Prevention of congenital rubella syndrome (CRS)

INTEGRATED MANAGEMENT OF PREGNANCY AND CHILDBIRTH (IMPAC)

The standard

In countries where rubella vaccine is included in the national immunization programme, women should be immunized against rubella before they become pregnant. In all countries, pregnant women with suspected rubella or exposure to rubella should be followed up and reported. In all countries, infants with suspected congenital rubella syndrome (CRS) should be assessed and reported.

Aim

To prevent congenital rubella syndrome (CRS).

Requirements

☐ In countries where rubella vaccine is included in the national immunization programme, a policy to provide vaccine for women of childbearing age is available; a national policy, national immunization programme and locally adapted guidelines on rubella immunization are available and are correctly implemented to ensure sustained high coverage.

☐ The vaccine, equipment and supplies (cold chain, auto-disable syringes, needles, etc.) needed to conduct rubella immunization are readily available in the health facilities.

☐ Health personnel have the knowledge and skills to determine when and how to vaccinate against rubella (including injection safety and safe waste disposal), and to advise pregnant women on prevention of rubella.

☐ A system is in place to monitor coverage with rubella vaccine in women of childbearing age.

☐ Surveillance is conducted for rubella in all age groups and for congenital rubella syndrome in children <12 months of age using appropriate case definitions. Investigation of cases of rubella in pregnancy and rubella exposure during pregnancy is given priority.

☐ Health education activities are carried out to increase community awareness on the importance of preventing rubella and congenital rubella syndrome.

NOTE: Recommendations in this standard are restricted to those relevant to management of women in the pre-pregnancy, antenatal and postpartum periods, and the neonate. Extensive recommendations on rubella and congenital rubella syndrome are available from the WHO Department of Immunization, Vaccines and Biologicals.
Applying the standard

**Prior to pregnancy and in the postpartum period**

In countries where rubella vaccine has been introduced into the national immunization schedule, health providers of maternal and child services must:

- Vaccinate children aged 12 months or older and/or schoolgirls and/or women of childbearing age against rubella, according to national policy and guidelines.

**During pregnancy**

In all countries, health providers of maternal and neonatal services, and skilled attendants in particular, must:

- Ensure that rubella vaccine is not offered to pregnant women and that women are advised to avoid pregnancy for one month after rubella vaccination.
- Inform pregnant women of the importance of avoiding contact with individuals with rubella.
- Report and investigate suspected rubella in pregnancy, exposure of a pregnant woman to rubella, and infants with suspected CRS.
- Be able to counsel women with confirmed rubella infection during pregnancy on the risk of fetal abnormalities and relevant laws and regulations with respect to termination of the pregnancy, if they so wish.
- Report and investigate cases of suspected congenital rubella syndrome in newborns and infants promptly, as required by the national communicable disease surveillance system.

**Audit**

**Input indicators**

- National guidelines for immunization of women against rubella are available in the health facilities and are known to the health care staff.
- Rubella vaccine is available and is correctly stored.
- Health providers correctly offer and administer rubella vaccine to women as recommended by the national policy (either in mass campaigns, to adolescents in or out of school, in the workplace, at family planning clinics, in the premarital period, or postpartum).
- A system is in place to monitor rubella vaccine coverage in women.
- There is a functioning surveillance system for rubella in all age groups, with priority for investigation of suspected rubella or exposure to rubella in pregnant women, and for congenital rubella syndrome in children <12 months of age.
- Health providers advise pregnant women on rubella prevention.

**Process and output indicators**

- The number and proportion of women of childbearing age vaccinated against rubella by district and by month.
- The proportion of women of childbearing age who are seropositive for rubella.

