Control of rubella and congenital rubella syndrome (CRS) in developing countries, part 2: vaccination against rubella

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In 1995–96 we conducted a review of rubella immunization strategies. Worldwide, 78 countries (more than one-third) reported a national policy of using rubella vaccine. This was closely related to country economic status. Based on the United Nations country classification, rubella vaccine is used in 92% of industrialized countries, 36% of those with economies-in-transition, and 28% of developing countries. Cases of congenital rubella syndrome (CRS) may be prevented as follows: by providing direct protection to women and/or schoolgirls (a selective vaccination strategy); by vaccinating boys and girls to provide indirect protection by reducing the transmission of rubella virus (a childhood vaccination strategy); or by a combination of these approaches (a combined strategy). A combined strategy was most commonly reported (60% of countries); seven countries (9%) reported a selective strategy; and 24 countries (31%) reported only childhood immunization. Experience has shown that it is essential to include vaccination of women of childbearing age in any rubella control strategy. Childhood vaccination alone may pose a risk of an increase in CRS cases. Although many countries have introduced rubella vaccine, few report any data on the impact of vaccination. Countries using rubella vaccine need to establish surveillance for rubella and CRS and monitor coverage in each of the target groups.

Introduction

Live attenuated rubella vaccines were licensed in the USA in 1969 and introduced throughout much of the industrialized world soon afterwards. Rubella vaccine has, however, not been recommended for inclusion in the Expanded Programme on Immunization (EPI) in developing countries (*1*) since when sustained high coverage cannot be guaranteed its introduction could increase the susceptibility of adult women by slowing, but not interrupting, rubella transmission (*2*). Even without a global recommendation, some countries have added rubella vaccine to their national immunization programmes, reflecting the high coverage levels (>80%, often >90%) with childhood vaccines in these countries, as well as a national response to studies documenting the burden of congenital rubella syndrome (CRS) (*3*).

There is considerable documentation of the burden of disease related to CRS in some developing countries (*3*). Approximately 50 developing countries have already conducted substantial studies to assess their CRS disease burden. For countries that have not yet done so, part 1 of this review provides guidance on various methods suitable for surveillance of CRS. In part 2, we present information on the current use of rubella vaccine in different WHO regions, with emphasis on developing countries. Summarized are lessons learned about the effect of different vaccination policies on rubella and CRS control, and recommendations are made for developing comprehensive rubella control programmes in those countries that have or are considering a rubella vaccination policy.

Methods

We conducted a literature review of congenital rubella syndrome, acquired rubella, and rubella vaccine in developing countries as well as referring to key articles on rubella immunization in industrialized countries. In addition, we consulted UNICEF, which facilitates vaccine purchases for the poorest countries, about rubella vaccine prices.

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In 1995, the WHO Global Programme for Vaccines and Immunization carried out a global survey of rubella immunization policies. Information was gathered from national governments, and updates as reported to WHO by June 1996 are included in this review. We classified immunization strategies according to the primary target group. Cases of CRS may be prevented as follows: by directly protecting women and/or schoolgirls (a selective vaccination strategy); by vaccinating boys and girls in childhood to provide indirect protection by reducing the transmission of rubella virus (a childhood vaccination strategy); or by a combination of these approaches (a combined strategy).

To examine the effect of economic status on use of rubella vaccine, we classified countries according to two schemes; first, using a United Nations scheme, which considers countries as industrialized, economies-in-transition (including Eastern European countries and most of the newly independent states of the former Soviet Union), or developing (*4*); second, according to categories for vaccine support developed by the WHO Global Programme for Vaccines and Immunization (*5*). The latter classification combines information on population and income to assess the capacity of a country to be self-sufficient in vaccine supply; band A consists of small low-income countries that should continue to receive support for vaccines from donors; and band B consists of countries that currently need donor support, but which will gradually assume financial responsibility for vaccine purchases. Bands C and D include countries that are already able to procure vaccines independently, while band E consists of high income countries.

