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SPANISH ASSOCIATION OF PAEDIATRICS

Immunisation schedule of the Spanish Association of Paediatrics: 2016 recommendations☆

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Abstract The Advisory Committee on Vaccines of the Spanish Association of Paediatrics (CAV-AEP) annually publishes the immunisation schedule which, in our opinion, estimates optimal for children resident in Spain, considering available evidence on current vaccines. We acknowledge the effort of the Ministry of Health during the last year in order to optimise the funded unified Spanish vaccination schedule, with the recent inclusion of pneumococcal and varicella vaccination in early infancy.

Regarding the funded vaccines included in the official unified immunisation schedule, taking into account available data, CAV-AEP recommends 2 + 1 strategy (2, 4 and 12 months) with hexavalent (DTPa-IPV-Hib-HB) vaccines and 13-valent pneumococcal conjugate vaccine.

Administration of Tdap and poliomyelitis booster dose at the age of 6 is recommended, as well as Tdap vaccine for adolescents and pregnant women, between 27 and 36 weeks gestation.

The two-dose scheme should be used for MMR (12 months and 2–4 years) and varicella (15 months and 2–4 years).

Coverage of human papillomavirus vaccination in girls aged 11–12 with a two dose scheme (0, 6 months) should be improved. Information for male adolescents about potential beneficial effects of this immunisation should be provided as well.

Regarding recommended unfunded immunisations, CAV-AEP recommends the administration of meningococcal B vaccine, due to the current availability in Spanish communitary pharmacies, with a 3 + 1 scheme (3, 5, 7 and 13–15 months). CAV-AEP requests the incorporation of this vaccine in the funded unified schedule. Vaccination against rotavirus is recommended in all infants.

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◊ Members of the Advisory Committee on Vaccines of the Spanish Association of Paediatrics (CAV-AEP) are presented in Appendix.

Annual influenza immunisation and vaccination against hepatitis A are indicated in population groups considered at risk.

PALABRAS CLAVE
Vacunas;
Calendario de vacunación;
Enfermedades inmunoprevenibles;
Niños

Calendario de vacunaciones de la Asociación Española de Pediatría (CAV-AEP): Recomendaciones 2016

Resumen El CAV-AEP publica anualmente el calendario de vacunaciones que estima idóneo para los niños residentes en España, teniendo en cuenta la evidencia disponible sobre las vacunas. Reconocemos el esfuerzo del Ministerio de Sanidad, en el último año, por optimizar el calendario común, con la inclusión de la vacunación frente al neumococo y la varicela en la primera infancia.

En cuanto a las vacunas financiadas incluidas en el calendario común, con los datos disponibles actualmente, y dada la falta de disponibilidad del componente de tosferina, se recomienda emplear esquemas 2 + 1 (2, 4 y 12 meses) con las vacunas hexavalentes y con la antineumocócica conjugada 13-valente.

Se aconseja un refuerzo de Tdpa a los 6 años, junto con una dosis de polio, así como vacunación con Tdpa en adolescentes y embarazadas, entre las semanas 27–36.

Se emplearán esquemas de 2 dosis para triple vírica (12 meses y 2–4 años) y varicela (15 meses y 2–4 años).

Se deben incrementar las coberturas frente al papilomavirus en niñas de 11–12 años con 2 dosis (0–6 meses), así como informar a los varones de los beneficios potenciales de la vacunación.

Respecto a las vacunas recomendadas no financiadas, dada su disponibilidad en las farmacias comunitarias, se recomienda la vacuna frente al meningococo B, con esquema 3 + 1 (3, 5, 7 y 13–15 meses), solicitando su entrada en el calendario. Es recomendable vacunar a todos los lactantes frente al rotavirus.

La vacunación antigripal anual y la inmunización frente a la hepatitis A están indicadas en grupos de riesgo.

Introduction

The Advisory Committee on Vaccines of the Spanish Association of Paediatrics (CAV-AEP) updates the immunisation schedule every year, taking into account current evidence to propose the recommendations on vaccination that it considers most appropriate for children residing in Spain.

This year, major changes have been made to the recommendations of this Committee, as can be seen in Fig. 1, partly due to new developments that have taken place in recent months, such as the inclusion of the pneumococcal conjugate vaccine and the vaccine against varicella in the official immunisation schedules in 2015 and 2016.[1] The Ministry of Health, Social Services and Equality (Ministerio de Sanidad, Servicios Sociales e Igualdad [MSSSI]) has taken into consideration these two important demands of the CAV-AEP, to the great delight of paediatricians and society. It has also announced the distribution of the vaccine against varicella in community pharmacies, and the long-awaited arrival of the meningococcal B vaccine, also demanded by paediatricians.

Due to the short supply of the pertussis vaccine, and for the purpose of optimising the immunisation schedule, adapting it to current epidemiological conditions, increasing its efficacy and converging towards the homogenisation of vaccination schedules in Europe, the CAV-AEP has made various modifications, implementing 2 + 1 schedules with hexavalent vaccines.

Ideally, scientific societies would be taken into account in the decision-making process, and the autonomous communities (ACs) and the MSSSI would make a greater collective effort to fund a more comprehensive routine immunisation schedule for Spanish children. Alternative systems should be set up to assist families in paying for vaccines that are not funded by the state, as is done in other countries in the European Union and in Spain in relation to commonly used medications.

Due to the space restrictions of this document, we recommend the reading of the expanded overview of these recommendations available at our website, www.vacunasaep.org.

In 2015, the case of diphtheria in Olot and the two cases of poliomyelitis in Ukraine underscored the need to continue vaccinating every child, striving to maintain high vaccination coverage rates and to persuade parents that refuse vaccination.

