



## Congenital rubella syndrome: a matter of concern

Efrén Martínez-Quintana,<sup>1</sup>  
Carlos Castillo-Solórzano,<sup>2</sup>  
Nuria Torner,<sup>3</sup> and  
Fayna Rodríguez-González<sup>4</sup>

**Suggested citation:** Martínez-Quintana E, Castillo-Solórzano C, Torner N, Rodríguez-González F. Congenital rubella syndrome: a matter of concern. *Rev Panam Salud Publica.* 2015;37(3):179–86.

### SYNOPSIS

*Congenital rubella syndrome (CRS), an important cause of severe birth defects, remains a public health problem in a significant number of countries. Therefore, global health experts encourage use of rubella vaccination, with the primary aim of preventing CRS. While large-scale rubella vaccination during the last decade has drastically reduced or eliminated both the virus and CRS in Europe and the Americas, many countries in Africa, South-East Asia, the Eastern Mediterranean, and the Western Pacific have not yet incorporated any type of rubella-containing vaccine into their immunization schedule. As a result, through travel and migration, rubella has been imported into countries that had successfully eliminated the virus, leading to outbreaks and the reestablishment of endemic transmission. The objective of this study was to identify the key factors required for CRS elimination (prevalence reduction, vaccination strategies, and surveillance methods) by reviewing publications in PubMed on rubella and CRS (systematic reviews, country experiences, and position papers from the World Health Organization (WHO) and other intergovernmental organizations). Based on the results of the review, to eliminate rubella and CRS in endemic areas and reduce re-emergence in previously disease-free areas, all countries should carry out two types of mass rubella vaccination campaigns: 1) one single mass national immunization campaign targeting all men and women 5–39+ years old (with the upper age limit depending on the year in which the rubella-containing vaccine was in-*

*roduced and the epidemiology of rubella in the country) and 2) incorporation of an rubella-containing vaccine in routine childhood immunization programs, including regular vaccination campaigns for 12-month-olds and measles follow-up campaigns. In addition to mass rubella immunization campaigns and routine childhood vaccination programs, the following measures should be taken to help fight rubella and CRS: 1) surveillance of the number of susceptible women of childbearing age, and the emergence of imported cases; 2) coverage of susceptible populations with “second-chance” (“catch-up”) campaigns (vaccination of older children and adults who may have missed earlier immunization programs); 3) rapid response to outbreaks; 4) strengthening of CRS surveillance; 5) involvement of the private sector in awareness and vaccination campaigns; and 6) reduction of the number of false-positive laboratory test results.*

**Key words:** rubella; rubella syndrome, congenital; prevalence; vaccination; Africa; Americas; Asia, Southeastern; Europe; Mediterranean region; Pacific Islands.

Rubella infection is usually mild with nonspecific (subclinical) symptoms and is therefore often undiagnosed or misdiagnosed. However, the rubella virus remains an important public health problem due to the teratogenic effects and risk of miscarriage and stillbirth that may result from congenital infection, particularly when the mother becomes infected during the first trimester of pregnancy (1–3).

Rubella was first described in the mid-18th century and remains endemic in many developing countries that do not include a rubella-containing vaccine (RCV) in their mass immunization programs (national campaigns and childhood vaccination schedules). Children 5–9 years old account for most cases of rubella infection, many of which are contracted in schools where susceptible individuals are in close contact. In countries without an RCV in their national immunization program, the proportion of women of childbearing age susceptible to rubella is high (4, 5). To reduce overall prevalence of the virus, global health experts recommend that all countries incorporate an RCV in routine childhood vaccination programs, including regular vaccination campaign for 12-month-olds and measles follow-up campaigns. To help prevent congenital rubella syndrome (CRS), additional efforts are needed to reduce the number of susceptible women of childbearing age. Strategies include vaccination at family planning clinics, schools, and in the workplace (before pregnancy) and in-hospital vaccination after delivery for women who give birth (“postpartum vaccination”) to protect their future offspring. Countries wishing to eliminate rubella and CRS should carry out a mass national immunization

<sup>1</sup> Cardiology Service, Complejo Hospitalario Universitario Insular-Materno Infantil, Las Palmas de Gran Canaria, Spain. Send correspondence to: Efrén Martínez-Quintana, efrencardio@gmail.com

<sup>2</sup> Family and Community Health, Pan American Health Organization, Washington, District of Columbia, United States of America.

<sup>3</sup> Department of Public Health, Universidad de Barcelona, Barcelona, Spain.

<sup>4</sup> Ophthalmology Service, Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas de Gran Canaria, Spain.

program that includes an RCV covering all males and females 5–39+ years old (6, 7). The upper age limit will depend on the year in which the RCV was introduced and the epidemiology of rubella in the country.

The objective of this study was to identify the key factors required for CRS elimination (prevalence reduction, vaccination strategies, and surveillance methods) by reviewing publications in PubMed on rubella and CRS (systematic reviews, country experiences, and position papers from the World Health Organization (WHO) and other intergovernmental organizations).

