¿Están protegidos nuestros lactantes frente al sarampión?

Mª José Cilleruelo Ortega

Hospital Universitario Puerta de Hierro Majadahonda

Comité Asesor de Vacunas -AEP

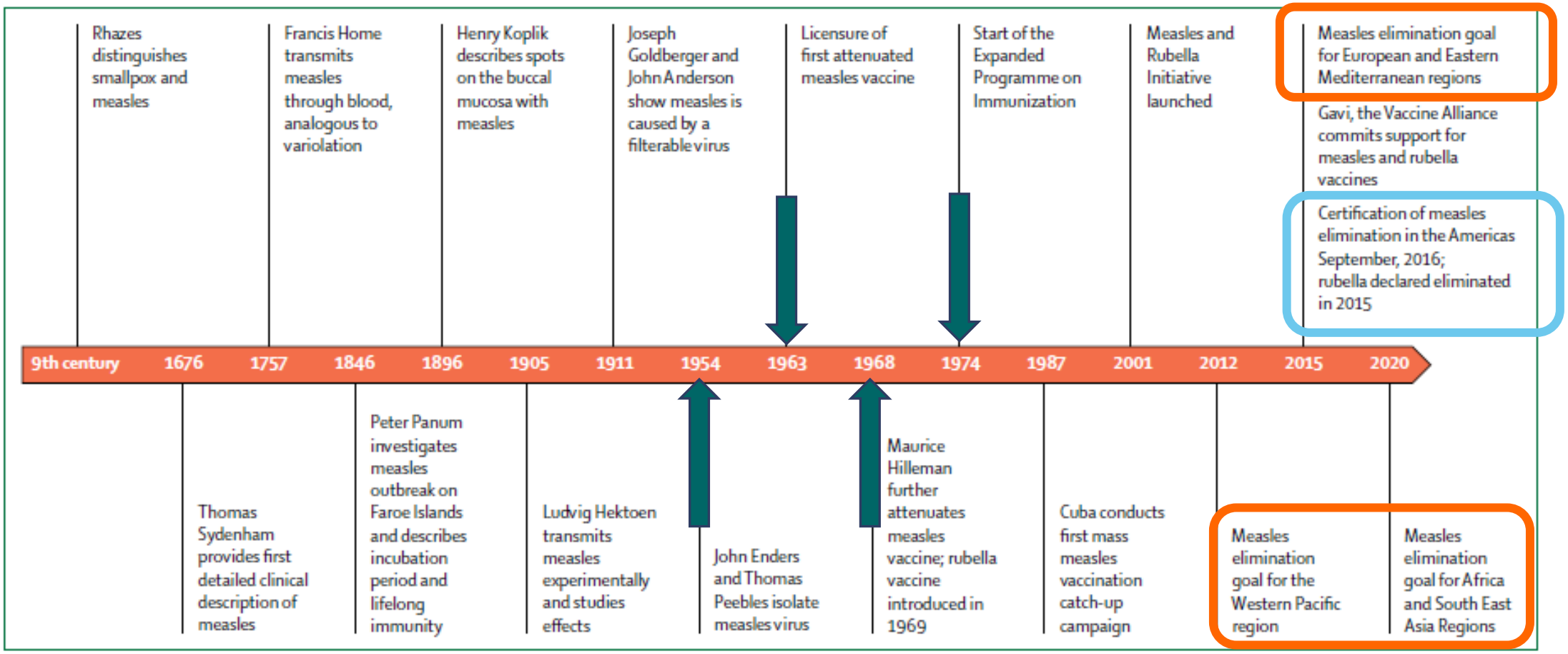
08/10/2020

Declaración de potenciales conflictos de intereses

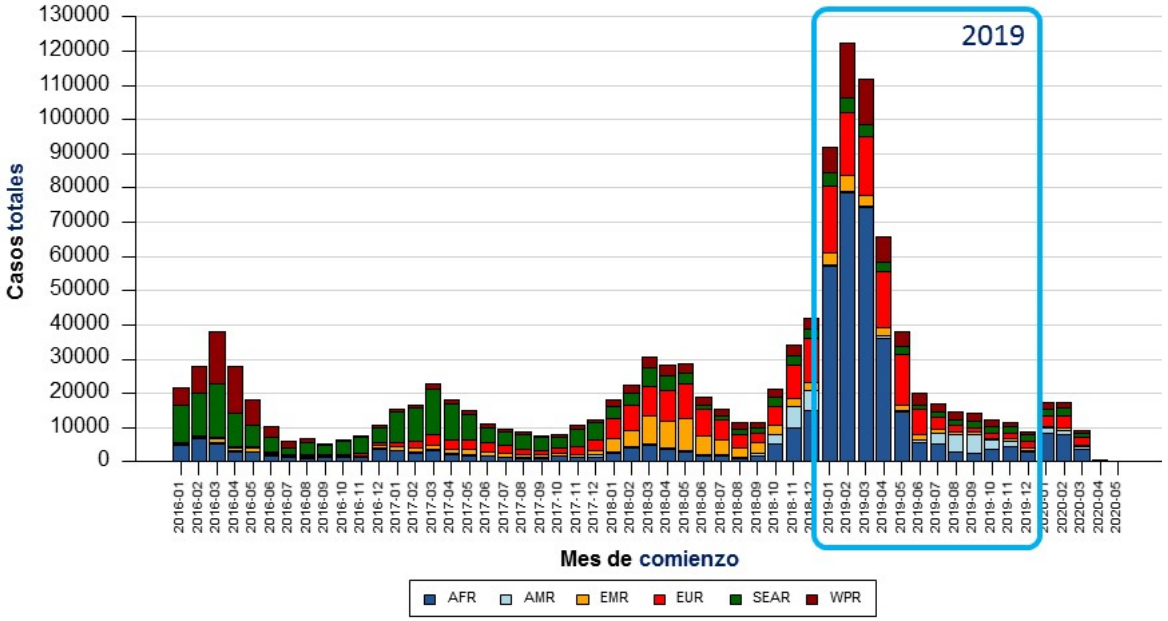
- **Relativas a esta presentación NO existen potenciales conflictos de intereses**

Hitos en la historia del sarampión

Moss WJ, et al. Lancet 2017; 390: 2490



Casos de sarampión, según meses y regiones de la OMS, 2016-2019



OMS, vigilancia epidemiológica del sarampión y la rubeola, 5 de mayo de 2020 (los datos de 2020 son provisionales)
https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_monthlydata/en/

