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Measles Epidemiology in Spain after Introduction of the National Indigenous Measles Elimination Plan

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Abstract: The Action Plan for Measles Elimination in Spain was introduced in 2001. This work analyzes the incidence, outbreaks, complications, admissions, disease mortality and vaccination coverages of measles.

Since 2001, measles incidence in Spain has been <1/100,000 inhabitants, with 1384 confirmed cases, mostly in infants aged <16 months (32%) and people aged >20 years (43%). Eight genotypes have been identified (47% of European origin). Hospitalization was required in 18% of cases and the most common complication was otitis. One death has been recorded.

Sustained high vaccination coverages and good epidemiological surveillance may make elimination of the indigenous transmission of measles possible in the near future but recent outbreaks show the need to continue and intensify measles control activities.

Keywords: Elimination plan, epidemiological surveillance, incidence, measles, outbreaks, vaccination coverage.

INTRODUCTION

Measles is a highly-contagious acute viral disease caused by the measles virus, an RNA virus of the genus *Morbillivirus* of the *Paramyxoviridae* family, which was characterized in 1954 by Enders and Peebles [1]: 23 different genotypes are known.

Measles is characterized by rash, fever, and cough, coryza or conjuntivitis and is transmitted by pharyngeal or nasal secretions, normally from four days before to four days after the onset of rash. The incubation period is normally 10-14 days and the possible complications include otitis media, laryngotracheobronchitis, pneumonia, diarrhoea, encephalitis and secondary bacterial infections. Children aged < 5 years who are living in poor conditions or are malnourished, and adults or patients with immune deficiencies have a greater risk of severe complications [2]. Subacute sclerosing panencephalitis (SSPE), a degenerative neurological disease that occurs several years after measles infection is an associated complication [1].

Measles has been a reportable disease in Spain since 1901, with numerical and weekly report of suspected cases [3]; since the introduction of the National Epidemiological Surveillance Network (RENAVE) in 1997, an annual report with the individual characteristics of age, sex, vaccination status, type of case, week of report and geographic area has also been required [4]. In 2001, measles surveillance in Spain was intensified, with the introduction of the Action Plan for Measles Elimination in Spain (APMES) in accordance with the objectives of the World Health Organization (WHO) which, in 1998, among the objectives of "Health for all in the 21st century" contemplated the elimination of measles in the European Region by 2007 [5] urging European countries to establish national indigenous measles elimination plans [6]. In 2003, after reviewing the situation of measles in Europe, the WHO European Region postponed this date to 2010 and later incorporated the objectives of control of congenital rubella and the elimination of endemic rubella in the region by 2010 to the plan [7, 8].

The fundamental objective of APMES is to collect and analyze the specific nature of measles epidemiology in Spain in order to facilitate continuous adaptation of measles elimination strategies, which include intensification of epidemiological surveillance, reinforcement of the role of the laboratory in measles surveillance and definition of vaccination strategies to accelerate measles control and maintain elimination [9].

In Spain, health care is devolved to the Autonomous Regions (AR), whose responsibilities include the APMES objectives of reaching and maintaining vaccination coverages > 95% for both doses of vaccine and reinforcing epidemiological surveillance to facilitate rapid detection of community

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circulation of the measles virus. The objective of APMES is involves the reporting and investigation of suspected cases, laboratory confirmation, urgent detection of outbreaks and the adoption of correct control measures, and permanent evaluation to control the quality of the surveillance system, reflected by the annual measles surveillance reports [9]. In 2003, the WHO published guidelines for the surveillance of measles and congenital rubella syndrome, and in 2004 it established controls on the exhaustiveness and timeliness of monthly reports of measles cases to the WHO as a measure for evaluating the plan [7]. Regionally, the exhaustiveness threshold is considered to be achieved when at least 80% of monthly reports are received by the WHO and the timeliness threshold when 80% of monthly reports are received at least before day 25 of the month following the report.

Measles vaccination began in Spain in 1978 with the univalent vaccine (Schwartz strain) at 9 months of age. This was replaced in 1981 by the measles-mumps-rubella (MMR) vaccine at 15 months of age. In 1995, the Interterritorial Council of the National Health System incorporated a second dose of MMR at 11-13 years, although more than half the ARs had already introduced it [10]. In 1996, a National Seroepidemiological Survey showed that the seroprevalence of detectable measles antibodies was > 95% in all age groups except the 6-9 years age group (90.8%) and 15-19 years age group (94 %). In people aged > 20 years the prevalence was > 98%, compatible with natural infection before the introduction of vaccination [11]. For these reasons, in 1999 it was decided to advance administration of the second dose to 3-6 years to eliminate the pocket of 5% of susceptible subjects at 6-9 years [10].

Vaccination coverages rose slowly after 1982 and have been maintained at 90% since 1993 and > 95% since 1999 [10].

