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CLINICS AND PRACTICE

Vaccines and vaccination calendar for people with Down's syndrome

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The immune dysfunction associated with Down's syndrome (DS) causes a susceptibility of suffering from infectious diseases and with a severe and recurrent course, particularly during the first 5 years of life and in advanced ages. The structural anomalies common to the syndrome, especially the respiratory tract, contribute to their presence and location.

Vaccinations can prevent a good number of these infections. The characteristics and extent of the immunological anomalies of the syndrome are not contraindications of vaccines. They are well tolerated and their immunogenicity is generally good, although inconsistent against some antigens, and perhaps last less so against some of them. The humoral responses generated are occasionally lower than normal, but usually reach levels considered protective[1]. These potential deficiencies require that individuals with DS strictly comply with the standard vaccine guidelines and require their recognition as a risk group with the benefit of systematically receiving vaccines with the usual selective indication.

Recent investigations have increased the knowledge, still incomplete and fragmentary, on the active immunization of this group, which should be reflected in their vaccination calendars.

Hepatitis B vaccine. DS causes a predisposition to hepatitis B, to the chronic carrying of the virus and its transmissibility. Early vaccination is important, given that the vaccine efficacy decreases with age and may be compromised with the concurrence of the, not uncommon, comorbidities of the syndrome (obesity, coeliac disease, diabetes). Studies in children and adults show a vaccine immunogenicity comparable to that obtained in the general population[2], although low seroconversion rates have recently been reported in a correctly vaccinated cohort of children and adolescents[3]. *Given the immune deficiencies of DS and the virulence of the infection due to hepatitis B in these patients, it would be advisable to confirm the presence of seroprotection after the vaccination.*

DTaP/Tdap Vaccines. While the immunogenicity of the diphtheria toxoid has shown to be sufficient[4], the anti-tetanus and acellular pertussis components appear to induce suboptimal responses. Insufficient formation of specific antibodies has been documented, as well as a possible deficiency in immunological memory against the tetanus toxoid[5]. As regards the acellular pertussis component, the acquisition of lower than usual geometric IgG titres have been reported after receiving the 2nd and 3rd doses of the vaccine series[6]. Due to these findings, the need to strictly comply with vaccination recommendations throughout life is advised, as well as *to take into account the eventual need to strengthen immunopreventive measures in risk situations: co-administration of immunoglobulins and anti-tetanus vaccines, or the prescribing of additional anti-pertussis vaccine.*

Vaccine against *Haemophilus influenzae* type b (Hib). IgG_2 deficiency has been found to be more common in DS children

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than in the rest of the population, which would make them more susceptible to encapsulated infections and, a potential vaccine failure. In the event of the coexistence of this deficiency, it would be advised *to document the vaccine response*, although it seems functionally sufficient, like that obtained with other polysaccharide vaccines in these same patients[7].

Vaccine against mumps, measles, and rubella. The studies available on the immunogenicity of the triple viral vaccine in seronegative people with DS report seroconversion rates of around 100% against mumps and measles. They were less, but not significant, against rubella[4]. This data suggests that it may be worthwhile *to certify the seroconversion against rubella* in children with DS after their vaccination.

Vaccines against poliomyelitis. The oral poliomyelitis vaccine (OPV) induces specific antibody titres similar to those obtained in the general population for poliovirus 2 and 3, but *lower for type 1,* in institutionalized seronegative individuals with DS[8]. There are no studies with parenteral inactivated vaccines in DS.

Influenza vaccine. Yearly vaccine systematically recommended in Spain for people older than 60-65 years. It is selectively indicated for other patients with complications risk factors. Anomalies have been detected in the immune response to influenza vaccines in people with DS, which converts them into patients at risk, regardless of the possible co-participation of other predisposing factors[9]. For this reason, the Down's Syndrome Medical Interest Group (DSMG), a reference group for the care of people with DS, includes their *yearly universal vaccination* against influenza amongst its "strong" recommendations[10], an indication that they be included in the specific health programs for the syndrome for those over 6 months-old.

Pneumococcal Vaccines. Its application is *particularly indicated, given the increased frequency of infections in which the principal bacteriological agent is pneumococcal:* otitis media, sinusitis, pneumonia. Particularly in children, but also in adults, the complications and lethality due to invasive pneumococcal diseases (IPD) –sepsis, meningitis, and bacteremic pneumonias– are especially common. The polysaccharide 23-valent vaccine (PVN23) has shown an immunogenicity equal to or a little less in DS than in the general population, often sub-optimal in both cases[11]. Recent works noted a good serum response to the conjugated 13-valent vaccine (PVC13) in children with trisomy 21, and also to its sequential PVC13/PPV23 vaccination[7]. Currently, the consideration that DS is an "increased risk" for IPD, justifies the systematic immunization of the affected group of children with PVC13 during their first two years of life and subsequently, between 2 and 5-6 years, and to receive a dose of PPV23. Not previously well vaccinated adults should receive PPV23, and those, on the other hand, that could currently benefit from a dose of PVC13[12], accepted for all age groups and already approved in some Spanish Autonomous Region calendars for its systematic administration in adults with DS.

