Situation of Rubella in Spain in the Elimination Phase. Rubella and Congenital Rubella Syndrome, 1997-2007

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Summary: *Objective*: To analyze the situation and evolution of rubella and congenital rubella syndrome in Spain and to evaluate the objective of elimination proposed by the World Health Organization for the European Region.

Methods: Analysis of the evolution of rubella incidence and vaccination coverages (l980 and 2007). Morbidity data were obtained from the National Epidemiological Surveillance Network and mortality and population data from the National Institute of Statistics.

Results: In 1979, a policy of selective rubella vaccination was introduced in Spain, targeting 11-year-old girls. In 1981, immunisation with the measles-mumps-rubella vaccine was introduced, at 15 months of age and a second dose was introduced in 1995.

Vaccination coverages since 1999 exceed 95% for the first dose and 90% for the second. The incidence of rubella has fallen drastically to < 1/100,000 since 2000 in all regions. Only small outbreaks or clusters have been detected, except for one large outbreak in Madrid that affected young adult males and fertile women from countries with low vaccination coverages. Since 1997, 13 cases of congenital rubella syndrome have been detected.

Conclusions: The situation in Spain favours the elimination of rubella. However, pockets of susceptible subjects remain, mainly young adult males and immigrants, who have increased substantially in numbers in the last decade. Fertile women with high birth rates from countries with a high rubella incidence have a high risk of congenital rubella syndrome.

Keywords: Rubella, congenital rubella syndrome, rubella susceptibility, elimination, congenital infection, immunopreventable diseases.

INTRODUCTION

Rubella is a mild viral illness which is less contagious than measles [1] and is characterized by mild febrile maculopapular rash that is benign in children and causes arthralgia and, less frequently, arthritis, in adults. Between 25 and 50% of infections are asymptomatic. Although rare, complications such as thrombocytopenia, encephalitis, Guillain-Barre syndrome, myocarditis and pericarditis may occur in adults [2]. The principal health problem is the teratogenic effects of congenital rubella syndrome (CRS). When a pregnant woman is infected with rubella virus, there is a 90% chance of passing the virus on to the fetus, which can lead to miscarriage, fetal death or the birth of an infant with CRS. As many of 90% of newborns whose mothers were infected during the first 11 weeks of pregnancy may be affected and up to 20% when infection occurs during the first 20 weeks [3]. Deafness is the most common defect, but CRS also cause defects in the eyes, heart, and brain. An estimated >100,000 cases of CRS occur annually in developing countries [2-5].

Measles and rubella vaccines can induce long term immunity with an effectiveness of 90–95%. Interrupting the indigenous transmission of measles requires maintaining very low levels of susceptibility throughout the population (<5%). CRS can be prevented by ensuring women of childbearing age are protected both through vaccination and by preventing their exposure to indigenously circulating rubella virus. A single dose of rubella vaccine at 12 months of age or older, which confers immunity in 95% or more of recipients, should be sufficient [6].

The eradication of rubella and CRS is currently not a major global public health priority, because other diseases such as poliomyelitis and measles have historically resulted in greater morbidity and mortality. However, rubella eradication should be possible, since infection is limited to humans, prolonged shedding is limited to children with CRS, and vaccine efficacy is high [6].

The Health For All Policy Framework [7], approved by the WHO Regional Committee for Europe in 1998, identi-

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fied targets for nine vaccine-preventable diseases, including measles elimination by 2007 and control of CRS (<1 case per 100,000 live births by 2010) [7]. Strategic plans for measles elimination and the control of congenital rubella infection in the WHO European Region 2003-2005 [8] were developed to meet these objectives. In 2005, given that most member states had incorporated a combined measles-rubella (MR) vaccine into the vaccination schedule, the WHO Regional Committee for Europe approved the inclusion of rubella elimination into the strategic plan for 2005-2010, considering that rubella elimination will be feasible within the framework of the measles elimination strategy [6, 9, 10]. Member states were urged to give high priority to achieving measles and rubella targets by 2010, mindful that there are high-risk and vulnerable populations within the European Region that still lack adequate immunization coverage because of limited access to primary health care services for geographical, cultural, ethnic or socioeconomic reasons, as well as unfounded mistrust of vaccinations.

