



SPANISH ASSOCIATION OF PAEDIATRICS

## IMMUNISATION SCHEDULE OF THE SPANISH ASSOCIATION OF PAEDIATRICS: 2020 RECOMMENDATIONS<sup>☆</sup>



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**Abstract** The CAV-AEP annually publishes the immunisation schedule considered optimal for children resident in Spain, taking into account the available evidence.

The 2 + 1 schedule is recommended (2, 4, and 11 months) with hexavalent vaccines (DTPa-VPI-Hib-HB) and with 13-valent pneumococcal conjugate.

A 6-year booster is recommended, preferably with DTPa (if available), with a dose of polio for those who received 2 + 1 schemes, as well as vaccination with Tdpa in adolescents and in each pregnancy, preferably between 27 and 32 weeks.

Rotavirus vaccine should be systematic for all infants.

Meningococcal B vaccine, with a 2+1 schedule, should be included in routine calendar.

In addition to the inclusion of the conjugated tetravalent meningococcal vaccine (MenACWY) at 12 years of age with catch up to 18 years, inclusive, the CAV recommends this vaccine to be also included at 12 months of age, replacing MenC. Likewise, it is recommended in those over 6 weeks of age with risk factors or who travel to countries with a high incidence of these serogroups.

Two-dose schedules for MMR (12 months and 3-4 years) and varicella (15 months and 3-4 years) will be used. The second dose could be applied as a tetravalent vaccine.

Universal systematic vaccination against HPV is recommended, both for girls and boys, preferably at 12 years, and greater effort should be made to improve coverage. The 9 genotype extends coverage for both genders.

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### Calendario de vacunaciones de la Asociación Española de Pediatría: recomendaciones 2020

**Resumen** El CAV-AEP publica anualmente el calendario de vacunaciones que estima idóneo para los niños residentes en España, teniendo en cuenta la evidencia científica disponible.

Se mantiene el esquema 2 + 1 (2, 4 y 11 meses) con vacunas hexavalentes (DTPa-VPI-Hib-HB) y con antineumocócica conjugada 13-valente.

Se aconseja un refuerzo a los 6 años, preferentemente con DTPa (si está disponible), junto a una dosis de polio para aquellos que recibieron esquemas 2 + 1, así como vacunación con Tdpa en adolescentes y en cada embarazo, preferentemente entre las 27 y las 32 semanas.

La vacuna del rotavirus debería ser sistemática para todos los lactantes.

Se sigue proponiendo la incorporación en el calendario de la vacuna antimeningocócica B, con esquema 2 + 1 en lactantes.

Además de la inclusión de la vacuna antimeningocócica conjugada tetravalente (MenACWY) a los 12 años con rescate hasta los 18 años, inclusive, el CAV recomienda que esta vacuna sea introducida también a los 12 meses de edad, sustituyendo a MenC. Igualmente, se recomienda en los mayores de 6 semanas de edad con factores de riesgo o que viajen a países de elevada incidencia de estos serogrupos.

Se emplearán esquemas de 2 dosis para triple vírica (12 meses y 3-4 años) y varicela (15 meses y 3-4 años). La segunda dosis se podría aplicar como vacuna tetravírica.

Se recomienda la vacunación sistemática universal frente al VPH, tanto a chicas como a chicos, preferentemente a los 12 años, debiendo realizar un mayor esfuerzo para mejorar las coberturas. La de 9 genotipos amplía la cobertura para ambos sexos.

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**INTRODUCTION**

The Advisory Committee on Vaccines of the Spanish Association of Paediatrics (CAV-AEP) updates its recommendations for vaccination of children and adolescents compared to last year<sup>1</sup> (Figure 1) taking into account the current scientific

evidence on vaccine effectiveness, and vaccine safety, as well as the epidemiology of vaccine-preventable diseases in Spain.