Vaccination against hepatitis B

2016 recommendation: *We recommend the vaccination of infants with three doses of hexavalent vaccine at 2, 4 and 12 months of age. Previously unvaccinated older children and adolescents will receive 3 doses of the monovalent vaccine alone or combined with the hepatitis A vaccine at 0, 1 and 6 months.*

In Spain, the annual incidence of hepatitis B (HBV) rose slightly in 2013 compared to 2012 (1.53 and 1.27 cases per 100,000 inhabitants, respectively).[2] In 2015, the first dose was given at birth in more than half of the ACs, a schedule that should be maintained if it is believed that there is suboptimal screening of pregnant women.

There is evidence that delaying the age at which the last dose of the vaccine is administered and increasing the interval between doses can improve immunological memory, offering greater protection against HBV in adults,[3] and this can be achieved with a 2 + 1 schedule.

The vaccination of newborns is always to be performed with the monovalent vaccine, which will be prescribed to children born to mothers that are HBsAg-positive or of unknown serological status. Babies born to HBsAg-positive mothers should also be given anti-hepatitis B immune globulin (HBIG), preferably in the first 12 h of life.

Four-dose schedules may be administered in infants that were vaccinated as newborns.

Fig. 2 presents a decision algorithm for the management of at-risk patients.

Vaccination against diphtheria, tetanus, pertussis, poliomyelitis and *Haemophilus influenzae* type b

2016 recommendation: *We recommend primary vaccination with the hexavalent DTaP-IPV-Hib vaccine at 2, 4 and 6 months. The first dose can be given earlier at 6 weeks post birth. A booster dose, also of the hexavalent vaccine, should be administered at 12 months of age (2 + 1 schedule), with subsequent boosters with the Tdap-IPV vaccine at age 6 years and with the Tdap vaccine at age 11–12 years. Vaccination with a dose of Tdap is recommended in all pregnant women between weeks*

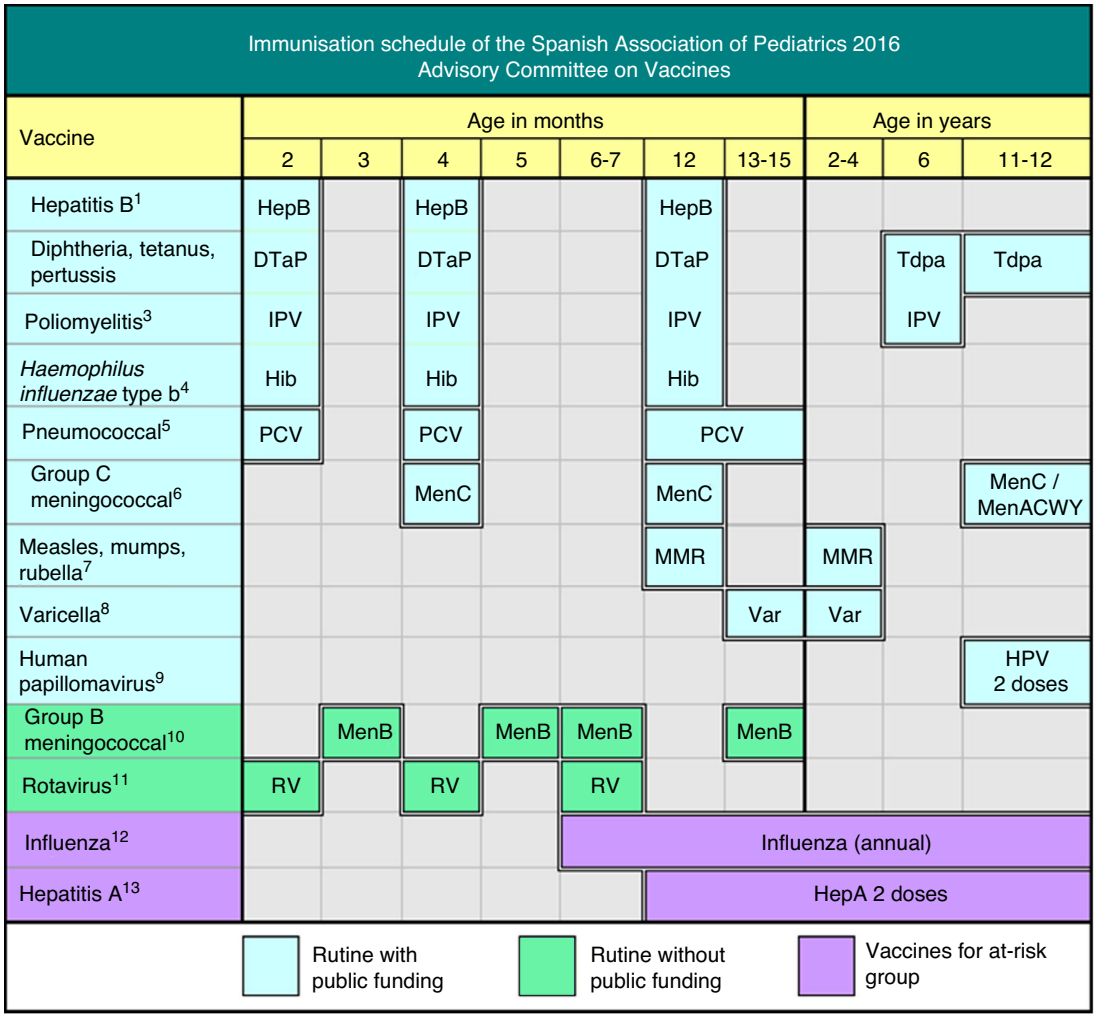

Figure 1 Immunisation schedule of the Spanish Association of Paediatrics 2016. Recommendations of the Advisory Committee on Vaccines.

This immunisation schedule, designed for childhood and adolescence, specifies the ages recommended for the administration of the vaccines considered by the CAV-AEP to have the profile of a **publicly funded routine vaccine**—vaccines that every child in Spain should receive and offered for free as part of the official immunisation programme of each of the ACs; of **non-funded routine vaccines**, which exhibit the profile of a routine vaccine and the CAV-AEP recommends be given to every child, but that due to cost-effectiveness reasons is prioritised based on the economic resources for its public funding; and vaccines that **target at-risk groups**, such as those indicated for individuals whose environmental or personal circumstances increase the likelihood that they will develop severe forms of infection or experience decompensation of an underlying disease. The recommended accelerated or catch-up schedules should be applied whenever vaccination is not performed at the specified ages. We recommend consulting the immunisation schedule of the corresponding autonomous community or city. Adverse reactions must be reported to the health authorities.