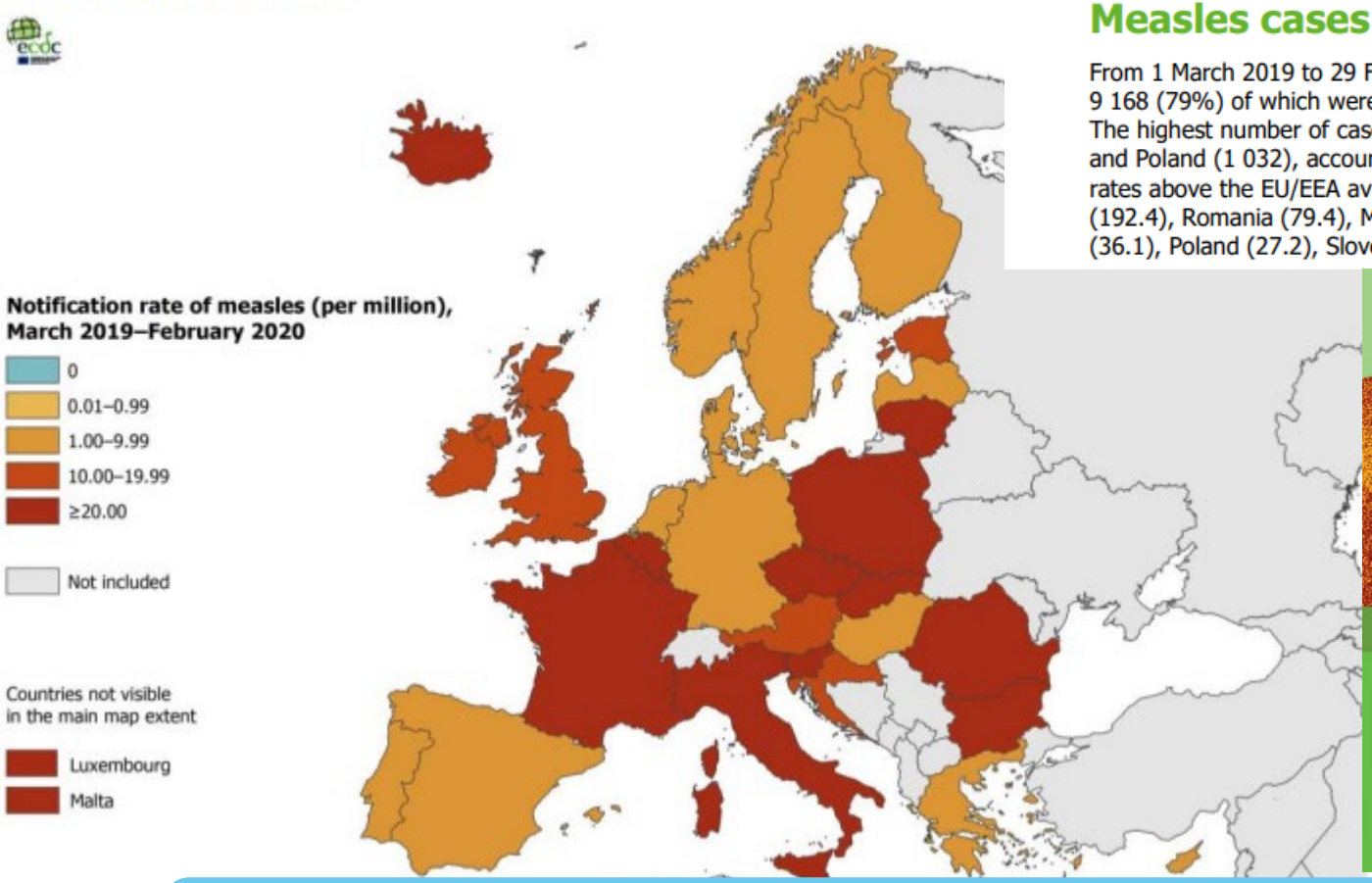
CASOS DE SARAMPIÓN SEGÚN MESES DEL AÑO, 2016-2019

En el año 2019 se han triplicado las cifras del año anterior, que, a su vez, había mostrado un leve aumento comparado con el año previo. El incremento de casos en 2019 se ha repartido de forma desigual entre las regiones de la OMS, siendo máximo en la región africana, seguida de la región europea y la del Pacífico occidental.

- En 2019: número de casos notificados 527 636; estimación del número real de casos, unos 20 millones.
- En 2018: casos estimados 8,5 millones, muertes estimadas 140 000.
- En 2017: casos notificados 173 330; número de casos reales estimados 6,7 millones; muertes estimadas 110 000.

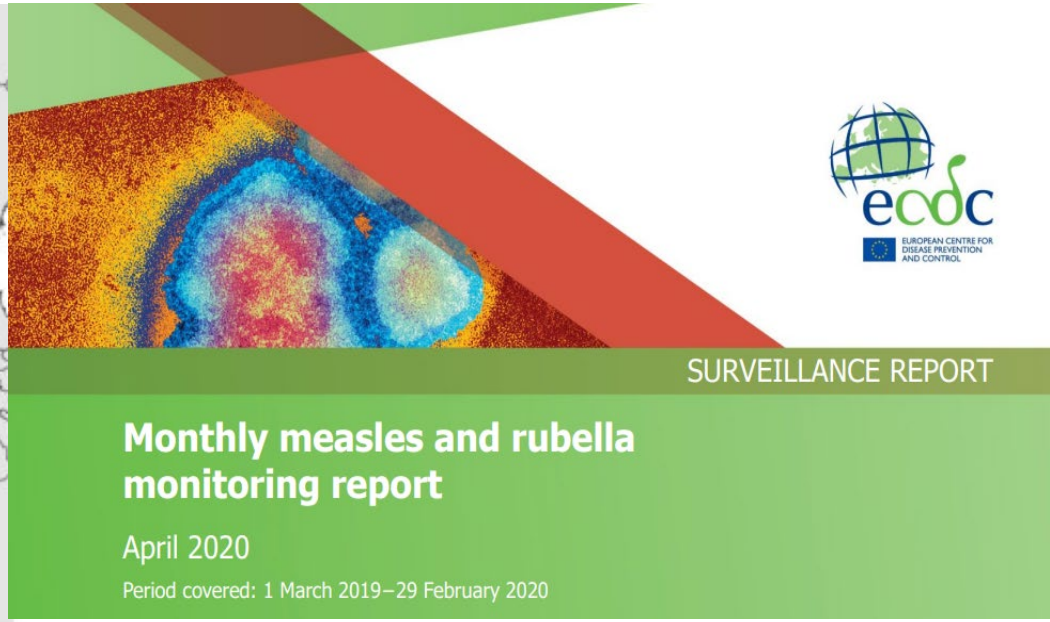
Cortesía A. Hernández Merino

Figure 2. Measles notification rate per million population by country, EU/EEA and the UK, 1 March 2019–29 February 2020