We recommend reading the expanded version of these recommendations in the CAV-AEP website, which provides the detailed arguments that support

ROUTINE IMMUNISATION SCHEDULE OF THE SPANISH ASSOCIATION OF PEDIATRICS 2020 Advisory Committee on Vaccines												
VACCINE	Age in months						Age in years					
	2	3	4	5	11	12	15	3-4	6	12	14	15-18
Hepatitis B <sup>1</sup>	HB		HB		HB							
Diphtheria, tetanus and pertussis <sup>2</sup>	DTaP		DTaP		DTaP				DTaP / Tdpa		Tdpa	
Poliomyelitis <sup>3</sup>	IPV		IPV		IPV				IPV			
Haemophilus influenzae type b <sup>4</sup>	Hib		Hib		Hib							
Pneumococci <sup>5</sup>	PCV		PCV		PCV							
Rotavirus <sup>6</sup>	RV	RV	(RV)									
Meningococcal B <sup>7</sup>		MenB		MenB		MenB						
Meningococcal C and ACWY <sup>8</sup>			MenC			MenACWY					MenACWY	
Measles, mumps and rubella <sup>9</sup>						MMR			MMR Var / MMRV			
Varicella <sup>10</sup>								Var				
Human papillomavirus <sup>11</sup>												HPV (2 doses)

**Figure 1** Routine immunisation schedule of the Spanish Association of Pediatrics 2020.

**(1) Hepatitis B vaccine (HB).**- 3 doses of hexavalent vaccine at ages 2, 4 and 11 months. Children of HBsAg-positive mothers or mothers of unknown serologic status will also be given one dose of monovalent HB vaccine at birth, in addition to 0.5mL of hepatitis B immune globulin (HBIG) if maternal HBsAg-positive status is confirmed. Infants vaccinated at birth will adhere to the routine schedule for year 1 of life, and thus will receive 4 doses of HB vaccine. Unvaccinated children and adolescents should be given 3 doses of monovalent vaccine on a 0-, 1- and 6-months schedule.

**(2) Diphtheria, tetanus and acellular pertussis vaccine (DTaP/Tdap).**- 5 doses: primary vaccination with 2 doses, at 2 and 4 months, of DTaP (hexavalent) vaccine; booster at 11 months (third dose) with DTaP (hexavalent) vaccine; at 6 years (fourth dose) with the standard load vaccine (DTaP-IPV), preferable to the low diphtheria and pertussis antigen load vaccine (Tdap-IPV), and at 12-14 years (fifth dose) with Tdap.

**(3) Inactivated poliovirus vaccine (IPV).**- 4 doses: primary vaccination with 2 doses, at 2 and 4 months, and booster doses at 11 months (with hexavalent) and 6 years (with DTaP-IPV or Tdap-IPV).

**(4) Haemophilus influenzae type b conjugate vaccine (Hib).**- 3 doses: primary vaccination at 2 and 4 months and booster dose at 11 months (with hexavalent).

**(5) Pneumococcal conjugate vaccine (PCV).**- 3 doses: the first two at 2 and 4 months, with a booster dose starting at 11 months of age. The vaccine recommended in Spain by the CAV-AEP continues to be the PCV13.

**(6) Rotavirus vaccine (RV).**- 2 or 3 doses of rotavirus vaccine: at 2 and 3-4 months with the monovalent vaccine or at 2, 3 and 4 months or 2, 4 and 5-6 months with the pentavalent vaccine. It is very important to start vaccination between 6 and 12 weeks of life in order to minimise risks, and to complete it before 24 weeks for the monovalent vaccine or 32 weeks for the pentavalent vaccine. Doses must be given at least 4 weeks apart. Both doses may be given at the same time as any other vaccine.

**(7) Meningococcal B vaccine (MenB).**- 4MenB. 3 doses: if vaccination starts at age 3 months, 2 doses at least 2 months apart with a booster starting at age 12 months and at least 6 months after the last dose in the primary vaccination series. If vaccination starts at 2 months, 4 doses are needed. Administration at least 15 days apart from other injectable inactivated vaccines is recommended up to age 18 months to minimise potential reactogenicity. The separation by a 15-day interval is not necessary for the varicella, MMR and rotavirus vaccines.

**(8) Meningococcal C conjugate vaccine (MenC) and meningococcal ACWY conjugate vaccine (MenACWY).**- 1 dose of conjugate MenC-TT at age 4 months. The CAV-AEP recommends 1 dose of the MenACWY conjugate vaccine at age 12-14 years, and a progressive catch-up vaccination schedule to be completed by age 18 years. If parents choose not to administer the MenACWY vaccine at age 12 months, the MenC-TT vaccine funded by the regional government must be administered instead. Administration of the MenACWY vaccine is still recommended in children and adolescents that are to live in countries where the vaccine is administered at this age (United States, Canada, Argentina, Austria, Greece, Netherlands, Italy, United Kingdom or Switzerland) and for children with risk factors for IMD: anatomic or functional asplenia, complement component deficiency, treatment with eculizumab, hematopoietic progenitor transplant recipients, HIV infection, prior episode of IMD caused by any serogroup, and contacts of an index case of IMD caused by serogroup A, W or Y in the context of an outbreak.