(1) Hepatitis B vaccine (HepB).- Three doses of hexavalent vaccine at ages 2, 4 and 12 months. Children of HBsAg-positive mothers will also be given a dose of monovalent HepB vaccine at birth along with 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth. When maternal serological status is unknown, the neonatal dose should be administered and maternal serology tested immediately, and should the mother test positive, HBIG should be administered to the neonate as soon as possible, and always in the first week of life. The administration of four doses of HepB vaccine is generally acceptable, and advisable in children born to HBsAg-positive mothers with birth weights below 2000 g that were vaccinated at birth, as the neonatal dose in these cases should not be counted as part of the series. Unvaccinated children and adolescents should be given three doses of monovalent HepB vaccine or the combined HepA&B vaccine on a 0, 1, and 6-month schedule at any age.

(2) Diphtheria, tetanus and acellular pertussis vaccine (DTaP/Tdap).- Five doses: primary vaccination with two doses, at ages 2 and 4 months, of DTaP (hexavalent); booster doses at 12 months (third dose) with DTaP (hexavalent), at 6 years (fourth dose) with the vaccine with reduced-antigen diphtheria and pertussis content (Tdap-IPV) and at 11–12 y ears (fifth dose) with Tdap.

(3) *Haemophilus influenzae* type b conjugate vaccine (Hib).- Three doses: primary vaccination at 2 and 4 months and booster at 12 months (third dose).

Figure 1 (*Continued*)

27 and 36 of gestation, and in all household members that will be in contact with the newborn (especially any postpartum mothers that were not vaccinated during pregnancy).

The incidence of pertussis has increased worldwide,[4] with infants suffering the highest burdens and most severe forms of disease. Preventive strategies must prioritise the protection of this group. Vaccination of women with the Tdap during the third trimester of gestation is safe and efficacious, and it is the most effective and efficient method for preventing pertussis in infants.[5]

The 2 + 1 primary vaccination and booster schedule is used in many European countries. We believe that this schedule, which is both safe and immunogenic, optimises the available doses of vaccine, as one less dose is used for primary vaccination.[6]

We uphold the recommendation of the WHO (2014) of administering one dose of OPV or IPV to travellers residing or meaning to stay for more than 4 weeks in countries affected by polio. This dose must be received within 4 weeks to 12 months of travel. The recent occurrence of two cases of poliomyelitis in unvaccinated children in Ukraine caused by

(4) Inactivated polio vaccine (IPV).- Four doses: primary vaccination with two doses and boosters at 12 months (third dose) and 6 years (fourth dose).

(5) Meningococcal C conjugate vaccine (MenC).- Three or four doses of monovalent conjugate vaccine (1+1+1 or 2+1+1 schedule): one dose at 4 months of age, another at 12 months of age, and a last dose at 11–12 years. Depending on the vaccine preparation, primary vaccination may require one dose (at 4 months) or two (at 2 and 4 months of age). At present, only two ACs use the two doses in the first year (Madrid, 2 and 4 months and Catalonia, 2 and 6 months). For the 12-year dose, substitution of the MenC by of one dose of the tetravalent (A, C, W and Y) meningococcal conjugate vaccine (**MenACWY**) could be considered.

(6) Pneumococcal conjugate vaccine (PCV).- Three doses: the first two at 2 and 4 months with a booster at 12 months of age (third dose). If routine childhood immunisation is not publicly funded, the 3+1 schedule applies: three doses (at 2, 4 and 6 months) in the first year of life and a fourth dose at 12 months of age. The vaccine currently recommended in Spain is the PCV13.

(7) Measles, mumps, rubella vaccine (MMR).- Two doses of MMR vaccine: the first one at 12 months, and the second at age 2–4 years, preferably at 2. Vaccination of susceptible patients outside these age ranges with two doses at least 1 month apart.

(8) Human papillomavirus vaccine (HPV).- Only for girls. Two doses between ages 11 and 12 years. The vaccination schedule depends on the preparation used: for the tetravalent vaccine, a two-dose course (at 0 and 6 months) for girls aged 9 to 13 years and a three-dose course (at 0, 2, 6 months) for ages 14 and up; for the bivalent vaccine, a two-dose course (0 and 6 months) for girls aged 9 to 14 years and a three-dose course (0, 1, 6 months) for ages 15 and up. They can be administered concomitantly with the MenC, HepA, HepB, and Tdap vaccines.

(9) Varicella vaccine (Var).- Two doses: the first at 15 months (12 months is also acceptable) and the second at 2–4 years of age, preferably at 2. Susceptible patients outside those age ranges will be vaccinated with two doses at least one month apart.

Figure 1 (*Continued*)

vaccine-derived poliovirus type 1 underscores the need to maintain high coverage rates of vaccination against polio. The 2 + 1 primary vaccination series with hexavalent vaccine calls for the administration of a polio booster at age 4–6 years with the Tdap-IPV vaccine, as many countries have been doing. Spain is one of the few European countries that do not administer this booster dose after age 2 years.

