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# Vaccination schedule for childhood and adolescence: comparing recommendations

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**Abstract**

**Objectives:** To present the criteria used to define a vaccination schedule for childhood and adolescence, comparing the recommendations of national and international excellence institutions.

**Sources of data:** Review of publications by the Brazilian Society of Pediatrics, the Brazilian Health Ministry, the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP) and the Centers for Disease Control and Prevention (CDC) covering the period from 2000 to 2005.

**Summary of the findings:** Local epidemiological and socioeconomic factors and the available infrastructure often define the priorities of immunobiological recommendations. The publications reviewed, both national and international, differ in terms of the vaccination schedule for tuberculosis, poliomyelitis, rotavirus, pertussis, pneumococcus, meningococcus, varicella and hepatitis A. In Brazil, there are Special Immunobiology Referral Centers (CRIE - Centros de Referência de Imunobiológicos Especiais), which, according to specific criteria, offer the population immunobiologicals that are unavailable on the public health network.

**Conclusions:** While the use of a universal schedule is impossible due to epidemiological and operational differences, there are similarities that can be incorporated with different populations, as long as technical and scientific criteria are respected.

*J Pediatr (Rio J). 2006;82(3 Suppl):S4-14:* Vaccination schedule, childhood, adolescence, vaccines, immunobiologicals.

## Introduction

Historically, many different vaccination schedules have been proposed – to meet legal obligations, in response to epidemiological data or to incorporate new vaccines. Before defining a vaccination schedule, however, it is necessary to consider fundamental aspects of vaccination such as individual and social characteristics, the epidemiological profile of regional diseases and also the state of the available infrastructure. These issues are of major importance when comparing, for example, developed and developing nations. In the latter, socioeconomic and sanitary issues, the endemic character of diseases and the lack of infrastructure must direct the focus of mass vaccination campaigns. It is in these regions that combining vaccinations is most indicated, in order to reduce the number of appointments.[1,2]

From an epidemiological point of view, when planning a vaccination schedule, long intervals between successive vaccines should be avoided. Vaccination should begin as early as possible and take into account the immune response to products at different ages and the history of diseases in the population. In order to be acceptable, planning should assess: the population's travel habits; climactic changes that interrupt community actions; local beliefs and customs that could represent obstacles to publicizing and executing the program. With relation to operational issues, schedules should specify the minimum possible number of visits to any given individual and should optimize simultaneous administration of vaccines and the use of combined vaccines. There should be periodic review and revision of the criteria established, considering the responses achieved and new scientific data to demonstrate the efficacy of the schedule implemented.[3] One example is the immunization schedule that represents the consensus of the American Academy of Pediatrics (AAP), the Advisory Committee on Immunization Practices (ACIP), the Centers for Disease Control and Prevention (CDC) and the American Academy of Family Physicians (AAFP) on routine immunization during childhood and adolescence in the USA. This policy is reviewed periodically and presented annually, in order to incorporate new vaccines and revised recommendations. The World Health Organization (WHO) publishes a recommended schedule for their expanded program on immunization. National health ministries can modify this schedule to meet local demands.[4]

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In Brazil the Health Ministry (HM) published its latest review of the *Programa Nacional de Imunizações* (PNI – Brazilian National Immunization Program) vaccination schedule in the form of a directive.[5] This directive establishes that fulfillment of the schedule is mandatory and must be confirmed through vaccination certificates issued by public health services or private vaccination clinics, as long as they are compliant with relevant legislation. The certificate must identify the vaccinating institution, the immunobiological administered, the manufacturing laboratory and the batch number. It should be signed by the physician or nurse responsible for the service. As part of the PNI, the HM has set up Special Immunobiology Referral Centers (CRIE – Centros de Referência de Imunobiológicos Especiais) that provide expensive high-tech products and target a special segment of the Brazilian population who, for some reason, are unable to take advantage of the routine services and materials available through the public health system. At these referral centers, the conditions of patients can be evaluated and their requirements for vaccination and the most appropriate vaccination program established.

In 2005 the Brazilian Society of Pediatrics (Sociedade Brasileira de Pediatria – SBP) published its vaccination schedule for childhood and adolescence, developed by their Infectology Scientific Department.[6] The previous recommendation (2003) stated that vaccines categorized as optional should be used according to availability and possibility.

In January 2006, ACIP published the latest revision of its vaccination schedule for childhood and adolescence for the current year. There are several changes and additions in relation to the previous schedule.[7]

For 2005/2006, the Sociedade Brasileira de Imunizações (SBIm, Brazilian Society of Immunizations) has recommended a different proposal for the vaccination of children, women, adolescents/adults and for professionals in a variety of occupations. These schedules are characterized by an up-to-date focus, employing new immunobiological presentations, emphasizing their availability on the public and private health networks and presenting clinical and epidemiological justification for their indication.[8]

The objective of the present study is to make a comparative analysis of the vaccine schedules for childhood and adolescence recommended by the HM, SBP and ACIP, demonstrating their similarities and highlighting the differences.

Some important observations:

1. Within the "comments" on each vaccine, information considered important by the authors has been included that may not be mentioned in the suggested schedule (Table 1).
2. Different HM sources may offer conflicting information concerning indications for vaccination in specific situations and it is suggested that updates be sought on institutional websites (Table 2) and CRIE guidelines (Table 3).[9]
3. The vaccine against rotavirus, one of the primary etiologic agents of severe diarrhea worldwide, was added to the PNI 2006 infant vaccination schedule, by means of a technical standard.[10]

## Tuberculosis vaccine (BCG)

**Use and efficacy.** Protection against tuberculosis. Efficacy is between 46 and 100% during the first year of life, especially against hematogenous dissemination and its most severe manifestations, such as meningoencephalitis. Its efficacy against pulmonary tuberculosis is questionable (0 to 80%).[11] The need for revaccination between 6 and 10 years of age as recommended by the HM remains controversial.[5,12]

**Indications.** The HM and the SBP recommend routine BCG vaccination. The ACIP does not include this vaccine in its routine schedule.