**(9) Measles, mumps and rubella vaccine (MMR).**- 2 doses of measles-mumps-rubella vaccine (MMR). The first at age 12 months and the second at age 3-4 years. The tetravalent MMRV vaccine may be administered for the second dose. Susceptible patients outside the specified ages will be vaccinated with 2 doses of MMR at least 1 month apart.

**Table 1** Abbreviation, generic names and brand names of vaccines recommended for routine immunisation by the CAV-AEP currently available in Spain.

Abbreviation / type of vaccine	Generic name	Brand name (manufacturer)	
DTaP-IPV-Hib-HB	Hexavalent (standard-load diphtheria, tetanus, standard-load acellular pertussis, inactivated poliovirus, Hib and hepatitis B vaccine)	Hexyon (Sanofi Pasteur), Infanrix Hexa (GSK) and Vaxelis (MSD)	
Tdap	Tetanus, reduced diphtheria toxoid and reduced-load acellular pertussis	Boostrix (GSK) and Triaxis (Sanofi Pasteur)	
Tdap-IPV	Tetanus, reduced diphtheria toxoid, reduced-load acellular pertussis and inactivated poliovirus	Boostrix Polio (GSK)	
PCV13	Pneumococcal 13-valent conjugate vaccine	Prevenar 13 (Pfizer)	
MenC-TT	Meningococcal group C vaccine conjugated with tetanus toxoid	NeisVac-C (Pfizer)	
MenACWY	Meningococcal A, C, W and Y vaccine conjugated with CRM	Menveo (GSK)	
	Meningococcal A, C, W and Y vaccine conjugated with tetanus toxoid	Nimenrix (Pfizer)	
MenB	Meningococcal group B vaccine	Bexsero (GSK)	
MMR	MenB-fHbp	Trumenba (Pfizer)	
		Measles, mumps, rubella vaccine	MMRVaxPro (MSD) and Priorix (GSK)
MMRV	Tetravalent vaccine (Measles, mumps, rubella and varicella)	ProQuad (MSD)	
Var	Varicella	Varilrix (GSK) and Varivax (MSD)	
HPV	HPV2	2-valent human papillomavirus vaccine	Cervarix (GSK)
	HPV4	4-valent human papillomavirus vaccine	Gardasil (MSD)
	HPV9	9-valent human papillomavirus vaccine	Gardasil 9 (MSD)
RV	RV1	Monovalent rotavirus vaccine	Rotarix (GSK)
	RV5	Pentavalent rotavirus vaccine	RotaTeq (MSD)

the recommendations. In addition, the recommendations for special situations and risk groups can also be found in the [Online Vaccine Manual of the AEP](#). [Table 1](#) presents a list with the vaccines currently included in the schedule.

These recommendations are aimed at paediatricians, family physicians, nurses, midwives, families and in general at anyone wishing to obtain updated information on paediatric immunisations.

Our objectives are to promote adherence with official immunisation schedules and offer health care providers options for catch-up vaccination in individuals with incomplete vaccination and to expand individual protection with the vaccines that are currently not included in official immunisation schedules.

We pursue the above objectives taking into account the local epidemiological circumstances and prioritising safety as a key component.

**(10) Varicella vaccine (Var).**- 2 doses: the first at age 15 months (age 12 months is also acceptable) and the second at age 3-4 years. The tetravalent vaccine (MMRV) may be used for the second dose. Susceptible patients outside the specified ages will be vaccinated with 2 doses of Var at least 1 month apart.