Results

Rubella vaccine

Between 1965 and 1967, several live, attenuated rubella strains were developed, and most industrialized countries began rubella vaccination soon afterwards. The live rubella vaccine currently distributed in most countries contains the RA 27/3 strain, which is prepared in human diploid cell culture (*6*). The vaccine is produced in monovalent form (rubella only), and in the following combinations: measles–rubella (MR) vaccine and measles–mumps–rubella (MMR) vaccine. The 1996 UNICEF discounted prices per dose for the neediest countries (those in bands A and B) were US$ 0.15 (monovalent rubella vaccine), US$ 0.55–0.59 (MR vaccine), US$ 0.72–0.95 (MMR vaccine) (J. Gilmartin, personal communication, 1996). However, UNICEF reports that the total annual number of doses ordered was <500000 over the period 1992–95, suggesting that most rubella vaccine purchases are made using other mechanisms, such as national tenders. For developing countries in the Region of the Americas, PAHO offers rubella-containing vaccines at a discounted price through a revolving fund. Also, in the private sector of some countries, MMR is less expensive than MR, because of the greater demand (S. Migasena, personal communication, 1996).

In clinical trials, ≥95% of susceptible persons who received a single dose of rubella vaccine when they were at least 12 months of age developed antibody (*7*), and some studies have shown 99–100% seroconversion (*8*, *9*). In India, >95% of children seroconverted after being vaccinated at 9 months of age (*10*) and, as in South Africa (*11*), there was no difference in seroconversion rates when rubella vaccine was given at 9 months or 15 months of age.

Clinical efficacy and challenge studies indicate that >90% of vaccinees are protected against both clinical rubella and viraemia for at least 15 years (*12–15*), and vaccine-induced protection is generally assumed to be lifelong. Reinfection of antibody-positive individuals has, however, been demonstrated by significant rises in antibody titre after exposure (*16*), and is more likely among vaccinees than among those with natural immunity (*17*, *18*). Although the risk of infection of the fetus is much lower than after primary infection (*19*, *20*), occasional cases of CRS have been reported in babies born to vaccinated women who had previously had at least one antibody-positive report (*21*).

As with other live virus vaccines, there has been concern that rubella vaccine should not be administered during pregnancy, since it can infect the fetus — although the isolation rate is low (3%) for RA27/3 vaccine (*22*), and the detection of vaccine virus in some aborted fetuses of vaccinated women does not mean that it can multiply to the level required to produce congenital defects (*23*). England and Wales, Germany, Sweden, and the USA have kept registries of women who inadvertently received rubella vaccine within 3 months of conception and continued their pregnancy (*24*). None of the 515 infants born to known seronegative women have had congenital anomalies compatible with CRS; thus the observed risk of vaccine-associated CRS is zero. The maximum theoretical risk of vaccine-associated CRS, based on a binomial distribution of cases with 95% confidence limits, is <1%, lower than the risk of major malformations among all pregnancies (2–3%). In the USA, the registry was closed in 1988 (*25*). Most advisory bodies continue to consider pregnancy a contraindication to rubella vaccination because of the theoretical risk of

vaccine-associated CRS. However, there is agreement that if a pregnant women is vaccinated inadvertently, the risk of vaccine-associated defects is so small as to be negligible, and should not ordinarily be a reason to consider interruption of pregnancy (*26*).

A review of adverse events associated with vaccination carried out in 1991 by the U.S. Institute of Medicine concluded that available evidence was consistent with a causal relationship between RA27/3 vaccination and transient acute arthritis (*27*). Self-limiting joint symptoms that resolve spontaneously are estimated to occur among 13–15% of women following vaccination with a dose of RA27/3 rubella vaccine, with much lower frequencies among children, adolescents, and adult men. The risk of chronic arthritis among women vaccinated with RA27/3 vaccine has been reported in three recent studies. A double-blind historical cohort study in Israel found no evidence for an association between postpartum rubella vaccination and subsequent development of arthritis (*28*), nor did a large retrospective cohort study in the USA (*29*). The preliminary results of a prospective study in Canada that provided postpartum rubella vaccine or placebo indicate no significant difference in the subsequent occurrence of arthritis/arthralgia in these two groups (*30*).

Current use of rubella vaccine in national immunization programmes

Worldwide, 78 countries (> one-third of all countries) reported a national policy of rubella vaccination (Fig. 1, Table 1). This does not include countries where rubella vaccine is only used in certain areas or the private sector. No countries in the African Region include rubella vaccine in their national immunization schedules. Rubella vaccine is used by approximately half the countries in the Region of the Americas and the Eastern Mediterranean Region, 64% in the European Region, and 31% in the Western Pacific Region. In the South-East Asia Region, Sri Lanka and Thailand introduced rubella vaccine in 1996. Of the 78 countries that use rubella vaccine, a combined strategy was reported by 47 (60%); 7 (9%) reported selective immunization of women and/or schoolgirls; and 24 (31%) reported only childhood immunization.