### Maternal rubella infection

In maternal rubella infection, which usually occurs five to seven days after maternal inoculation, the virus spreads across the placenta hematogenously, leading to the potentially devastating effects of congenital infection on the developing fetus, including miscarriage, stillbirth, and various teratogenic effects (Table 1) (8, 9). In maternal rubella infection with a rash, the frequency of congenital infection is more than 80% during the first 12 weeks of pregnancy, about 54% at 13–14 weeks, and about 25% at the end of the second trimester. When any type of maternal rubella infection occurs after 16 weeks of pregnancy, there is no risk of CRS for the newborn (10).

### Epidemiology of CRS

Before the introduction of the rubella vaccine in 1969, the global incidence of CRS ranged from 0.8–4.0

per 1 000 live births (during rubella epidemics) to about 0.1–0.2 per 1 000 live births (during endemic periods) (11). Currently, the vast majority of CRS cases worldwide occur in developing countries that do not include an RCV in their mass national immunization program (12).

Recognizing CRS as a cause of preventable morbidity (including childhood blindness and deafness, which create lifelong special health and social needs), WHO advocates two approaches for rubella vaccination. One approach focuses exclusively on reducing CRS by immunizing adolescent girls or women of childbearing age, or both, to provide individual protection. The second approach is more comprehensive, focusing on interrupting rubella virus transmission and thereby eliminating rubella as well as CRS. The latter approach requires RCVs to be introduced into the routine childhood immunization schedule and combined with the vaccination of older age groups who are susceptible to rubella. Depending on the burden of CRS and available resources, countries should define their goal and the time frame for achieving it (13).

Rubella vaccination programs were started in some countries in the early 1970s. The first WHO rubella vaccine position paper was published in 2000 to guide the introduction of RCV in childhood immunization schedules (5). In the last few decades the number of WHO member states that include an RCV in their routine childhood immunization schedule has increased from 83 or 43% (in 1996) to 132 out of 194 or 68% (in 2012). By 2014, 141 countries had introduced an RCV in their routine childhood schedules and seven countries had plans to introduce it in 2015 (Figure 1).

**TABLE 1. Case definitions for congenital rubella syndrome (CRS), 2009<sup>a</sup>**

Suspected	Probable	Confirmed	Infection only
If the child does not meet the criteria for a probable or confirmed case, he/she must have one or more of the following clinical findings:	If the child does not have laboratory confirmation of rubella infection, he/she must have at least two of the following clinical findings:	At least one of the clinical findings for rubella and one of the following four types of laboratory data:	No clinical symptoms or signs of rubella but any of the laboratory data that confirm a case
Cataracts	Cataracts	Isolation of rubella virus	
Congenital glaucoma	Congenital glaucoma	Detection of rubella-specific IgM antibody	
Congenital heart disease	Congenital heart disease	High antibody levels <sup>b</sup>	
Hearing impairment	Hearing impairment	PCR-positive for rubella virus	
Pigmentary retinopathy	Pigmentary retinopathy		
Purpura	OR one of the above plus one or more of the following:		
Hepatosplenomegaly	Purpura		
Jaundice	Hepatosplenomegaly		
Microcephaly	Jaundice		
Developmental delay	Microcephaly		
Meningoencephalitis	Developmental delay		
Radiolucent bone disease	Meningoencephalitis		
	Radiolucent bone disease		

**Source:** Council of State and Territorial Epidemiologists 2009 position statement (8).

<sup>a</sup> CRS is characterized by low birth weight, ophthalmic problems (cataracts, glaucoma, pigmentary retinopathy, chorioretinitis, and microphthalmia); auditory problems (sensorineural hearing impairment); cardiac problems (ventricular septal defects, patent ductus arteriosus, peripheral pulmonary artery stenosis, and hypoplasia or coarctation of the aorta); and/or neurologic problems (intracranial calcifications, microcephaly, behavior disorders and meningoencephalitis). Other abnormalities such as hepatosplenomegaly, hepatitis, thrombocytopenia, osteitis, interstitial pneumonitis, type I diabetes mellitus, and thyroiditis may also be seen (9).

<sup>b</sup> Those that persist at a higher level and for a longer period of time than expected from passive transfer of maternal antibody (i.e., a rubella titer that does not drop at the expected rate of a twofold decline per month).

Table 2 shows rubella and CRS control and elimination activities by WHO region (Africa, Americas, Eastern Mediterranean, Europe, South-East Asia, and Western Pacific) for the years 2000, 2009, and 2012 (12, 14).