In the pre-vaccination era, measles incidence in Spain was very high, with an accumulated annual mean incidence until 1977 of 429 per 100,000 (150,000 cases per year) (Fig. **1**). In 1982, there was a significant increase in cases corresponding to the incorporation of NHS physicians to the compulsory reporting system as well as to the low coverages achieved in the first years of vaccination. In 1986, the number of cases increased again. After consolidation of the infant vaccination programme and the maintenance of high vaccination coverages, measles incidence has fallen greatly in all Spanish ARs and provinces. This reduction has continued in recent years, with the lowest annual incidence being reached in 2005 (0.05 per 100,000 inhabitants) (Table **1**) [12].

The objective of this study is to analyze the situation of measles in Spain after the attainment and maintenance of high vaccination coverages and the introduction of APMES, which mandates exhaustive surveillance of each suspected case.

MATERIAL AND METHODS

Data sources: RENAVE data base of reportable diseases in Spain, which has received data on the variables included in APMES since 2001. Study period 2001-2008. The definition of a suspected case "maculopapular rash, high fever, and cough or coryza or conjuntivitis" is sensitive enough to guarantee very few cases are not detected. Suspected cases are classified as: confirmed by laboratory or epidemiological link, confirmed by compatible clinical manifestations, and discarded.

Confirmed cases are classified according to the origin of the infection as indigenous or imported (between 7 and 18 days abroad or contact with somebody with these conditions during the incubation period). Information is also collected on the clinical tests carried out, the vaccination status of cases, complications, hospital admission and disease evolution and the study of contacts (persons in contact with a confirmed case of measles during the four days before and four days after rash onset in the case). Investigation of contacts allows detection of immune subjects (due to natural infection or correct immunization) and susceptible subjects (who should receive the same tests as cases, with the corresponding control measures, isolation and/or immunization. When no new cases are detected after investigation of susceptible contacts, the case is classified as an *isolated case.*

Biological specimens should be collected from all suspected cases of measles to confirm or discard the diagnosis. The diagnostic criterion of choice is the detection of measles-specific IgM antibodies in sera but samples of urine or oropharyngeal/nasopharyngeal exudate should also be col-

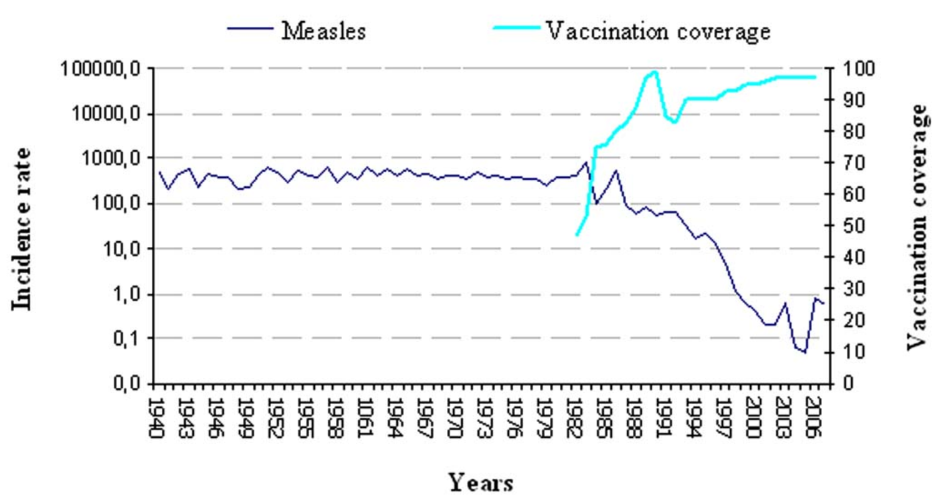

Fig. (1). Measles incidence per 100,000 population in Spain 1940-2008 and vaccination coverages 1982-2008.

Table 1. Measles Incidence and Classification of Cases. Spain 2001 - 2008

Year	Total Suspected Cases	Confirmed (% Suspected)	Compatible (% Suspected)	Discarded (% Suspected)	Incidence (Confirmed and Compatible*100,000 Inhab)	Vaccination Coverages (%)
2001	136	36 (26%)	17 (13%)	83 (61%)	0.13	96.5
2002	212	64 (30%)	15 (7%)	133 (63%)	0.16	97.2
2003	518	243 (47%)	12 (2%)	263 (51%)	0.62	97.7
2004	120	25 (21%)	1 (1%)	94 (78%)	0.06	97.3
2005	100	20 (20%)	2 (2%)	78 (78%)	0.05	96.8
2006	545	362 (66%)	15 (3%)	168 (31%)	0.83	96.9
2007	483	255 (53%)	12 (2%)	215 (45%)	0.59	97.1
2008	475	229 (48%)	70 (15%)	176 (37%)	0.67	97.8

lected in order to isolate the virus. Study of the urine sample and/or pharyngeal exudate allows the virus genotype and its sequence, epidemiological markers important for tracing the transmission of outbreaks between countries, to be determined.

