Advisory Committee on Vaccines of the Spanish Association of Pediatrics

A minimum unified immunisation schedule for Spain: Position of the CAV-AEP

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The remarkable status quo in Spain, with 19 official schedules that differ both in the included vaccines and in the immunisation schemes[1] and which have not been justified from either a public health or a social perspective, is unique in the world. There are other countries, albeit only a few, that also have different official schedules, but not in the amount or disparity to be found in Spain, a fact that discredits the Spanish healthcare system, both within our country and at an international level.

The stance of the Spanish scientific societies on the current situation

It has been a few years since scientific associations started demanding a unified immunisation schedule. Thus, AEP (Asociación Española de Pediatría / Spanish Association of Paediatrics), through its Advisory Committee on Vaccines (CAV-AEP) founded in May 1994, set as one of its main objectives the achievement of a unified immunisation schedule for all of Spain[2]. Since then, CAV-AEP has published a yearly immunisation schedule, including the one featured in the current issue of *Anales de Pediatría*[3], that diverges in different points from the one proposed by the CISNS (Interterritorial Council of the

Spanish National Health Service)[4], and the different schedules of Spain's various autonomous communities[1].

In April 2011, the AEV (Asociación Española de Vacunología / Spanish Association of Vaccinology) and the AEP released a document with a series of suggestions and their justification to assist in developing a reasonable unified immunisation schedule[5]. In addition, they supported the creation of a **Spanish Advisory Committee on Vaccines** to be developed from the current Whitepaper on the Program and Register of Vaccinations of the Ministry of Health (the Ministry's advisory body on vaccines), and which would engage the active participation of the main scientific societies involved in recommendations about vaccination. A technical body of this kind, which has been in place in other countries for years, could be the key to having a unified immunisation schedule in all the autonomous communities, which would not require them to renounce their competencies on the matter, and that could be supported by scientific associations, taking into account the importance of healthcare professionals in advising about vaccines, and in their prescription and administration.

And the Ministry's unified immunisation schedule did arrive … but of minimum services

In March 2013 the schedule of the Ministry and the CISNS was published[6], with the mandate to implement the unified schedule nationwide starting in January 2014[4]. However, instead of the widespread applause that would have been expected at the presentation of this eagerly-awaited initiative, the reaction was one of disappointment, as the proposed schedule offered minimum services and was a step backwards in some aspects, concerns that were voiced by both the AEP and scientific societies[7]. These organisations perceived the obvious generalised disappointment, and were compelled to evaluate this proposal as a "minimum-service schedule"[8].

The proposed unified schedule did not take into account the opinions and recommendations expressed by scientific associations, nor the technical considerations and recommendations of the Ministry's own Whitepaper on the Program and Register of Vaccinations from its advisory body on vaccines, published in a document that resulted from an audio conference that had been

held for that particular purpose on February 16 2012 at the MSSSI (Ministry of Health, Social Services, and Equality). The decision made by the Ministry-CISNS was a political one, with a clear focus on economic concerns, ignoring the technical recommendations of its own Advisory Committee and the opinions of scientific societies. The outcome has been a minimum-service schedule that is inadequate, incomplete, of poor quality, and which will probably not result in a unified implementation.

The vaccines and schemes that must have been included in the unified immunisation schedule

Among the most important criticisms, there is the exclusion of the **routine immunisation against pneumococcal disease**. Universal vaccination against pneumococcus was recommended by the AEP in 2003[9] and it was also recommended as a routine immunisation for all Spanish children by the Ministry's own Whitepaper on the Program and Register of Vaccinations in a technical document produced in 2009 (which the Ministry did not divulge) which literally stated that *"It would be advisable for the corresponding authorities to take this report into account when considering the introduction of a broad-spectrum conjugate pneumococcal vaccine, one specifically covering the invasive serotypes most commonly isolated in our country, in the routine paediatric immunisation schedule"*[10].