Fig. 1. **Countries that include rubella vaccine in their national immunization programme** (data reported to WHO up to June 1996).

Table 1: **Countries/areas using rubella vaccine, based on information reported to WHO up to June 1996**

WHO Region	No. of countries/areas using rubella vaccine	% of population represented by countries/areas using rubella vaccine[a]
African	0/48 (0)[b]	0
Americas	22/47 (47)	43
Eastern Mediterranean	11/23 (48)	12
European	32/50 (64)	55
South-East Asia	2/10 (20)	5
Western Pacific	11/36 (31)	11[c]
Global total	78/214 (36)	20

[a] Ref (*4*).
[b] Figures in parentheses are percentages.
[c] Excluding China, 46% of the population is represented by countries using rubella vaccine in the Western Pacific Region.

Use of rubella vaccine is related to national economic status. Based on the United Nations country classification (*4*), rubella vaccine is used by 92% of industrialized countries, 36% of economies-in-transition, and 28% of developing countries. A similar pattern emerges when countries are classified according to vaccine support criteria (*5*). Among high-income countries (band E), 92% use rubella vaccine. Among countries that are self-sufficient in vaccine financing (bands C and D), 48% use rubella vaccine. This contrasts with countries that need external support for vaccine purchase: only 21% of countries in band B and 4% of the poorest countries (band A) use rubella vaccine.

Region of the Americas. In the Americas, 22 countries (representing 43% of the total population in the region) reported national use of rubella vaccine (Table 1). The island countries of the Caribbean were the first developing countries in the Americas to introduce rubella vaccine on a national basis (*31*). Recently, regional strategies and activities for rubella control have interlinked with those of measles elimination. A plan of action for measles elimination by the year 2000 calls for achievement and maintenance of 95% measles vaccine coverage in all districts, with complementary periodic vaccination campaigns and careful surveillance of measles-like illnesses, including laboratory confirmation of the diagnosis (*32*). A regional measles laboratory network has been established, and in many instances sera that test negative for measles are screened for dengue and rubella.

In the English-speaking Caribbean (CAREC), laboratory testing of specimens from the rash and fever surveillance system from 1990–95 indicated widespread circulation of rubella virus. A review of all rubella seroprevalence studies in the Caribbean showed that 30–50% of women of childbearing age remain susceptible. By 1996, all CAREC countries should use a rubella-containing vaccine as part of their routine infant immunization schedule, and all will try to include this in the follow-up campaigns of children under 5 years of age conducted for the measles elimination programme (*33*). The CAREC rubella control policies also include vaccinating all women of childbearing age, vaccinating as many 5–18-year-old schoolchildren as possible, and initiating surveillance for CRS and rash-in-pregnancy (*33*).

In Cuba, rubella epidemics occurred every 5–7 years during the pre-vaccine era. In 1982, selective vaccination of 12-year-old girls was introduced, and in 1985–86 mass campaigns were conducted first for 18–30-year-old females (rubella vaccine), followed by those for 1–14-year-old males and females (MR vaccine). Since 1988, MMR vaccine has been given routinely to children at 12 months of age. With this combination of strategies, rubella infection has virtually been eliminated in Cuba.

São Paulo State, Brazil, has used a similar approach to Cuba, but did not include vaccination of adult women. From the age-specific seroprevalence in a community-based survey in Caieiras city, São Paulo, the average age at infection was estimated to be 6 years (*34*). In 1992, the Brazilian Ministry of Health decided to conduct a nationwide vaccination campaign against measles for children between 9 months and 15 years of age. São Paulo State used MMR vaccine for children under 10 years of age in the campaign, and has subsequently implemented routine MMR vaccine for children. One year after the campaign, the average rubella seroprevalence among children aged 1–15 years had increased from 40% to 97% (*35*). The decrease in rubella transmission in São Paulo State has reduced the chance of exposure among pregnant women who are still susceptible, but it is important to continue monitoring rubella transmission among adults as well as the potential introduction of rubella from neighbouring states.