**HM.** Recommends routine vaccination at birth. Revaccination between 6 and 10 years has not been implemented in some states, awaiting the conclusions of studies into the efficacy of the second dose.[5]

**SBP.** Recommends routine vaccination at birth. The second dose of the BCG vaccine should be given, or not, in accordance with the local health policy (state or municipal).[6]

**ACIP.** Not routinely given in the USA. Tuberculosis control is based on rigorous epidemiological surveillance, with early identification and diagnosis of cases and contacts and follow-up of treatment.[4,13]

**Comments.** According to HM directives, the minimum weight for BCG administration is 2 kg. In the absence of vaccine scar 6 months after administration, vaccination should be repeated without prior tuberculin testing.[14] Both the WHO and HM recommend vaccination of the newborn infants (NB) of HIV-infected mothers and of asymptomatic seropositive children without immunodepression.[15] The WHO does not recommend BCG revaccination.[12]

## Hepatitis B vaccine

**Use and efficacy.** Prevention of hepatitis B and D. Efficacy of up to 95% in children and adolescents.[4] Certain factors can reduce the efficacy of this vaccine: immunodepression, diabetes, obesity, smoking, renal insufficiency, gluteal administration and older age.[4] Prophylactic administration associated with hepatitis B immune globulin (HBIG) to NBs of HBsAg and HBeAg positive mothers within 12-24 hours of birth is 85 to 95%

**Table 1 -** Suggested schedule for immunization of children and adolescents

| Age | Vaccine |
|---|---|
| Newborn | BCG, hepatitis B* |
| 1 month | Hepatitis B* |
| 2 months | Poliomyelitis†, diphtheria, tetanus and pertussis‡, *haemophilus* (Hib)§, rotavirus¦, pneumococcal conjugate (PCV7)¶ |
| 3 months | Meningococcal C conjugate** |
| 4 months | Poliomyelitis†, diphtheria, tetanus and pertussis‡, *haemophilus* (Hib)§, rotavirus¦, pneumococcal conjugate (PCV7)¶ |
| 5 months | Meningococcal C conjugate** |
| 6 months | Poliomyelitis†, diphtheria, tetanus and pertussis‡, *haemophilus* (Hib)§, hepatitis B*, pneumococcal conjugate (PCV7)¶ influenza†† |
| 7 months | Meningococcal C conjugate**, influenza†† |
| 9 months | Yellow fever‡‡ |
| 12 months | Measles, rubella and mumps, varicella§§, hepatitis A¦¦ |
| 15 months | Poliomyelitis†, diphtheria, tetanus and pertussis‡, *haemophilus* (Hib)§, pneumococcal conjugate (PCV7)¶ |
| 18 months | Hepatitis A¦¦ |
| 4 to 6 years | Diphtheria, tetanus and pertussis‡ and measles, rubella and mumps |
| 6 to 10 years | BCG¶¶ |
| 11 to 19 years*** | Diphtheria, tetanus and pertussis†††, hepatitis B, yellow fever‡‡, measles, rubella and mumps‡‡‡, varicella§§ |

Vaccines recommended as routine by the Health Ministry (HM).
The references used are the vaccination schedules for childhood and adolescence published by the HM, Brazilian Society of Pediatrics (Sociedade Brasileira de Pediatria – SBP) and the Advisory Committee on Immunization Practices (ACIP).[5-7]

* Hepatitis B vaccine: the first dose of vaccine should be given within the first 12 hours of life. If the mother is confirmed as HBsAg negative, then the hepatitis B vaccine can be administered at 2, 4 and 6 months of age, using presentations combined with other vaccines recommended at those ages.

† Poliomyelitis vaccine: the vaccine of choice is the inactivated version (IPV).

‡ Diphtheria, tetanus and pertussis vaccine: the presentation of choice is the acellular vaccine (DTaP).

§ *Haemophilus influenzae* type b (Hib) vaccine: the HM provides tetravalent vaccine (DTwP + Hib) for the first 3 doses (2, 4 and 6 months) and does not indicate a booster dose. The SBP recommends that if a combined vaccine containing DTaP and Hib is used for the basic course, then a fourth dose of Hib should be given at 15 months.

¦ Rotavirus vaccine (RV): given orally in 2 doses. The maximum age for administering the first dose is 14 weeks and for the second it is 24 weeks. Despite being packaged in syringes, the vaccine must only be given orally.

¶ 7-valent pneumococcal conjugate vaccine (PCV7): recommended by the SBP for all children aged 2 to 23 months.

** Meningococcal C conjugate vaccine: recommended by the SBP depending on the local or regional epidemiological situation. Can be given in two or three doses , depending on the manufacturer.

†† Influenza (flu) vaccine: recommended by the SBP and ACIP, annually, during the autumn, for healthy children aged 6 to 23 months. The first year the vaccine is used it should be given twice with a 1 month interval between doses.

‡‡ Yellow fever vaccine: indicated for residents of or travelers to endemic areas (Brazilian states: AP, TO, MA, MT, HM, RO, AC, RR, AM, PA, GO and DF), transitional areas (some regions of the states: PI, BA, MG, SP, PR, SC and RS) and areas of potential risk (some regions of the states: BA, ES and MG). Vaccinate 10 days before traveling.

§§ Varicella vaccine: recommended by the SBP and ACIP as routine from 1 year of age.

¦¦ Hepatitis A vaccine: recommended by the SBP and ACIP as routine from 1 year of age.

¶¶ Tuberculosis vaccine (BCG): there is still ongoing debate on the efficacy of the second dose. To be given or not according to state or municipal health policy.