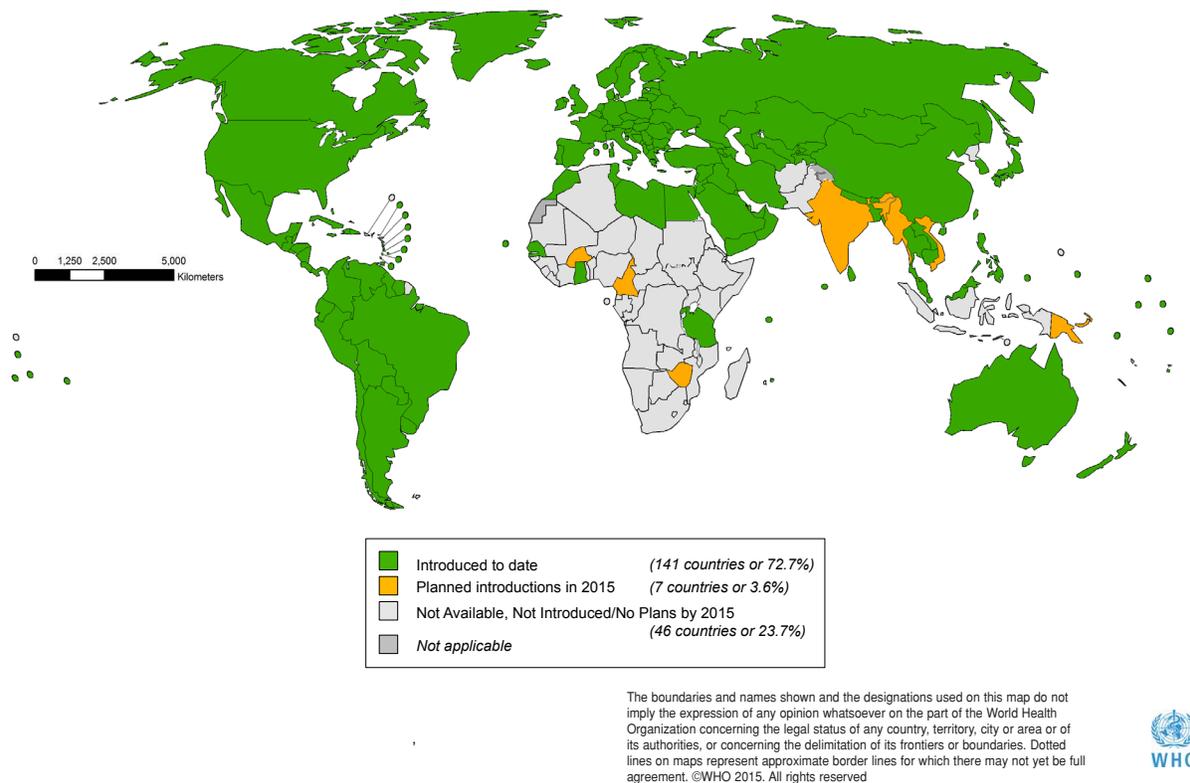
### WHO regions

**Europe.** In 1998, the WHO Europe region declared two public health goals: 1) eliminating indigenous (non-imported) measles, including rubella and 2) controlling congenital rubella (15). By 2005, most European countries included an RCV in their routine childhood immunization schedules, and a strategic plan for total eliminating endemic measles (including rubella) and preventing CRS (< 1 case per 100 000 live births) by 2010 was in place (16). However, in September 2010,

the end-date for achievement of these goals was postponed to 2015 due to the emergence of new cases of the virus in some European countries (17).

Between 2003 and 2011, the number of cases reported for the region dropped from 304.390 to 9 672.0 (a decrease of almost 97%). However, in 2012, there was a threefold increase in reported cases of rubella. More than 92% of the cases occurred in Romania and Poland. The epidemiology of rubella in these and other countries in the region has usually reflected national rubella immunization policies. For example, outbreaks in Poland (2007–2008 and 2011–2013) and Romania (2011–2012) predominantly affected sex and age groups that had not been targeted by rubella immunization programs, according to reports from WHO missions to these countries (16, 18, 19).

FIGURE 1. Countries with rubella vaccine in the national immunization program and planned introductions in 2015<sup>a</sup>



**Source:** World Health Organization Immunization, Vaccines and Biologicals (IVB) Database, 5 March 2015. Reprinted with permission from WHO.

<sup>a</sup> Countries with rubella vaccine to date: Albania, Andorra, Antigua and Barbuda, Argentina, Armenia, Australia, Austria, Azerbaijan, Bahamas, Bahrain, Bangladesh, Barbados, Belarus, Belgium, Belize, Bhutan, Bolivia, Bosnia and Herzegovina, Brazil, Brunei Darussalam, Bulgaria, Cabo Verde, Cambodia, Canada, Chile, China, Colombia, Cook Islands, Costa Rica, Croatia, Cuba, Cyprus, Czech Republic, Denmark, Dominica, Dominican Republic, Ecuador, Egypt, El Salvador, Estonia, Fiji, Finland, France, Georgia, Germany, Ghana, Greece, Grenada, Guatemala, Guyana, Haiti, Honduras, Hungary, Iceland, Iran (Islamic Republic of), Iraq, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kazakhstan, Kiribati, Kuwait, Kyrgyzstan, Lao People's Democratic Republic, Latvia, Lebanon, Libya, Lithuania, Luxembourg, Malaysia, Maldives, Malta, Marshall Islands, Mauritius, Mexico, Micronesia (Federated States of), Monaco, Mongolia, Montenegro, Morocco, Nauru, Nepal, Netherlands, New Zealand, Nicaragua, Niue, Norway, Oman, Palau, Panama, Paraguay, Peru, Philippines, Poland, Portugal, Qatar, Republic of Korea, Republic of Moldova, Romania, Russian Federation, Rwanda, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Samoa, San Marino, Saudi Arabia, Senegal, Serbia, Seychelles, Singapore, Slovakia, Slovenia, Solomon Islands, Spain, Sri Lanka, Suriname, Sweden, Switzerland, Syrian Arab Republic, Tajikistan, Thailand, The former Yugoslav Republic of Macedonia, Tonga, Trinidad and Tobago, Tunisia, Turkey, Turkmenistan, Tuvalu, Ukraine, United Arab Emirates, United Kingdom, United Republic of Tanzania, United States of America, Uruguay, Uzbekistan, Venezuela, Yemen. Countries with planned introductions in 2015: Burkina Faso, Cameroon, India (partial), Myanmar, Papua New Guinea, Viet Nam, Zimbabwe. Countries for which no information was available or that have not introduced the vaccine and have no plans to in 2015: Afghanistan, Algeria, Angola, Benin, Botswana, Burundi, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic People's Republic of Korea, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Guinea, Guinea-Bissau, Indonesia, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Namibia, Niger, Nigeria, Pakistan, Sao Tome and Principe, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Swaziland, Timor-Leste, Togo, Uganda, Vanuatu, Zambia.