Vaccination against pneumococcal disease

2016 recommendation: *Vaccination against pneumococcal disease is recommended for all children younger than 5 years and children that are immunocompromised or otherwise at risk at any age. Routine vaccination can be performed starting in infancy with a 2 + 1 series* (at 2, *4, 12–15 months), but in the absence of routine vaccination, the series should follow a 3 + 1 schedule. We recommend the use of the 13-valent pneumococcal conjugate vaccine (PCV13) based on epidemiological data for Spain, its demonstrated effectiveness in reducing the rate of all forms of noninvasive disease and its capacity to induce herd immunity in all age groups.*

The evidence of the capacity of pneumococcal conjugate vaccines (10-valent [PCV10] and PCV13) to cause a marked reduction in the rate of invasive pneumococcal disease (IPD) continues to grow.[7,8] These two vaccines also have a significant impact on noninvasive pneumococcal disease, having led to a reduction in the number of hospitalisations for pneumonia caused by pneumococcus or of other aetiologies in vaccinated as well as unvaccinated individuals.[9]

The PCV13 significantly reduces nasopharyngeal colonisation by vaccine serotypes, including 19A.[10] It is almost

(10) Meningococcal B vaccine (MenB).- Four doses: the first three at 2.5–3, 4.5–5 and 6–7 months, with a booster dose at 13–15 months of age to minimise vaccine reactogenicity and avoid concomitant vaccination with MenC.

(11) Rotavirus vaccine (RV).- Three doses of rotavirus vaccine: at 2, 4, 6 months or at 2, 3, 4 months. The course must start between 6 and 12 weeks of life and must be completed before age 32 weeks. Doses must be administered at least 4 weeks apart.

(12) Influenza vaccine (Flu).- Annual vaccination of patients with risk factors and their household contacts (older than 6 months). One dose in individuals older than 9 years; children aged 6 months to 9 years will be given two doses at least 1 month apart the first time they are vaccinated and a single dose in subsequent years if they remain at risk.

(13) Hepatitis A vaccine (HepA).- Two doses, at least 6 months apart, starting at 12 months of age or older. Vaccination is indicated for patients travelling abroad to countries with moderate or high endemicity or that belong to risk groups.

Figure 1 (*Continued*)

certain that this fact accounts for the marked reduction brought by this vaccine on noninvasive forms of pneumococcal disease such as pneumonia[11,12] and acute otitis media,[13] as well as for the herd immunity against IPD and pneumonia in both children and adults.

There are fewer studies on the impact of PCV10 on nasopharyngeal colonisation and noninvasive forms of pneumococcal disease. The PCV10 produces a considerable reduction of hospitalisations due to pneumonia,[9] although this reduction is not as significant as the one achieved by

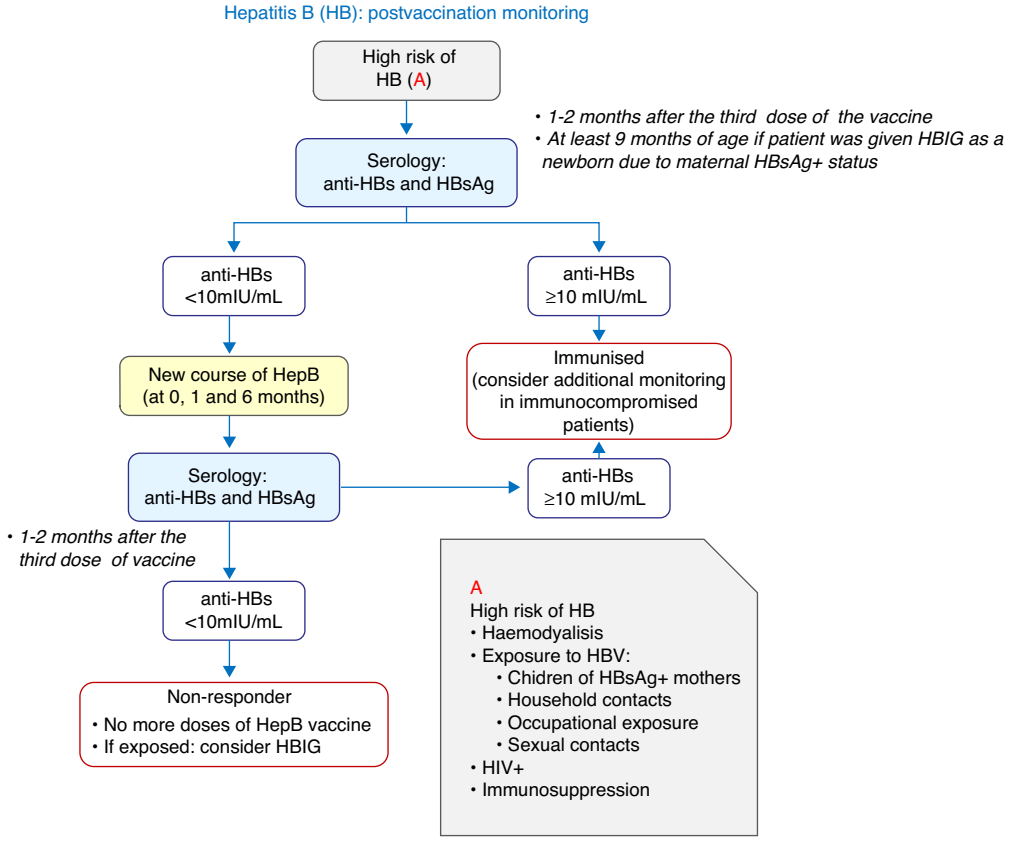

Figure 2 Decision algorithm for postvaccination monitoring in individuals at high risk for hepatitis B.

At-risk group	Disease or situation
Immunocompetent children	Chronic respiratory disease: severe asthma, bronchopulmonary dysplasia, cystic fibrosis, α1-antitrypsin deficiency, bronchiectasis
	Chronic heart disease, especially congenital cyanotic heart defects or diseases involving heart failure or haemodynamic alterations
	Down syndrome[a]
	Individuals with neurologic disorders that carry a risk of pulmonary aspiration of fluids or secretions, such as cerebral palsy or recurrent convulsive seizures
	Diabetes mellitus type 1
	Chronic liver disease
	Subarachnoid pleural fistula
	Children with cochlear implants
Children with asplenia (anatomic or functional)[b]	Sickle cell anaemia and other severe haemoglobinopathies
	Congenital or acquired asplenia, splenic dysfunction
Immunocompromised children[b]	HIV infection
	Primary immunodeficiencies (excluding asymptomatic isolated IgA deficiency)
	Chronic kidney failure and nephrotic syndrome
	Diseases requiring treatment with immunosuppresive drugs or radiotherapy (including leukaemia, lymphoma, bone marrow or solid organ transplant)
Preterm infants born before 32 weeks' gestation or with birth weights <1700 g[c]	

a Follow the recommendations for immunocompromised children only in case of a documented immunodeficiency with high risk for IPD.
b High-risk patients: follow specific recommendations for vaccination against pneumococcal disease (see figure 4)

c Preterm newborns (especially those <32 weeks or <1700g) are at higher risk of having invasive disease by *streptococcus pneumoniae* than full term newborn, so administration of the PCV13 following a 3+1 schedule is recommended in these children, without later doses of PPSV23, unless there are additional risk factors.