*** The start of adolescence is an important time to review susceptibility to and/or immunity from diseases and to catch up with the vaccination schedule. Based on risk factors and local epidemiology, indications for vaccination against hepatitis A and meningococcus C should be assessed.

††† Diphtheria, tetanus and acellular pertussis vaccine for adolescents and adults (dTap): already recommended as routine by both the ACIP and SBP for revaccination at adolescence, as an alternative to the dT vaccine to maintain protection against pertussis.

‡‡‡ Measles, mumps and rubella vaccine (MMR) or measles and rubella vaccine (MR): recommended by the HM for women aged 12 to 49 years and for men up to 39 years of age who have no proof of earlier vaccination.

**Table 2 -** Electronically updated references

| | |
|---|---|
| HM – General | http://portal.saude.gov.br/saude/ |
| Publications | http://dtr2001.saude.gov.br/svs/pub/pub00.htm |
| Directives | http://portalweb05.saude.gov.br/portal/arquivos/pdf/calendarios_vacin_2004.pdf |
| PNI | http://portalweb05.saude.gov.br/portal/saude/visualizar_texto.cfm?idtxt=21461 |
| CRIE | http://portalweb05.saude.gov.br/portal/saude/visualizar_texto.cfm?idtxt=21614 |
| SBP | www.sbp.with.br |
| SBIm | www.sbim.org.br/institucional.htm |
| CDC – General | www.cdc.gov |
| Schedules and recommendations | www.cdc.gov/nip/home-hcp.htm |
| ACIP Recommendations | www.cdc.gov/nip/publications/acip-list.htm |
| AAP | www.aap.org |
| AAFP | www.aafp.org |
| WHO | www.who.int/en |

**Table 3 -** Indications* for the use of special immunobiologicals at CRIE referral centers[9]

| | |
|---|---|
| **Human hepatitis B immunoglobulin** | Indications: NBs of hepatitis B surface antigen positive mothers (HBsAg+); accidental percutaneous exposure to blood or mucosal contamination; sexual contacts of acute hepatitis B patients; victims of sexual abuse; the immunodepressed, even when previously immunized due to one of the indications above. |
| **Human rabies immunoglobulin** | Indication: People who require anti-rabies serum, but have a history of allergy to the heterologous serum; people who require anti-rabies serum, whose test for serum sensitivity was positive and who, during desensitization with serum presented hypersensitivity reactions; immunodepressed people requiring anti-rabies prophylaxis (irrespective of the type of accident). |
| **Human tetanus immunoglobulin** | Indications: People who require anti-tetanus serum (AST) with history of allergic reaction to the heterologous serum; newborns with potentially tetanogenic injuries and whose mothers' vaccination status is either unknown or inadequate. |
| **Human varicella-zoster immunoglobulin** | Recommended for the following groups of susceptible people who have had significant contact: pregnant women; the newborn infants of mothers with varicella onset during the last 5 days of pregnancy or up to 48 hours after birth; premature newborn infants, with 28 or more weeks' pregnancy and whose mothers have no history of varicella; premature newborn infants, with less than 28 weeks' pregnancy (or less than 1,000 g at birth), regardless of maternal history of varicella; immunodepressed children or adults, irrespective of their previous history of varicella or vaccination. |
| **Inactivated poliomyelitis vaccine** | Indications:<br>a) Immunodepressed children (with congenital or acquired immune deficiency) who have not been vaccinated or who were given an incomplete course of vaccination against poliomyelitis.<br>b) The children of HIV+ mothers before diagnosis is defined. If the inactivated vaccine is unavailable, infected children with the HIV virus (symptomatic or not) and the children of HIV+ mothers can be given the OPV.<br>c) Premature newborn infants who are hospitalized in a neonatal unit when they reach vaccination age.<br>d) Children who have been in contact at home or in hospital with immunodepressed people and require the poliomyelitis vaccine.<br>e) People undergoing transplantation of bone marrow or solid organs.<br>f) History of paralytic complications (flaccid paralysis) after an earlier dose of OPV. |
| **DTaP** | Indications:<br>Children up to 6 years old who<br>a) after receiving any of the doses in a DTwP or DTwP+Hib course present the following adverse reactions: convulsions in the first 72 hours; hypotonic hyporesponsive episode (HHE) during the first 48 hours.<br>b) present lung disease or chronic heart disease with risk of decompensation in case of fever.<br>c) present incapacitating chronic neurological diseases.<br>d) present chronic convulsive diseases.<br>A basic course is also recommended for extremely premature newborn infants (< 1,000 g or < 31 weeks' gestation) or newborn infants who are hospitalized in a neonatal unit when they reach vaccination age. |
| **Diphtheria and tetanus pediatric vaccine** | Indications: Children less than 7 years old who present encephalopathy during the first 7 days after receiving the DTwP vaccine, DTwP+Hib or the DTaP vaccine (the pertussis vaccine is contraindicated) |
| **Conjugate *Haemophilus influenzae* type b vaccine** | Indications:<br>a) Children less than 1 year old with indications for DTaP (who are unable to receive the tetravalent vaccine currently available on the public health system).<br>b) Immunodepressed children aged 12 to 59 months.<br>c) Unvaccinated children and adolescents, at least 5 and less than 19 years old, in the following situations: lung disease (including persistent moderate or severe asthma), chronic renal or cardiac disease; diabetes mellitus; immunodepression, including asymptomatic HIV infections; anatomic or functional asplenia; hemoglobinopathies; with trisomies; before elective splenectomy.<br>d) Bone marrow transplantation patients of any age. |
| **Conjugate meningococcal vaccine** | Indications: people with congenital or acquired asplenia (sickle-cell anemia and thalassemia, post-splenectomy patients); congenital immunodeficiencies (complement deficiency, agammaglobulinemia, etc.); people with indications for cochlea implantation; bone marrow transplantation patients; deposit disease sufferers. |
| **Hepatitis A vaccine** | Indications: Individuals who are chronically positive for hepatitis B surface antigen (HBsAg+); other chronic liver disease patients; transplant patients and bone marrow and solid organ donors; immunodeficiency caused by neoplasms or treatment; HIV positive children (less than 13 years old); individuals with trisomy; deposit disease patients. |
| **Varicella vaccine** | Indications:<br>Pre-exposure: immunodepressed patients (as recommended in the literature): acute lymphoblastic leukemia and solid tumors in remission (at least 12 months), if patients have at least 1,200 lymphocytes/$mm^3$ without radiotherapy; humoral immunodepression; health professionals, people susceptible to the disease and their relatives and immunocompetent people who come into hospital or domestic contact with immunodepressed patients; donors and candidates for solid organs; bone marrow donors; bone marrow transplant patients on protocols; people who will be subjected to chemotherapy, on research protocols; chronic nephropathies; nephrotic syndrome; infection by HIV/AIDS (A1N1); people with chronic severe dermatological diseases; people on chronic salicylates use; people with anatomic or functional asplenia ; trisomy patients.<br>Post-exposure: immunocompetent people who have contact with cases on wards. |