**TABLE 2. Control and elimination activities for rubella and congenital rubella syndrome (CRS) by World Health Organization (WHO) region and year (2000, 2009, and 2012)<sup>a-c</sup>**

WHO regions (no. of member states)	Rubella			CRS	
	Member states with RCV <sup>d</sup> in schedule (%)	No. of member states reporting (%)	No. of cases reported	No. of member states reporting (%)	No. of cases reported
<b>2000</b>					
Africa (46)	2 (4)	7 (15)	865	3 (7)	0
Americas (35)	31 (89)	25 (71)	39 228	18 (51)	80
Eastern Mediterranean (22)	12 (55)	11 (50)	3 122	6 (27)	0
Europe (53)	40 (75)	41 (77)	621 039	34 (64)	48
South-East Asia (11)	2 (18)	3 (27)	1 165	2 (18)	26
Western Pacific (27)	12 (44)	15 (55)	5 475	12 (44)	3
Total (194)	99 (51)	102 (53)	670 894	75 (39)	157
<b>2009</b>					
Africa (46)	2 (4)	38 (83)	17 388	15 (33)	47
Americas (35)	35 (100)	34 (97)	18	34 (97)	20
Eastern Mediterranean (22)	15 (68)	15 (68)	2 030	10 (45)	67
Europe (53)	53 (100)	46 (87)	11 623	43 (81)	17
South-East Asia (11)	4 (36)	9 (82)	17 208	4 (36)	3
Western Pacific (27)	21 (78)	25 (93)	73 077	17 (63)	11
Total (194)	130 (67)	167 (87)	121 344	123 (63)	165
<b>2012</b>					
Africa (46)	3 (7)	41 (89)	10 830	20 (43)	69
Americas (35)	35 (100)	35 (100)	21	35 (100)	3
Eastern Mediterranean (22)	14 (64)	18 (82)	1 698	9 (41)	20
Europe (53)	53 (100)	46 (87)	30 536	42 (79)	60
South-East Asia (11)	5 (45)	11 (100)	6 670	6 (55)	14
Western Pacific (27)	22 (81)	23 (85)	44 275	17 (63)	134
Total (194)	132 (68)	174 (90)	94 030	129 (66)	300

**Source:** U.S. Centers for Disease Control and Prevention (12, 14).

<sup>a</sup> Reporting of rubella and CRS cases in a region depends on the number of regional member states with surveillance systems and the quality of the systems. As a country makes progress on rubella control and CRS prevention the number of reported cases might increase even when the actual number of infections decreases.

<sup>b</sup> Many of the numbers provided by some WHO regions are underestimated. For example, based on seroprevalence data and statistical models, it is estimated that 46 621 infants with CRS will be born annually in the South-East Asia region. Similar estimates are given for the Africa region, where most countries have not yet included rubella vaccination in their national immunization program.

<sup>c</sup> By 2014, 141 countries had introduced the rubella vaccine, and in 2015, seven more countries will include it, for a total of 148 countries.

<sup>d</sup> RCV: rubella-containing vaccine.

**Americas.** Before 1990, only 6 of the 44 countries and territories in the Americas included an RCV in their routine childhood vaccination programs. In 2003, the Pan American Health Organization (PAHO), the regional office of the WHO, established the goal of eliminating rubella in the Americas by the year 2010 (20). By 2007, about 99% of new birth cohorts in the region had introduced an RCV in their routine childhood schedules. However, in 2007, the Americas experienced a resurgence of rubella cases due to importations of the virus into countries that had only targeted females in their mass immunization campaigns, such as Brazil and Chile. In each area where surveillance detected transmission of the virus and the occurrence of CRS, the mass immunization campaigns had omitted adult males. As a result of the rubella outbreaks in the region during 2008–2009, there were 13 reported cases of CRS in Chile and 14 in Brazil (21). No endemic CRS cases were reported in 2010 or 2011.