**(11) Human papillomavirus vaccine (HPV).**- Universal routine vaccination of all girls and boys, preferably at age 12 years, to prevent oncological diseases associated with this virus. All 3 HPV vaccines are authorised for use in male individuals, although there is little data on the use of the HPV2 vaccine in this sex. Administration of 2 doses at age 12 years. The vaccination schedule depends on the vaccine used: for the tetravalent vaccine, a 2-dose series (at 0 and 6 months) aged 9 to 13 years and a 3-dose series (at 0, 2 and 6 months) in those aged  $\geq 14$  years; for the 2-valent and 9-valent vaccines, a 2-dose series (at 0 and 6 months) aged 9 to 14 years and a 3-dose series (at 0, 1-2 [depending on the vaccine used] and 6 months) in those aged  $\geq 15$  years. The HPV vaccine may be administered at the same time as the MenC, MenACWY, hepatitis A and B and Tdap vaccines. There are no data on its coadministration with the varicella vaccine, although it should not cause any problems.

From the CAV-AEP, we once again emphasise the goal of promoting the establishment of a unified immunisation schedule to uphold the principle of equality in disease prevention and in the services offered by the public health systems of all the autonomous communities of Spain.

We need to structure systems for debate to advance in other important aspects, such as improving Primary Care as the cornerstone of the National Health System and the setting where vaccination is performed, gaps in vaccination coverage addressed in specific age groups, populations and geographical areas, considering approaches to the co-funding of vaccines that are not included in official immunisation schedules, establishing a system for compensation of adverse events that, while rare and unpredictable, may result from vaccination, and developing a platform with information on all aspects of vaccination.

As has been done in other countries, we need to promote a new technological and scientific infrastructure at the national level for providing evidence-based advice on policy issues related to vaccination, as recommended by the WHO, which would allow the synchronization of the various scientific, social and health administration perspectives at play.

The AEP is open and willing to participate and collaborate with the Ministry of Health, Consumption and Social Welfare of Spain, the governments of the different autonomous communities and any other parties involved in tasks and processes aimed at improving immunisation.

## VACCINATION AGAINST HEPATITIS B

**2020 recommendation:** *We recommend the vaccination of infants with 3 doses of hexavalent vaccine at 2, 4 and 11 months of age. Previously unvaccinated older children and adolescents will receive 3 doses of the monovalent vaccine in a 0-, 1- and 6-months schedule.*

In Spain, the annual incidence of hepatitis B remains under 2 cases per 100 000 inhabitants. In 2016, a total of 530 cases were notified, corresponding to an incidence of 1.14 cases per 100 000 inhabitants.<sup>2</sup>

Since 2018, every autonomous community initiate the hepatitis B series at age 2 months with the hexavalent vaccine.

Newborns of mothers who are HBsAg-positive or of unknown serologic status should be vaccinated as early as possible regardless of birth weight and always with the monovalent vaccine. They should also be given hepatitis B immune globulin in the first 12 hours post birth if the mother is HBsAg-positive. Newborns vaccinated at birth will adhere to the routine immunisation schedule for the first year of life, so they will receive a total of 4 doses of hepatitis B vaccine.

## VACCINATION AGAINST DIPHTHERIA, TETANUS, PERTUSSIS, POLIOMYELITIS AND HAEMOPHILUS INFLUENZAE TYPE B

**2020 recommendation:** *We recommend a 2+1 schedule with the hexavalent vaccine at 2, 4 and 11 months. Children that have received the 2+1 series should be given DTaP-IPV,*

*preferably, or Tdap-IPV at age 6 years and Tdap at age 12-14 years. We recommend vaccination with Tdap of all pregnant women in each pregnancy, preferably between 27 and 32 weeks of gestation, as early as possible within this window. In case of known risk of preterm birth, vaccination could be given starting at 16 weeks.*

The 2+1 schedule is sufficiently immunogenic and allows optimising the use of available doses. Earlier administration of the first dose at 6 weeks post birth is allowed.

The goal of vaccination during pregnancy is to prevent pertussis in infants aged less than 3 months and to reduce transmission. Vaccination of pregnant women with Tdap is the priority, without neglecting the primary vaccination series, booster doses and vaccination of health care staff employed in obstetrics and paediatrics settings.