* The indications for the immunobiologicals provided at CRIEs are constantly being updated and it is suggested that the HM website be consulted for revisions (Table 2).

**Table 3 -** continuation

| | |
|---|---|
| **Influenza vaccine** | Indications: Priorities for influenza vaccination at CRIEs: people with lung disease (including asthma) or cardiovascular chronic, nephropathy chronic, diabetes mellitus, liver disease chronic, anatomic or functional asplenia and related diseases, hemoglobinopathies, HIV+, trisomy, incapacitating neurological diseases; patients subjected to transplantation of solid organs and bone marrow, cochlea implantation, chronic salicylates use; donors of solid organs and bone marrow; immunodepressed; domestic contacts of immunodepressed patients; health professionals. |
| **Typhoid vaccine** | Indications: People exposed as a result of living in or visiting endemic areas. |
| **7-valent conjugate and 23-valent polysaccharide pneumococcal vaccines** | Indications: HIV/AIDS; the immunodepressed; congenital or acquired asplenia and related diseases; hemoglobinopathies; chronic lung disease (including severe asthma with corticoids in immunosuppressive doses); chronic heart diseases; chronic nephropathies (including nephrotic syndrome); diabetes mellitus; liver disease chronic; solid organ and bone marrow transplantation patients; cerebrospinal fluid fistula; incapacitating chronic neurological diseases; deposit diseases; trisomies; cochlea implantation. |

effective at preventing acute and chronic infections by the hepatitis B virus (HBV) in these children. These levels of protection are only achieved if the NBs are given another two doses of the hepatitis B vaccine by 6 months of age. If the vaccine is used in isolation (without HBIG), in the same situation, efficacy is 70 to 95%.[4,16]

**Indications.** The HM, SBP and ACIP recommend routine hepatitis B vaccination within the first 12 hours of life[5-7,14] or before hospital discharge.[7]

**HM.** The basic scheme is in three doses, with intervals of 30 days between the first and second and 180 days from the first to the third dose. The vaccine is available on the public health service for children and adolescents up to 19 years without proof of previous vaccination. In cases of incomplete vaccination, the course already started should be completed.[5] The vaccine is also available for people of any age in special circumstances (for example: the sexual contacts of a person with acute hepatitis B).[17]

**SBP.** Children with birth weight ≤ 2 kg should be given the first dose at birth, the second on reaching 2 kg, the third 1 month after the second and a fourth dose 6 months after the first. Unvaccinated adolescents and adolescents who have never had the disease constitute a priority group for vaccination against hepatitis B.[6]

**ACIP.** Only the monovalent vaccine is indicated at birth. Later doses can be monovalent or combined, and three or four doses can be given in total. If the first dose is given at birth, the second should be given at 1-2 months. The first dose can be given at 2 months if the mother is confirmed as HBsAg negative. The final dose (whether third or fourth) cannot be given before 24 weeks of life.[4,7] Infants born to HBsAg positive mothers should be given the vaccine and 0.5 mL of HBIG, in different locations, during the first 12 hours of life.[4] These children should be tested for HBsAg and anti-HBs between 9 and 18 months of age.[7] When the mother's HBsAg status is unknown, infants should receive their first dose of vaccine during the first 12 hours of life. The mother should be tested as quickly as possible and, if the result is positive, HBIG should be given within a maximum of 7 days.[4,7]

**Comments.** Despite the recommendation by both the HM and SBP that the first dose of vaccine be given within the first 12 hours of life, this conduct is unfortunately not yet routine in Brazil. The state of São Paulo has passed a law to make this practice mandatory.[18] Pre-vaccination screening of children and adolescents without risk factors is not recommended.[4] Routine serological testing (anti-HBs) is recommended after the full vaccination course is complete for people at risk, (for example: drug users).[4] The combined hepatitis A and B vaccine can be given from 1 year of age onwards, in three doses, at 0, 1 and 6 to 12 months.[19,20] The adult presentation of this combined vaccine can be administered to children aged 1 to 15 years, in two doses (0 and 6 to 12 months).[21,22]

### Live oral poliomyelitis vaccine (OPV) and inactivated poliomyelitis vaccine (IPV)

**Use and efficacy.** Prevention of poliomyelitis. Seroconversion in 95% of individuals vaccinated after two doses and in 99 to 100% after three doses.[4] Prolonged immunity, possibly lifelong.[4] The IPV version offers mucosal immunity, but at lower intensity than the OPV.[4]