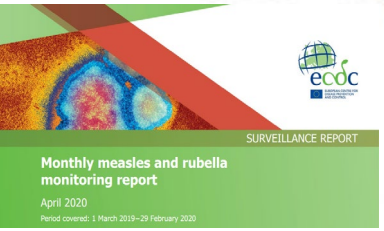
Measles cases March 2019–February 2020

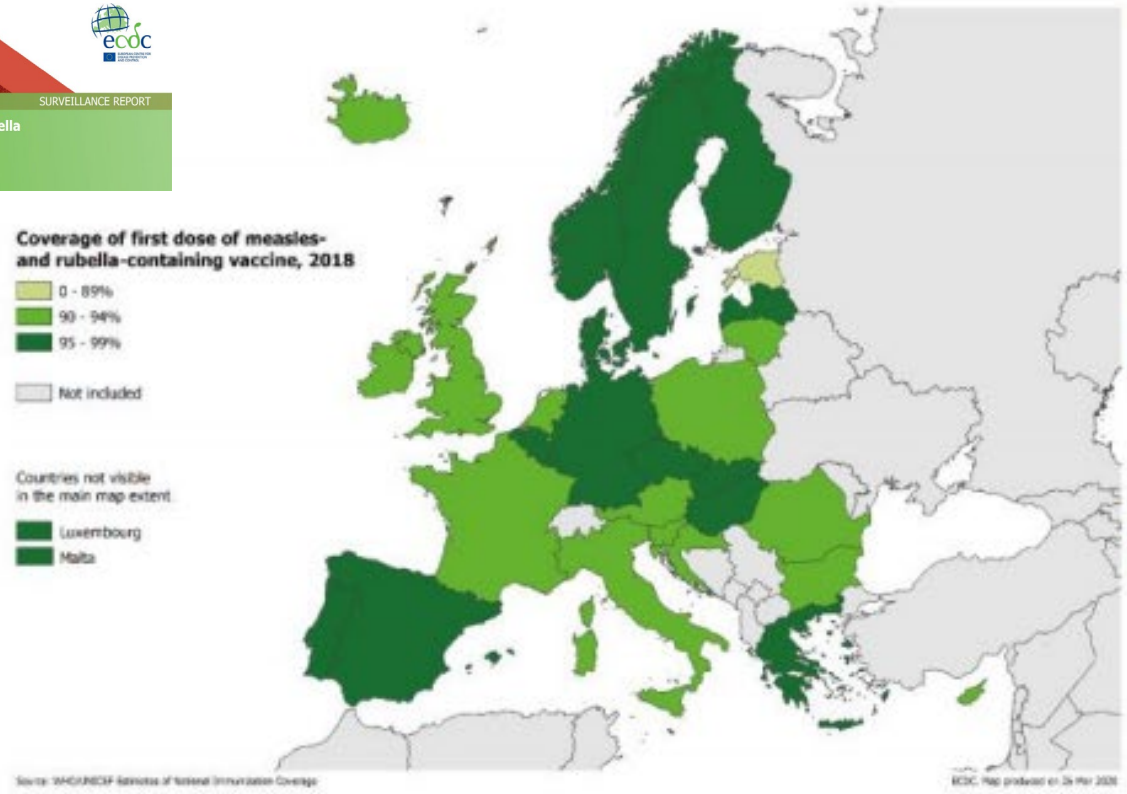
From 1 March 2019 to 29 February 2020, 29 EU/EEA Member States and the UK reported 11 576 cases of measles, 9 168 (79%) of which were laboratory confirmed. No countries reported zero cases during this 12-month period. The highest number of cases were reported by France (2 466), Romania (1 542), Italy (1 353), Bulgaria (1 347) and Poland (1 032), accounting for 21%, 13%, 12%, 12% and 9% of all cases, respectively (Table 1). Notification rates above the EU/EEA average of 22.9 cases per million population were reported by Lithuania (268.4), Bulgaria (192.4), Romania (79.4), Malta (68.9), Slovakia (43.9), Luxembourg (40.7), Belgium (38.2), France (36.8), Czechia (36.1), Poland (27.2), Slovenia (25.9), Italy (22.4) and Iceland (22.4); see Figure 2.

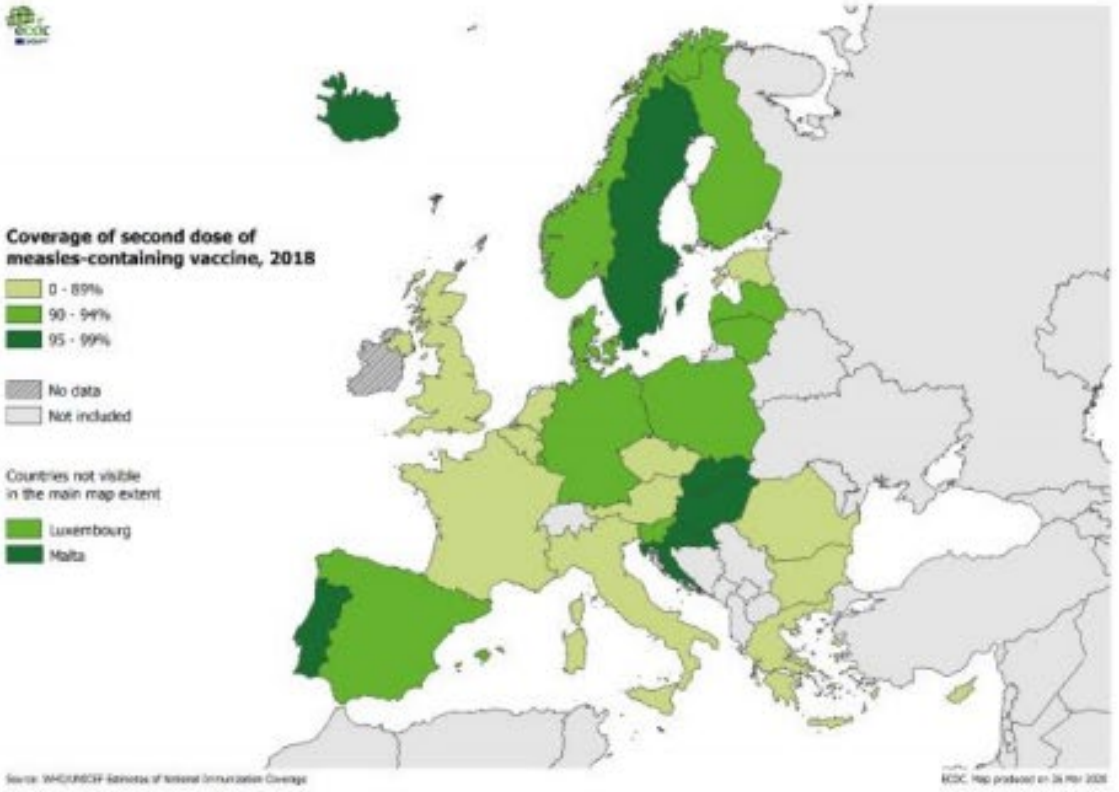


Of the 10 828 cases with known age, 3 023 (28%) were in children under five years; 5 824 (54%) cases were aged 15 years or older. The highest notification rates were observed in infants under one year of age (238.4 cases per million) and in children aged 1–4 years (87.8 cases per million).

Figure 4. Vaccination coverage for first (left) dose of a measles- and rubella-containing vaccine and second (right) dose of a measles-containing vaccine, EU/EEA and the UK, 2018







El 71% de los casos no vacunados

Casos en < 1 año: 1029 (87% no vacunados)

Casos en 1-4 años: 1836 (63% no vacunados)

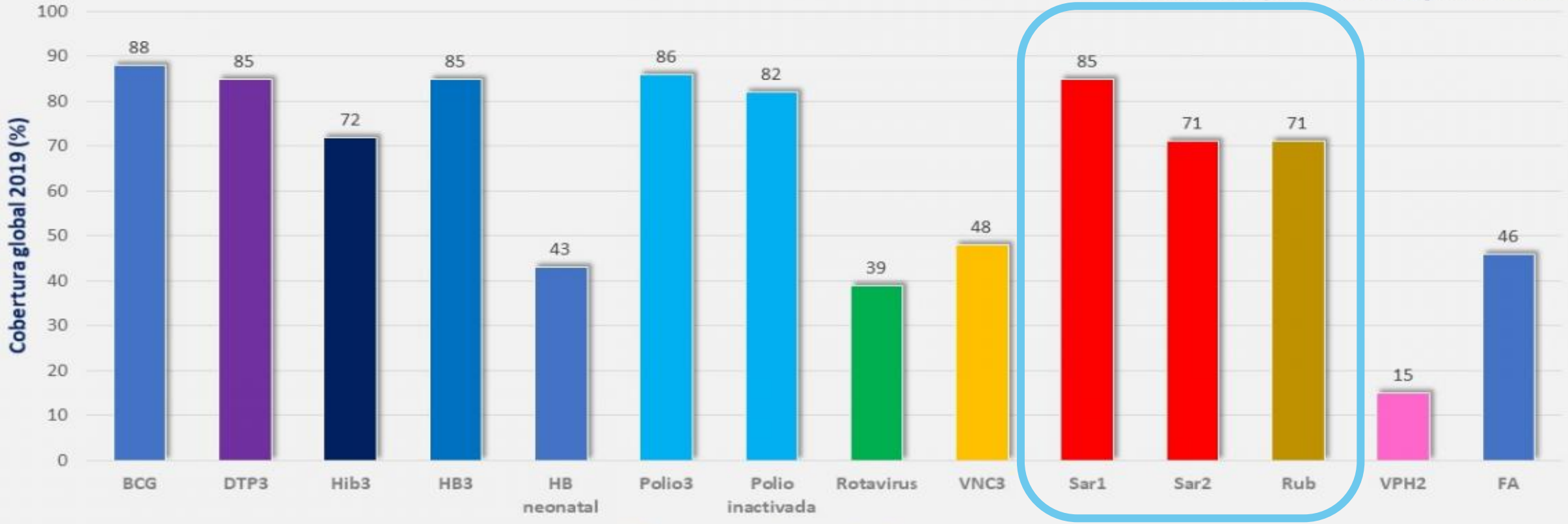
Sólo 5 países coberturas 1ª y 2ª dosis >95%: Eslovaquia, Hungría, Malta, Portugal y Suecia

Vacunaciones infantiles básicas

Coberturas vacunales en el mundo, OMS, 2019

https://vacunasaep.org/
@CAV_AEP
Agosto, 2020

Fuente: adaptado de OMS, julio de 2020



• Polio inactivada: una dosis de VPI en países que usan la vacuna atenuada • Rotavirus: pauta completa • FA: fiebre amarilla en países endémicos

Cortesía A. Hernández Merino

¿Están protegidos nuestros lactantes frente al sarampión?