In the United States, from 2004–2011, four cases of CRS were reported in infants. The virus contracted by the first infant, who was born in 2003, was classi-

fied as imported from Nigeria. The virus contracted by the second infant, who was born in 2004, was classified as imported from Cote d'Ivoire. Both infants' mothers had unknown vaccination status. The mother of the third infant with CRS (who was born in 2008) was exposed to rubella outside the United States, most likely in India. The mother of the fourth infant (also born in 2008) had documented receipt of one dose of an RCV and had not traveled outside the United States during pregnancy, so the source of that rubella infection is unknown. This case was unusual case, as reports of CRS in children of vaccinated mothers are extremely rare (22, 23).

In the Americas region, remarkable progress toward the elimination of rubella and CRS has been made, with a reduction of 99.99% of confirmed cases between 1998 and 2013. Region-wide vaccination of adolescents and young adults—male and female—has helped to maintain elimination of the disease. In addition, experience with mass immunization of millions of women of childbearing age in the region has allowed for the follow-up of more than 33 000 women who were vaccinated without knowing they were

pregnant. About 3.6% of babies of women vaccinated early in their pregnancy showed positive results for rubella virus IgM antibodies, but none of them developed CRS abnormalities.

**Africa, Eastern Mediterranean, South-East Asia, and Western Pacific.** In 1996, an estimated 22 000 babies were born with CRS in Africa, along with about 46 000 in South-East Asia, and close to 13 000 in the Western Pacific (13). By 2012, very few countries in Africa and South-East Asia had introduced RCV. Therefore, the current burden of CRS in those two regions is thought to be similar to that estimated for 1996 (24). The Western Pacific region aimed to significantly accelerate efforts to reduce the prevalence of rubella and CRS (to < 1 case per 100 000) by 2015 (25, 26). In the Eastern Mediterranean region, 16 of 22 countries have introduced the rubella vaccine into their expanded program on immunization schedule and 13 have developed a national target for rubella and CRS elimination. The 13 countries achieved coverage of more than 90% with the first dose of RCV (RCV1) in 2012, as reported in 2013 (25).

### Vaccination programs

**Strategies.** Incorporating the rubella vaccine into routine childhood vaccination schedules is a cost-beneficial and cost-effective (27) means of preventing congenital rubella infection and CRS. Countries should only consider this strategy if they are able to achieve and maintain 80% or higher coverage with their regular childhood measles vaccination campaigns (22). Including an RCV in regular childhood measles vaccination campaigns that cover less than 80% of the child population could result in decreased rubella virus circulation, which could increase the average age of rubella infection for females from childhood to the childbearing years. Therefore, in cases where regular childhood measles vaccination coverage is less than 80%, to protect women of childbearing age from giving birth to babies with CRS, mass immunization of everyone < 40 years old with the measles-rubella (MR) vaccine is recommended (28).

Systematic review of rubella vaccination strategies implemented in the Americas found that a combination of the two types of mass vaccination programs (routine childhood vaccination and mass immunization of all males and females aged 5–39+ years) led to the interruption of rubella virus circulation, the elimination of endemic disease, and the prevention of CRS, in a shorter period of time than expected, compared with routine childhood vaccination alone or in combination with risk-reduction approaches for the adult population such as postpartum vaccination and screening programs for immunity (29). Nevertheless, other research showed that immunity screening combined with selective postpartum vaccination can significantly reduce both the number of susceptible women and the number who experience rubella infection during pregnancy (30, 31).

**Vaccine formulations, dosage, and schedules.** Rubella vaccines are available in monovalent formulations (“rubella vaccine”) and in combination with other vaccine viruses (“RCV”). One dose of either type of vaccine is recommended for persons  $\geq 12$  months old to prevent rubella. Follow-up studies indicate that one dose of rubella vaccine can provide long-lasting immunity and that an RCV provides safety from the infection (low susceptibility to rubella disease), with antibody levels decreasing over time (32). Despite these findings, most countries currently have a two-dose vaccine schedule (with the first dose administered at age 12–15 months and the second at age 3–5 years) (33) using an RCV—the combined measles-mumps-rubella (MMR) vaccine. This is a cost-effective strategy, given that 1) the clinical symptoms of rubella and measles are similar and 2) rubella and measles affect the same age groups.

### Rubella elimination

**Strategies.** Strategies for rubella elimination can be divided into those for: 1) countries that introduced an RCV more than 20 years ago in a routine childhood vaccination programs; 2) countries that have conducted a mass rubella immunization campaigns (targeting both males and females ages 5–39+ years); 3) countries that have conducted partial rubella immunization activities (by cohort, sex, risk group, or geographic area); and 4) countries that have not yet introduced an RCV in their childhood vaccination programs.

Other vaccination strategies (e.g., immunization of concentrated populations, institutional immunization programs, and door-to-door vaccination programs) can also be used depending on the target population, the characteristics of the department or district (with different geographic and socioeconomic areas) carrying out the rubella elimination campaign, and the phase of the campaign. Vaccination of concentrated populations (e.g., at schools or a workplace) should be based on census lists by target age group. Institutional vaccination programs should focus on women of childbearing age (e.g., hospital vaccination of women post-delivery or post-abortion). Door-to-door vaccinations could be used to cover vulnerable populations not reached by health services or fixed vaccination posts (33). For school-aged children, including vaccination as a school-entry requirement has proved to be an effective strategy for achieving and maintaining high vaccine coverage.