**Indications.** The HM, SBP and ACIP recommend routine poliomyelitis vaccination.

**HM.** The HM recommends the OPV as routine, from 2 months age, in four doses.[5] For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP suggests that the IPV can replace the oral vaccine in all doses, preferably for the first two doses. All children younger than 5 years of age should be given the OPV on national vaccination days.[6]

**ACIP.** The ACIP only recommends the IPV as routine.[7]

**Comments.** If the OPV is inadvertently administered to a family member of an immunodepressed person, physical contact between the two should be avoided for 4 to 6 weeks.[4] The childhood OPV course is in four doses, at 2, 4, 6 and 15 months of age. The IPV is given in four doses, in the same sequence as the OPV[17] or at 2, 4, 6-18

months and at 4-6 years of age.[7] In countries were the disease has been eradicated, there is a tendency towards exclusive utilization of the inactivated vaccine in order to avoid the risk of paralysis from the live vaccine.[4,7]

### Rotavirus vaccine (RV)

**Use and efficacy.** Prevention of rotavirus diarrhea, by means of a monovalent vaccine produced from an attenuated human strain of the G1,P[8] serotype. According to studies carried out in Finland, Mexico and 10 Latin American countries, after the administration of two doses of the vaccine, efficacy against severe rotavirus gastroenteritis varied from 68.5 to 90.0% and against hospitalizations caused by RV disease, from 65.4 to 93.0%.[10,23-26]

**Indications.** The HM and SBP recommend routine RV vaccination. In February 2006 the ACIP approved the use of a pentavalent RV vaccine (Rotateq® - Merck Sharp & Dohme) at 2, 4 and 6 months in the USA.[27,28]

**HM.** The HM recommends routine RV vaccination, in two doses, exclusively orally – the first dose between 6 and 14 weeks of life and the second between 14 and 24 weeks, with a minimum interval of 4 weeks between them. The second dose should not be given after 24 weeks.[10]

**SBP.** In a technical statement produced by the Infectology Scientific Department, the SBP recommended that the RV vaccine be added to the childhood vaccination schedule and that the manufacturer's instructions be followed for administration.[29]

**ACIP.** In February 2006 the ACIP approved the use of a pentavalent RV vaccine (Rotateq® - Merck Sharp & Dohme) at 2, 4 and 6 months in the USA.[27,28]

**Comments.** Breastfeeding does not interfere with absorption of the vaccine. Administration is exclusively by oral route: in case of vomiting, spitting out or regurgitation, the doses should not be repeated. Clinical trials have reported no increase in cases of intussusception with the use of this vaccine. There are no reports of interference in immune response or increases in adverse reactions if given simultaneously with other vaccines used at these ages, including combined vaccines.[10,23-26]

### Diphtheria, tetanus and whole-cell pertussis vaccine (DTwP), diphtheria, tetanus and acellular pertussis vaccine (DTaP) and pediatric diphtheria, tetanus vaccine (DT)

**Use and efficacy.** Protection against pertussis, tetanus and diphtheria. Efficacy against pertussis: more than 80% with three doses, declining over time.[30] Atypical disease may affect vaccinated people or some may present the disease due to a natural decrease in antibodies. Efficacy of the vaccine against tetanus: three doses confer protection to most people for at least 10 years.[4] Efficacy of the vaccine against diphtheria: there is only epidemiological evidence demonstrating the efficacy of the vaccine.[4] Revaccination after 6-12 months with the DTwP/DTaP/DT vaccines has a booster effect on all components, with persistent levels that generally last more than 10 years.[4] The different versions of the DTaP vaccine, with three or five fractions of the pertussis component have comparable clinical efficacy.[4]

**Indications.** The HM, SBP and ACIP recommend routine vaccination against pertussis, tetanus and diphtheria.

**HM.** The HM recommends a course of three doses of the combined DTwP + Hib vaccine (tetravalent) at 2, 4 and 6 months of age and two boosters with DTwP, the first at 15 months and the second between 4 and 6 years.[5] The ministry makes DTaP available for those children who exhibit significant reactions to DTwP[17] and DT for children less than 7 years old for whom the pertussis component is contraindicated.[17] For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP states that the DTwP vaccine is effective and well tolerated, but when possible, the acellular vaccine should be given as it has lower reactogenicity.[6]

**ACIP.** The ACIP only use the DTaP vaccine as routine. The fourth dose can be given at 12 months of age, as long as the minimum interval of 6 months since the third dose is respected and there is a chance the child may not return at 15-18 months. The fifth dose should be given after 4 years of age.[7]

**Comments.** Reactions such as convulsions (with or without fever), occurring within 3 days; persistent, inconsolable crying or screaming for 3 or more hours within 48 hours of vaccination; collapse or a state similar to shock (hypotonic-hyporesponsive episode) within the first 48 hours; temperature of 40.5 ºC or more within 48 hours, with no other obvious cause, do not contraindicate subsequent doses of DTwP or DTaP, but the decision to administer them must be considered with care. Preferably, DTaP should be used to reduce the possibility of further adverse reactions.[4-6,17,31] The repetition of such reactions may justify the interruption of immunization for pertussis.[4] In children with high fever and persistent crying after previous doses of DTwP, prophylaxy with paracetamol is recommended, or, preferably, that DTaP be used.[5] If the fourth dose is administered after 4 years of age then the fifth dose is not necessary.[4]

### Diphtheria, tetanus and acellular pertussis vaccine for adolescents and adults (dTap) and adult diphtheria and tetanus vaccine (dT)

**Use and efficacy.** Prevention of tetanus, diphtheria and pertussis in children, adolescents and adults. Tetanus

vaccine : for most people, three doses confer protection for at least 10 years.[4] Efficacy of the vaccine against diphtheria: there is only epidemiological evidence demonstrating the efficacy of this vaccine.[4] Pertussis vaccine: reported efficacy in adolescents and adults after one dose of the vaccine dTap is 85%.[32]

**Indications.** The HM, SBP and ACIP recommend the adult tetanus and diphtheria vaccine and/or the diphtheria, tetanus and acellular pertussis vaccine for adolescents and adults as routine.