Vaccination of pregnant women is effective, preventing disease (90%-93%) and death (95%) in infants aged less than 2 months.<sup>3</sup> The vaccine is highly immunogenic, and some studies have found a higher immunogenicity when it is administered early at 13 to 25 weeks compared to after 26 weeks of gestation,<sup>4</sup> but further research is required to confirm that the incidence of pertussis in infants aged less than 2 months does not increase with the former schedule. If vaccination is performed in the third trimester, a higher level of antibodies is achieved if performed between 27 and 30 weeks of gestation.<sup>5</sup>

Some authors recommend a 3+1 schedule in preterm infants, as studies in this subpopulation were carried out using this schedule, but it is unknown whether it is necessary. Many European countries maintain the 2+1,<sup>6</sup> which facilitates adherence to the schedule, as vaccination may be delayed or incomplete in some of these children.

Children that received a 2+1 primary vaccination series with hexavalent vaccine should be given a booster dose at age 6 years, preferably with the DTaP-IPV vaccine.

Due to the increase in the incidence of poliomyelitis caused by wild poliovirus in Pakistan and Afghanistan, it is important to be careful in case of international travel.

## VACCINATION AGAINST PNEUMOCOCCAL DISEASE

**2020 recommendation:** *Vaccination against pneumococcal disease is recommended for all children younger than 5 years and children that are at risk due to underlying disease at any age. A 2+1 series (at 2, 4 and 11 months) is recommended for routine vaccination of infants. The CAV-AEP continues to recommend the use of the 13-valent pneumococcal conjugate vaccine (PCV13) on account of the current epidemiology of pneumococcal infections in Spain prior to the introduction and use of this vaccine.*

The impact of pneumococcal conjugate vaccines (decavalent [PCV10] and VNC13) on invasive pneumococcal disease (IPD) and non-invasive pneumococcal disease caused by vaccine serotypes has resulted in few cases of IPD being caused by these serotypes. Childhood vaccination is expected to achieve the near eradication (90% decrease) of IPD by vaccine serotypes within 10 years if high vaccination coverage rates are achieved. Therefore, the future impact of pneumococcal conjugate vaccines will depend on replacement

by nonvaccine serotypes and the ability to maintain high vaccination coverage.

The increase in IPD caused by nonvaccine serotypes reflects changes in nasopharyngeal carriage, which aside from vaccination is determined by complex factors that are difficult to control, such as the invasiveness of specific serotypes.<sup>7</sup> This explains the observed variability in replacement in different countries, even those using the same vaccine.

The increase in IPD by nonvaccine serotypes, which has been greater in the population aged more than 65 years, reduces, but does not nullify, the overall benefits of vaccination.<sup>7,8</sup> Another factor at play is the phenomenon of serotype replacement, which can change the distribution of the different forms of IPD.

The United States is an exception in serotype replacement, as there has been no evidence of an increase in the incidence of IPD by nonvaccine serotypes in any age group.<sup>7,9</sup> In Madrid, there has also been no increase in IPD by nonvaccine serotypes in individuals aged less than 15 years, but there has been an increase in other age groups in the incidence of IPD caused by serotypes 8, 3, 12F, 22F, 12B and 24F.

Although there has been a strong increase in the incidence of IPD by serotype 19A in countries using the PCV10, a study conducted in Kenya found that the incidence of IPD by this serotype did not change and did not detect replacement by other nonvaccine serotypes.<sup>10</sup>

Recently, it has been confirmed that the level of specific antibodies required to prevent nasopharyngeal colonization (which is key to achieve herd immunity) is greater compared to the level required to prevent IPD and different for each serotype.

## VACCINATION AGAINST ROTAVIRUS

**2020 recommendation:** *Vaccination against rotavirus (RV) should be included in the routine immunisation schedule for all infants.*

To date, more than 100 countries have introduced vaccination against RV in their immunisation schedules. The public health benefits of this intervention have been enormous, and in Europe vaccination programmes have led to reductions in the burden of disease of 60% to 90% both in terms of primary care visits and hospital admissions.<sup>11</sup>

In Spain, a review of studies published in the past 10 years reveals a high effectiveness, with a reduction of 83% to 96% in the number of hospital admissions due to RV.<sup>12</sup>

Vaccination also indirectly and positively affects the unvaccinated environment, which substantially enhances the impact and efficiency of this intervention. On account of their vulnerability, preterm infants deserve special attention, and they should receive the vaccine without delay, even if they are hospitalised, before 12 weeks post birth.<sup>13</sup>

The benefits of vaccination far exceed the risk of intussusception, the only severe adverse event associated with the RV vaccine, which is very rare (1 to 5 cases per 100 000 vaccinated children).<sup>14</sup>