1. **Sí**
2. **No**
3. **Podría mejorar**

¿Por qué está pasando?

¿Por qué está pasando?

1. Rechazo a la vacunación

2. Exclusión social

3. Disminución de la duración de la protección materna

4. Otros

¿Por qué está pasando?

1. Rechazo a la vacunación

2. Exclusión social

3. Disminución de la duración de la protección materna

4. Otros

Vaccine Scheduler

Measles: Recommended vaccinations

Back to search | Export to spreadsheet

- General recommendation
- Recommendation for specific groups only
- Catch-up (e.g. if previous doses missed)
- Vaccination not funded by the National Health system
- Mandatory vaccination

	Months											Years														
	6	9	11	12	13	14	15	16	17	18	23	2	3	4	5	6	7	8	9	10	11	12	13	14-16	17	18
Austria		MEAS[1]										MEAS														
Belgium				MEAS											MEAS					MEAS				MEAS		
Bulgaria					MEAS																	MEAS				
Croatia				MEAS											MEAS[2]											
Cyprus					MEAS									MEAS												
Czech Republic					MEAS										MEAS											
Denmark							MEAS[4]							MEAS												
Estonia				MEAS																			MEAS			
Finland				MEAS[5]												MEAS										
France		MEAS[6]		MEAS				MEAS								MEAS[7]										
Germany			MEAS[8]				MEAS					MEAS														
Greece				MEAS				MEAS						MEAS		MEAS										
Hungary							MEAS														MEAS[12]					
Iceland										MEAS												MEAS				
Ireland				MEAS										MEAS												
Italy					MEAS											MEAS										
Latvia				MEAS													MEAS[13]					MEAS[14]				
Liechtenstein				MEAS			MEAS																			
Lithuania							MEAS									MEAS										
Luxembourg				MEAS				MEAS																		MEAS[15]
Malta					MEAS								MEAS													
Netherlands						MEAS													MEAS							
Norway							MEAS														MEAS					
Poland					MEAS															MEAS	MEAS[16]					
Portugal				MEAS											MEAS											
Romania				MEAS											MEAS											
Slovakia						MEAS														MEAS						
Slovenia				MEAS											MEAS											
Spain				MEAS									MEAS													
Sweden										MEAS						MEAS[17]										
United Kingdom				MEAS									MEAS							MEAS[18]						


Duración anticuerpos maternos
Respuesta inmune a la vacuna
Riesgo de infección

Duración de los anticuerpos maternos

Cambios epidemiológicos

- *Wilkins et al* apuntaron ya en 1972 que los esquemas de vacunación deberían adaptarse con el tiempo debido al cambio en la protección conferida por mujeres vacunadas no infectadas. *Wilkins J et al. Am J Res Child. 1972*

- Tres cambios en la epidemiología de la enfermedad:
  1. **La mayoría de las mujeres en edad fértil están vacunadas y no han pasado la infección natural**
  2. **La edad media de las madres ha aumentado**. Mayor intervalo de tiempo entre la vacunación y el nacimiento de los hijos y posiblemente un **descenso en la protección transmitida**
  3. **Escasa circulación del virus. Menos refuerzos naturales (*booster*). Niveles de anticuerpos inferiores en la población**

Sato H. Am J Dis Child 1979; Glezen WP. Vaccine 2003; Markowitz LE. Pediatrics 1996

Anticuerpos maternos en hijos de madres con inmunización natural vs vacunadas

- **Menor concentración y menor duración** de anticuerpos específicos en madres vacunadas que en aquellas que han adquirido la infección de forma natural
- **Pérdida de protección más rápida** en hijos de madres vacunadas

Período ventana en el que los lactantes son susceptibles a la infección por la pérdida de estos anticuerpos antes de haber iniciado la vacunación

Lennon JL et al. J Pediatr. 1986; Jenks P. Epidemiol Infect. 1988; Black. Prog Med Virol. 1989; Sood. J Pediatr. 1995; Johnson. Vaccine. 2000; Gagneur. Expert Rev Antinfect Ther. 2010; Zhang. Vaccine. 2012; Waaijenborg. J Infect Dis. 2013; Guerra. Vaccine. 2018

Available online at www.sciencedirect.com
ScienceDirect
Vaccine 25 (2007) 6296–6304
Vaccine
www.elsevier.com/locate/vaccine

Review

Passive transmission and persistence of naturally acquired or vaccine-induced maternal antibodies against measles in newborns

E. Leuridan *, P. Van Damme

Centre for the Evaluation of Vaccination, University of Antwerp, Campus Drie Eiken, Universiteitsplein 1, 2610 Wilrijk, Belgium

Received 23 March 2007; received in revised form 8 June 2007; accepted 11 June 2007
Available online 29 June 2007

Table 1
Comparison of study populations

Reference (year)	Country	Study design	*N* infants from Nat[a] mothers	*N* infants from Vac[b] mothers
[29] (1986)	USA	423 paired sera mother-cord and 59 infants		
[30] (1988)	UK	52 infants	34	18
[31] (1992)	Canada	278 infants	164	114 Vac 1[c]: $N=60$ Vac 2[d]: $N=54$
[46] (1995)	Canada	125 infants	60	65 VacA[e]: $N=22$ VacB[f]: $N=43$
[32] (1995)	Israel	300 infants		300
		mothers + 78 full term infants and 78 mothers		

[a] Nat: children from naturally infected mothers.
[b] Vac: children from vaccinated mothers.
[c] Vac 1: mother received 1–3 killed + 1 attenuated vaccine.
[d] Vac 2: mother received 1 attenuated.
[e] Vac A: mother received 1 killed + 1 attenuated vaccine.
[f] Vac B: mother received 1 attenuated vaccine.

En todos los estudios se comprueba pérdida de protección más rápida en hijos de madres vacunadas
Adelanto de vacuna de 15 a 12 meses

Vaccine 36 (2018) 1248–1255

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

Waning of measles maternal antibody in infants in measles elimination settings – A systematic literature review

Fiona M. Guerra [a], Natasha S. Crowcroft [a,b,c], Lindsay Friedman [a], Shelley L. Deeks [a,b], Scott A. Halperin [d,e,f,g], Alberto Severini [h,i], Todd F. Hatchette [d,e,f,g], Shelly Bolotin [a,b,*], on behalf of the Immunity of Canadians and Risk of Epidemics (iCARE) Network

ABSTRACT

Introduction: Most infants are born with immunity to measles through maternal antibodies transferred in pregnancy, which decay over time. However, in measles elimination settings, where measles does not circulate endemically and most immunity is from immunization rather than infection, maternal antibody levels are lower. This results in infant immunity that wanes earlier, and a wider susceptibility gap between maternal antibody decay and infant immunization than in non-eliminated settings. We aimed to systematically quantify the extent and duration of protection from measles in infants in settings that have sustained measles elimination.