**HM.** The HM recommends dT as the routine vaccine for booster doses, at 10 year intervals, shortened to 5 years in cases of pregnancy or wounds suspected of causing tetanus.[5]

**SBP.** The SBP routine included routine dT vaccine boosters every 10 years. As an alternative to the dT vaccine, the dTap vaccine can be given at 15 years.[6]

**ACIP.** As of 2006, the ACIP recommends that the first booster after early childhood be at the start of adolescence (11-12 years). The dTap vaccine and the next boosters should be given with dT every 10 years.[7]

**Comments.** People previously vaccinated with a complete course should be given a booster every 10 years. Those whose course was never completed should complete it with one or two doses.[4,14] People who have never been vaccinated should receive three doses: the intervals between doses vary from one reference source to another. The HM recommends administration at 0, 2 and 4 months,[5] and the ACIP, 0, 2 and 8 months.[4] The minimum interval between doses is 30 days. These vaccines are recommended for prophylaxis after wounding, together with equine anti-tetanus serum (ATS)[14] or human tetanus immunoglobulin (TIG),[4] for those non-immunized or partially immunized against tetanus. If vaccination is necessary during pregnancy it is given in the first prenatal consultation,[14] or in the second trimester[4] and before 15 days prior to the estimated date of birth, providing adequate protection for the NB.[4] Women who have not previously been vaccinated should receive three doses, two during pregnancy, with 4 to 8 weeks between them, and the third after birth. Partially vaccinated women who have had one or two doses should only complete the three dose course, irrespective of the time elapsed.[4,14] Only dT is indicated for expectant mothers who require immunization against tetanus. The ACIP does not contraindicate dTap during pregnancy, but neither does it indicate the vaccine as routine in this situation.[33]

### *Haemophilus influenzae* type b (Hib) vaccine

**Use and efficacy.** Prevention of invasive diseases caused by Hib. It has a significant epidemiological impact since it reduces the carrier status of Hib by inhibiting colonization, thus reducing transmission.[34] Clinical efficacy after the first grade in school is estimated at 95 to 100%.[30] After this period, the concentration of antibodies falls and a booster dose is recommended at 12-15 months.[4]

**Indications.** The HM, SBP and ACIP recommend routine Hib vaccination.

**HM.** The HM recommends a course of three of the tetravalent combined DTwP + Hib vaccine at 2, 4 and 6 months, without the Hib booster dose at 15 months.[5] For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP states that if the combined vaccine with DTaP and Hib is used for the basic course, a fourth dose of Hib vaccine should be given at 15 months of life.[6]

**ACIP.** The ACIP gives its support to the three basic doses of vaccine plus a booster dose between 12 (minimum age) and 15 months.[7]

**Comments.** Administration of the Hib vaccine without the booster at 15 months is being questioned, since there have been reports of increased Hib meningitis cases in countries adopting vaccination schedules restricted to the first year of life.[34,35] If the ACIP course is followed, and vaccination is started between 2 and 6 months of age, three doses are indicated at 2 month intervals, and then a fourth dose between 12 and 15 months. Starting between 7 and 11 months, two doses are given at 2 month intervals and a third between 12 and 15 months. Between 12 and 14 months, two doses are indicated with at least 2 months between them. From 15 to 59 months, a single dose should be given, unless the child in question suffers from pathologies that predispose to Hib infection. In that case, two doses should be given with an interval from 6 to 8 weeks between them.[4] Children less than 2 years old who present invasive Hib disease do not develop immunity and should be vaccinated. Vaccinated children who develop invasive disease should have their immune status evaluated.[4]

### Pneumococcal conjugate vaccine

**Use and efficacy.** Prevention of diseases caused by pneumococcus. A study carried out in Brazil estimates that the protective coverage of the 7-valent vaccine is 58 to 70% against invasive pneumococcal infections caused by the serotypes contained in the vaccine.[36] North-American sources describe efficacy of 89 to 97% for invasive diseases (meningitis and bacteremia), of up to 70% for pneumonia and from 6 to 56 % for otitis caused by pneumococci present in the vaccine.[37] Six of the seven serotypes present in the vaccine are those most often associated with penicillin resistance.[37] The vaccine has significant epidemiological impact, since it reduces the carrier status of pneumococcus by inhibiting colonization, reducing the transmission and occurrence of disease,

including in other age groups, primarily young adults and seniors.[38,39]

**Indications.** The HM does not recommend routine pneumococcus vaccination, while both the SBP and ACIP do.

**HM.** The PCV-7 vaccine is not included in the routine HM vaccination schedule. For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP indicates the PCV-7 vaccine for all children from 2 to 23 months.[6]

**ACIP.** The ACIP indicates PCV-7 for all children from 2 to 23 months of age and for those aged 24 to 59 months who are at risk of pneumococcal disease. Children attending daycare are considered at risk and should be vaccinated. Additionally, the 23-valent pneumococcal polysaccharide vaccine (PPV-23) is indicated from 2 years onwards in high risk cases (for example, immunodepressed individuals).[7,40]

**Comments.** If the course of PCV-7 vaccination is begun between 2 and 6 months of age, administer three doses with a 6 to 8 week interval and a fourth dose between 12 and 15 months. If started at 7 to 11 months, administer two doses with a 6 to 8 week interval between them and a third dose between 12 and 15 months. Starting at 12 to 23 months, give two doses with a 6 to 8 week interval between them. If vaccination takes place between 24 and 59 months it should be a single dose, with the exception of children with sickle-cell anemia, asplenia, HIV, chronic diseases or immunosuppression, in which cases two doses are given, with an interval of 6 to 8 weeks between them (at least 30 days). In these cases, 6 to 8 weeks after the second PCV-7 dose, a dose of the PPV-23 vaccine is given, and there is a revaccination dose, also PPV-23, after 3-5 years.[7]