These risk groups require a mixed vaccination course with PCV13 + PPSV23

This risk group requires only PCV13 (3+1) and no PPSV23

Figure 3 Situations involving risk of severe or recurrent pneumococcal disease in childhood and adolescence.

the PCV13.[11,12] This may be due to the nonexistent impact of the PCV10 on the rate of nasopharyngeal colonisation by serotype 19A,[14] which in fact increases after vaccination with the PCV10.[15] Moreover, given the importance of nasopharyngeal colonisation as regards herd immunity, it is unlikely that the PCV10 with achieve this protection against serotype 19A, as illustrated by the experience in Finland, where the number of cases of PID by this serotype has increased significantly in unvaccinated individuals and overall in the entire population.[16]

Figs. 3 and 4 show the groups at risk for pneumococcal disease and the recommendations for vaccination against pneumococcus.

Vaccination against group C meningogoccal disease

2016 recommendation: *We recommend three to four doses of the monovalent meningococcal conjugate vaccine (series of 1 [or 2] + 1 + 1), with the following schedule: a first dose at 4 months (or two doses at 2 and 4 months, depending on the vaccine used), another at 12 months, and a last one at 12 years of age. In adolescents, this last dose may be replaced by one dose of tetravalent meningococcal conjugate vaccine.*

There is extensive evidence on the effectiveness of this vaccine.[17] The rate of invasive meningococcal disease (IMD) by serogroup C remained very low in Spain during the 2012–2013 season (0.06 cases per 100,000 inhabitants). The incidence of meningococcal disease by other serogroups (W, Y and A) continues to be low in Spain at less than 5%. The availability of tetravalent conjugate vaccines (Menveo® and Nimenrix®),[18] reserved for vaccination of travellers to endemic regions, provides an ideal alternative for booster doses in adolescence, given the increased frequency of travel in this age group. The use of this vaccine is recommended at any age, especially in immunocompromised patients at high risk of IMD (complement deficiency, congenital or functional asplenia), for whom the CDC recommends revaccination every 5 years.[19]

Vaccination against measles, mumps and rubella (MMR)

2016 recommendation: *We recommend that a first dose of MMR vaccine be given at 12 months of age, with a second dose given between 2 and 4 years of age, preferably at 2, for the early remediation of any potential primary vaccine failures.*

Between Juland June 2015, the number of reported cases of measles in the WHO European Region decreased, although it continued to be unacceptably high; as did the number of rubella cases and outbreaks of mumps. The incidence of these diseases in Spain is low, but nevertheless shows the same trends.[20] It is essential that high coverage rates and thorough surveillance are maintained if we are to eradicate these diseases. The administration at 12 months of a single dose of vaccine achieves seroconversion rates of 95% and higher for all three viruses, rates that approximate 100% after administration of the second dose.

Vaccination against varicella

2016 recommendation: *It is recommended that all children be vaccinated against varicella with two doses: one at 15 months and another at 2–4 years of age. It is also recommended that a two-dose catch up vaccination be done in children and adolescents that have not had the disease and are unvaccinated (or that the series is completed in those who have only received one dose in the past).*

The MSSSI has approved the inclusion of vaccination against varicella with a two-dose schedule (at 12–15 months and 3–4 years) starting in 2016.[21] The two vaccines currently available (Varilrix® and Varivax®)[18] have

1. In light of the existing body of evidence, the CAV-AEP reasserts the need to include the routine vaccination against pneumococcus of all Spanish children aged less than 5 years, taking into account that at present the PCV13 vaccine offers the best coverage against the serotypes circulating in Spain and can have the most impact in controlling pneumococcal disease.

2. For as long as routine vaccination against pneumococcus is not implemented, 3+1 vaccination schedules should be followed (a three-dose primary vaccination series and one booster dose in the second year of life). If vaccination coverage rates are low, the lack of protection by herd immunity can make some children susceptible to certain serotypes, such as 6B and 23F, when they have only received two doses and until they are given the booster dose in the second year of life.

3. The CAV-AEP stresses the need to vaccinate individuals that are immunocompromised or otherwise at high risk for developing severe pneumococcal infections (Figure 3) following the recommended mixed schedule with administration of the PCV13 and the 23-valent polysaccharide pneumococcal vaccine (PPSV23).

   a. For children that are immunocompromised or have anatomic or functional asplenia (sickle cell disease or other haemoglobinopathies) aged 5 years or less: 1) *always use 3+1 schedules* when vaccination is initiated at 2 months concomitantly with other vaccines in the immunisation schedule; 2) if they have not received at least two doses of PCV13 in the first year of life, they must be given at least two doses of this vaccine; 3) children aged 2–5 years that have never received a dose of PCV13 must be given two doses of PCV13 at least two months apart; 4) When vaccination with PCV13 is complete, children aged more than 2 years must be given one dose of PPSV23 followed by single booster dose of PPSV23 five years later (no more than two doses of PPSV23 will be administered).

   b. Children at risk that are neither immunocompromised or asplenic, but at risk of having recurrent or severe pneumococcal infections aged 5 years or less (Figure 3) can be vaccinated with the schedule established for immunocompromised children or the routine vaccination schedule, completing vaccination after age 2 years with a single dose of PPSV23 at least two months apart from the last dose of PCV13.

   c. For all children at risk (Figure 3) aged 6–17 years: 1) administer a dose of PCV13; 2) administer a dose of PPSV23 at least 2 months apart from the dose of PCV13; 3) administer second and last dose of PPSV23 five years after the first PPSV23 dose only to immunocompromised and asplenic individuals.