Incidence rates are calculated according to the 2001 Spanish census and projections made by the National Institute of Statistics (NIS) [13].

Hospitalizations since 2001 are analysed using the RENAVE database included in APMES and the complications of measles come from reported cases. In addition, hospitalizations are analysed using the Minimum Basic Data Set (CMBD) of hospital discharges from 2001 to 2007, (the last year for which national data are available). The CMBD was created in 1992 by the Ministry of Health and records hospital discharges by means of 22 variables. Diagnoses are coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The main diagnosis is coded in the CMBD as the condition shown by tests to be the cause of hospital admission, even when complications or other disorders (classified as secondary diagnoses) appear during the hospital stay [14].

The variables collected for each case are: date of birth, sex, place of residence, date of admission, date of discharge, type of discharge (1 - Home; 2 - Transfer to Hospital; 3 - Voluntary; 4 - Death; 5 - Transfer to social health centre; 6 - Unknown), main diagnosis, other diagnoses.

The ICD-9 codes corresponding to measles are: 055 measles, 055.0- post-measles encephalitis, 055.1- post-measles pneumonia, 055.2- post-measles otitis media, 055.7-measles with other specified complications, 055.71 - keratoconjunctivitis due to measles, 055.79 - other complications of measles, 055.8-measles with other non-specified complications, 055.9-measles without complications.

Only cases with a principal discharge diagnosis of measles or its complications are analyzed.

Spanish mortality due to measles is obtained from the NIS, which uses the ICD-10 [13]. The codes for measles are B05 (B05.0, B05.1, B05.2, B05.3, B05.4, B05.8 and B05.9). Measles mortality since 2001 is also studied using the RENAVE database of cases reported to APMES.

Data on global measles mortality are available from 1901 to 1950 (for age groups only), since 1980 (for age and sex) and since 1990 (age, sex and geographic distribution).

APMES evaluation indicators are at least 1 suspected case of measles studied per 100,000 inhabitants in 80% of AR and laboratory tests in > 80% of suspected cases and investigation of transmission chains and genotypes of circulating viruses.

The WHO criteria for measles elimination are interruption of transmission, variability in circulating genotypes and reproduction rate or effective reproductive number, R<1 [15]. Interruption of transmission and virus circulation is defined as the absence of cases for a time greater than the maximum incubation period of the disease in all of Spain.

RESULTS

Measles incidence in Spain has been <10 per 100,000 inhabitants since 1997, continuing the progressive reduction that began in 1988 resulting from high vaccination coverage. Since 2001, this reduction has continued, interrupted by an increase in 2003 due to an outbreak in Andalusia, [16] and in 2006-2008 when 12 outbreaks in seven ARs were detected in accordance with events in other WHO European Region countries [17-21]. This increased incidence has resulted in a modification of the downward trend since 2001, and in 2006 the incidence was 0.86 confirmed cases per 100,000 inhabitants, the highest since the introduction of APMES (Table **1**).

From 2001 to 2008, 2,559 suspected cases were reported through APMES, of which 1,384 were confirmed; 1,241 by laboratory or epidemiological link (48.3% female) with 143 (42.3% female) classified as compatible cases. Measles virus was not found in 45.8% of suspected cases (1,175, 43.3% female) and the presence of other diseases was confirmed in 10.3% of cases.

The distribution of confirmed and compatible cases by age group showed that the most-affected groups were those not covered by vaccination: children aged <16 months (32% of confirmed cases) and adults aged > 20 years (43%). This pattern was more evident during the last three years of the study. The age distribution was similar for both sexes in confirmed, suspected and discarded cases (Fig. **2**).