Methods: We conducted a systematic review of studies of measles maternal antibody waning in infants in measles elimination settings. We searched MEDLINE, Embase, CINAHL, Scopus, BIOSIS Previews, and Global Health databases for relevant studies. Studies were included if they were set in countries that had eliminated measles for ≥3 years, and if the study cohort included healthy, full-term, unvaccinated infants ≤12 months, born to healthy mothers, and reported a relevant measure of measles maternal antibody in infants. We assessed study quality using the MetaQAT tool.

Results: We identified 4692 unique citations, eight of which met inclusion criteria. One study reported anti-measles antibody in cord blood, six reported antibody in infant sera, and one reported both. Two studies reported that 80 and 100% of infants were protected from measles at birth. One study reported no protection amongst 3–7 month old infants, and another reported limited protection in infants >4 months. The remaining studies reported the proportion of infants with detected antibody, but not the proportion immune.

Conclusion: Although limited, these data suggest that in settings that have sustained measles elimination, some infants are susceptible to measles well before the age of routine measles immunization. Setting-specific seroprevalence and vaccine effectiveness studies are required to evaluate this in different jurisdictions.

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Summary of studies reviewed.

Study	Setting		Population				Test method			Measures of measles immunity		
	Study year	Country	N	Gestational age	Infant age (number)	Sample	Antibody type	Test	Cut off[a]	Titre	Detectable antibody	Protective antibody
[33]	1997–1999*	USA	113	≥36 weeks	6 months (n = 42)	Sera	Neutralizing	PRNT	<1:4 = negative (measuring detectable antibody)*	13 (CI: 7–26)	26/42 (61.9%)	–
					9 months (n = 35)					4 (CI: 2–8)	15/35 (42.9%)	–
					12 months (n = 36)					1 (CI: 1–1)	0/36 (0%)	–
[34]	1998–2000*	USA	134	≥36 weeks	6 months (n = 73)	Sera	Neutralizing	PRNT	<1:4 = negative (measuring detectable antibody)*, ≥120 mIU/mL = protective	–	47/73 (64.4%)	–
					9 months (n = 61)					–	24/61 (39.3%)	–
					12 months (n = 53)					–	1/53 (1.9%)	
[32]	1994–2002	USA	133	≥36 weeks	6 months (n = 29)	Sera	Neutralizing	PRNT	<1:4 = negative (measuring detectable antibody), >120 mIU/mL	47 mIU/ml (CI: 31–71)	15/29 (51.7%)	–
					6 months (n = 24)*					91 mIU/mL	–	4.2%
					7 months (n = 24)*					75 mIU/mL	–	0.0%
					8 months (n = 26)*					78 mIU/mL	–	0.0%
					9 months (n = 27)*					75 mIU/mL	–	0.0%
					10 months (n = 25)*					80 mIU/mL	–	4.0%
					11 months (n = 25)*					75 mIU/mL	–	0.0%
					2 months (n = 11)	Sera	Neutralizing	PRNT	≥120 mIU/mL = protective	225.1 mIU/mL	–	63.6%
					4 month (n = 11)					82.4 mIU/mL	–	27.3%
					6 months (n = 6)					25.9 mIU/mL	–	16.7%
					7–11 months (n = 5)					32.1 mIU/mL	–	0.0%

En entornos en los que se ha eliminado el sarampión, los lactantes pierden la protección antes de los 12 meses de vida (incluso a los 6 meses)

Vaccine 38 (2020) 460–469

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

The effect of time since measles vaccination and age at first dose on measles vaccine effectiveness – A systematic review

Stephanie L. Hughes [a], Shelly Bolotin [a,b,c], Sumaiya Khan [a], Ye Li [a,b], Caitlin Johnson [a], Lindsay Friedman [a], Andrea C. Tricco [b,d], Susan J.M. Hahné [e], Jane M. Heffernan [f], Alya Dabbagh [g], David N. Durrheim [h,i,j], Walter A. Orenstein [k,l], William J. Moss [m], Mark Jit [n,o], Natasha S. Crowcroft [a,b,c,p,*]

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The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

The Journal of Infectious Diseases® 2019;220:594–602

Early Measles Vaccination During an Outbreak in the Netherlands: Short-Term and Long-Term Decreases in Antibody Responses Among Children Vaccinated Before 12 Months of Age

Iris D. Brinkman,[1,2] Jelle de Wit,[1] Gaby P. Smits,[1] Hinke I. ten Hulscher,[1] Maria C. Jongerius,[1] Taymara C. Abreu,[1] Fiona R. M. van der Klis,[1] Susan J. M. Hahné,[1] Marion P. G. Koopmans,[2] Nynke Y. Rots,[1] Debbie van Baarle,[1,3] and Robert S. van Binnendijk[1]

Measles immunity gaps and the progress towards elimination: a multi-country modelling analysis

Filippo Trentini*, Piero Poletti*, Stefano Merler, Alessia Melegaro

Summary

Background The persistent circulation of measles in both low-income and high-income countries requires a better characterisation of present epidemiological trends and existing immunity gaps across different sociodemographic settings. Serological surveys, which provide direct measures of population protection against the infection, are underexploited and often supply fragmentary estimates of population immunity. This study aims to investigate how measles immunity has changed over time across different socioeconomic settings, as a result of demographic changes and past immunisation policies.

Lancet Infect Dis 2017

Published Online August 11, 2017 http://dx.doi.org/10.1016/S1473-3099(17)30421-8

See Online/Comment http://dx.doi.org/10.1016/

The Journal of Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Effectiveness of Early Measles, Mumps, and Rubella Vaccination Among 6–14-Month-Old Infants During an Epidemic in the Netherlands: An Observational Cohort Study

Tom Woudenberg,[1] Nicoline A. T. van der Maas,[1] Mirjam J. Knol,[1] Hester de Melker,[1] Rob S. van Binnendijk,[2] and Susan J. M. Hahné[1]

Vaccine xxx (2017) xxx–xxx

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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Progress and challenges in measles and rubella elimination in the WHO European Region

Siddhartha Sankar Datta [a,*], Patrick Michael O'Connor [a], Dragan Jankovic [a], Mark Muscat [a], Myriam Corrine Ben Mamou [a], Simarjit Singh [a], Theodoros Kaloumenos [a], Susan Reef [b], Mark Papania [b], Robb Butler [a]

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Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Duration of immunity to measles, rubella and mumps during the first year of life

María José Cilleruelo [a], Aurora Fernández-García [b,d], Serena Villaverde [a], Juan Echevarría [b,d], Miguel Ángel Marín [a], Juan Carlos Sanz [c,d], Agustín López [a], Ana Royuela [a,d], Belén Ruiz Antoran [a], Fernando de Ory [b,d,*]

[a] Servicio de Pediatría, Instituto de Investigación Sanitaria Puerta de Hierro-Segovia de Arana (IDIPHISA), Hospital Universitario Puerta de Hierro, 28222 Majadahonda, Spain
[b] National Reference Laboratory for Measles and Rubella Elimination, National Centre for Microbiology, Institute of Health Carlos III, 28220 Majadahonda, Spain
[c] Laboratorio Regional de Salud Pública, Comunidad de Madrid, 28052 Madrid, Spain
[d] Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP), Spain

Funding

The study was funded by the Fondo de Investigación Sanitaria (FIS PI12/02006), AF-G was funded by CIBER de Epidemiología y Salud Pública (ESPG13).