4. Preterm newborns (especially those born before 32 weeks' gestation or weighing less than 1700 g) are more likely to develop invasive disease by *Streptococcus pneumoniae* than full term newborns, so administration of the PCV13 is specifically recommended in this population, following a 3+1 schedule and without subsequent doses of PPSV23, unless there are other associated risk factors.

Figure 4 Recommendations for vaccination against pneumococcal disease.

demonstrated high effectiveness in reducing the incidence of cases and complications, both in vaccinated and the unvaccinated individuals,[22,23] while exhibiting an excellent safety profile.[24]

Varicella vaccination is being rigorously monitored in Europe, where its potential benefits and cost-effectiveness are under debate. The impact of the disease and the need to achieve high vaccination coverage rates with two doses are critical aspects that need to be researched.[24]

After nearly 20 years of vaccination in the United States, there has been no evidence of a shift in the age of disease.[23] There had been an increase in the incidence of herpes zoster (HZ) prior to the introduction of childhood vaccination against varicella,[25] and several studies have concluded that there is no evidence of vaccination having any influence on the incidence of HZ,[25,26] although its incidence is lower in vaccinated children than in children with a history of natural varicella.[27] Childhood vaccination against varicella can only be considered cost-effective if there is evidence that it is not associated with an increase in the incidence of HZ in the general population, and especially in individuals aged more than 50 years, while the potential impact of vaccinating the latter against HZ is being evaluated.[24]

The optimal interval between doses and the duration of the protection conferred by vaccination remain to be determined, and a rigorous epidemiologic surveillance is essential to this end.[24]

Vaccination against human papillomavirus (HPV)

2016 CAV-AEP recommendation: *Routine vaccination against HPV is recommended for all girls aged 11–12 years as a means to prevent cervical cancer and precancerous lesions in the female genital tract.*

We believe that the optimal age for vaccination is 11–12 years. The 2015 recommendation of the MSSSI already incorporated the appeal of the CAV-AEP for advancing vaccination to age 12 years.[1] The currently approved dosage allows the administration of two doses in adolescents.[18]

Population	Age	Doses	Intervals	Booster doses
Infants	2–5 months	3[a]	≥ 1 month	Yes, one dose at 12–15 months[b]
Unvaccinated infants	6–11 months	2	≥ 2 months	Yes, one booster dose given in the second year of life at least two months after primary vaccination [b]
	12–23 months	2	≥ 2 months	Yes, one booster dose given 12–23 months after primary vaccination[b]
Children	2–10 years	2	≥ 2 months	Need has not been established
Adolescents and adults	11–50 years[c]	2	≥ 1 month	Need has not been established

Source: Bexsero® summary of product characteristics approved by the EMA
a The first dose must be administered at age 2 months or older. The safety and efficacy of the MenB vaccine in infants less than 8 weeks of age have not been established.
b The need for and timing of other booster doses have not been established.
c There are no data for adults aged more than 50 years.

Figure 5 Schedule for vaccination against group B meningococcal disease.

The data that are currently available support both the efficacy and the effectiveness of universal vaccination programmes for the prevention of persistent infection by HPV, genital warts and preneoplasias, including high-grade lesions.[28,29] We expect that data supporting the use of the vaccine for the prevention of cervical cancer and other cancers associated with HPV will soon follow.

Both vaccines have exhibited an adequate safety profile and a favourable benefit-risk ratio.[29] Still, the average coverage rate in Spain has not grown past 75%. A greater effort is required of healthcare professionals to improve coverage.

The tetravalent vaccine has been approved for males[18] and included in the official vaccination schedule of countries such as the United States, Canada, Austria, Switzerland and some regions in Italy. There is growing evidence on the role of HPV in the aetiopathogenesis of some types of cancer that affect both sexes, but especially those with a greater incidence in males, such as anal cancer and cancers of the head and neck.[30] Information must be given and vaccination with the tetravalent vaccine considered for males aged 11–12 years.[30]

Vaccination against group B meningococcal disease

2016 recommendation: *The meningococcal B vaccine exhibits the profile of a routine vaccine to be administered to all children starting at 2 months of age.*

Clinical trials have demonstrated that the only vaccine currently authorised in Europe for the prevention of group B IMD (Bexsero®) from 2 months of age is immunogenic and safe in infants, children, adolescent and adults, and induces immunologic memory. The decision of the United Kingdom (UK) to include it in its official schedule starting in September 1, 2015 has been particularly relevant, introducing the vaccine in infants with a 2 + 1 schedule (at 2, 4 and 12–13 months).[31]

Clinical trials have shown that Bexsero® may be administered concomitantly with the rest of the vaccines in the schedule, although this increases its reactogenicity. Administration of prophylactic paracetamol reduces the incidence of adverse events and does not affect the immunogenicity of this vaccine or any other vaccines in the routine schedule that are given concomitantly.Its compatibility with meningococcal C vaccines remains to be demonstrated.The AEMPS has authorised the distribution of this vaccine in community pharmacies starting on October 1, 2015.[32]Based on current data, we recommend[33]:

1. Administration of Bexsero® without concomitant administration of other vaccines in the schedule, with doses at 3, 5 and 7 months or administered at least 2 weeks apart from other routine vaccines.
2. This schedule would not require the routine use of prophylactic paracetamol.
3. The booster dose should be given between 13 and 15 months of age to avoid an overlap with the meningococcal C vaccine.

The dosage of this vaccine is summarised in Fig. 5.

