubella associated arthritis. *Lancet* 1982; 1:1323-1325.

80. Tookey PA, Jones G, Miller BH, Peckham CS. Rubella vaccination in pregnancy. *CDR* 1991;1:R86-R88.

81. Lindegren ML, Fehrs LJ, Hadler SC, Hinman AR. Update: rubella and congenital rubella syndrome, 1980-1990. *Epidemiologic Reviews* 1991;13:341-348.

82. Morgan-Capner P, Miller E, Vurdien JE, Ramsay ME. Outcome of pregnancy after maternal reinfection with rubella. *CDR* 1991;1:R57-59.

83. Redhead KA, Copsey GJ, Suchak K, Ahmed M. Rubella antibody screening. *British Journal of General Practice* 1993;43:435.

84. Ferson MJ, Robertson PW and Whybin LR. Cost effectiveness of prevaccination screening of health care workers for immunity to measles, mumps and rubella. *The Medical Journal of Australia* 1994;160:478,480-482.

85. Murray DL, Lynch MA. Determination of immune status to measles, rubella and varicella-zoster viruses among medical students; assessment of historical information. *American Journal of Public Health* 1988;78:836-838.

86. Edmond E and Zealley H. The impact of a rubella prevention policy on the outcome of rubella in pregnancy. *British Journal of Obstetrics and Gynaecology* 1986;93: 563-567.

87. Pelissero C , Marena C, Aguzzi F, Bevilacqua M, Rebatsi F. Seroepidemiology, morbidity and vaccination strategies against rubella infection. Eight years experience in Oltrepò Pavese. *European Journal of Epidemiology* 1993; 9:322-326.

88. Varughese P and Acres SE. Observations on Rubella Trends in Canada. *CDWR* 1979;5:81-88.

89. Robertson SE, Cochi SL, Bunn GA, Morse DL, Preblud SR. Preventing rubella; assessing missed opportunities for immunization. *American Journal of Public Health* 1987;77:1347-1349.

90. Rossier E. A preventable case of congenital rubella syndrome and its public health implications. *Canadian Journal of Public Health* 1991;82:229-230.

91. Braun C, Kampa D, Fressle R, Willke E, Stahl M and Haller O. Congenital rubella syndrome despite repeated vaccination of the mother: acoincidence of vaccine failure with failure to vaccinate. *Acta Paediatrica* 1994;83:674-677.

92. Lee SH, Ewert DP, Frederick PD, Mascola L. Resurgence of congenital rubella syndrome in the 1990s. Report on missed opportunities and failed prevention policies among women of childbearing age. *JAMA* 1992;267:2616-2620.

93. Rushworth RL,Bell SM, Rob MI, Taylor PT. Diagnostic testing during pregnancy: a descriptive analysis of utilization data. *Australian Journal of Public Health* 1994;18:401-6. See 102

94. Eisele CJ.Rubella susceptibility in women of childbearing age. *JOGNN* 1993;22: 260-263.

95. Mersey DJ and Madlon-Kay D. Rubella screening at drug rehabilitation centers. *JAMA* 1992;268:2377.

96. Miller CL, Miller E, Sequeira PJL, Cradock-Watson JE, Longson M, Wiseberg EC. Effect of selective vaccination on rubella susceptibility and infection in pregnancy. *BMJ* 1985;291:1398-1401.

97. Charbonneau S, Valiquete L, Bédard L, Carsley J, Perron L, Saintonge F, Tremblay M, Guérard L. Survey of postpartum rubella vaccination, Montréal, Laval, and Montérégie, Quebec, 1992. *CCDR* 1996;22:38-41.

98. Division of Disease Control and Epidemiology, Department of Health, Government of Newfoundland and Labrador. *Immunization Manual for Public Health Nurses.* 1992.

99. Laboratory Centre for Disease Control. A new rubella vaccine: RA 27/3. *CDWR* 1979;5:88.

100. Community Health Division, Department of Health, Government of Newfoundland and Labrador. *Annual Reports.* 1972-1992

101. Division of Disease Control and Epidemiology, Government of Newfoundland and Labrador. *Communicable Disease Reports of Newfoundland.* 1981-1992.