The formation of local committees for political, technical, and operational support seems important for improving the coordination and implementation of rubella elimination campaigns, and the creation of a broad partnership through outreach to many sectors of society (e.g., education, public safety, and faith-based groups; nongovernmental organizations (NGOs); industry and trade groups; community leaders; and professional associations and scientific societies) is essential. Likewise, working with government and international agencies, including WHO, provides

support throughout campaign planning and implementation. Finally, having experienced vaccination campaign supervisors, using graphs and activity timetables to monitor progress, and having rapid access to all available information may be helpful at the operational level, and innovative promotion strategies, including local participatory events, highly visible messages, and advertising, can help increase community awareness of the importance of preventing rubella and CRS (34, 35).

### Surveillance

Goals for rubella surveillance may differ according to country context. In countries where rubella is endemic, surveillance should focus on areas where the virus is circulating. In countries with vaccination programs for control and elimination of the virus, surveillance should include 1) investigation and characterization of sporadic cases and outbreaks and their chains of transmission; 2) rapid and appropriate public health response; 3) identification of populations or groups at risk; 4) determination of disease prevalence and incidence as well as transmission mechanisms; 5) identification of the geographic origin and genotype of the circulating viruses, and 6) the collection of data to better inform future priority-setting to achieve and maintain high levels of population immunity. Laboratory testing of rubella cases is another critical component of surveillance providing timely confirmation or rejection of suspected rubella cases, and determination of the genotypic characteristics of the circulating virus (36).

Routine surveillance for CRS should identify all infants less than one year old and determine and record infected pregnant women's case classification ("laboratory confirmed," "clinical symptoms," or "epidemiologically linked") and pregnancy outcome (e.g., miscarriage, termination, infant with CRS, etc.). Use of some method for predicting the number of CRS cases, such as the model used in Japan (37), may help enhance detection of this often under-reported syndrome.

**Public benefits.** The development and implementation of rubella elimination strategy has provided opportunities for improving access to and quality of care for those with congenital disabilities. For example, neonatal deafness programs created to strengthen CRS surveillance by allowing for early detection of hearing impairments in newborns help improve the quality of life for hearing-impaired children by providing new diagnostic technologies, educational interventions, and effective rehabilitation (38).

In addition, screening of all pregnant mothers with TORCH (toxoplasmosis, syphilis, rubella, cytomegalovirus, and congenital herpes infections) immunoglobulin titers, a practice taken for granted in many developed countries, should be enhanced (33).

### Conclusions

One single mass national immunization campaign targeting all men and women 5–39+ years old and incorporation of an RCV in routine childhood immunization programs, including regular vaccination campaigns for 12-month-olds, can, in "one stroke," eliminate rubella and CRS. However, importations of rubella viruses from other countries and regions through travel and migration are fairly common and can lead to outbreaks and even reestablish endemic transmission of the disease. Therefore, in addition to mass immunization, the following measures should be taken to help prevent rubella and CRS: 1) surveillance of the number of susceptible women of childbearing age, and the emergence of imported cases; 2) coverage of susceptible populations with "second-chance" ("catch-up") campaigns (vaccination of older children and adults who may have missed earlier immunization programs); 3) rapid and appropriate response to outbreaks (i.e., all sporadic illnesses clinically consistent with rubella thoroughly investigated and adequate specimens obtained for laboratory confirmation); 4) strengthening of CRS surveillance; 5) involvement of the private sector in awareness and vaccination campaigns; and 6) reduction of the number of false-positive laboratory test results.

**Conflicts of interest.** None.

---

### SINOPSIS

#### Síndrome de rubéola congénita: un motivo de preocupación

*El síndrome de rubéola congénita (SRC), una causa importante de defectos congénitos graves, sigue siendo un problema de salud pública en un número significativo de países. Por consiguiente, los expertos mundiales en salud promueven el uso de la vacunación antirrubéolica con el objetivo primario de prevenir el SRC. Aunque, durante el último decenio, la vacunación antirrubéolica administrada a gran escala ha reducido drásticamente o eliminado tanto el virus como el SRC en Europa y la Región de las Américas, muchos países de África, Asia Sudoriental, el Mediterráneo Oriental y el Pacífico Occidental aún no han incorporado ningún tipo de vacuna con componente antirrubéolico en su calendario de vacunaciones. Como resultado, y a consecuencia de los viajes y las migraciones, la rubéola se ha importado a países que habían eliminado eficazmente el virus, provocando brotes y el restablecimiento de la transmisión endémica. El objetivo de este estudio fue determinar los factores clave requeridos para la eliminación del SRC (reducción de la prevalencia, estrategias de vacunación y métodos de vigilancia) mediante la revisión de publicaciones aparecidas en PubMed sobre la rubéola y el SRC (revisiones sistemáticas, experiencias de países y documentos de posición de la Organización Mundial de la Salud y otras organizaciones intergubernamentales). Con base en los resultados de la revisión,*