Vaccination against rotavirus

2016 recommendation: *Vaccination against rotavirus is an advisable and safe health intervention for all infants.*

Since the introduction of the rotavirus (RV) vaccines in 2006, the morbidity and mortality of gastroenteritis due to RV infection in infants and young children has decreased considerably both in developing and developed countries.

Universal vaccination against rotavirus is recommended by the WHO for infants in every country of the world, and a significant decrease of morbidity and mortality caused by RV has been observed since the introduction of this vaccine in the official immunisation schedules of more than 77 countries (September 2015).

There is also evidence of a marked decline in the circulation of RV in European countries that have implemented routine vaccination, as can be observed in the UK after 2 years of universal vaccination.[34]

There has been a strict post-marketing surveillance, with a special focus on intussusception, for which a low risk has been observed (1–5 cases per 100,000 vaccinated children).[35] It is important that the parents of children that are going to be vaccinated are informed of the benefits and risks of this vaccine, explaining the warning signs for intussusception so parents can act quickly and avoid the complications of a delayed diagnosis (it is important that vaccination is initiated before 12 weeks). The benefits of vaccination against rotavirus continue to significantly outweigh the hypothetical risks of intussusception.[36]

The pentavalent vaccine, RotaTeq®, continues to be the only one available in Spain. It is administered orally and can be given at the same time as other vaccines in the schedule.

Vaccination against influenza

2016 CAV-AEP recommendation: *Vaccination against influenza is recommended for children and adolescents in the following circumstances: (a) risk groups: children aged 6 months and older and adolescents that are at risk due to specific circumstances or underlying disease; (b) children aged 6 months and older, adolescents and adults that are healthy and living with at-risk individuals.*

Fig. 6 summarises the recommendations of the CAV-AEP for vaccination against influenza, and Fig. 7 the dosage of the vaccine. Additional information can be found in the annual document released by this Committee specifically devoted to the influenza vaccine.[37]

Vaccination against hepatitis A

2016 recommendation: *Vaccination against hepatitis A with 2 doses at least 6 months apart is recommended in specific risk situations. Its administration should be considered for children aged more than 12 months attending child-care centres.*

The preparations, dosage and indications for this vaccine for children and adolescents at risk are presented in Fig. 8.[38] The vaccine has a 95% efficacy and it is estimated that anti-HVA antibodies persist for at least 14–20 years.[39]

1) At-risk groups: children aged 6 months and older and adolescents in the following situations or with underlying disease:
   - ❒ Chronic respiratory disease (such as cystic fibrosis, bronchopulmonary dysplasia, bronchiectasis, asthma, bronchial hyperresponsiveness etc).
   - ❒ Severe cardiovascular disease (congenital or acquired).
   - ❒ Chronic metabolic disease (such as diabetes mellitus, inborn errors of metabolism, etc).
   - ❒ Chronic kidney disease (such as kidney failure, nephrotic syndrome, etc) or liver disease.
   - ❒ Chronic inflammatory bowel disease.
   - ❒ Immunodeficiency, either congenital (excluding asymptomatic isolated IgA deficiency) or acquired (including long-term administration of highdose systemic corticosteroids).
   - ❒ Functional or anatomic asplenia.
   - ❒ Malignant disease.
   - ❒ Moderate or severe haematologic disease (such as clinically significant haemoglobinopathy, leukaemia, etc).
   - ❒ Chronic neuromuscular disease and moderate or severe encephalopathy.
   - ❒ Moderate or severe malnutrition.
   - ❒ Morbid obesity (BMI 3 or more standard deviations above the mean).
   - ❒ Down syndrome or other genetic disorders with risk factors for influenza.
   - ❒ Ongoing treatment with acetylsalicylic acid (due to the risk of Reye's syndrome in case of infection by the influenza virus).
   - ❒ Pregnancy in adolescents.
2) Healthy children aged 6 months or older, and healthy adolescents and adults (household members and caregivers) living with at-risk patients.[a]

This Committee, in agreement with other scientific associations in Spain, would like to emphasise the recommendation that all health care professionals that have contact with patients be vaccinated against influenza.

Notes:

a Likewise, we want to stress the recommendation of vaccinating household contacts of at-risk infants aged less than 6 months, as the latter cannot be given the influenza vaccine.

Figure 6 Recommendations of the CAV-AEP for vaccination against seasonal influenza 2015–2016 (with trivalent inactivated vaccines).[37]

6 months to 8 years	- Between ages 6 and 35 months, the dose is 0.25 mL, although some studies have shown greater immunogenicity with doses of 0.5 mL. - Starting at 36 months the dose is 0.5 mL. - 2 doses at least 4 weeks apart. - A single dose suffices if the patient has received at least 2 doses of the vaccine in the past, which need not have been administered in the course of a single season.
9 years and older	- 0.5 mL dose. - One dose each season, regardless of history of influenza vaccination in previous seasons.

Figure 7 Dosage of the influenza vaccine by age and vaccination history.[37]