### Meningococcal conjugate vaccine

**Use and efficacy.** Prevention of meningococcal disease caused by serogroup C. The immunogenicity of the serogroup C conjugate vaccine is up to 100%.[41] Recent studies carried out to evaluate efficacy after the introduction of the conjugate vaccine against meningococcus C in England found evidence that efficacy was reduced after routine vaccination at 2, 3 and 4 months of age and in children under 3 years vaccinated with a single dose during a catch-up campaign.[42,43]

**Indications.** Neither the HM nor the SBP recommend routine meningococcus vaccination. The ACIP recommends the quadrivalent conjugate meningococcal vaccine (groups A/C/Y/W135).

**HM.** The HM does not include this vaccine in its routine schedule. For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP indicates the conjugate C vaccine from 2 months of age, depending on local epidemiology. Two or three doses of vaccine are given during the first year of life, depending on manufacturer. After 12 months a single dose should be given.[6]

**ACIP.** In 2006, the ACIP began to recommend routine immunization with the quadrivalent conjugate meningococcal vaccine (groups A/C/Y/W135) for adolescents. The recommendation is to use the conjugate vaccine, but if this is not available, the polysaccharide quadrivalent vaccine (groups A/C/Y/W135) can be used. They also recommend the polysaccharide vaccine for children with deficiencies of the terminal complement or asplenia (anatomically or functionally) from 2 to 10 years old. Above this age the conjugate vaccine is preferred.[7]

**Comments.** The conjugate meningococcal C vaccine with tetanus toxoid has been approved for use in two doses, with a 2 month interval, before 1 year of age. If the conjugate vaccine with diphtheria proteins is employed before 1 year it is applied in three doses, with 2 months' intervals. When given after 1 year of age, the vaccines are administered in a single dose.[44,45] Recent data suggest the need for a booster dose for children vaccinated during the first year of life.[42,43,46] Polysaccharide vaccines are not recommended as routine vaccines, but are used for children and adults during outbreaks and for those traveling to high risk areas (for example, sub-Saharan Africa).[4] The quadrivalent meningococcal vaccines (groups A/C/Y/W135) recommended by the ACIP, either the conjugate or the polysaccharide versions, are not yet available in Brazil.

### Influenza (flu) vaccine

**Use and efficacy.** Prevention of diseases caused by the influenza virus. Efficacy of 30 to 90%, depending on age and the health status of those being vaccinated.[46] Seniors and the immunodepressed respond less; however these groups have more pressing indications for the vaccine since their morbidity and mortality are elevated.[4,15,47,48]

**Indications.** The HM does not recommend the flu vaccine as routine, while the SBP and ACIP do.

**HM.** This vaccine is not included on the routine HM schedule. For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP recommends routine vaccination for the 6 months to 2 years age group and, after 2 years for high-risk groups.[6]

**ACIP.** The ACIP recommends routine annual vaccination of children from 6 to 23 months,[7,47] and from 6 months onwards, in any age group, for patients with underlying diseases that predispose to infection by influenza or when such an infection could aggravate their primary disease.

Vaccination is also recommended for the contacts of healthy children from 0 to 5 months of age and for expectant mothers.[7,47]

**Comments.** The influenza vaccine should be administered during the months preceding the period of greatest flu prevalence.[4,47] Expectant mothers (risk group for flu complications) should also be vaccinated if pregnancy occurs during the flu season, preferably from the second trimester on, or at any point of the pregnancy if the person has a high risk condition.[31,47] Vaccination is recommended by the HM, from 6 months onwards, for those with chronic diseases, especially the immunodepressed, lung and heart disease patients, donors and transplant patients of bone marrow and solid organs and for those that frequent the homes of immunodepressed patients.[14,17,47,48] The influenza immunization course is detailed in Table 4.

**Table 4 -** Recommendations for influenza vaccine[4]

| Age | Dose | No. of doses | Interval | Route |
|---|---|---|---|---|
| 6-35 months | 0.25 mL | 1-2 * | 1 month | IM |
| 3-8 years | 0.5 mL | 1-2 * | 1 month | IM |
| 9 years or more | 0.5 mL | 1 | | IM |

IM = intramuscular.
* Two doses are only given during the first year the child is vaccinated. In the second year of vaccination, even if the child has only been given one dose previously, just one dose is given.

### Yellow fever vaccine

**Use and efficacy.** Prevention of yellow fever. Approximately 90% of people who are vaccinated exhibit neutralizing antibodies in serum by the 10th day after vaccination, which can last for more than 10 years.[30,49]

**Indications.** The HM and the SBP recommend routine yellow fever vaccination. The ACIP does not include this vaccine in its vaccination schedule.