The main key strategies to achieve this target are: 1) to achieve and maintain high vaccination coverages within childhood immunization programs (>=95 % with two doses of measles and at least one dose of rubella vaccines) and target susceptible populations, including women of childbearing age, ensuring a low level of susceptibility to rubella in this female population (<=5%), and 2) to improve rubella and CRS surveillance, increasing sensitivity and specificity. In the elimination phase, when disease incidence approaches 1 per 100,000, surveillance needs to be of sufficient quality in sensitivity and specificity to detect clusters and sporadic cases, with rigorous epidemiological investigation and laboratory confirmation, ensuring the capacity of laboratories to investigate >=80% of all suspected measles and rubella cases and characterize circulating viruses [6].

Member states should all assess the capacity of their surveillance to ensure it is of sufficient quality to monitor, measure and report and communicate effectively, in a timely manner, to enable appropriate public health action and reach the target objective [6].

In 1979, a policy of selective rubella vaccination was implemented in Spain, targeting 11-year-old girls. In 1981, immunisation with the measles-mumps-rubella (MMR) vaccine was introduced, and the age of administration was moved back to 15 months. In 1995, a second dose of MMR was introduced for both sexes at 11 years of age, substituting the rubella vaccine in girls, and in 1999 the age of administration of this second dose was moved to 3-6 years, with vaccination of children aged 11-13 years who had not received the second dose before the age of 6 years being maintained since 1999. In the first years after introduction of the vaccine coverages were low but they increased progressively to reach 80% by 1986; since 1999 coverages exceed 95% for the first dose and 90% for the second.

A National Serosurvey in 1996, targeting the 2-39 years age group (born between 1955 and 1994) showed a prevalence of rubella antibodies of 93.8% in the general population and > 96% in women. In males, only the 2-5 years age group (born between 1992 and 1994) and the 30-39 years age group (born before 1966) had a prevalence >95%. The lowest prevalence was observed in men born between 1967 and 1982 (86%-93%) [11, 12].

The measles elimination plan was introduced in 2001 in Spain in the context of high MMR vaccination coverages, low disease incidence and sufficient technical capability to establish the required surveillance system. Surveillance is based on the National Epidemiological Surveillance Network (RENAVE), coordinated by the National Epidemiology Centre, which is well-established in all 19 Autonomous Regions (AR) and includes a network of reference laboratories, coordinated by the National Microbiology Centre with the capacity to confirm cases and characterize the viruses detected [13].

Systematic annual evaluations of the measles elimination plan have verified the quality of the surveillance system, reaching the quality standards (sensitivity, timeliness of the investigation and laboratory diagnosis) established by the WHO for almost all indicators [14].

The plan for the elimination of rubella in Spain was approved in this context in 2007 and was introduced in 2008, with a specific surveillance protocol with the same strategy established for measles elimination [15].

The objective of this study is to analyze the epidemiological situation and evolution of rubella and CRS (incidence, severity and mortality, risk populations) in Spain and to evaluate the possibility of achieving elimination.

MATERIAL AND METHODS

Incident Cases

Data Sources: Data Base of Reportable Diseases of the RENAVE System

Incident cases of rubella reported weekly from 1982 (introduction of rubella surveillance in Spain) to 2007. Since 1997, reports of cases of rubella contain individualized information (sex, age, vaccination status and final classification of the case). Cases of CRS are reported annually with individualized information [16] and CRS surveillance is complemented by active search for CRS cases in the Minimum Basic Data Set (MBDS) of hospital admissions, Ministry of Health and Social Policy.

Mortality data were obtained from the National Death Register, National Institute of Statistics (NIS).

Population data were obtained from the NIS. Incidence rates were calculated according to census data and the demographic distribution by sex, age and country of origin were calculated using census data and municipal voting registers.

The annual rate of live births, used to calculate the incidence of CRS and the proportion of births attributable to foreign mothers was obtained from the Natural Population Movement register (NIS).