Eastern Mediterranean Region. In the Eastern Mediterranean Region 11 countries (12% of the regional population) reported national use of rubella vaccine (Table 1). Interest in vaccination increased during 1990–93 when rubella outbreaks were reported in Bahrain (*36*), Islamic Republic of Iran (*37*), Iraq (M.H. Wahdan, personal communication, 1993), Kuwait (*36*), and Oman (*38*). Subsequently, retrospective reviews also identified increases in rubella incidence in Saudi Arabia and the United Arab Emirates (*36*). In Saudi Arabia, which implements

postpartum vaccination as well as childhood MMR vaccination, only 9% of 10824 women attending antenatal clinics in 1992–93 were seronegative (*39*). There was an increase in CRS cases, none the less, with 10 neonatal CRS cases being seen at one referral hospital over a 12-month period in 1992–93 compared with a total of 27 CRS cases over the previous 11 years. In December 1995, the six Gulf states agreed to adopt standard case definitions for measles, rubella, and CRS; to implement surveillance of rash illness (including serological confirmation of measles and rubella); and to focus efforts on preventing CRS through high coverage with a combined rubella immunization strategy (*36*). The Eastern Mediterranean Region plans to conduct workshops to examine rubella epidemiology and control strategies for other groups of countries in the region.

European Region. In 1984, the European Region established a goal to eliminate CRS by the year 2000. The operational targets were as follows: all countries should have at least 90% rubella vaccine coverage and effective rubella and CRS surveillance by 1995; and by 1996, all countries should be investigating every suspected CRS case. However, many countries have had difficulty in financing their national vaccination programmes. As of mid-1996, 32 countries in the European Region (representing 56% of the regional population) reported national use of rubella vaccine (Table 1), but only 36% of the Eastern European countries have introduced rubella vaccine.

A combined vaccination strategy has operated since 1976 in Croatia (at that time part of Yugoslavia) with 92–96% coverage of <3-year-olds and 96–98% coverage of 14-year-old girls; a large rubella outbreak occurred in 1989, in which 9% of reported cases were aged ≥20 years (*40*). In 1992–93, rubella outbreaks were reported in several Eastern European countries, including Poland (*41*), and rubella incidence also increased in England and Wales (*42*).

In Israel, rubella vaccination began in 1973, after a major rubella epidemic in 1972 that resulted in 542 confirmed and 739 suspected rubella cases during pregnancy (*43*). For the first 6 years, only schoolgirl vaccination was practised. Despite very high coverage levels, the biggest rubella epidemic ever recorded occurred in 1979, leading to 45 CRS cases (*44*) and over 480 rubella-associated abortions (*45*). The proportion of legal abortions due to rubella was 10% during this epidemic, equal to that in 1972, but fewer CRS cases were documented than in 1972 (*46*). This epidemic showed the importance of protecting women of childbearing age, and in 1980 postpartum vaccination was introduced and soon extended to all women of childbearing age as well as to special risk groups. By 1983, 75% of seronegative women at family health clinics were vaccinated, and the overall susceptibility of women of childbearing age fell from >20% to <10%. In the next rubella epidemic, in 1983, only 3% of cases involved women of childbearing age, with the incidence among them being only 21% of that in 1971–80, and no increase in CRS being seen (*47*). None the less, outbreaks of rubella continued to occur, especially among adolescent males, and in 1989 a combined strategy was adopted by the addition of MMR vaccine at 15 months of age. In 1987, 98% of 220 female military recruits and 88% of male recruits aged 18–19 years were seropositive for rubella (*48*).

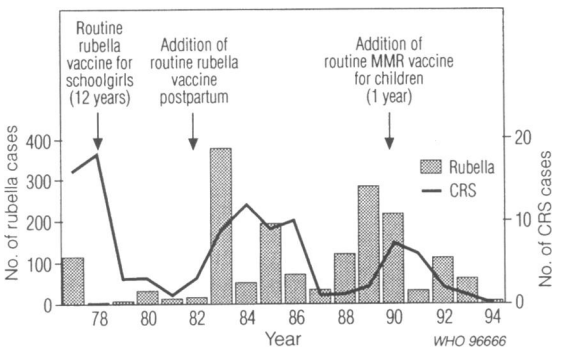
Western Pacific Region. In the Western Pacific Region, 11 countries (representing 11% of the regional population) reported national use of rubella vaccine (Table 1). Fiji, Japan, and Macao conduct selective vaccination of schoolgirls.