102. Mathias R. Congenital Rubella Syndrome - Newfoundland. *CDWR* 1976;2:170-171.

103. Ratnam S, Butler RW, Tobin AM, Hockin J. Rubella screening in Newfoundland and Labrador. *CDWR* 1983; 9:161-163.

104. Statistics Canada. *Ethnic Origin - The Nation.* (Catalogue 93-315) Ottawa: Minister of Industry, Science and Technology, 1993.

105. Dean AG, Dean JA, Burton AH, Dicker RC. *Epi-Info* Version 6.02. A word processing , database and statistics system for epidemiology on microcomputers. Stone Mountain, GA: USD Incorporated, 1994.

106. Van den Brant PA, Schouten LJ, Goldbohm RA, Dorant E, Hunen PMH. Development of a record linkage protocol for use in the Dutch Cancer Registry for epidemiological research. *International Journal of Epidemiology* 1990;19:553-558.

107. Colton T. *Statistics in Medicine,* 6th edition. Boston: Little, Brown and Company, 1974.

108. Tennis P, Andrews E, Bombardier C, Wang Y, Strand L, West R, Tilson H, Doi P. Record linkage to conduct an epidemiologic study on the association of rheumatoid arthritis and lymphoma in the Province of Saskatchewan, Canada. *Journal of Clinical Epidemiology* 1993;46:685-695.

APPENDIX ONE
RUBELLA REPORTING DEFINITION

Case Definitions

Confirmed Case
Even in the absence of symptoms any one of the following:

1. Virus detection.
2. A 4-fold rise in serologic titre.
3. Rubella specific IgM in the serum.

Clinical Case
Both of the following:

1. Fever and rash and one or more of arthritis/arthralgia, lymphadenopathy, conjunctivitis.
2. In a community with documented rubella activity or epidemiologically linked to a confirmed case.

Preventable Case
A case in a Canadian resident who meets all of the following criteria:

1. At least 13 months of age.
2. Born after 1956.
3. Lacking documented receipt of live rubella vaccine on or after first birthday.
4. Without medical contraindication to receiving vaccine.
5. Without valid philosophic/religious exemption.

Surveillance System

General surveillance method.

Source: Canadian communicable disease surveillance system: disease-specific case definitions and surveillance methods. *CDWR* 1991;17S3:p.29.

APPENDIX ONE
CONGENITAL RUBELLA SYNDROME REPORTING DEFINITION

Case Definitions

Confirmed Case
Includes live and stillborn children. Clinically compatible defects and one or more of the following:

1. Isolation of rubella virus.
2. Detection of rubella specific IgM.
3. Persistence of rubella specific IgG higher than that expected from passive transfer of maternal antibody.

Clinical Case
Clinically compatible defects without laboratory confirmation. The following laboratory findings must not exist:

1. Rubella antibody titre absent in the infant.
2. Rubella antibody titre absent in the mother.
3. Rubella antibody titre declines in the infant consistent with the normal decline after birth of passively transferred maternal antibody.

Preventable Case
Case in an infant whose mother was eligible for immunization or had been previously tested and recognized as rubella susceptible.

Surveillance System

1. General surveillance method.
2. Surveillance of birth records, hospital discharge data and laboratory data.

Source: Canadian communicable disease surveillance system: disease-specific case definitions and surveillance methods. *CDWR* 1991;17S3:p.29.

APPENDIX TWO
DATA SOURCE 3: POSTNATAL REFERRAL FORM
Record of Livebirth Notification

LIVE BIRTH NOTIFICATION

Government of Newfoundland and Labrador
Department of Health

..... MCP number .....

..... Registration number .....

SECTION A – Mandatory for Registration of Birth (required within 48 hours of delivery)

CHILD

1. Surname, Given Name(s)
2. Sex ☐ M ☐ F ☐ Unknown
3. Date of Birth (Y/M/D)
4. Hospital
H. Code
Birth location (City, municipality/place)
SRCode
5. Hosp. Adm. No.