a

b

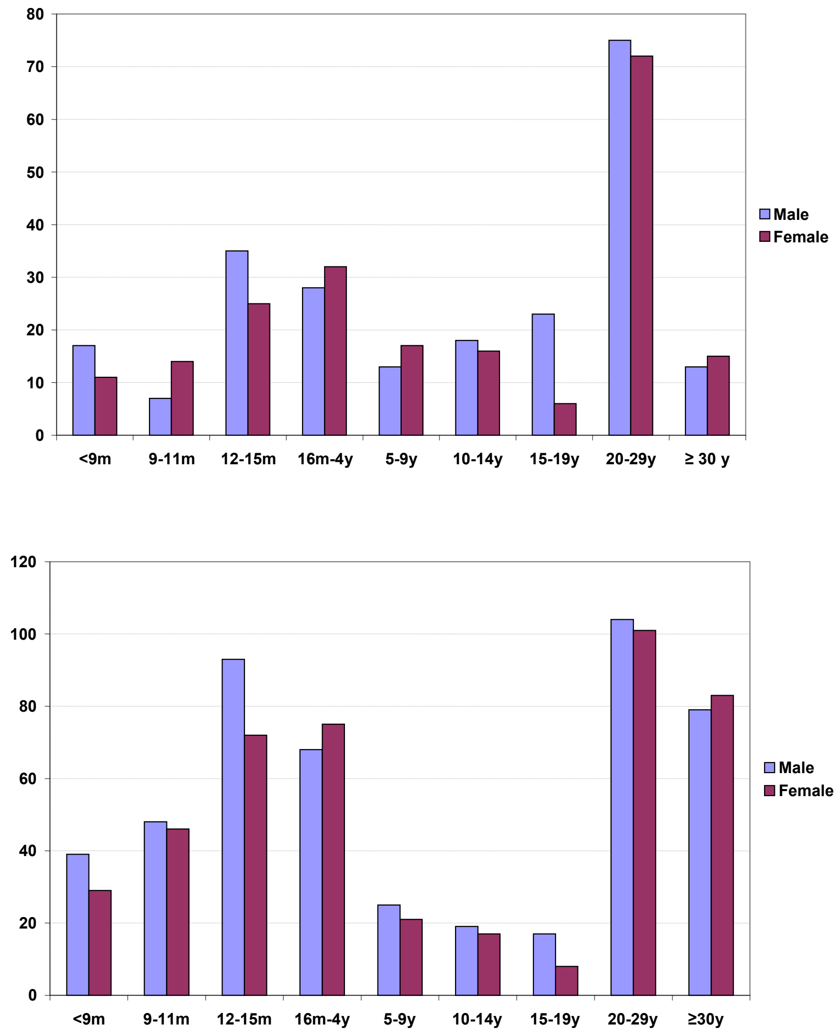

Fig. (2). Distribution of confirmed and discarded cases of measles according to age and sex. Spain 2001-2005 (**a**) and 2006-2008 (**b**).

From the first year of APMES there was a progressive reduction in avoidable cases (cases that should have been vaccinated due to their age and were not). Avoidable cases are those occurring in people aged 16 months -14 years of age with no vaccine dose and 5-14 years with a single dose, due to the fact that high vaccination coverages were not reached in Spain until the 1990s. However, in 2005, the year with the lowest measles incidence in Spain (0.05 per 100,000 inhabitants corresponding to 22 confirmed cases) 50% of cases might have been avoided (Table **2**).

A total of 10.6% (147 cases) were classified as isolated cases, with a source of infection outside Spain having been identified in 23% (34 cases).

Table **3** shows reported measles outbreaks in Spain since the introduction of APMES summarized according to AR, origin of the infection and genotype isolated, number of cases according to sex and age group, and the length and type of transmission of the outbreak. The longest outbreaks occurred in 2006 in Catalonia and 2008 [19] in Andalusia (11 months) [20] and Madrid (7 months), [18] and in 2003 in Andalusia (6 months) [16].

In recent years, the greatest number of imported cases have come from other European Region countries, accounting for 67% of cases with a known source of infection in 2005 and 81% in 2006. However, in 2007 no case was imported, because all cases belonged to an outbreak of imported origin during the previous year; in 2008, 80% of cases with a known source of origin were imported from other European countries (Table **4**).

Since the introduction of APMES, some type of sample has been collected in 2,268 suspected cases (88%). Samples of urine or exudate were collected in 60% of suspected cases.

Analysis of urine samples collected since 2001, enabled 8 disease-causing genotypes, and thus the origin of the outbreaks, to be identified (Fig. **3**).

All discarded cases of measles should be screened for rubella. However, since the introduction of APMES, rubella screening was made in only 20% of discarded cases in 2002, 70% in 2003, 42.7% in 2004, 66.6% in 2005, 47.6% in 2006, 78% in 2007 and 12% in 2008; 58 cases of rubella were confirmed in the 1,175 discarded cases of measles. Twenty cases

Table 2. Cases of Measles According to Year, Age Group and Vaccination Status. Spain 2001-2008