Malaysia, one of the larger countries in the region (1994 population, 19.7 million) used a different approach. In 1987, a mass campaign of females aged 12–44 years was conducted at numerous sites, including health clinics, factories, offices, markets and shopping malls. Altogether, 2.3 million doses of rubella vaccine were delivered (*49*). Rubella immunization requirements were introduced for government workers, female school and university personnel, and all women working in health care. The prevalence of rubella infections, diagnosed through TORCHES screening (*Toxoplasma gondii*, rubella virus, cytomegalovirus, herpes simplex virus, and syphilis) of newborns (mostly "weak and immature newborns"), decreased from 6.8% in 1987 to 2% in 1991 (*50*).

In Singapore, vaccination of 11-year-old schoolgirls began in 1976, and 96% coverage was reached. Vaccination was extended to schoolboys and servicemen in 1982. The immunization programme increased the immunity levels of women of childbearing age from 56% seropositive in 1975–79, to 85% in 1987. However, the risk of CRS was still high, since 15% remained susceptible. Between 45 and 77 abortions per year were carried out for cases of clinical rubella during pregnancy, and an average of five CRS cases were reported per year over the period 1983–87 (*51*).

In Hong Kong, a selective vaccination strategy, introduced in 1978, reduced the incidence of CRS, but recurrent rubella outbreaks showed that spread to pregnant women was still a possibility (Fig. 2). In 1990, Hong Kong introduced a combined rubella immunization strategy (*52*).

Fig. 2. **Annual reported number of cases of rubella and congenital rubella syndrome (CRS) in Hong Kong, 1977–94; MMR: measles–mumps–rubella** (ref. *52*).



Discussion

A variety of factors may influence the choice of a strategy for rubella vaccination. According to Plotkin, vaccination of all infants will probably eradicate CRS in 30–40 years; vaccination of all schoolgirls will presumably eradicate CRS in 10–20 years; and vaccination of adult women will eradicate CRS immediately, but only if 100% are immunized (*6*). However, eradication of CRS based on immunization of a single target group remains to be demonstrated. Moreover, the achievement of high coverage may not be equally easy in each potential target group. Table 2 summarizes the advantages and disadvantages encountered with the different strategies reviewed in this article. Irrespective of the strategy selected, it is important that high coverage of the selected target groups be attained and sustained.

Experience in several countries shows that it is essential to include vaccination of women of childbearing age in any strategy (*43*, *51*, *53*, *54*). In this respect, it is important to define this age group, taking into account the age-specific fertility pattern of the country, since this will influence the costs of strategies that include vaccination of all women of childbearing age. To avoid the theoretical risk of vaccinating pregnant women, postpartum vaccination has been the usual strategy. In several industrialized countries antenatal serological screening with postpartum vaccination of seronegative women has been difficult to implement (*53*, *54*). It may therefore be more practical to vaccinate all postpartum women without prior screening. The cost of the extra vaccine needs to be balanced against that of screening and the potentially higher coverage achievable without serological screening. However, this would still leave primigravidae unprotected, among whom 40% of reported CRS cases occur in the United Kingdom (*55*) and 50–60% in the USA (*54*). Vaccine should, therefore, be offered to all post-pubertal women at all opportunities; the usual procedure being to counsel women to avoid becoming pregnant for 3 months after being vaccinated (*26*). Vaccination of women of childbearing age through routine health services may be feasible in some countries, but in many developing countries would be difficult since a lifetime immunization record would be needed to determine whether they have been vaccinated previously. An alternative is a mass campaign for women of childbearing age, such as in Cuba and Malaysia.

Selective vaccination of teenage girls directly protects the vaccinees, but has very little effect on overall transmission of rubella. In countries that cannot guarantee sustained high coverage of childhood vaccination, this strategy has the advantage of not shifting the average age at infection into childbearing ages, but it requires high rates of female attendance at school and good liaisons between school and health authorities. Potentially, vaccination against rubella can be conducted at the same time as school-based tetanus toxoid vaccination at a small marginal cost. However, coverage must be monitored since although high coverage of schoolgirls was attained in Bahrain (*36*), Hong Kong (*52*), Israel (*47*), Kuwait (*36*), Singapore (*51*) and Slovenia (A. Kraigher, personal communication, 1996), other industrialized (*56*, *57*) and developing countries have had difficulty in attaining this. In Jamaica, where schoolgirl vaccination was introduced in 1978, only 60–70% were immunized in many parishes in 1986 (*58*), and in the late 1980s, 31% of 2448 females aged 15–45 years from all parishes were still seronegative by enzyme immunoassay (*59*). In Trinidad and Tobago, approximately 10 years after the start of schoolgirl vaccination, 41% of antenatal clinic attendees were still seronegative (*60*). The current rubella outbreaks in Guyana and Jamaica that began in 1995, coupled with evidence of widespread rubella virus circulation throughout the Caribbean, are thus of great concern (*33*).