y con objeto de eliminar la rubéola y el SRC en las zonas endémicas y reducir su reaparición en las zonas previamente libres de la enfermedad, todos los países deben llevar a cabo dos tipos de campañas de vacunación antirrubéolica masivas: 1) una única campaña de vacunación masiva a escala nacional dirigida a todos los hombres y mujeres de 5 a 39 años de edad (el límite superior de edad depende del año de introducción de la vacuna con componente antirrubéolico y de la epidemiología de la rubéola en el país), y 2) la incorporación de una vacuna con componente antirrubéolico en los programas sistemáticos de vacunación infantil, incluidas las campañas regulares de vacunación dirigidas a lactantes de 12 meses de edad y las campañas de seguimiento de las enfermedades exantemáticas. Además de las campañas de vacunación masiva contra la rubéola y los programas sistemáticos de vacunación infantil, se deben aplicar las siguientes medidas para ayudar a combatir la rubéola y el SRC:

1) la vigilancia de las mujeres en edad fecunda susceptibles, y de la aparición de casos importados; 2) la cobertura de las poblaciones vulnerables mediante campañas de "segunda oportunidad" ("puesta al día") (vacunación de niños mayores y adultos a los que no hubieran alcanzado los programas de vacunación anteriores); 3) la respuesta rápida ante los brotes; 4) el fortalecimiento de la vigilancia del SRC; 5) la participación del sector privado en las campañas de concientización y vacunación; y 6) la reducción del número de resultados de pruebas de laboratorio falsamente positivos.

**Palabras clave:** rubéola (sarampión alemán); síndrome de rubéola congénita; prevalencia; vacunación; África; Américas; Asia Sudoriental; Europa (continente); región mediterránea; islas del pacífico.

## REFERENCES

- Gillam S. The Jeanne Manery Fisher Memorial Lecture 1994. Molecular biology of rubella virus structural proteins. *Biochem Cell Biol.* 1994;72(9-10):349-56.
- Hobman T, Chanter J. Rubella virus. In: Knipe DM, Howley PM. *Fields virology*. 5th ed. Philadelphia: Wolters Kluwer; 2007. Pp. 1069-100.
- Cooper LZ. The burden of congenital rubella syndrome. In: de Quadros CA, editor. *Vaccines: preventing disease & protecting health*. Washington: Pan American Health Organization; 2004. Pp. 53-64.
- Cutts FT, 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. *Bull World Health Organ.* 1997;75(1):55-68.
- Dewan P, Gupta P. Burden of congenital rubella syndrome (CRS) in India: a systematic review. *Indian Pediatr.* 2012;49(5):377-99.
- Webber R. Pregnancy and infection. In: Webber R, editor. *Communicable diseases: a global perspective*. 4th ed. Cambridge, MA: CAB International; 2012. Pp. 278-90.
- Barrabeig I, Torner N, Martínez A, Carmona G, Ciruela P, Batalla J, et al. Results of the rubella elimination program in Catalonia (Spain), 2002-2011. *Hum Vaccin Immunother.* 2013;9(3):642-8.
- Council of State and Territorial Epidemiologists. Public health reporting and national notification for congenital rubella syndrome. Position statement 09-ID-61. Atlanta: The Council; 2009.
- Plotkin SA, Reef SE, Cooper LZ, Alford Jr CA. Rubella. In: Remington JS, Klein JO, Wilson CB, Nizet V, Maldonado YA, editors. *Infectious diseases of the fetus and newborn infant*. 7th ed. Philadelphia: Elsevier Saunders; 2011. Pp. 861-98.
- Miller E, Craddock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet.* 1982;2(8302):781-4.
- World Health Organization. Rubella vaccines: WHO position paper—recommendations. *Vaccine.* 2011;29(48):8767-8.
- Centers for Disease Control and Prevention (US). Rubella and congenital rubella syndrome control and elimination—global progress, 2000-2012. *MMWR Morb Mortal Wkly Rep.* 2013; 62(48):983-6.
- World Health Organization. Rubella vaccines: WHO position paper. *Wkly Epidemiol Rec.* 2011;86(29):301-16.
- Centers for Disease Control and Prevention (US). Progress toward control of rubella and prevention of congenital rubella syndrome—worldwide, 2009. *MMWR Morb Mortal Wkly Rep.* 2010;59(40):1307-10.
- World Health Organization. Eliminating measles and rubella and preventing congenital rubella. WHO European Region Strategic Plan 2005-2010. Geneva: WHO; 2005.
- Zimmerman L, Rogalska J, Wannemuehler KA, Haponiuk M, Kosek A, Pauch E, et al. Toward rubella elimination in Poland: need for supplemental immunization activities, enhanced surveillance, and further integration with measles elimination efforts. *J Infect Dis.* 2011;204 Suppl 1:S389-95.
- World Health Organization. Controlling rubella and preventing congenital rubella syndrome—global progress, 2009. *Wkly Epidemiol Rec.* 2010;85(42):413-8.
- Paradowska-Stankiewicz I, Czarkowski MP, Derrough T, Stefanoff P. Ongoing outbreak of rubella among young male adults in Poland: increased risk of congenital rubella infections. *Euro Surveill.* 2013;18(21). pii: 20485.
- Janta D, Stanescu A, Lupulescu E, Molnar G, Pistol A. Ongoing rubella outbreak among adolescents in Salaj, Romania, September 2011-January 2012. *Euro Surveill.* 2012;17(7). pii: 20089.
- Castillo-Solórzano C, Marsigli C, Bravo-Alcántara P, Flannery B, Ruiz Matus C, Tambini G, et al. Elimination of rubella and congenital rubella syndrome in the Americas. *J Infect Dis.* 2011;204 Suppl 2:S571-8.
- Pan American Health Organization. Plan of Action for the documentation and verification of measles, rubella, and congenital rubella syndrome elimination in the region of the Americas. Washington: PAHO; 2011. Available from: [http://www.paho.org/hq/index.php?option=com\\_docman&task=doc\\_view&gid=16739&Itemid=270&lang=en](http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&gid=16739&Itemid=270&lang=en)
- Centers for Disease Control and Prevention (US). Documentation and verification of measles, rubella and congenital rubella syndrome: elimination in the region of the Americas. United States national report, March 28, 2012. CDC Report: Elimination of Measles, Rubella, and CRS. Atlanta: CDC National Center for Immunization and Respiratory Disease; 2012. Available from: <http://www.cdc.gov/measles/downloads/report-elimination-measles-rubella-crs.pdf>
- McLean H, Redd S, Abernathy E, Icenogle J, Wallace G. Congenital rubella syndrome. In: Roush SW, Baldy LM, editors. *Manual for the surveillance for vaccine-preventable diseases*. 5th ed. Atlanta: Centers for Disease Control and Prevention; 2012. Available from: <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt15-crs.pdf>
- World Health Organization. Global measles and rubella strategic plan: 2012-2020. Geneva: WHO; 2012. Available from: <http://www.measles>