2001	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	9	3	3	0	2	5	0	22
1 dose	0	3	0	0	1	2	0	6
2 doses	0	0	0	0	0	0	0	0
N/A	0	0	1	0	1	6	0	8
Total	9	6	4	0	4	13	0	36
% by age	25%	17%	11%	0%	11%	36%	0%	100%
% avoidable								22%
2002	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	12	6	2	5	3	18	1	47
1 dose	0	7	5	0	1	3	0	16
2 doses	0	0	2	1	0	1	1	5
N/A	1	2	0	0	2	5	1	11
Total	13	15	9	6	6	27	3	79
% by age	16.5%	19.0%	11.4%	7.6%	7.6%	34.2%	3.8%	100.0%
% avoidable								20%
2003	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	51	12	4	9	5	24	4	109
1 dose	5	13	2	4	2	19	5	50
2 doses			2	2	1	1		6
N/A	9		3	8	11	50	9	90
Total	65	25	11	23	19	94	18	255
% by age	25.49%	9.80%	4.31%	9.02%	7.45%	36.86%	7.06%	100.00%
% avoidable								12%
2004	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	8	1	1			5	3	18
1 dose		2				1		2
2 doses								
N/A						2	2	4
Total	8	3	1			8	5	25
% by age	32.0%	12.0%	4.0%	0.0%	0.0%	32.0%	20.0%	100.0%
% avoidable								8%
2005	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	1	4	4	3				12
1 dose		4					1	5
2 doses								0
N/A	1			1		3		5
Total	2	8	4	4		3	1	22
% by age	9.1%	3.4%	18.2%	18.2%	0.0%	13.6%	4.5%	100.0%
% avoidable								50%

Table 2. Cont….

2006	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	143	30	11	8	2	34	36	264
1 dose	12	25	2		1	14	2	56
2 doses			2	4		3		9
N/A	1	4	1		5	25	13	49
Total	156	59	16	12	8	76	51	378
% by age	41.3%	15.6%	4.2%	3.2%	2.1%	20.1%	13.5%	100.0%
% avoidable								14%
2007	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	104	21	6	3	1	34	59	228
1 dose	1	17				7	1	26
2 doses			2	4				6
N/A		1				1	5	7
Total	105	39	8	7	1	42	65	267
% by age	39.3%	14.6%	3.0%	2.6%	0.4%	15.7%	24.3%%	100.0%
% avoidable								12%
2008	**< 16 Months**	**16 Months - 4 Years**	**5-9 Years**	**10-14 Years**	**15-19 Years**	**20-29 Years**	**>30 Years**	**General Total**
0 dose	50	13	8	4	4	27	13	119
1 dose	9	11		2		6	2	30
2 doses				1	1			2
N/A	7	21	14	10	11	54	31	148
Total	66	45	22	17	16	87	46	299
% by age	24.7%	16.9%	8.2%	6.4%	6.0%	32.6%	17.2%	112.0%
% avoidable								10%

of postvaccination measles were diagnosed: 3 in 2001, 5 in 2004, 1 in 2005, 4 in 2006, 2 in 2007 and 5 in 2008; the distribution by sex was similar. Other identified diagnoses included parvovirus, scarlet fever, herpes virus 6, Epstein Barr virus, cytomegalovirus, nonspecific rashes, and others.

Measles complications were analysed using RENAVE surveillance data and CMBD hospitalization data.

Of the 1,384 confirmed and compatible cases since 2001, 252 cases (18%) required hospital admission, with a similar distribution between sexes. Fifty per cent of hospitalized patients were aged > 20 years and the 5-19 years age group had the fewest hospitalizations (10%). The frequency of hospitalizations by age remained constant over time.

Complications were reported in 162 of hospitalized cases (11.7%) with no differences between sexes. By age, 14% of cases aged > 15 years presented complications (13% in males and 15% in females) and 11% of cases in infants aged < 16 months (12% in males and 9% in females) and 9% in both sexes aged 16 months to 14 years. The most-frequent complications were pneumonia 15% (24 cases) and otitis 18% (30 cases). Table **5** shows data on admissions and complications (pneumonia and otitis) from 2001 to 2008. One case of encephalitis was recorded in a patient in whom measles was discarded.

MBDS results from 2001 to 2007 show slightly different data. A total of 209 patients were discharged with a diagnosis of measles (28 less than the RENAVE figures for the same period). Notably, 7 cases of encephalitis were identified: one in 2001, 2002, and 2005, respectively and four in 2003: four occurred in children aged 1-14 years, two in people aged 15-44 years and one in a male aged > 7 years. Five occurred in males and two in females.

There were 24 cases of pneumonia: one male and one female aged 1-14 years in 2001; one female aged <1 year, two males aged 1-14 years and one male and five females aged 15-44 years in 2003, one female aged 1-14 years in 2004, one female aged 1-14 years, four males and two females aged 14-44 years in 2006, and 1 female aged <1 year, 1 female aged 1-4 years and 2 males and 1 female aged 15 - 44 years in 2007.