**Outcome indicators**

- Number of cases of rubella in all age groups.
- Number of cases of rubella in pregnant women.
- Number of cases of congenital rubella syndrome in infants <12 months of age.
- Perinatal mortality due to congenital rubella.
### Rationale

#### Burden of suffering

Rubella infection occurs worldwide. It is a mild, self-limiting infection in children and adults but its effects on the fetus can be devastating (1). Fetuses infected with rubella early in pregnancy are at greatest risk of intrauterine death, spontaneous abortion and congenital malformations of major organ systems (1). Typically, congenital rubella syndrome (CRS) is characterized by congenital heart disease, cataracts and deafness, but infants with CRS may also present with single or combined defects including microcephaly, microphthalmia, congenital glaucoma, meningoencephalitis, mental retardation, purpura, hepatosplenomegaly and bone disease (1,2). Severe and moderate cases are recognized at birth, but mild cases with only slight cardiac involvement or deafness may not be detected until later in infancy or in childhood. CRS also has late-onset manifestations, including autism, diabetes mellitus, and thyroiditis (3). A large prospective study in England and Wales that followed infants for a mean period of 26 months, found that the risk of rubella birth defects was 90% when the mother was infected in the first 11 weeks of pregnancy; 33% in weeks 11-12; 11% in weeks 13-14; and 24% in weeks 15-16 (4). A study in Sweden found that the risk was 2% when the mother was infected during weeks 17-20 of pregnancy, with deafness as the sole defect (5).

In 1996, WHO sponsored a global epidemiology review to assess the evidence for the occurrence of CRS in developing countries (6). More than 50 developing countries were found to have conducted studies on the burden of CRS, and 14 of these provided incidence rates for number of CRS cases per 1000 live births. In the outbreak setting, the incidence of CRS was 0.6-2.2 per 1000 live births. These rates are similar to those reported in industrialized countries before vaccination was introduced. These data exclude abortion and are underestimates of congenital malformations, since only anomalies that were manifest at birth or during the first months of life were included. Altogether 43 developing countries had conducted rubella serosurveys in healthy women of childbearing age with a sample size of at least 100 women. In 12 countries ≥25% of women of childbearing age were susceptible and in 20 countries 10-24% were susceptible; high susceptibility rates indicate that there are many women at risk for delivery of an infant with CRS. Based on serosurvey data, a model was developed which predicted there were some 110,000 new cases of CRS in infants in developing countries (excluding those in the European Region) in 1996 (7).

Guidelines on surveillance for rubella in persons of all ages, during pregnancy, and for CRS in infants were published by WHO (8,9). Since 2000, all countries have been requested to report the annual number of cases of rubella and CRS on the WHO-UNICEF Joint Reporting Form, and these data are maintained by the WHO Department of Immunization, Vaccines and Biologicals in Geneva. In recent years, there has been enormous improvement in the global understanding of rubella epidemiology, thanks to the nearly 700 laboratories (reference, regional, national, and subnational) participating in the WHO Global Measles/Rubella Laboratory Network. WHO regions with rubella elimination targets (the Americas and Europe) have standards for reporting cases of rubella and CRS weekly or monthly. In the Region of the Americas, countries report cases of rubella and CRS weekly, with publication of these data (http://www.paho.org/english/AD/FCH/IM/Measles.htm). In the European Region, 47 of 52 countries have established rubella surveillance and these data are reported monthly (http://www.euro.who.int/vaccine).

By 2003, some 131 countries/territories (60%) out of a total of 215 countries/territories have added rubella vaccine to their national immunization system. Two WHO regions - the Americas and Europe - have established regional targets for elimination of rubella and CRS by the year 2010 (10-14).

#### Efficacy and effectiveness

There is no specific therapy for maternal or congenital rubella infection. The value of immunoglobulin given after exposure early in pregnancy has not been established. The primary means of preventing CRS is by rubella immunization. Rubella vaccine is highly effective: a single dose of the most commonly used RA27/3 rubella vaccine strain leads to seroconversion in at least 95% of vaccinees and is thought to afford lifelong protection (3). All studies that have examined cost-effectiveness of rubella vaccination have found a positive cost-benefit ratio (15). A WHO position paper on rubella vaccines
Prevention of congenital rubella syndrome (CRS)

Standards

**CRS congenital rubella syndrome** provides extensive guidance for countries (3). WHO recommends that all countries should assess their rubella situation and, if appropriate, make plans for the introduction of rubella vaccine.