The absence of such a pneumococcal vaccine in the unified schedule is particularly harmful to preventative paediatric care in Spain, and to the image of our country, especially considering that Spain and Portugal are the only countries in Western and Northern Europe that do not include it in the routine child immunisation schedule, as mentioned by the Centers for Disease Control and Prevention (CDC) in their 2013 report[11].

In some aspects, we can even consider this unified schedule as a step backward, as it calls for some autonomous communities to discontinue immunisations (against pneumococcus and varicella) currently included in their schedules with unequivocal positive results in health outcomes, as is the case of the **varicella immunisation** in the communities of Navarra[12], Ceuta, Melilla, and Madrid[13]. The latter has already announced that it will remove it from its

schedule in January 2014 to adapt to the unified immunisation schedule of the Ministry[14].

When it comes to discontinuing immunisations previously included in regional schedules, Madrid already stopped funding routine pneumococcal vaccination in June 2012 despite the positive outcomes of its implementation[15] and the direct opposition of its technical Advisory Committee on vaccines of the Community of Madrid. As from today, we still do not know what is going to happen to the pilot programme for immunisation against pneumococcus in Galicia, which started in January 2011[16], or the inclusion of this immunisation in the routine schedule of the Basque Country, which had been planned for 2014[17]. Removing a routine immunisation from the schedule for purely economic reasons when it had positive public health outcomes and posed no safety or quality concerns, as has been the case of the removal of the pneumococcal vaccine from the immunisation schedule of the Community of Madrid, is a political move, one that has nothing to do with technical issues and is not justified from a public health perspective, something unheard of in developed countries. Vaccines should never be seen as measures to be implemented or discontinued for reasons unrelated to public health. In addition to the extent to which this discredits the government's immunisation policy in the eyes of the general public, the negative effects it may have on social, ecological, and public health levels remain to be seen.

The most recent outrage committed by the AEMPS (Agencia Española de Medicamentos y Productos Sanitarios / Spanish Agency on Drugs and Health Products) has been to block the distribution and sale in pharmacies of one of the vaccines against varicella, **Varivax®** (Sanofi Pasteur MSD), since the summer of 2013, which has resulted in the unavailability of vaccines against varicella outside the hospital network to this day. What is most puzzling about the situation is that this took place when there had been no changes to the product data sheet, no safety concerns associated to the vaccine, nor any production issues.

According to public data obtained from IMS Health Spain (a company that offers healthcare information), in the five years between 2008-12 medical prescriptions in Spain (excluding the four autonomous communities, Madrid, Navarre, Ceuta, and Melilla, which routinely vaccinate children against

chickenpox) resulted in the sale of 1,114,023 doses of the varicella vaccine paid by the private sector (parents). From this number of prescribed doses, the AEP estimates that in this five-year period approximately 716,421 children were immunised, and an estimated 600,000 cases of chickenpox were prevented (85% efficacy), with an average of 125,000 prevented cases per year. Likewise, it prevented about 6,000 hospital admissions in this five-year period (1% of cases), as well as several deaths. This information, which was relayed to the Ministry, was not enough to prevent the removal of the vaccines from the Spanish market, despite the absence of safety alerts or any negative epidemiological circumstances, a removal that was based on unproven assumptions, with the result that healthy Spanish children can no longer be immunised against varicella in the private market. It is obvious that with their distribution-blocking policy and in the absence of routine immunisation of children in Spain, the Ministry is willing to assume 125,000 more cases a year of varicella, thousands of complications, and hundreds of hospitalisations that were being prevented by paediatricians in recent years.

Once again, the AEP, AEV, and SEMPSPH scientific associations published a statement expressing their concern about the unavailability of the varicella vaccine[18] and sent a letter to the AEMPS and the Ministry of Health presenting the same concerns, to which they received no reply. Later on, the CAV-AEP published a public statement for professionals and another one for families, analysing the situation and explaining the most controversial issues[19]. The AEP reiterated its absolute disagreement with the restrictions on the distribution and sale of these vaccines that were approved by the EMA with specific indications that the AEMPS is not adhering to, something that the AEMPS has not justified, or has justified based on false assumptions, in our opinion.