Table 3. Outbreaks of Measles in Spain 2001-2008

Place	Origin	Geno Type	Nº Cases (% Women)	Ages Affected				% Vaccinated	Duration	Type of Transmission
				0-15 Months	16m-4 Years	5-19 Years	> 19 Years			
				Year 2001						
Galicia	China		3 (33%)			100%		0.0%		Family and schoolchild
Balearic I.		D7	7 (29%)	75.20%	28.6%			0.0%	May-July	Day-care centre and family
Catalonia	Morocco		5 (0%)	20.00%	0.0%	0%	80%	0.0%	April-May	Family
Madrid		D7	10 (30%)	10.00%			90%	0.0%	April-July	Community and family
				Year 2002						
Valencia	Girl Bosnian origin		15 (46.7%)	26.60%			60%	13.3%	January-February	Community
Extremadura	Morocco		3 (33%)						January	Family
Madrid			3 (0%)		100.0%			0.0%	February	Family and school-child
Balearic I.	Germany		12 (25%)	25.00%		16%	58%	0.0%	June-August	
Catalonia			11 (54.2%)			73%	27%		August	Antivaccination family
				Year 2003						
Andalusia	Algeria	B3	182 (46.1%	25.0%	6.1%	19.4%	49.4%	6.1%	January-June	Community
Murcia	Andalusia (Almeria)	B3	6 (66.6%)	50.0%		25.0%	25.0%	16.0%	March-April	Family, hospital, community
Madrid		D7	15 (40%)	13.3%			86.6%	46.6%	June-August	Hospital
Catalonia	Morocco		3 (66.6%)		66.6%	33.3%		0.0%	September-October	Family
Castile-La Mancha	Morocco	C2	4 (75%)	25.0%			75.0%		August	
Valencia		D8	10 (44%)	30%	10%	40%	20%	30.0%	April-June	
				Year 2004						
Catalonia		D5	8 (37.5%)	37.5%	12.5%	13.0%	37.5%	0.0%	June-August	Community and family
Balearic I.		D4	4 (50%)						August-September	Community and hospital
Catalonia	Thailand	D5	3 (66%)				100.0%		August	German airport
				Year 2005						
Catalonia	Rumania	D4	6 (83%)		33.0%	66.6%		0.0%	July	Family
Andalusia			4 (25%)	25%	25.0%	50%		0.0%	June-August	Ethnic gypsy family & group

Table 3. cont….

Place	Origin	Geno Type	Nº Cases (% Women)	Ages Affected				% Vaccinated	Duration	Type of Transmission
				0-15 Months	16m-4 Years	5-19 Years	> 19 Years			
Year 2006										
La Rioja		D6 (=Rumania)	18 (66%)	66.7%	16.7%		16.7%	61.1%	December 05 - February	Hospital, nursery schools
Madrid	United Kingdom	B3	177 (50%)	26.0%	10.0%	12.0%	52.0%	15.8%	February-August	Hospital, community
Catalonia	Rumania	D4	3 (66%)	75.0%	25.0%			0.0%	February	Family
Canary I.	United Kingdom	B3	13 (50%)		14.0%	7.0%	79.0%	38.5%	January-March	Family, hospital, community
Valencia	Madrid	B3	3 (50%)				100.0%		February	Family
Canary I.	Germany	D6	3 (0%)	33.0%	33.0%	33.0%		75.0%	April-June	Family
Catalonia	Italy	D4	381 (48.5%)	62.0%	19.0%	10.0%	9.0%	9.7%	August 06-June 07	Family, hospital, community, day-care centre
Year 2007										
Castile and Leon		D4	16 (53%)				100%	11.8%	February-April	Community
Year 2008										
Madrid		D4	11 (38%)	19%			69%	0%	May	Community
Andalusia (Cadiz)		D4	248 (44%)				100%	11.8%	February	Community, family, schoolchild.
Andalusia (Granada)		D9	2 (0%)				100%	0%	July	Family
Madrid	Equatorial Guinea	B3	19 (42%)	95%			5%		September-October	Day-care centre

In 1901, 18,463 deaths due to measles were recorded: between 1902 and 1922 the annual number was between 5,000 and 10,000 and from 1923 to 1943 between 1,000 and 5,000. Since 1972 the annual number of deaths has fallen to < 100.

From 1951 to 1972, 53.4% of deaths occurred in infants aged <1 year and 39.4% in children aged 1-4 years, with adult mortality being negligible. The largest number of deaths between 1973 and 2005 (43%) occurred in children aged 1-4 years, followed by infants aged < 1 year (28%), but mortality in people aged > 25 years rose to 8.4% of the total.

In 1996, 1997, 1998 and 2002 no deaths were recorded.

Since 2001, deaths have been recorded by reports to APMES with only one death being reported (in 2003). However the death register of the National Institute of Health recorded 11 deaths due to measles between 2001 and 2007 (5 females and 6 males; three aged <19 years, seven aged 24-49 years and one aged 71 years).

For clarification, these 10 more deaths were investigated in the AR in which they were detected and it was concluded that they were caused by late complications of measles acquired in childhood, with the majority being diagnosed as SSPE, a complication that occurs between 8 and 10 years after measles infection and which has a specific ICD-10 code (A81.1) different from that of measles and its complications. Two of the cases are still being studied.