To eliminate CRS and postnatal rubella, childhood vaccination needs to be included in national programmes. The introduction of routine childhood vaccination alone, however, is not recommended, since CRS will continue subsequently for 20 years or more, until the cohorts that were vaccinated as children reach childbearing age. Mathematical models show how intermediate coverage levels for childhood vaccination can increase the average age at infection and thus the incidence of CRS. For example, in countries such as the United Kingdom and USA, with an average age at infection prevaccination of 9 years, childhood vaccination would lead to an increase in cases of CRS at coverage levels

Table 2: **Advantages and disadvantages of rubella vaccination strategies**

Strategy	Advantages	Disadvantages
Selective vaccination of schoolgirls	Direct protection to future mothers before first pregnancy Relatively inexpensive if school health services already in place Ongoing rubella transmission in children adds to protection	No effect on rubella transmission Delay of ⩾10 years for impact on CRS
Selective vaccination of schoolgirls and postpartum women	As above, plus: direct protection to women of childbearing age with no theoretical risk relating to vaccine in pregnancy. Performed well (e.g. Australia).	No effect on rubella transmission Primigravidae not reached for ⩾10 years If antenatal serological screening conducted with postpartum vaccination of susceptibles, difficult to reach high coverage
Selective vaccination of schoolgirls and all women of childbearing age	As above, plus: immediate protection to women of all gravidities Performed well (e.g. Israel)	Vaccination costs higher Need to conduct pregnancy counselling[a]
Childhood vaccination alone	In principle, high coverage may eventually eliminate rubella transmission	Indirect protection to women of childbearing age NOT guaranteed Very long time until impact seen **This strategy is not recommended**
Combined routine immunization of children, schoolgirls, and all women of childbearing age	Impact on CRS potentially immediate In longer term, potential to eliminate rubella	May be costly to maintain Need to conduct pregnancy counselling[a] May be difficult to achieve high coverage of each target group
Mass campaign for 1–14-year-olds with routine MR or MMR vaccination of children[b]	Potentially interrupts rubella transmission, at least in short term (e.g. São Paulo)	Leaves a pool of older susceptibles unprotected May get resurgence of rubella in teens/adults leading to CRS **This strategy is not recommended**
Mass campaign for women of childbearing age and 1–14-year-olds with routine MR or MMR vaccination of children	If implemented effectively, potential to eliminate rubella (e.g. Cuba)	Most costly Need to conduct pregnancy counselling[a] Rubella transmission could still continue among adult males

[a] Women should be advised to avoid pregnancy for 3 months after vaccination; women who are pregnant should not receive vaccine.
[b] MR: mumps–rubella; MMR: mumps–measles–rubella.

<50%. In countries, such as Brazil, with an average age at infection of 6 years (*3*), an increase in CRS would occur unless at least 80% coverage were achieved (*2*).

The experience of childhood rubella vaccination in the USA supports the predictions from these mathematical models. At the beginning of the programme in the USA, rubella vaccine was predominantly targeted at 1–12-year-old boys and girls, and 65% coverage of this age group was reached by 1975. This greatly reduced the incidence of acquired rubella and interrupted the pattern of epidemics, but had proportionately less effect on CRS incidence. Although rubella vaccine was available for susceptible women of childbearing age, coverage of this group was low (*54*), there were substantial missed opportunities (*61*), and the proportion of susceptible women of childbearing age remained unchanged at 10–20% (*62*). In 1978–79 and 1989–91 rubella epidemics led to substantial numbers of CRS cases (*63*).