RESULTS

Rubella Incidence

The mean annual disease incidence per 100,000 inhabitants prior to introduction of the MMR vaccine, based on cases reported to the surveillance system, was 430 cases of measles and 440 cases of rubella. By 2000, the annual reported incidence per 100,000 had fallen to 0.4 for measles and 0.85 for rubella. Since then, this falling trend has continued, with the detection of isolated cases and small outbreaks

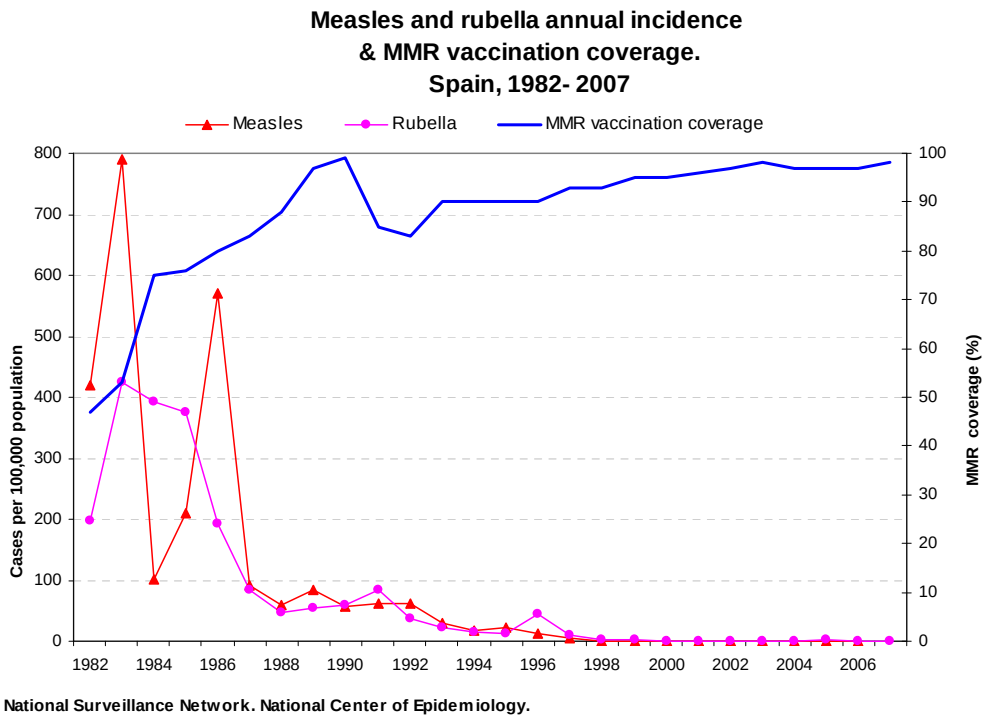

Fig. (1). Measles and rubella annual incidence and MMWR vaccination coverage, Spain 1982-2007.

or clusters, except for 2005 when there was a large rubella outbreak in Madrid [17] that raised the national incidence to 1.35 per 100,000. Since 2005, the incidence has continued to fall and in 2007 was 0.15 cases per 100,000 (Fig. **1**).

The falling incidence of rubella was evident in all ARs. Three regions have maintained rates < 1 per 100,000 since 1997 (Basque Country, Catalonia and Cantabria) and all 17 ARs (except Madrid in 2005) have maintained an incidence lower than or very close to 1 per 100,000 since 2001. Only the autonomous cities of Ceuta and Melilla (Spanish cities located in North Africa with a population of 71,034 and 65,540, respectively, population census 2001) have had higher incidences in some years (annual mean incidence 2001-2007: 4.6 per 100,000 population). The highest incidences in 2007 occurred in Ceuta (1.34 per 100,000) and the Canary Islands (1.14 per 100,000).