## VACCINATION AGAINST MENINGOCOCCAL DISEASE

**2020 recommendation:** *Routine vaccination against meningococcus B is recommended in all infants starting at 3 months of age with a 2 + 1 schedule. For all other age groups, including adolescents, the decision whether to vaccinate should be made on a case-by-case basis.*

We also recommend administration of the MenC-TT vaccine at age 4 months and replacing the MenC dose at age 12 months by a dose of MenACWY. It is essential that, should a child not be given the latter vaccine, the dose of MenC is administered without fail. We continue to recommend administration of the MenACWY vaccine to adolescents, and catch-up vaccination is recommended up to age 18 years.

In Spain, 2 vaccines are available for prevention of invasive meningococcal disease (IMD) due to group B meningococcus: the 4CMenB vaccine (from age 2 months) and the MenB-fHbp vaccine (authorised in Europe for use from age 10 years), both of which contain subcapsular protein antigens.

Since IMD by serogroup B is rare, conventional cost-benefit analyses of this vaccine are unfavourable. However, the CAV-AEP considers that it should be included in the routine immunisation schedule for 2 reasons:

- 1) IMD is a devastating disease and the most frequent serogroup isolated in infants aged less than 12 months in Spain is group B.<sup>15</sup>
- 2) It is an effective vaccine, as demonstrated by its impact after the introduction in the vaccination schedule in England in 2015, with a 2 + 1 series given in infancy.

The outcomes after the first 10 months of the programme showed an effectiveness of 83% against all group B strains and a reduction of 50% in the number of cases in the target population.<sup>16</sup> Three years after its introduction, there is evidence of an overall adjusted effectiveness of 58.9% (95% confidence interval [CI], -31.5%-87.1%), and an effectiveness of 70.5% against strains theoretically covered by the vaccine. Since 2015, 277 cases of IMD due to group B meningococcus have been prevented, and the annual incidence observed in the 3 vaccinated cohorts has been lower than predicted,<sup>17</sup> with no evidence of safety concerns. It is possible that the 4CMenB vaccine may offer cross-protection against other serotypes.

Assuming the degree of uncertainty that is to be expected in relation to any recently developed vaccine, the CAV-AEP considers that there are sufficient data on its impact and safety to recommend administration of the 4CMenB vaccine to all infants, the age group with the highest incidence of IMD, with a 2 + 1 series starting at age 3 months. Two autonomous communities in Spain (Castilla y León and the Canary Islands) have already included the 4CMenB vaccine in their routine childhood immunisation schedules.

The CAV-AEP recommends vaccination against group B meningococcus in all adolescents to improve individual protection, but not as a routine measure, as these vaccines do not reduce the prevalence of nasopharyngeal carriage or generate herd immunity.<sup>18</sup>

There is ample evidence of the effectiveness of the monovalent vaccine against group C meningococcus. The incidence rate of IMD due to serogroup C in Spain remained very low in the 2017-2018 season (0.08 cases/100 000 inhabitants).<sup>14</sup>

Starting in 2000, there has been a marked increase in the incidence of IMD by serogroups W and Y in Europe,<sup>19</sup> leading many countries to change their vaccination policy against IMD by replacing the dose of MenC by a dose of MenACWY at age 2 years and/or in adolescence. Some countries in America, such as the United States, Canada, Chile and Argentina, have also included the MenACWY vaccine in their immunisation schedules.<sup>20</sup>

In Spain, from the 2014-15 season, there has been an increase in the annual incidence of IMD, a trend that has been sustained year after year due to the increase in the incidence of IMD by groups W and Y. The latest data from the Centro Nacional de Epidemiología (National Epidemiology Centre), corresponding to week 32 of 2019, reflect a clear increase: 77 cases of IMD by group W (incidence, 0.16/100 000) and 48 by group Y (incidence, 0.10/100 000).<sup>15</sup>

With these data, the Comisión de Salud Pública (Public Health Committee) published a document in 2019 with recommendations on vaccination against IMD. When it came to the MenACWY vaccine, the committee considered vaccination of adolescents and young adults a priority, replacing the MenC dose at 12 years by a dose of MenACWY and planning catch-up vaccination of adolescents aged 13 to 18 years in the span of 2 to 3 years to achieve an epidemiologically significant impact as soon as possible.<sup>21</sup> Meanwhile, the government of Castilla y León has included the MenACWY vaccine in the official immunisation schedule at ages 12 months and 12 years. Andalusia will add it to its routine schedule in 2020.