The move in many countries towards accelerated control and elimination of measles raises the question of the marginal cost of including rubella control strategies with this initiative. Through vaccination it should be easier, in principle, to reduce transmission of rubella than that of measles, in view of the lower basic reproductive rate of rubella (*2*); in practice, however, elimination of rubella may be more complex. Unlike the situation with measles in the pre-vaccination era, all adults cannot be assumed to be immune against rubella, and it is precisely the occurrence of rubella in adult (pregnant) women that must be avoided. The age group to include in mass campaigns for rubella control or elimination needs careful study. For measles, the age group <15 years was selected in the Americas, because campaigns were implemented approximately 15 years after the vaccination programme began, and older persons were assumed to be immune (*64*). For rubella, however, older individuals may need to be included, especially in countries where ⩾25% of the

adult population is susceptible to the disease. Mass vaccination of women of childbearing age may provide direct protection to the target group for prevention of CRS, but it is plausible that rubella could continue to circulate for some years among adult males, and it will be important to maintain protection of girls entering their childbearing years after the campaign ends. Additional vaccination activities targeted towards areas with high densities of adult males (*26*) might help reduce transmission further, but as recent experience in Scotland shows (*65*), transmission may be widespread in the community and not confined to institutions.

Recommendations

A total of 38% of all countries currently include rubella vaccine in their national immunization programmes (Table 1); it is a cause for concern that several countries report only a childhood vaccination strategy. For countries already using rubella vaccine and those considering its use, the experience reported in this article leads to the following recommendations.

• ***Ensure protection of women of childbearing age.*** It is important for countries with national rubella vaccination programmes to ensure that their strategies include protection of women of childbearing age. Whether to achieve this using a one-time mass campaign or routine vaccination of women of childbearing age, with or without prior screening for susceptibility, will depend on the local situation and the capacity to attain high coverage.

• ***Monitor vaccine coverage.*** Coverage of rubella vaccine should be monitored in each of the target groups. This should be straightforward for children under 2 years of age, by incorporating information on rubella vaccine in the national EPI coverage system. For schoolgirls, the cooperation of school health authorities and the Ministry of Education will be needed. Routine monitoring of coverage will probably be most difficult for women of childbearing age, and a lifetime immunization record will probably be needed, as for tetanus toxoid vaccine. Missed opportunity surveys should be conducted in settings where rubella vaccine is indicated (*61*).

• ***Conduct surveillance of CRS and acquired rubella.*** Proposed methods for carrying out such surveillance have been described in part 1 of this review (*3*). Strengthening of laboratory and epidemiological capacity for rubella investigation, as part of EPI surveillance of rash illnesses in all countries, is strongly recommended. This should be integrated with activities to strengthen measles and dengue surveillance, with extension of surveillance to adults with rash illnesses. In countries where therapeutic abortions are available, abortion conducted because of a rash illness in pregnancy may be a much more sensitive indicator of programme impact than the reported incidence of CRS (*46*, *51*, *55*, *66*).

• ***Establish serological surveillance of susceptibility if resources permit.*** Ongoing (longitudinal) serological surveillance may be a useful adjunct to clinical surveillance for monitoring the effect of the programme on susceptibility in different age groups, particularly among women of childbearing age. The simplest method is to monitor susceptibility among women attending antenatal clinics (*53*); ideally, this should be combined with postpartum vaccination of seronegative women. In countries aiming for elimination, monitoring changes in age- and sex-specific seroprevalence provides data on which to base additional vaccination strategies (*67*).

• ***Investigate the effect of partial childhood vaccination coverage.*** Because of concerns about the effect of partial coverage with childhood rubella vaccination, there is a need to investigate the effect of childhood MMR vaccination in countries with low coverage, or in those where vaccination is conducted in the private sector only. If a substantial proportion of children is vaccinated via the private sector, for example in urban areas, the average age at infection could increase, potentially raising the risk of exposure of pregnant women. Information on differences in rubella and CRS epidemiology between areas with and without MMR vaccination is needed.

• ***Update models of the effectiveness of different vaccination strategies.*** In the past, mathematical models have been helpful for illustrating the potential effect of childhood versus selective vaccination strategies at different coverage levels (*2*). However, such models deal with industrialized country settings, and do not include alternative vaccination approaches such as initial mass campaigns of different potential age groups. The effectiveness of the various approaches outlined here, in developing countries with a range of demographic and epidemiological situations, should be susceptible to modelling. Ideally, empirical data should be obtained on the costs of different strategies, so that models can include this important element.

• ***Countries considering introduction of rubella vaccine must be able to sustain a control programme.*** National governments should ensure that they have the economic and logistical capacity to sustain a rubella and CRS control programme in

the long-term, before introducing vaccination. For countries considering whether to introduce vaccine, data on the burden of disease should be obtained using the methods described in part 1 of this review (*3*).