**HM.** The HM recommends the yellow fever vaccine starting at 9 months of age for people living in or traveling to endemic areas (Brazilian states: AP, TO, MA, MT, HM, RO, AC, RR, AM, PA, GO and DF), transitional areas (some parts of the states: PI, BA, MG, SP, PR, SC and RS) or potential risk areas (some areas of the states: BA, ES and MG). Vaccination is also recommended for those traveling to endemic areas outside Brazil. Vaccination should be performed at least 10 days before traveling.[5]

**SBP.** The SBP recommends vaccination for residents of and travelers to endemic, transitional and potential risk areas.[6]

**ACIP.** The ACIP does not include this vaccine in its routine schedule.

**Comments.** This vaccine is contraindicated for children under 6 months (increased risk of encephalitis) and for people with severe egg allergies.[14,30,49] According to the CDC and the ACIP, this vaccine is not recommended between 4 and 9 months of age, except in special exposure situations, evaluating the cost-effectiveness of vaccination (post vaccination encephalitis).[4,49] The vaccine is contraindicated during pregnancy and for immunodepressed people, except if there is a high risk of transmission and allowed by the patient's clinical status.[49] Boosters are required every 10 years.[5,14,49]

### Measles, mumps and rubella vaccine (MMR)

**Use and efficacy.** Used for the prevention of measles, mumps and rubella. When given in the two recommended doses, after 1 year of age and with a minimum interval of 1 month, efficacy is more than 99% for measles.[4] A single dose after 12 months of age induces 95% protection from rubella and mumps.[4]

**Indications.** The HM, SBP and ACIP recommend the MMR vaccine as routine.

**HM.** The HM recommends two doses of the vaccine, the first at age 1 year and the second between 4 and 6 years. The measles and rubella vaccine or the MMR are recommended by the HM for women aged 12 to 49 years and for men up to 39 years of age who have no proof of earlier vaccination.[5] For recommendations that are not covered by the routine schedule, see the CRIE indications (Table 3).

**SBP.** The SBP recommends two doses of the vaccine, the first at 1 year of age. The second can be given from 4 to 6 years of age, or during catch-up campaigns. All children and adolescents should receive two doses of MMR, with a minimum interval of 1 month. Additional doses are not required.[6]

**ACIP.** The ACIP recommends vaccination at 12 months of age and revaccination between 4 and 6 years of age. If necessary, the second dose can be given 4 weeks after the first.[4,7,50,51]

**Comments.** The MMR vaccine containing the Jeryl-Lynn mumps strain should be the first choice because it is associated with lower rates of post-vaccination encephalitis.[29] In situations of measles outbreaks or travel to risk areas the vaccine (monovalent or combined) can be given from 6 months of age on, although at this age it may not be effective due to interference by maternal antibodies.[4] Neither neomycin contact dermatitis nor hypersensitivity reactions (even anaphylactic shock) to hen's eggs contraindicate vaccination, but care should be taken.[4] Vaccination is contraindicated during pregnancy and for immunodepressed individuals.[4] Vaccinated women should avoid conception for 28 days,[5,52,53] but if the vaccine is given inadvertently to pregnant women, termination of the pregnancy is not recommended.[4,5]

### Varicella vaccine

**Use and efficacy.** In the presence of pre-exposure, this vaccine provides 70 to 85% protection from mild infection and 99% from moderate or severe infection in children aged 1 to 12 years.[4] From 13 years of age, immune response is observed in 78% of people who are given one dose of the vaccine and in 99% of those who receive a second dose, justifying the requirement for two doses from this age on.[4] In the presence of post-exposure, efficacy is up to 80% if the vaccine is given within the first 3 to 5 days of contact.[4]

**Indications.** The HM does not recommend routine varicella vaccination, while both the SBP and the ACIP do.

**HM.** The HM only provides this vaccine in special circumstances (Table 3).

**SBP.** The SBP recommends the vaccine for all children from 12 months on and for susceptible adolescents. Unvaccinated or not previously infected adolescents are a priority group for varicella vaccination.[6]

**ACIP.** The ACIP routine vaccination schedule recommends this vaccine from 12 months of age for susceptible people.[7]

**Comments.** Between 12 months and 12 years of age a single dose is given. Thereafter, two doses are given with a 4 to 8 week interval.[4,7] The ACIP recommends a second dose of the varicella vaccine for children between 12 months and 12 years in situations of varicella outbreaks, with a minimum interval of 3 months after the first dose.[54] The quadruple viral vaccine (measles, mumps, rubella and varicella), already licensed by the FDA for use with children aged 12 months to 12 years, should be recommended in two doses, the same course used for the triple vaccine.[55] Salicylates should be avoided for 6 weeks after the vaccine because of links between the disease/salicylates and Reye's syndrome.[4] The vaccine is contraindicated during pregnancy (avoid conception for 28 days[52]) and for immunodepressed people.[4] Human varicella-zoster immune globulin (VZIG) can also be used after exposure, but for special cases (example: exposed immunodepressed individuals).[4,17]

### Hepatitis A vaccine

**Use and efficacy.** Studies using modified ELISA have demonstrated protective levels of anti-HVA in 88 to 99% of those vaccinated 15 days after the first dose of the vaccine and in 100% 30 days after the second dose.[4]

**Indications.** The HM does not recommend routine hepatitis A vaccination, while both the SBP and ACIP do.

**HM.** The HM only makes this vaccine available under special circumstances (Table 3).

**SBP.** The SBP recommends vaccination of all children from 12 months of age.[6]

**ACIP.** The ACIP recommends routine vaccination for children aged 12 to 23 months.[7]

**Comments.** Post-immunization serum testing is not indicated because of the vaccine's high immunogenicity (approximately 100%). In populations where the disease is endemic, pre-immunization serum testing can be considered, always assessing the cost-benefit ratio. Studies demonstrate that maternal antibodies can interfere with the immune response of this vaccine if it is given before 1 year of age. The CDC schedule was changed in 2006, making the indication for this vaccine universal from 1 year on and reducing the age of administration from 2 years to 1 year.[4,7]

### Final comments

The definition of a vaccination schedule must take into account epidemiological, immunological, technological, logistical and socioeconomic variables. Likewise, the proposal must be easy to understand and manage, in addition to being socially acceptable. The inclusion of a vaccine as part of the routine schedule should be based on the possibilities of preventing conditions that are public health issues. While a single, universal schedule is not appropriate, there are institutional recommendations at the national and international levels that should serve as benchmark for the development of immunization strategies, as long as they are kept up to date.

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