The CAV-AEP supports the replacement of the dose of MenC by a dose of MenACWY in adolescence, but also at age 12 months, given the increasing trend in the incidence of IMD by groups W and Y in children aged less than 5 years. In case the MenACWY vaccine is not given at 12 months, it is important to ensure administration of a dose of MenC to prevent a drop in vaccination coverage.

## VACCINATION AGAINST MEASLES, MUMPS AND RUBELLA (MMR)

**2020 recommendation:** *We recommend the administration of a first dose of MMR vaccine at 12 months of age, with a second dose given between 3 and 4 years of age. The tetravalent vaccine (MMRV) may be used for the second dose.*

Due to suboptimal vaccination coverage in some countries, the prevalence of measles has exhibited a sustained increase in the past 6 years in 6 World Health Organization (WHO) regions. In the European Region, in the first semester of 2019, the incidence doubled compared to the same period in 2018,<sup>22</sup> and 4 countries have lost their measles-free status (not including Spain). There are still outbreaks of mumps, while rubella stays stable.<sup>23</sup> Maintaining vaccination coverage rates above 95% for the 2 doses and strict epidemiological surveillance are of the essence to eradicate these diseases.

Some studies have detected an increased risk of suffering convulsive seizures when the MMRV vaccine is used for the first dose given to children aged less than 2 years, so for the time being we recommend giving these 2 vaccines separately (MMR and varicella) in this age group.<sup>24</sup>

## VACCINATION AGAINST VARICELLA

**2020 recommendation:** *We recommend vaccination of all children against varicella with 2 doses administered at ages 15 months and 3–4 years (the MMRV vaccine may be used for the second dose). We also recommend catch-up vaccination with a 2-dose series (or completion of the 2-dose series when applicable) for all children and adolescents that have not had the disease.*

Since 2016, vaccination against varicella has been included in the immunisation schedule of every autonomous community with a 2-dose series (at 15 months and 3–4 years).<sup>25</sup> There are two monovalent and two tetravalent vaccines with evidence of a high effectiveness (92%–97.3%).<sup>26</sup>

In 2019, 9 autonomous communities in Spain introduced the use of the MMRV vaccine for the second dose, facilitating adherence to the immunisation schedule.

The strategy of universal vaccination against varicella has proven cost-effective.<sup>27</sup> After 20 years of use in the United States, there is evidence of an overall decline in the incidence of disease<sup>28</sup> and in the incidence of herpes zoster in the paediatric population.<sup>29</sup> There is no evidence of shift toward older ages or of an increase in the incidence of herpes zoster in the overall population.<sup>30</sup>

## VACCINATION AGAINST HUMAN PAPILLOMAVIRUS (HPV)

**2020 recommendation:** *Routine vaccination against HPV is recommended in both girls and boys, preferably at age 12 years, as a means to prevent oncological diseases associated with this virus.*

The optimal age for vaccination is 12 years, with administration of a 2-dose series, with the aim of maximizing immunogenicity and its possible benefits prior to sexual debut and pursuing the broadest possible vaccination coverage. The recommendation also extends to older ages if vaccination has been delayed, as well as to at-risk groups, given the benefits that it may continue to provide.

In girls, the evidence on the efficacy and effectiveness of this vaccine in preventing persistent HPV infection, genital warts and precancerous cervical lesions continues to grow, with a reduction of up to 85% in the incidence of high-grade dysplasias, even 10 years after vaccination.<sup>31,32</sup>

In male individuals, the efficacy of the vaccine in preventing HPV-related cancer is greater in those that receive it prior to their sexual debut.<sup>33</sup>

These vaccines are extremely safe and have a very favourable risk-benefit ratio.<sup>31</sup> The only adverse events described are anaphylaxis, which may occur with administration of any vaccine, and syncope.<sup>34</sup> In spite of this, the coverage in Spain continues to be considerably low compared to all other vaccines in the routine immunisation schedule.<sup>35</sup>

Vaccination of male individuals is already included in the schedules of 29 countries, with the recent addition of Germany and the United Kingdom.<sup>34,36</sup> There are relevant data on the role of HPV in the aetiology of certain types of cancer affecting both sexes but with a higher incidence in males, such as rectal cancer and head and neck cancer.<sup>37</sup> The immunogenicity achieved is comparable to the one achieved in girls.<sup>38</sup> For all the above reasons, the CAV-AEP also recommends vaccination of male adolescents.