In the past, rubella has not been considered a public health priority in developing countries, which is probably appropriate for the poorest countries where infant, child, and maternal mortality rates are high and the health and education services infrastructure is lacking. However, developing countries represent a wide range of economies and demographic structures, with some having taken the initiative to include rubella vaccine in their national immunization programmes, while others are considering doing so. It is therefore important to evaluate programmes that are in progress, including the cost-effectiveness of different control strategies.

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Résumé

Lutte contre la rubéole et la rubéole congénitale dans les pays en développement, deuxième partie : vaccination contre la rubéole

En 1995–96, nous avons mené une enquête mondiale sur les stratégies de vaccination contre la rubéole. Au total, 78 pays (plus du tiers) ont signalé qu'ils avaient une politique nationale de vaccination contre cette maladie; dans ce nombre ne figurent pas les pays où la vaccination antirubéolique n'est pratiquée que dans quelques régions ou par le secteur privé. Aucun pays de la Région africaine n'a inscrit la rubéole dans son calendrier national de vaccination. Environ la moitié des pays de la Région des Amériques et de la Région de la Méditerranée orientale, 64 % des pays de la Région européenne et 31 % de ceux de la Région du Pacifique occidental utilisent le vaccin antirubéolique. Dans la Région de l'Asie du Sud-Est, Sri Lanka et la Thaïlande ont commencé à l'utiliser en 1996.

Les cas de rubéole congénitale peuvent être prévenus en protégeant directement les femmes et/ou les écolières (stratégie de vaccination sélective), en vaccinant les enfants (garçons et filles) pour réduire la transmission du virus et obtenir ainsi une protection indirecte (stratégie de vaccination des enfants), ou en associant ces deux méthodes (stratégie combinée). La majorité des pays (60 %) ont indiqué qu'ils avaient adopté la stratégie combinée. Seulement sept pays (9 %) ont déclaré avoir adopté une stratégie sélective de vaccination des femmes et/ou des écolières, tandis que 24 pays (31 %) ont signalé qu'ils ne pratiquaient que la vaccination des enfants. L'utilisation du vaccin antirubéolique est étroitement liée au niveau économique du pays. Si l'on reprend la classification des pays par les Nations Unies, on constate que le vaccin est utilisé dans 92 % des pays industrialisés, 36 % des pays à économie de transition et 28 % des pays en développement.

Si beaucoup de pays ont introduit le vaccin antirubéolique dans leur programme, peu d'entre eux fournissent des données sur l'impact de la vaccination. Dans la Région des Amériques, on a constaté une circulation généralisée du virus de la rubéole dans les Caraïbes anglophones au cours de la période 1990-95. Malgré les programmes nationaux de vaccination, 30 à 50 % des femmes des Caraïbes en âge de procréer restent sensibles à la maladie; on s'efforce donc actuellement d'améliorer la couverture vaccinale des femmes. Dans la Région de la Méditerranée orientale, des flambées de rubéole se sont produites entre 1990 et 1993 à Bahreïn, en Iraq, en République islamique d'Iran, au Koweït, à Oman, en Arabie saoudite et dans les Emirats arabes unis. En 1996, les six pays du Golfe ont établi un système de surveillance des maladies éruptives (avec confirmation sérologique pour la rougeole et la rubéole) et ont décidé de signaler régulièrement les cas de rubéole et de rubéole congénitale répondant à la définition officielle. Dans la Région européenne, une flambée de rubéole s'est produite en 1989 en Croatie (qui faisait alors partie de la Yougoslavie) et une importante épidémie a eu lieu en Pologne en 1992-93.

Avant d'introduire le vaccin antirubéolique, les gouvernements devraient s'assurer qu'ils disposent des moyens économiques et logistiques nécessaires pour appliquer un programme à long terme de lutte contre la rubéole et la rubéole congénitale. Ils devraient également réunir des données afin

d'évaluer le fardeau que représente pour eux la rubéole congénitale.

Les pays qui utilisent déjà le vaccin antirubéolique devraient s'assurer que les femmes en âge de procréer sont prises en compte dans leur stratégie de lutte contre la rubéole. Une solution pratique pourrait être la vaccination des femmes après l'accouchement. Les autres possibilités sont la vaccination de masse des femmes en âge de procréer et/ou la vaccination des écolières. Les pays devraient également contrôler la couverture vaccinale de chacun des groupes cibles. Le renforcement des moyens de laboratoire et d'étude épidémiologique de la rubéole, dans le cadre de la surveillance de la rougeole et des autres maladies éruptives, est fortement recommandé.

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