Since 2000, three significant rubella outbreaks have occurred, the first in Madrid in 2003 with 19 cases, of whom 14 were fertile women of Latin American origin [18]. The second and largest outbreak occurred in Madrid in 2005 [17] and affected 476 people, mostly non-vaccinated young adults aged 20-29 years; 58% were of foreign, mainly Latin American, origin and 43% were female, of which 92% were of childbearing age. Immigrants made up 39% of male patients and 84% of female patients. Thirty-three percent of cases were in immigrant women of childbearing age compared with 6% in Spanish women of childbearing age. Only 5% of patients recalled being vaccinated against rubella. Regional health services reported three voluntary abortions due to the risk of CRS and four associated cases of CRS affecting newborns of immigrant women. In 2005, an outbreak occurred in Catalonia that affected 8 people, all non-vaccinated fertile women of Brazilian nationality [19].

Fig. (**2**) shows the distribution by age group and sex of the 746 confirmed cases with information individualized reported since 1997: 84.3% of cases were in young people and young adults: 52.3% were males aged 15-39 years and 32% females in the same age group, 14% were aged <14 years and 2% >39 years.

Incidence of CRS

From January 1997 to December 2007, 13 cases of CRS, all of them laboratory confirmed, have been detected in Spain: 1997: three cases; 1998: two cases; 1999: one case; 2003: one case; 2004: one case; 2005: five cases (four associated with the Madrid rubella outbreak). No cases have been detected since 2005 [20].

Eight cases were reported to the National Surveillance Network according to protocol and the other five were detected by active search in hospital registries.

Six cases of CRS were in babies born to foreign women from the Philippines (one case in 1997), Africa (one case in 1999 and another in 2005) and Latin America (three cases in 2005). Three cases of CRS were in children of Spanish women (born in 1998, 2003 and 2005, respectively); in 4 cases the maternal nationality was unknown (2 cases in 1997, 1 in 1998 and another in 2004). These mothers did not attend pregnancy check ups and the diagnosis of CRS was unexpected [20].

CRS incidence from 1997 to 2004 in Spain ranged from 0 in 2002 to 0.22 per 100,000 live births in 2004. In 2005 CRS incidence was 1.07 per 100,000 live births [20].

Risk Population

Data from the 1996 seroprevalence survey showed the existence of a pocket of susceptible subjects in people born between 1967 and 1982 (7%-14%) [11]. Women of all ages

had a susceptibility of < 5%. However, between 1998 and 2007 there has been a large increase in immigration to Spain, mainly of young people and young adults. In 1998, 637,085 people (1.6% of the total resident population) were foreign born and in 2007 the figure was 4,519,534 people (10.0% of the total population) (Fig. **3**).

In 2007, 70% of foreigners resident in Spain were aged 15-49 years; 12.0% of men and 10.5% of women were foreign born.

Foreign residents came from Europe (i.e. 41 % with 54% from Western Europe and 46% from Eastern Europe), Latin America (34.3%), Africa (17.9%) and Asia (4.9%) (Table **1**). Morocco was the country with the highest percentage susceptibility(13.6%).

In 1997, 13,545 (3.7%) of total births in Spain (368,361) were in foreign-born mothers compared to 16.6% (79,985) of total births (481,295) in 2007.

In 2007 38.7% of foreign-born mothers giving birth in Spain were Latin American, 27.6% African, 27.0% European and 6% Asian (Table **1**).

DISCUSSION AND CONCLUSIONS

The current epidemiological situation of rubella in Spain favours the achievement of the proposed WHO objectives. High national and regional levels of paediatric vaccination with two doses of MMR have been maintained and rubella incidence remains < 1 case per 100,000 inhabitants, with the occurrence of small clusters or local outbreaks indicating the practical absence of indigenous viral circulation.

Rubella susceptibility in fertile women was < 5% in the 1996 National Seroprevalence Survey, and this level has been maintained and has probably fallen due to the high vaccination coverages achieved.

The technological quality for quality surveillance in the elimination phase has been demonstrated by the measles elimination plan.

However, pockets of susceptible subjects remain in young adult Spaniards, immigrants from countries without or with insufficient rubella vaccination programmes, of whom a large proportion are fertile women, and were those most-affected in the most-recent outbreaks. The high susceptibility to rubella in these groups has been studied in Catalonia [21] and other countries [22, 23].