The quality indicators of the system are close to the quality standards established by the WHO of 80% until 2009. The most unfavourable indicators were those referring to the timeliness of the report, which has remained at the same level from the beginning of APMES (Table **6**).

Since 2002, there have been seventeen periods of >18 days free of measles cases ; the last two periods occurred in 2005 and 2006, due to two long outbreaks. There is wide variability in the circulating genotypes in the years for which this information is available. From 2002 to 2006, all estimated reproduction rates have been <1, with the maximum

Table 4. Imported Cases According to Origin and Year in Cases with Source of Infection Known. Spain 2001-2008

	2001	2002	2003	2004	2005	2006	2007	2008	Total	%
Morocco	1	3	9	1		1			15	21%
Germany		2	1			4			7	**10%**
China	2			1					3	4%
Thailand				3					3	4%
Philippines	1		1						2	3%
Italy		2				1		1	4	**5%**
Pakistan		2							2	3%
Bosnia		1							1	**1%**
Ukraine		1				4			5	**7%**
Algeria			1						1	1%
Equator				1					1	1%
France			1						1	**1%**
United Kingdom			1		1	1		3	6	**8%**
Indonesia (Bali)	1								1	1%
North Korea		1							1	1%
Equatorial Guinea	1							1	2	3%
India				1		2			3	4%
Rumania					1	5			6	**8%**
USA					1				1	1%
Ethiopia						1			1	1%
Greece						1			1	**1%**
Switzerland						1			1	**1%**
European source	**0%**	**50%**	**21%**	**0%**	**67%**	**81%**	**0%**	**80%**	**44%**	**47%**
Known source	6	12	14	7	3	21	0	5	73	93%

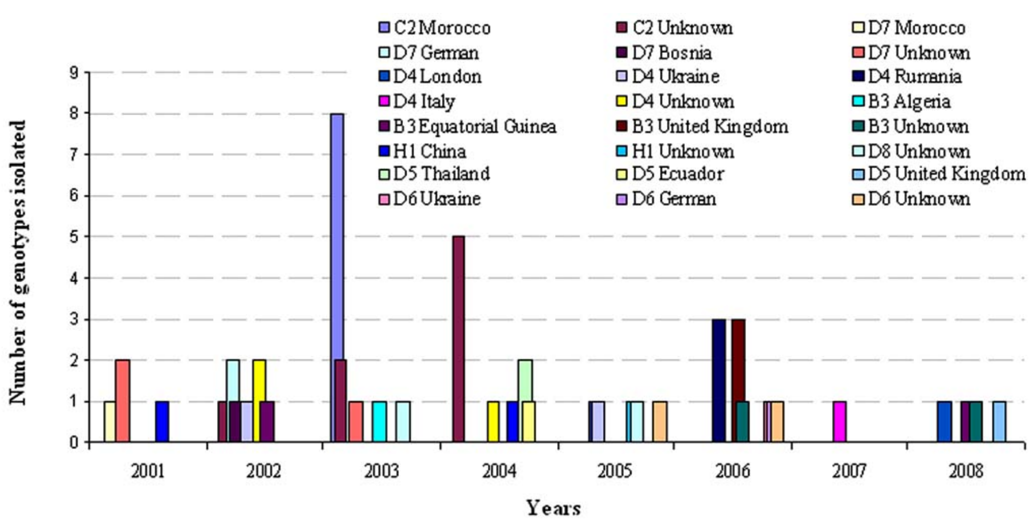

Fig. (3). Genotypes identified in Spain according to place of origin. 2001-2008.

Table 5. Admissions and Complications in Individual Reports to Renave According to Year of Admission

		Age < 1 Year		1-14 Years		15-47 Years		Total	Cases with Complications
		Male	Female	Male	Female	Male	Female		
Admitted									
	2001	1	-	-	-	-	-	1	3
	2002	3	-	-	2	-	2	7	-
	2003	9	7	2	6	19	16	59	25
	2004	-	2	-	-	3	5	10	5
	2005	-	1	1	-	1	1	4	-
	2006	21	19	10	10	23	21	104	44
	2007	7	1	4	1	16	14	43	67
	2008	3	3	2	-	8	8	24	18
	Total	44	33	19	19	70	67	252	162
Pneumonia	2001	-	-	1	-	-	-	1	
	2002	-	-	-	-	-	-	-	
	2003	-	-	1	1	2	5	9	
	2004	-	-	1	-	-	-	1	
	2006	-	-	1	-	2	4	7	
	2007	2	-	1	-	1	1	5	
	2008	1	-	-	-	-	-	1	
	Total	3	0	5	1	5	10	24 (10%)	15%
Otitis	2001	-	1	-	-	-	-	1	
	2002	-	-	-	-	-	-	-	
	2003	-	-	-	1	-	-	1	
	2004	-	-	-	-	1	-	1	
	2006	-	1	-	2	-	-	3	
	2007	3	3	4	3	2	6	21	
	2008	-	1	-	-	1	1	3	
	Total	3	5	4	6	3	6	30 (12%)	18%