ABSTRACT

Introduction and objectives: The MMR vaccine was included in the official vaccination schedule in Spain in 1981. Currently, most women of childbearing age are vaccinated and have not been naturally infected. Several studies have shown that vaccinated women have a lower antibody concentration than that achieved after natural infection, and a shorter duration of transplacentally acquired antibodies in their children. The objective of this study was to determine the antibody titer in mothers and their infants at birth and throughout the first year of life under current epidemiological circumstances.

Material and methods: Single-center, observational, descriptive and prospective study conducted between October 2013 and December 2014. One sample of serum and another of a dried blood spot on filter paper were taken from each mother. Dried blood spot samples on filter paper were taken from the children at birth, and at 3, 6, 9 and 12 months. In all the samples, levels of antibodies to the measles, rubella and mumps viruses were measured using standardized quantitative assays.

Results: 146 mother-child pairs were included. 78.4%, 86.9% and 67.1% of mothers had antibodies to measles, rubella and mumps, respectively. A decrease in the antibody titer in children was observed after 3 months, and no antibodies against the three diseases were detected by the age of 6 months. Comparisons revealed no statistically significant differences between the antibody titers of children of mothers born before or after 1981 during the first year of their life.

Discussion: The rapid loss of transplacentally acquired antibodies against measles, rubella and mumps, under current epidemiological conditions, suggests that bringing the MMR vaccination forward to 9 months might be justified. Larger population studies are needed to confirm these results.

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[b] National Reference Laboratory for Measles and Rubella Elimination, National Centre for Microbiology, Institute of Health Carlos III, 28220 Majadahonda, Spain
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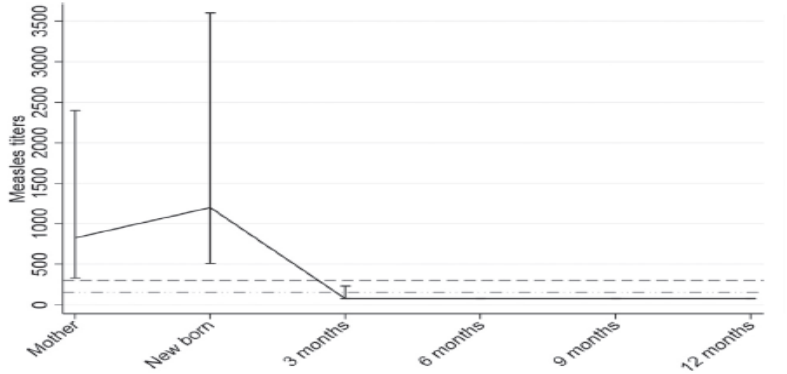
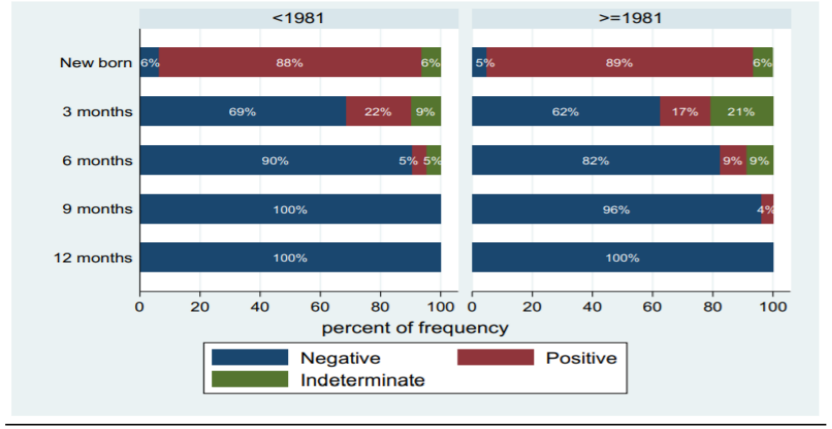


a. Median and IQR titers for measles



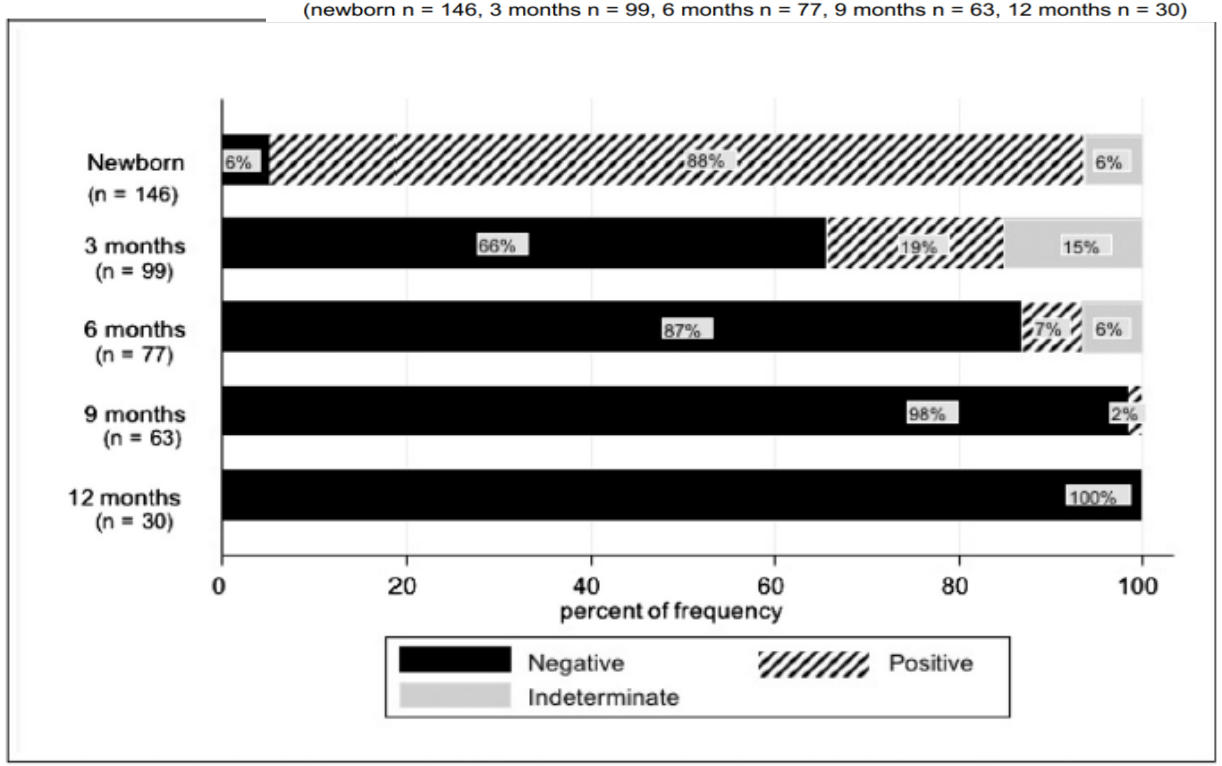
a. Time to negative antibody level of antibodies against measles by time of maternal birth (newborn n = 146, 3 months n = 99, 6 months n = 77, 9 months n = 63, 12 months n = 30)

3.2. Serological results

3.2.1. Measles

78.4% of mothers had antibodies against measles (13.7% indeterminate results). The median antibody titers were 825 mIU/ml (interquartile range (IQR): 330–2400 mIU/ml) for mothers, and 1200 mIU/ml (IQR: 510–3600 mIU/ml) in the newborns ($p = 0.072$) (Table 2). The antibody levels over time are shown in Fig. 1a. 88% of newborns had positive titers and only 19% continued to be positive at 3 months. All of them were seronegative at 12 months (Fig. 2a).