MOTHER

6. Surname, Given Name(s)
Birth Surname
7. MCP#
8. Hospital Admission Number
9. Date of Birth (Y/M/D)
10. Age
11 Birthplace (Province/Country outside Canada)
SRCode
12. Mother's Home Address
SRCode
Postal Code
13. Marital Status
1 ☐ Never Married
2 ☐ Married
3 ☐ Widowed
4 ☐ Divorced
5 ☐ Common Law
6 ☐ Separated

FATHER

14. Surname, Given Name(s)
15. Date of Birth (Y/M/D)
16. Age
17. Birthplace (Province/Country outside Canada)
SRCode

I certify that the information given is true and accurate to the best of my knowledge and belief.
Signature of Mother and/or Father
DATE YEAR MO DY

SECTION B – Health History and Medical Certification of Birth

PART 1 – HEALTH HISTORY

18. Education Attained (Parents)
a. Mother
b. Father
19. Baby's Religious Denomination
20. Number of Children Ever Born to this Mother (including this livebirth)
LiveBirth
StillBirth
21. Date of Last Delivery (if applicable)
YEAR MO DY
1 ☐ Live
2 ☐ Stillborn
22. Kind of Present Delivery
a. 1 ☐ Single 2 ☐ Twin 3 ☐ Other
b. Number of Stillborn
23. Multiple Birth Sequence
1 ☐ 1st 2 ☐ 2nd
3 ☐ Other – Specify
24. Birthweight (in grams)
g
25. Trimester Prenatal Care Began
1 ☐ None 3 ☐ 2nd
2 ☐ 1st 4 ☐ 3rd
26. Apgar score
1' 5' 10' 15'
27. Family Physician
28. Specialist for Prenatal Care
☐ No
☐ Yes → Trimester ☐ 1st ☐ 2nd ☐ 3rd
29. Familial Diseases (Up to and including second cousins of parents)
1 ☐ No 2 ☐ Deafness 3 ☐ Other (Please Specify Below)
ICD9 >
ICD9 >
ICD9 >
ICD9 >

PART 2 – PHYSICIAN SECTION

30. Mode of Delivery
C. Section
1 ☐ Spon. vert.
2 ☐ 1st
3 ☐ 2nd +
4 ☐ Forceps vert.-low
5 ☐ Breech (vaginal)
6 ☐ Forceps vert.-mid
7 ☐ Vacuum extraction
8 ☐ Vaginal Birth after Caesarean Section
31. Labour / Delivery
1 ☐ Induction 2 ☐ No complications 3 ☐ Fetal distress 4 ☐ Other complications — Specify
ICD9 >
ICD9 >
ICD9 >
ICD9 >
32. Complications of Pregnancy
1 ☐ None
2 ☐ Toxaemia or hypertension
3 ☐ Rhesus sommunization
4 ☐ Antepartum haemorrhage
5 ☐ Diabetes (Ins. Dep.)
6 ☐ IUGR
7 ☐ Anaemia < 100 G/L
8 ☐ Genital herpes
9 ☐ Viral or drug exposure (List Below)
ICD9 >
ICD9 >
ICD9 >
ICD9 >
10 ☐ Other (Complications of Pregnancy) (List below)
ICD9 >
ICD9 >
ICD9 >
ICD9 >
33. Neonatal Conditions/Birth Injuries noted at Birth 1 ☐ None 2 ☐ Yes (Specify)
ICD9 >
ICD9 >
34. Gestation Period
completed weeks
35. Congenital Anomalies
1 ☐ None
2 ☐ Anencephalus
3 ☐ Spina bifida
4 ☐ Hydrocephalus
5 ☐ Cleft lip / palate
6 ☐ Fetal alcohol syndrome
7 ☐ T-E fistula
8 ☐ Hypospadias/epispadias
9 ☐ Reduction deformity of limbs
10 ☐ Rectal / anal atresia / stenosis
11 ☐ Omphalocele / gastroschisis
12 ☐ Chromosomal anomalies ▶ ICD9 >
13 ☐ Other congenital anomalies ▶ ICD9 >