The primary purpose of rubella vaccination is to prevent CRS. Two approaches are recommended: (a) prevention of CRS only, through immunization of women of childbearing age; or (b) elimination of rubella as well as CRS, through immunization of young children as well as women of childbearing age (3). The decision to include rubella vaccine is made at the national level and the choice of approach should be based on the level of rubella susceptibility in women of childbearing age; the burden of disease due to CRS; the strength of the basic immunization programme as indicated by routine measles vaccine coverage (which should be >80% for several years before implementing childhood rubella vaccination); infrastructure and resources for child and adult immunization programmes; assurance of injection safety; and other disease priorities. A policy of rubella vaccination of women of childbearing age only is essentially free of risks of altering rubella transmission dynamics, whereas inadequately implemented childhood vaccination runs the risk of increasing the number of cases of CRS (16,17). Therefore, childhood rubella vaccine introduction is not recommended unless the national programme will be able to sustain high levels of coverage (above 80%) on a long-term basis.

Rubella vaccine should be avoided in pregnancy because of the theoretical but never demonstrated teratogenic risk (3). No case of CRS has been reported in more than 1000 susceptible pregnant women who inadvertently received rubella vaccine in early pregnancy; thus, inadvertent rubella vaccination during pregnancy is not an indication for abortion (18). If pregnancy is being planned, then an interval of one month should be observed after rubella vaccination. Generally, the adverse events following vaccination with RA27/3 rubella vaccine are mild (3). Common adverse events include pain, redness and induration at the site of injection. Joint symptoms are common in adolescent and adult women who receive rubella vaccine; they include arthralgia (25%) and arthritis (10%) that usually last a few days to 2 weeks. These transient reactions seem to occur in seronegative individuals only, for whom the vaccine is important. Although concerns have been raised that rubella vaccination of adult women might occasionally lead to chronic arthritis, large epidemiological studies have not supported a role for rubella vaccine in chronic joint disease (3).

Persons with a history of anaphylactic reaction to neomycin should not receive rubella vaccine. Rubella vaccine should not be given to immunodeficient individuals, although it is recommended for asymptomatic HIV-positive people (3). Persons with active tuberculosis should not receive rubella vaccine until treatment is established. Breastfeeding is not a contraindication to postpartum rubella vaccination. Although vaccine virus has been detected in breast milk and transmission can occur, no illness has been reported in infants (19,20).

Routine antenatal rubella IgG antibody screening is not recommended for all countries, as this is expensive. Rather, laboratory resources should be directed to diagnosis of rubella in pregnant women who have suspected rubella or have been exposed to rubella. A blood specimen needs to be obtained as soon as possible after suspected rubella infection and this should be sent for rubella IgM antibody testing. Where further clarification is needed, rubella IgG antibody tests may be helpful if these are available. Research is ongoing to determine how best to use rubella avidity tests as an additional diagnostic method for pregnant women.

Neonates with CRS shed rubella virus during the first months of life, and care should be taken that these infants are not in contact with pregnant women.

*CRS congenital rubella syndrome*
The table below summarizes the evidence from the most relevant studies. The level of evidence is presented using the NICE methodology which applies a coding from 1 (high level) to 4 (low level). For details, see also the Introduction to the Standards for Maternal and Neonatal Care and the Process to develop the Standards for Maternal and Neonatal Care on http://www.who.int/making_pregnancy_safer/publications/en. For an overview of a comprehensive list of evidence, please refer to the reference section of the standard.