Table 6. Surveillance Quality Indicators. Spain 2002-2008

Surveillance Indicators	2002	2003	2004	2005	2006	2007	2008
% of Autonomic Regions that communicate at least one suspected case	84%	84%	79%	74%	89%	58%	84%
% of cases reported in <=24 hours after onset of symptoms	13%	43%	25%	29%	30%	40%	54%
% of cases with blood samples or link	91%	98%	97%	97%	88%	84%	81%
% of cases with results < 7 days after reception	61%	91%	89%	86%	70%	70%	76%
% of confirmed cases with known source of infection	64%	83%	68%	36%	93%	96%	89%
% of outbreaks studied	100%	100%	100%	100%	100%	100%	100%

being reached in 2006 with an estimated value of R of between 0.92 and 0.95 using any of the methods for measuring R (Fig. **3**).

DISCUSSION

The effort involved in setting up APMES has resulted in more exhaustive control of each suspected case of measles and early identification of confirmed cases, which favours the rapid introduction of outbreak control measures.

One change in the pattern of measles after the impact of mass vaccination is the shift in cases to adulthood and the appearance of cases in non-vaccinated infants aged < 16 months, who accounted for a substantial part of the reported cases in 2006-2008, when the infection affected unvaccinated children from a day-care centre, changing the age pattern; cases in this age group rose from 25% in 2001-2005 to 35% in 2006-2008. However, in 2008 there were cases in children aged 4-19 years, an age group in which measles had been practically nonexistent. The shift to adulthood cases has continued in the last two years, with people aged > 20 years representing 42% of confirmed cases.

Current outbreaks are directly related to the distribution of pockets of susceptible subjects, a situation that suggests the need to improve vaccination coverage at all ages and ensure that high coverages are reached in all local population.

The differences observed in mortality between surveillance data and the national death register have been clarified by studies carried out by the AR in which each case was identified. The differences observed are due to them being coded as deaths by measles, late complications of measles i.e., not acute measles.

The discrepancies observed between the RENAVE and CMDB databases with respect to encephalitis may be due to the same reasons as the discrepancies in mortality. Encephalitis can be an acute complication of measles but also a sequela, which could be not coded correctly, as observed for mortality. There may be cases of acute encephalitis not reported to the surveillance network, although this seems strange. The discrepancy in the number of admissions between the two data bases may be due to the fact that the analysis presented here is only of cases hospitalized due to measles, not those in which the disease occurred during hospitalization or concurrently.

The indicator of reported cases in less than 24 hours shows very low figures, this fact could be explained because the access to health services does not happen always in the first 24 hours; so it is difficult to act on that indicator.

During 2005, several WHO European Region countries reported large outbreaks that were exported to other European Region countries, provoking a substantial number of outbreaks, some large, that continued during 2006 and 2007 [22].

The origin of imported cases of measles to Spain has followed the same trend in recent years, with the majority coming from other WHO European Region countries. Same situation had been observed in other European countries with importation came from spain [22]. This suggests that collective efforts are necessary to increase vaccination coverages.

The quality indicators of the system since 2002 indicate a good evolution of APMES, although the same trends have been observed from the beginning, with the worst results being obtained for the timeliness of reporting . This does not invalidate the system but shows where more efforts in measles surveillance are necessary.

According to the WHO elimination criteria, a safety limit of R of 0.7 and the criterion of several incubation periods free of cases both mean Spain still has not eliminated measles. This shows that the efforts carried out until now must continue and further improvements are necessary.

CONCLUSIONS

Elimination of the indigenous transmission of measles in Spain may be possible in the near future due to the current high vaccination coverages and levels of epidemiological surveillance. However, the last three years, in which the incidence has been nearly 1 per 100,000 inhabitants, shows that more efforts are needed to ensure elimination.

Epidemiological surveillance of each case should be reinforced, some quality indicators, especially the sensitivity and timeliness of reporting and investigation should be improved, and vaccination coverages > 95% in all ARs for both the first and second doses of vaccine should be reached and sustained, with special attention being paid to vulnerable groups.

The most-vulnerable groups include travellers to endemic regions or countries with current outbreaks, migrants from countries with different policies of infant immunization, nomadic populations, ethnic gypsies, and adopted children from countries with defective vaccination programmes. Susceptible groups in Spain include young adults born before and during the first years after introduction of the vaccine and infants aged <15 months who have not yet received the first dose of vaccine [20]. It is essential to maintain high coverages in health workers to avoid nosocomial transmission, as has occurred in some outbreaks [23].

In order to reach these objectives, the greatest possible diffusion of the measles elimination plan among all health workers, especially in adult primary health care, hospital emergency departments and all paediatric departments, is required.

APPENDIX

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