With respect to the year of birth, it was observed that in mothers born before 1981 the median antibody titer was 1200 mIU/ml (IQR: 695–5650 mIU/ml), while those born subsequently had titers of 590 mIU/ml (IQR: 320–1200) ($p < 0.001$). The median antibody titer in newborn children of mothers from the first period was 1900 mIU/ml (IQR: 470–5500 mIU/ml), and that of children of mothers born after 1981 was 710 mIU/ml (IQR: 450–1400 mIU/ml) ($p < 0.001$) (Fig. 3a).



a. Evolution of time to negative antibody level against Measles

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Measles Antibody Levels in Young Infants

Michelle Science, MD,[a,c,d] Rachel Savage, PhD,[c,f] Alberto Severini, MD,[g,h] Elizabeth McLachlan, PhD,[g] Stephanie L. Hughes, PhD,[c] Callum Arnold, MChem,[a] Susan Richardson, MD,[b] Natasha Crowcroft, MD (Cantab),[c,e,f,i] Shelley Deeks, MD,[c,f] Scott Halperin, MD,[j] Kevin Brown, PhD,[c,f,i] Todd Hatchette, MD,[j] Jonathan Gubbay, MBBS,[a,c,d,e] Tony Mazzulli, MD,[c,e,k] Shelly Bolotin, PhD[c,e,f]

BACKGROUND: Infants are often assumed to be immune to measles through maternal antibodies transferred during pregnancy and, in many countries, receive their first measles-containing vaccine at 12 to 15 months. Immunity may wane before this time in measles-eliminated settings, placing infants at risk for measles and complications. We investigated humoral immunity to measles in infants <12 months of age in Ontario, Canada.

METHODS: We selected sera collected at a tertiary pediatric hospital from infants <12 months who were born at ≥37 weeks' gestational age. We excluded infants with conditions that affect antibody levels. We selected ≤25 sera from 8 predetermined age bands and tested them for measles-neutralizing antibody using the plaque-reduction neutralization test. We calculated the proportion immune at each age band, and predictors of infant susceptibility were assessed by using multivariable logistic regression and Poisson regression.

RESULTS: Of 196 infant sera, 56% (110 of 196) were from boys, and 35% (69 of 196) were from infants with underlying medical conditions. In the first month, 20% (5 of 25) of infants had antibodies below the protective threshold, which increased to 92% (22 of 24) by 3 months. By 6 months, all infants had titers below the protective threshold. In a multivariable analysis, infant age was the strongest predictor of susceptibility (odds ratio = 2.13 for each additional month increase; 95% confidence interval: 1.52–2.97).

CONCLUSIONS: Most infants were susceptible to measles by 3 months of age in this elimination setting. Our findings inform important policy discussions relating to the timing of the first dose of measles-containing vaccine and infant postexposure prophylaxis recommendations.

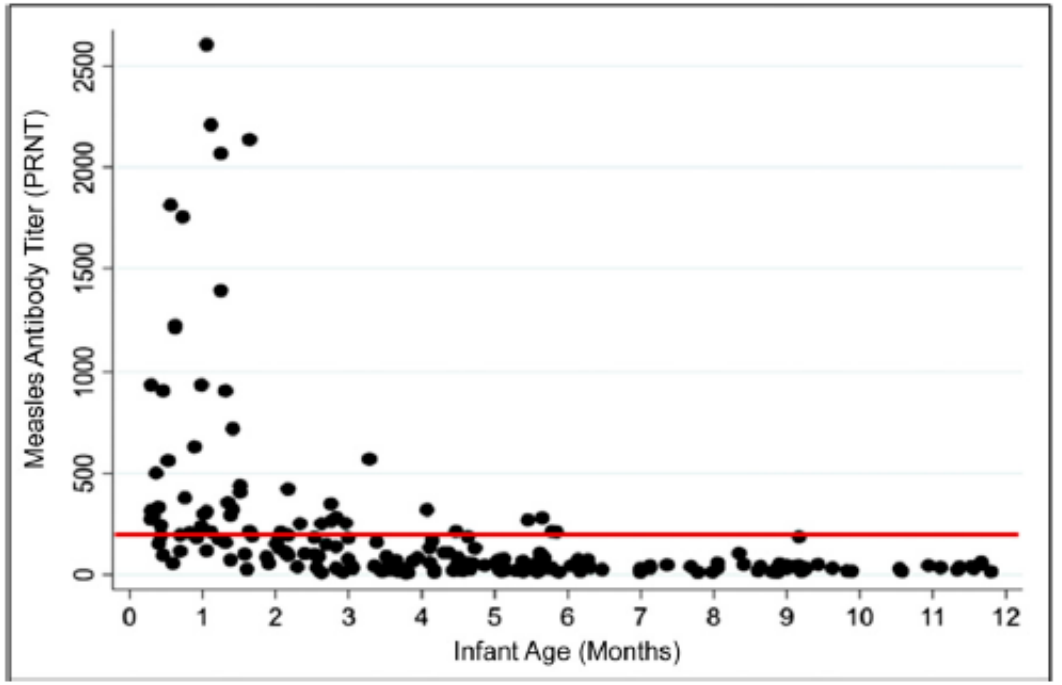


FIGURE 2
Scatterplot of the relationship between infant age in months and measles antibody titer in mIU/mL (N = 196). We considered infants above the threshold to be immune to measles infection and those below the threshold to be susceptible to measles infection.

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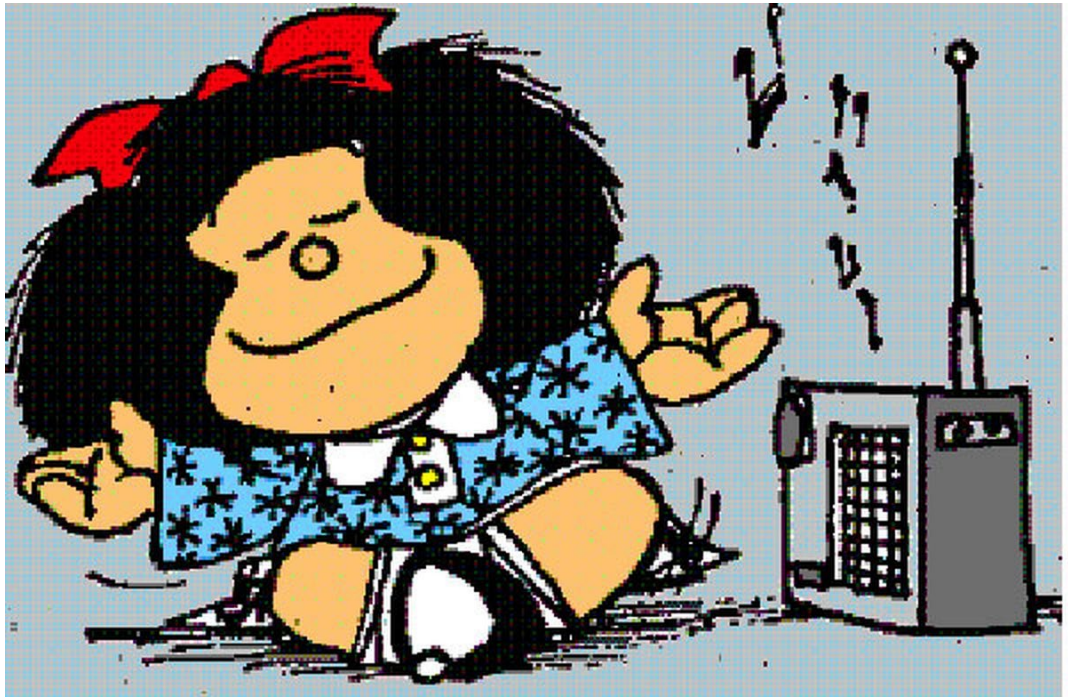
Duración anticuerpos maternos
Respuesta inmune a la vacuna
Riesgo de infección



Respuesta inmune a la vacuna

¿Se puede adelantar la edad de vacunación?