In Spain, 3 HPV vaccines are currently available: the 9-valent vaccine (HPV9), the 4-valent vaccine and the 2-valent vaccine.<sup>39,40</sup> All 3 confer protection against cervical cancer and precancerous lesions, although the first 2 also protect against genital warts. The HPV9 vaccine offers the widest direct coverage against cervical malignancies (90%) and potential prevention of HPV-related vulvar, vaginal and anal cancers (85%-95%).<sup>41</sup> All 3 are authorised for use in individuals of both sexes. In case vaccination against HPV is publicly funded, we recommend using the HPV vaccine that has been selected by each autonomous community.

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## CONFLICTS OF INTERESTS (LAST 5 YEARS)

FJAG has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer, Sanofi Pasteur and MSD and as a consultant in GlaxoSmithKline, Novartis, Pfizer, Sanofi Pasteur and MSD advisory boards.

MJCO has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer, Sanofi Pasteur and MSD, as a researcher in clinical trials for GlaxoSmithKline and Pfizer, and as a consultant in GlaxoSmithKline, Novartis, Pfizer, Sanofi Pasteur and MSD advisory boards.

JAA has collaborated in educational activities funded by Astra, GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD, as a researcher in clinical trials for GlaxoSmithKline and Sanofi Pasteur and as a consultant in GlaxoSmithKline, MSD, Sanofi Pasteur and Pfizer advisory boards.

MGS has collaborated in educational activities funded by Astra, GlaxoSmithKline, Pfizer y Sanofi Pasteur MSD, as a researcher in clinical trials for GlaxoSmithKline, Janssen and Sanofi Pasteur MSD and as a consultant in GlaxoSmithKline and Novartis advisory boards.

NGS has collaborated in educational activities funded by Sanofi Pasteur and MSD and attended educational activities funded by Novartis y Pfizer.

EGL has received funding to attend domestic educational activities, and has participated in educational activities funded by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD, collaborated as a researcher in clinical trials for GlaxoSmithKline and as a consultant in GlaxoSmithKline advisory boards.

AHM has received funding to attend domestic educational activities and has participated in educational activities funded by Pfizer.

AIA has collaborated in educational activities funded by GSK, Pfizer and Sanofi-Pasteur-MSD, has received funding from Pfizer to attend domestic educational activities, and has participated in educational activities funded by GSK, MSD and Pfizer.

MMM has collaborated in educational activities funded by GlaxoSmithKline, Pfizer, Sanofi Pasteur and MSD, as a researcher in clinical trials for GlaxoSmithKline, Pfizer, Sanofi Pasteur and MSD and as a consultant in Novartis advisory boards.

AMM has received funding from Pfizer to attend educational activities in Spain and abroad, but stopped accepting any type of sponsoring from any pharmaceutical laboratories for any type of activity (as an educator or as a learner) since becoming a member of the CAV-AEP.

MLNG has collaborated in educational activities funded by Gilead, GlaxoSmithKline, Janssen, Pfizer, MSD and ViiV, as a consultant for Abbott, Astra Zeneca, Novartis and ViiV advisory boards and as a researcher in clinical trials sponsored by GlaxoSmithKline, Pfizer, Roche and Sanofi Pasteur.

JRC has collaborated in educational activities funded by GlaxoSmithKline, Pfizer, Sanofi Pasteur and MSD and as a researcher in clinical trials for GlaxoSmithKline and Pfizer.

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- María Garcés-Sánchez. Paediatrician, Centro de Salud Nazaret, Valencia. Researcher affiliated to the Section on Vaccines, FISABIO, Valencia.
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- Elisa Garrote Llanos. Paediatrician, Department of Infectious Diseases, Hospital Universitario Basurto, Bilbao. Associate professor, School of Medicine, Universidad del País Vasco, UPV-EHU.
- Ángel Hernández Merino. Paediatrician, Centro de Salud La Rivota, Alcorcón, Madrid.
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