Delivered By (Surname, Given Names)
Code
Position/Title
Signature
DATE: YEAR MO DY

8-2370-73.1: 1992-07-17

Distribution: WHITE – Department of Health CANARY – Hospital BUFF – Community Health Nurse

APPENDIX TWO
DATA SOURCE 4: VACCINATION RECORD
Immunization and Health Record

GOVERNMENT OF NEWFOUNDLAND AND LABRADOR
DEPARTMENT OF HEALTH
IMMUNIZATION AND HEALTH RECORD

School Medical Office Follow-up

Child's Name _____ (Surname) (First name) (Second name)

Date and Year of Birth _____ Sex _____ MCP Number _____

Parents _____ Guardian _____

School Year	Name of School	Grade	Home Address (Street, City/Town)	Phone Numb

IMMUNIZATION RECORD

Immunization Permission

I hereby request that he/she be immunized/tested in accordance with the ongoing programmes of the Newfoundland Department of Health

Signature of Parent or Guardian _____

Date _____

DPT & Polio	DT & Polio	T - Tine Test M - 5 TU Mantoux	Other Antigens
		Test Result Test Result Test Result Test Result X-Ray	Allergies/Comments
MMR	**DT**	**Rubella**	

H-000-02
15-000-0652

APPENDIX TWO
DATA SOURCE 6: POSTNATAL RUBELLA VACCINATION RECORD
Rubella Immunization Consent

Rubella Immunization Consent

Name _____ Rubella Status ☐ Not Immune

Address _____ Family Dr. _____

M.C.P.# _____ Date _____

Rubella Vaccine should be administered only if the patient is not pregnant and agrees to avoid pregnancy for 3 months following vaccination.

SIGN CONSENT OR REFUSAL — NOT BOTH

CONSENT

I have discussed and understand the risks and benefits of Rubella Immunization. To the best of my knowledge, I am not pregnant and agree not to become pregnant for three months. I WANT to receive rubella vaccine.

_____ _____
Signature *Date*

REFUSAL

I have discussed and understand the risks and benefits of Rubella Immunization. I **DO NOT WANT** this immunization.

_____ _____
Signature *Date*

Record of Immunization
(to be completed by public health nurse)

Vaccine Name _____ Expiry Date _____ Lot # _____

Site of Administration _____ Dosage _____

This client has been counselled and has received information regarding the importance of avoiding pregnancy for the next three months - until after _____
Date

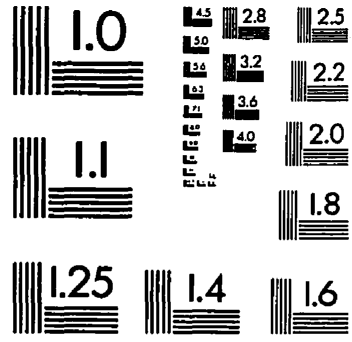
_____ _____
PHN Signature *Date*

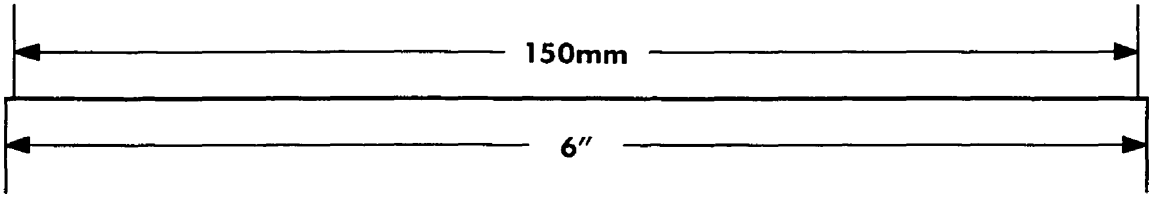
After completion of this form, by PHN, send:

Copy 1 (white) to - Disease Control & Epidemiology Division, Department of Health.

Copy 2 (yellow) to - health unit.

Copy 3 (pink) to - family doctor.





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