For these reasons, there is a risk of outbreaks due to imported cases in the susceptible population of young males and fertile women, such as the one that occurred in Madrid in 2005, with subsequent risk of CRS, particularly in women who have difficulties in accessing prenatal healthcare.

Given this situation, surveillance and vaccination measures should be optimized, especially in foreign-born fertile women and in the potentially-susceptible population namely males born between 1967 and 1982, immigrants and adopted

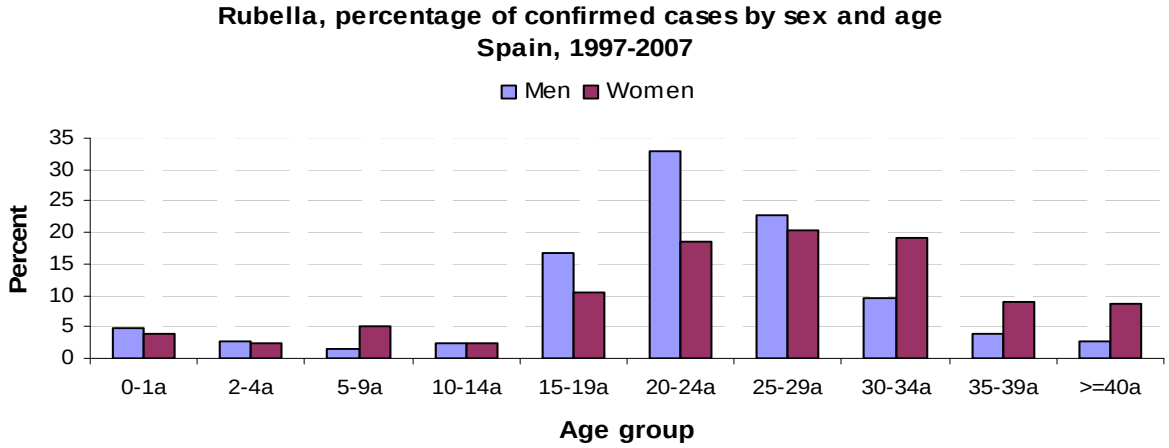

Fig. (2). Confirmed cases of rubella according to sex and age, Spain 1997-2007.

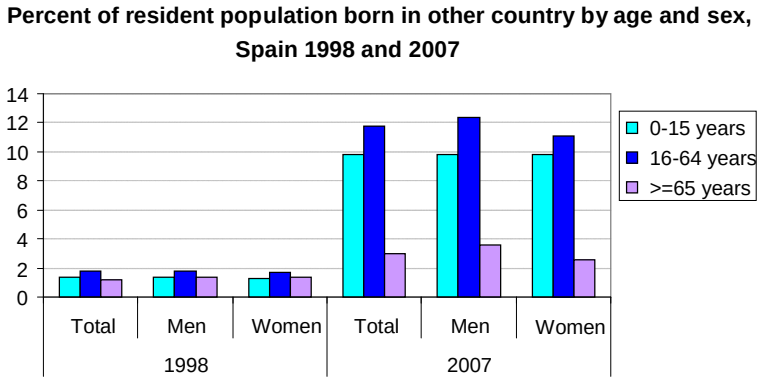

Fig. (3). Percentage of foreign-born residents according to age and sex. Spain 1998 and 2007.

Table 1. Foreign-Born Residents and Births to Foreign Mothers According to Region of Origin. Spain 2007

	Distribution of Foreign-Born Residents by Region of Origin			Percent of Births to Foreign Mother
Year 2007				
	Total	**Men**	**Women**	
Latin America	34.3	29.4	39.7	38.8
Europe	41.9	41.5	42.5	27.1
Africa	17.8	22.4	12.7	27.7
Asia	4.9	5.7	3.9	6.2
Other	1.1	1.0	1.2	0.2

Source: National Institute of Statistics.

children from countries with defective vaccination programmes and non-vaccinated travellers to endemic regions. Among other measures, vaccination with one dose of MMR of all potentially susceptible people accessing health care services is recommended.

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