- rubellainitiative.org/wp-content/uploads/2013/06/Measles-Rubella-Strategic-Plan.pdf
25. World Health Organization. The Measles & Rubella Initiative: 2013 Annual Report. Geneva: WHO; 2014.
  26. World Health Organization, Regional Office for the Western Pacific, Expanded Programme on Immunization. Measles-Rubella Bulletin. Manila: WHO; 2015. Available from: <http://www.wpro.who.int/immunization/documents/mrbulletinvol9issue3.pdf?ua=1>
  27. Hinman AR, Irons B, Lewis M, Kandola K. Economic analyses of rubella and rubella vaccines: a global review. *Bull World Health Organ.* 2002;80(4):264–70.
  28. Andrus JK, de Quadros CA, Solórzano CC, Periago MR, Henderson DA. Measles and rubella eradication in the Americas. *Vaccine.* 2011;29 Suppl 4:D91–6.
  29. Mongua-Rodríguez N, Díaz-Ortega JL, García-García L, Piña-Pozas M, Ferreira-Guerrero E, Delgado-Sánchez G, et al. A systematic review of rubella vaccination strategies implemented in the Americas: impact on the incidence and seroprevalence rates of rubella and congenital rubella syndrome. *Vaccine.* 2013;31(17):2145–51.
  30. Griffiths PD, Baboonian C. Is post partum rubella vaccination worthwhile? *J Clin Pathol.* 1982;35(12):1340–4.
  31. Okuda M, Yamanaka M, Takahashi T, Ishikawa H, Endoh M, Hirahara F. Positive rates for rubella antibody in pregnant women and benefit of postpartum vaccination in a Japanese perinatal center. *J Obstet Gynaecol Res.* 2008;34(2):168–73.
  32. McLean HQ, Fiebelkorn AP, Temte JL, Wallace GS; Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013: summary recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-04):1–34.
  33. Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L. Measles, mumps, and rubella—vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 1998;47(RR-8):1–57.
  34. Urquijo L, Pastor D, Velandia MP, Vicari AS. Rubella and congenital rubella syndrome elimination activities: Colombia, 2005–2006. *J Infect Dis.* 2011;204 Suppl 2:S603–7.
  35. Andrus JK, de Quadros CA. Perspectives on the role of surveillance in eliminating rubella and congenital rubella syndrome in the Americas. *Expert Rev Vaccines.* 2013;12(9):989–93.
  36. Bispo de Filippis AM, Icenogle J, Matus CR, Andrus JK. Enhanced laboratory surveillance for the elimination of rubella and congenital rubella syndrome in the Americas. *J Infect Dis.* 2011;204 Suppl 2:S652–8.
  37. Ohkusa Y, Sugawara T, Arai S, Satoh H, Okuno H, Tanaki-Taya K, et al. Short-term prediction of the incidence of congenital rubella syndrome. *PLoS Curr.* 2014;6. pii: ecurrents.outbreaks.8c74272f4348781c5d01c81e6150c2f7. doi: 10.1371/currents.outbreaks.8c74272f4348781c5d01c81e6150c2f7.
  38. Morice A, Avila-Aguero ML, Salas-Peraza D, Soriano A, Castillo-Solórzano C. Approach to verify the status of measles, rubella, and congenital rubella syndrome elimination in Costa Rica. *J Infect Dis.* 2011;204 Suppl 2:S690–7.

---

Manuscript received on 1 October 2014. Revised version accepted for publication on 17 March 2015.