Hepatitis A vaccine. People with DS do not have an increased susceptibility for an infection by the hepatitis A virus. However, and particularly in children, their physical contacts and their habitual attendance to special centres favour its *horizontal transmission, preventable by vaccination.* A co-infection in patients with chronic hepatitis B, to which DS is susceptible, would confer it with a special seriousness. The vaccine generates a good immune response in young children with DS[13]. These are circumstances that support their early vaccination against the disease.

Other vaccines. There are no studies available on vaccinations against rotavirus, varicella, meningococcal C, and human papillomavirus in DS. The last two are in all the Spanish systematic vaccination calendars, with trisomy 21 being an exception. Those for varicella and rotavirus are not contemplated, which should, in this case, be prescribed selectively, as done in other national calendars[14,15]. There are no reasons to contraindicate them, but they are recommended in children in whom favouring factors for clinical severity converge.

DS needs to be conceptualized as an "increased severity risk condition" for immuno-preventable disease, as already contemplated in countries that enjoy complete and adapted vaccination calendars. To ensure access by people with trisomy 21 to a "maximums calendar" suitable to their age, would significantly contribute to improve their health and life expectancy. It is a strong recommendation, which, together with a possibility of a sub-optimal response to some vaccines, supports its strict compliance and the occasional adoption of additional immuno-prophylactic measures.

Vaccinations calendar for people with Down's syndrome

The considerations expressed support the indication of an extended vaccinations calendar for people with DS, who without a doubt are susceptible to immunopreventable diseases and their complications.

Based on these assumptions, Down España and the Fundació Catalana Síndrome de Down (FCSD), with the collaboration and consensus of the Spanish Pediatric Association Vaccine Advisory Committee (CAV-AEP) and the Spanish Vaccinology Association (AEV), in 2012 prepared a first Spanish vaccinations calendar for this group. Basically following the recommendations of the CAV-AEP, an updated calendar has been configured, complementary to that recommended for the general population, and which is shown in the following table.

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Vaccination schedule recommended for people with Down's syndrome, Spain 2014

Vaccines	Age in months						Age in years			Adult
	0	2	4	6	12-15	15-18	2-3	4-6	11-12	
Hepatitis B[1]	HB	HB	HB	HB						
Diphtheria, tetanus, pertussis		Tdap	Tdap	Tdap		Tdap		DTaP/Tdap	Tdap	Td[2]
Poliomyelitis		IPV	IPV	IPV		IPV				
H. influenzae type b		Hib	Hib	Hib		Hib				
Meningococcal C		MenC[3]			MenC				MenC	
Pnemonococcal[4]		PVC	PVC	PVC	PVC		PPV23[5]			
Triple viral					MMR		MMR			
Human Papillomavirus[6]									HPV	
Rotavirus		RV (3d)[7]								
Varicella					Var		Var			
Influenza					Yearly					
Hepatitis A[8]					HA		HA			

Vaccines: DTaP: acellular diphtheria-tetanus-pertussis; HA: hepatitis A; HB: hepatitis B; Hib: Haemophilus influenzae type b; HPV: Human papillomavirus; Influenza: influenza; IPV: inactivated poliomyelitis; MenC: meningococcal serogroup C; MMR: mumps-measles-rubella; PPV23: Pneumococcal (polysaccharide 23-valent); PVC: Pneumococcal conjugate; RV: rotavirus; Tdap: Low antigen load acellular diphtheria-tetanus-pertussis; Var: varicella.

[1]In accordance with the current guidelines of each Autonomous Region. At any age, in the absence of previous vaccination, a series of 3 doses will be administered (0, 1, and 6 months). [2]Booster dose during adult life, following the guidelines of each Autonomous Region; ensure that a total minimum of 5 doses is received. [3]1 or 2 doses depending on the vaccine used. [4]The CAV-AEP recommends the pneumococcal vaccine with conjugated vaccines from 2 months to 5 years-old (up to 17 years in risk groups), with PVC13 offering the most cover in Spain according to current epidemiological and microbiological data. [5]A single dose of PPV23 from 2 years-old, with a minimum of 8 weeks after the last dose of PVC13. In severe immunodeficiency cases, administer a 2nd and last dose of PPV23 at 5 years form the first. In people over 5 years-old, a dose of PVC13 may be administered to those who have not received it previously. [6]In girls. [7]3 doses of RotaTeq®, the vaccine currently available. [8]The 2nd dose, at 6-12 months from the 1st.

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ERRATUM

In the "Letter to the Editor" published in *Rev Med Int Sindr Down*. 2014;18(1):18 the author's name was omitted. Full details of the signatory of this letter are:

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