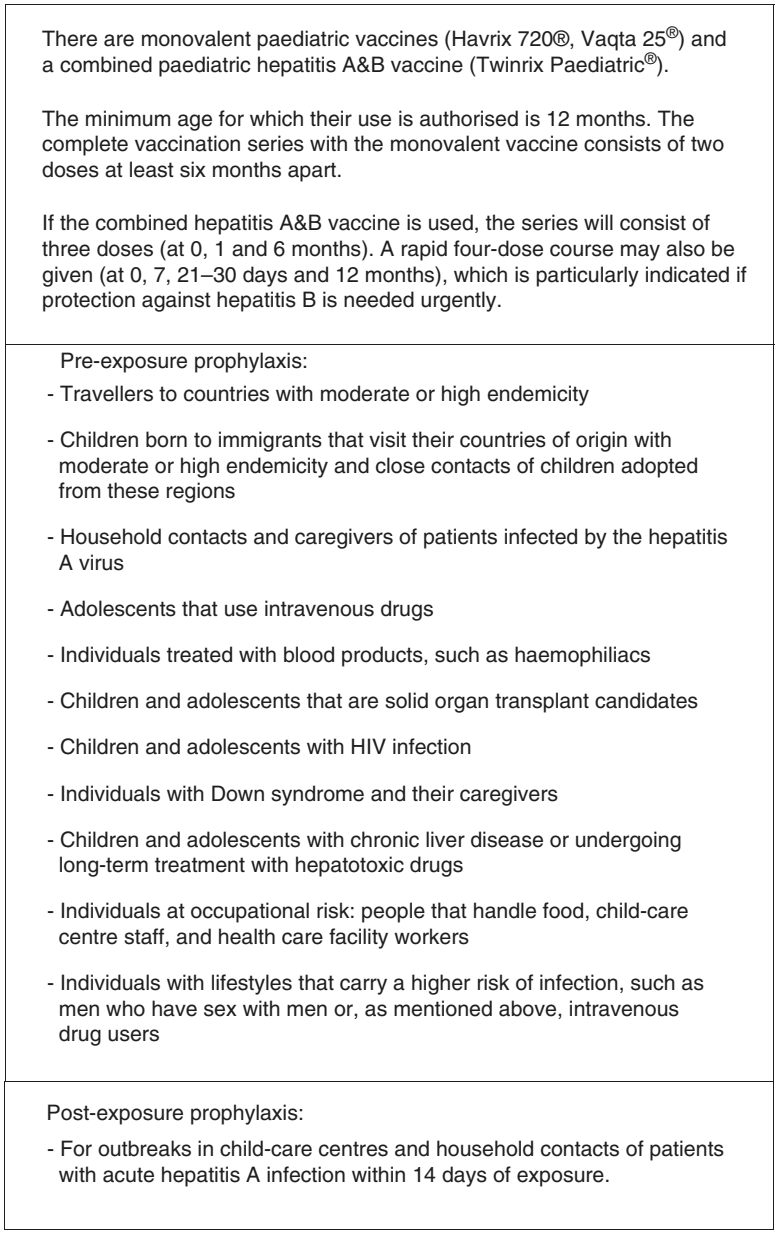

Figure 8 Preparations, dosage and recommendations of the CAV-AEP for vaccination against hepatitis A in children and adolescents that belong to at-risk groups.

Child-care centres that care for incontinent children are more likely to experience outbreaks of hepatitis A and transmit the virus to susceptible household contacts. For this reason, children aged more than 12 months that attend child-care centres could benefit from the administration of this vaccine, while benefitting their contacts indirectly.

Another special risk group are children born, most of them in Spain, to immigrants from endemic regions, as they are at a high risk of contracting the disease when they visit their countries of origin and subsequently transmitting the disease.[40]

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Conflicts of interest

Last 5 years:

- DMP has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer and Sanofi Pasteur MSD, as a researcher in clinical trials conducted by GlaxoSmithKline and as a consultant on the Astra-Zeneca, GlaxoSmithKline, Novartis and Pfizer advisory boards.
- FJAG has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer and Sanofi Pasteur MSD

and as a consultant on GlaxoSmithKline and Novartis advisory boards.
- JAF has collaborated in educational activities and as a research in clinical trials funded by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD, and as a consultant in GlaxoSmithKline and Novartis advisory boards.
- MJCO has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer and Sanofi Pasteur MSD, as a researcher in clinical trials conducted by Pfizer and as a consultant on GlaxoSmithKline, Novartis, Pfizer and Sanofi Pasteur MSD advisory boards.
- JMCR has collaborated in educational activities funded by GlaxoSmithKline, Sanofi Pasteur MSD and Novartis.
- NGS has collaborated in educational activities funded by Sanofi Pasteur MSD and has attended educational activities funded by Novartis and Pfizer.
- AHM has received funding to attend domestic educational activities.
- THSM has collaborated in educational activities funded by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD and as a researcher in clinical trials funded by GlaxoSmithKline and Pfizer.
- MMM has collaborated in educational activities funded by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD, as a researcher in clinical trials conducted by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD and as a consultant on a Novartis advisory board.
- LOC has collaborated in educational activities funded by GlaxoSmithKline, Novartis, Pfizer and Sanofi Pasteur MSD and as a researcher in clinical trials conducted by GlaxoSmithKline.
- JRC has collaborated in educational activities funded by GlaxoSmithKline, Pfizer and Sanofi Pasteur MSD and as a researcher in clinical trials conducted by GlaxoSmithKline and Pfizer.

Appendix. Composition and professional affiliation of the members of the Advisory Committee on Vaccines of the Spanish Association of Paediatrics

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- Francisco José Álvarez García. Pediatra. Centro de Salud de Llanera. Asturias. Profesor Asociado en Ciencias de la Salud. Departamento de Medicina. Universidad de Oviedo.
- Javier Arístegui Fernández. Unidad de Infectología Pediátrica. Hospital Universitario de Basurto. Bilbao. Departamento de Pediatría. Facultad de Medicina of the Universidad del País Vasco (UPV/EHU).
- María José Cilleruelo Ortega. Servicio de Pediatría. Hospital Universitario Puerta de Hierro-Majadahonda, Madrid. Departamento de Pediatría. Facultad de Medicina of the Universidad Autónoma de Madrid.
- José María Corretger Rauet. Consell Assessor de Vacunacions. Departament de Salut. Generalitat de Catalunya. Barcelona.
- Nuria García Sánchez. Pediatra. Centro de Salud Delicias Sur. Zaragoza. Profesora Asociada en Ciencias de la Salud. Departamento de Pediatría. Facultad de Medicina of the Universidad de Zaragoza.
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- Manuel Merino Moína. Pediatra. Centro de Salud El Greco. Getafe. Madrid. Profesor Colaborador de la Facultad de Medicina. Universidad Europea. Madrid.
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- Jesús Ruiz-Contreras. Servicio de Pediatría. Hospital Universitario 12 de octubre. Madrid. Departamento de Pediatría. Facultad de Medicina of the Universidad Complutense de Madrid.

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