<table>
<thead>
<tr>
<th>Study (Type &amp; Level of evidence)</th>
<th>Population &amp; Setting</th>
<th>Objective &amp; Intervention</th>
<th>Outcomes linked to the Standard</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>16. Panagiotopoulos et al. 1999</td>
<td>Children, adolescents and women of childbearing age Greece</td>
<td>To describe the events leading to the epidemic of CRS in Greece after a major rubella epidemic</td>
<td>1977: MMR vaccination optional 1989: MMR vaccination (one dose) compulsory for children 1 year old 1991: MMR vaccination (two doses) compulsory (at 15 months and 11–12 years) Average coverage with MMR in the 1990s: 50–60% Proportion of pregnant women susceptible to rubella during the 1980s: 12% (1980) → 36% (1990) Rubella epidemic: 1993 (Feb.–June); 64% of cases were 15 years old or over CRS epidemic: 1993 (Sept.–Dec.); 25 cases serologically confirmed with 7 deaths Rubella and CRS surveillance were passive, with likely high rates of underreporting</td>
<td>With low vaccination coverage, the immunization of children aged 1 year against rubella without any immunization of women in the postpartum period or in the childbearing age carries the risk of increasing the occurrence of CRS</td>
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<td>18. Vynnycky, Guy Cutts 2003</td>
<td>Dynamic transmission model</td>
<td>Assumes that MMR vaccination is restricted to young children</td>
<td>Model indicates that in countries with a medium to high force of rubella infection, levels of MMR* vaccine coverage &lt;80% would lead, in the long-term, to an increase in CRS</td>
<td>Highlights the risks of private sector MMR vaccination. Concludes that systematic rubella vaccination should be conducted among adult women</td>
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<tr>
<td>15. Hinman, Irons &amp; Kandola 2002</td>
<td>Different populations (children, women of childbearing age, infants) in different parts of the world 12 studies in developed countries; 10 studies in developing countries</td>
<td>To investigate whether the incorporation of rubella vaccination into immunization programmes in developing countries is economically justified</td>
<td>Annual cost of treating a CRS case Lifetime cost of treating a CRS case Benefit-to-cost ratio</td>
<td>Average US$ 2000–14 000 Average US$ 50 000–64 000 Always positive, ranging from 2 to 40 depending on the strategy adopted</td>
<td>Only results from developing countries reported here</td>
</tr>
<tr>
<td>7. Cutts &amp; Vynnycky. 1999</td>
<td>Rubella serosurvey data from developing countries abstracted for preparation of a simple catalytic model to estimate CRS incidence</td>
<td>To model the incidence of CRS in developing countries of different WHO regions (excluding Europe) in 1996</td>
<td>Estimated mean number of new cases of CRS in infants born in 1996 in developing countries, by WHO region</td>
<td>Africa 22,471 Americas 15,994 E. Mediterranean 12,080 SE Asia 46,621 W Pacific 12,634</td>
<td>Mean global total of 110,000 CRS cases in developing countries indicates CRS is an under-recognized health problem in many developing countries</td>
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* Measles, mumps and rubella
### 1.4 Prevention of congenital rubella syndrome (CRS)

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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Cutts, Robertson, Diaz-Ortega &amp; Samuel 1997</td>
<td>CRS surveillance studies with incidence data: 14 studies from 12 developing countries</td>
<td>To assess the incidence of CRS among infants in developing countries</td>
<td>Annual incidence of CRS per 1000 live births</td>
<td>Range from 0.6 - 2.2 CRS cases /1000 live births in the outbreak setting</td>
<td>Incidence comparable to that reported by industrialised countries in the pre-vaccination era</td>
</tr>
<tr>
<td>7. Cutts, Robertson SE, Diaz-Ortega JL, Samuel R. Control of rubella and congenital rubella syndrome (CRS) in developing countries, part 1: burden of disease from CRS.</td>
<td>Rubella (serum IgG) susceptibility in 45 developing countries, each of which had at least one serosurvey of healthy women with a sample size &gt;100</td>
<td>To assess the potential risk of CRS</td>
<td>Rubella susceptibility in women of childbearing age</td>
<td>&gt;25% susceptible in 12 countries; 10-24% susceptible in 20 countries; &lt;10% susceptible in 13 countries</td>
<td>Review limited to developing countries, since all industrialized countries had already adopted rubella vaccine</td>
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### References


**Links and additional sources**


IV. Expanded Programme on Immunization in the Americas. FLASOG to participate in the implementation of strategies to control rubella and prevent CRS in the Americas. *EPI Newsletter*, 2001, 23 (6):7.


Standards
for Maternal and
Neonatal Care