- **La edad óptima para la vacunación se basa en la edad a la que el mayor porcentaje de niños responderán correctamente a la vacuna:**
  - *Johnson et al* (1994): con una dosis de vacuna atenuada a los 6 meses se obtiene respuesta protectora en el 76% de los niños. Tras una segunda dosis a los 15 meses el 100% mostraba el mismo nivel de protección que los niños vacunados solo a los 15 meses
  - *Markowitz el al* (1996): TV 9 meses/12 meses, eficacia similar
  - *Kumar et al* (1998): respuesta menor en niños de 6 meses que en 15 meses
  - *Pabst et al* (1999): buena respuesta de Lf B y Lf T en niños de 6 meses nacidos de madres vacunadas
  - *Klinge et al* (2000): TV 9 meses efectiva independientemente del estado de vacunación de las madres

Immunogenicity, effectiveness, and safety of measles vaccination in infants younger than 9 months: a systematic review and meta-analysis

Laura M Nic Lochlainn, Brechje de Gier, Nicoline van der Maas, Peter M Strebel, Tracey Goodman, Rob S van Binnendijk, Hester E de Melker, Susan J M Hahné

Lancet Infect Dis 2019; 19: 1235–45
Published Online September 20, 2019
https://doi.org/10.1016/S1473-3099(19)30395-0

Summary

Background Measles is an important cause of death in children, despite the availability of safe and cost-saving measles-containing vaccines (MCVs). The first MCV dose (MCV1) is recommended at 9 months of age in countries with ongoing measles transmission, and at 12 months in countries with low risk of measles. To assess whether bringing forward the age of MCV1 is beneficial, we did a systematic review and meta-analysis of the benefits and risks of MCV1 in infants younger than 9 months.

Interpretation MCV1 administered to infants younger than 9 months induces a good immune response, whereby the proportion of infants seroconverted increases with increased age at vaccination. A large proportion of infants receiving MCV1 before 9 months of age are protected and the vaccine is safe, although higher antibody titres and vaccine effectiveness are found when MCV1 is administered at older ages. Recommending MCV1 administration to infants younger than 9 months for those at high risk of measles is an important step towards reducing measles-related mortality and morbidity.

Funding WHO.

Effect of measles vaccination in infants younger than 9 months on the immune response to subsequent measles vaccine doses: a systematic review and meta-analysis

Laura M Nic Lochlainn, Brechje de Gier, Nicoline van der Maas, Rob van Binnendijk, Peter M Strebel, Tracey Goodman, Hester E de Melker, William J Moss, Susan J M Hahné

Lancet Infect Dis 2019; 19: 1246–54

Published Online September 20, 2019 https://doi.org/10.1016/S1473-3099(19)30396-2

Summary

Background Vaccinating infants with a first dose of measles-containing vaccine (MCV1) before 9 months of age in high-risk settings has the potential to reduce measles-related morbidity and mortality. However, there is concern that early vaccination might blunt the immune response to subsequent measles vaccine doses. We systematically reviewed the available evidence on the effect of MCV1 administration to infants younger than 9 months on their immune responses to subsequent MCV doses.

Interpretation Our findings suggest that administering MCV1 to infants younger than 9 months followed by additional MCV doses results in high seropositivity, vaccine effectiveness, and T-cell responses, which are independent of the age at MCV1, supporting the vaccination of very young infants in high-risk settings. However, we also found some evidence that MCV1 administered to infants younger than 9 months resulted in lower antibody titres after one or two subsequent doses of MCV than when measles vaccination is started at age 9 months or older. The clinical and public-health relevance of this immunity blunting effect are uncertain.

Funding WHO.

Inmunidad celular

- La vacunación en los primeros meses de vida genera una respuesta de células T, incluso en presencia de anticuerpos maternos. ***Siegrist CA. Eur J Immunol 1998***
- Estos anticuerpos maternos no afectan la respuesta de Th1/Th2. ***Blomqvist G. Vaccine 2003***
- La vacuna de sarampión induce una potente respuesta inmune de células B y T cuando se administra a lactantes ≥ 6 meses hijos de madres vacunadas. ***Gans H. J Infect Dis 2004***

Vaccine 38 (2020) 20–28

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Review

The effect of maternal antibodies on the cellular immune response after infant vaccination: A review

Marjolein R.P. Orije [a,*], Kirsten Maertens [a], Véronique Corbière [b], Nasamon Wanlapakorn [c], Pierre Van Damme [a], Elke Leuridan [a], Françoise Mascart [b]

[a] Centre for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, University of Antwerp, Belgium
[b] Laboratory of Vaccinology and Mucosal Immunity, Université Libre de Bruxelles (U.L.B.), Faculty of Medicine, Belgium

ABSTRACT

During the last few decades, maternal immunization as a strategy to protect young infants from infectious diseases has been increasingly recommended, yet some issues have emerged. Studies have shown that for several vaccines, such as live attenuated, toxoid and conjugated vaccines, high maternal antibody titers inhibit the infant's humoral immune response after infant vaccination. However, it is not clear whether this decreased antibody titer has any clinical impact on the infant's protection, as the cellular immune responses are often equally important in providing disease protection and may therefore compensate for diminished antibody levels. Reports describing the effect of maternal antibodies on the cellular immune response after infant vaccination are scarce, probably because such studies are expensive, labor intensive and utilize poorly standardized laboratory techniques. Therefore, this review aims to shed light on what is currently known about the cellular immune responses after infant vaccination in the presence of high (maternal) antibody titers both in animal and human studies. Overall, the findings suggest that maternally derived antibodies do not interfere with the cellular immune responses after infant vaccination. However, more research in humans is clearly needed, as most data originate from animal studies.

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[a] Centre for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, University of Antwerp, Belgium
[b] Laboratory of Vaccinology and Mucosal Immunity, Université Libre de Bruxelles (U.L.B.), Faculty of Medicine, Belgium
[c] Center of Excellence in Clinical Virology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Thailand

3. Results and discussion

3.1. Cellular immune response after vaccination in the presence of inhibiting Abs

Table 2
Human studies reporting the immune response after infant vaccination in the presence of high maternal titers.

Maternal/passive Abs	Disease/vaccine	Number of participants	Effect of high maternal/passive Ab titers on the:		Refs.
			Humoral immune response	Cellular immune response	
maternal Abs*	Connaught measles vaccine		responses	5 years of age	et al. [38]

suppressed [39]. All these results correlate well with those from animal studies and suggest that although the presence of maternal Abs inhibits humoral immunity, they do not interfere with the CMI response. In addition, some publications even suggest that maternal Abs prime the body for a more robust CMI response that persists until booster vaccination and confers possible protection throughout the child's life [37,38]. However, to reach a clear conclusion, more research in humans is needed.

Overview of the reported human studies. MMR = measles, mumps and rubella; DTaP = diphtheria, tetanus and acellular pertussis.
* Pre-existing maternal Abs = antibodies that were not induced by maternal vaccination


. Y EL QUE NO HAYA ENTENDIDO, QUE LEVANTE LA MANO
ha
hi
hoy
VEAMOS, MANOLITO, ¿QUÉ ES LO QUE NO HAS ENTENDIDO?
DESDE MARZO HASTA AHORA, ¡NADA!

Comentarios finales

1. En las actuales condiciones epidemiológicas, los lactantes NO están bien protegidos frente al sarampión, especialmente entre los 6 y 12 meses de vida

2. El riesgo de infección depende de:
    1. Duración de la protección conferida por los anticuerpos maternos
    2. Respuesta inmune a la vacunación

3. Existen datos prometedores acerca de una protección correcta y duradera conferida por la inmunidad celular tras la vacunación

4. El adelanto de la primera dosis de vacuna frente a sarampión a los 9 meses es una opción segura, efectiva e inmunógena

MUCHAS GRACIAS