But this irregular situation in which vaccine lots are blocked from distribution to EU pharmacy networks is not the first one. This modus operandi started as early as 2010 with one of the **rotavirus vaccine, Rotarix®** (GlaxoSmithKline), when the AEMPS chose not to authorise the distribution of new lots of the vaccine, even though there were no data suggesting that the presence of porcine circovirus could pose a health hazard[20]. To this day, the AEMPS still upholds its decision not to release lots of Rotarix®. This decision

stands alone in the whole world, as no other country has adopted this measure, nor have the major international medicinal and drug regulatory agencies (EMA, FDA)[21]. Adding to the international puzzlement, and exacerbating the exotic originality of the AEMPS, there are currently 13 countries in Latin America (Bolivia, Brazil, Colombia, Dominican Republic, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Panama, Paraguay, Peru, and Venezuela) that routinely immunise all infants with Rotarix®, and starting in July 2013, in Europe, the United Kingdom has introduced this vaccine in the routine immunisation schedule for all its children. It is quite hard to understand why while Spain is halting this vaccine, several Latin American countries and countries in our immediate environment, such as the United Kingdom, are using the very same vaccine formulation to immunise all of their infants in their routine schedule[22], the product is available for its unrestricted use in the rest of the world, and its use is not restricted by international regulatory agencies (FDA and EMA).

Meanwhile, the much-anticipated new **meningococcal group B vaccine** (Bexsero®, Novartis vaccines), approved by the EMA for its use in all children over 2 months of age, has been restricted by the AEMPS as a hospital-only vaccine, blocking the only recourse currently available to medicine to prevent group B meningococcal disease, when group B is, at present, the most frequent serotype causing this deadly disease throughout Europe, including Spain. Scientific associations expressed their disagreement with this decision, and issued a public statement[23]. Recently, the *Lancet* journal saw fit to publish a letter denouncing the AEMPS's decision to restrict the meningococcal B vaccine to hospital use in Spain[24].

There are also other controversial points in the Ministry -CISNS unified schedule, which we present below:

The schedule proposed by the Ministry by which the **hepatitis B vaccine** would be administered at birth with a three-injection course at 0, 2, and 6 months of age affects the regions that immunise children at 2, 4, and 6 months of age (7 autonomous communities, plus Ceuta and Melilla, practically half of the country), when these regions do so precisely because they have an efficient pregnancy screening programme for hepatitis B surface antigen carriers that controls vertical transmission of the hepatitis B virus, so that they do not need to administer the first dose to neonates at the hospital. Enforcing the Ministry-

CISNS guidelines in every autonomous community only creates problems and raises costs while deriving no benefits in communities with a 2-4-6 months-of-age immunisation scheme. It requires bringing a dose of the hepatitis B vaccine to the hospital or clinic where the infant is born that would otherwise be administered in primary care during the 4-month routine visits scheduled for healthy children at no additional cost, as it would be given as part of a hexavalent vaccine, and requires the implementation of all the logistics involved in administering it at the hospital. All of this entails unnecessary expenses and brings no public health benefits. Furthermore, it once more disregards the proposals made by the AEP and by the Ministry's Whitepaper on the Program and Register of Vaccinations which, with regard to the hepatitis B immunisation in infants recommends that, word by word, *"the immunisation courses with doses at 0, 1-2, and 6 months or 2, 4, and 6 months shall be maintained*".

The proposal in the unified schedule of the Ministry-CISNS about administering the **human papillomavirus vaccination (HPV)** to girls at 14 years of age in every autonomous community, instead of at 11-13 years as some of them are doing with good reason, ought to be seen as another step backwards, as the coverage and acceptability would be potentially optimal if immunisation started earlier, at 11-12 years of age. It is a choice with a clear economic basis, which provides no benefits in terms of health. Once again, the decision ignored the recommendations of the AEP and of the Ministry's Whitepaper on the Program and Register of Vaccinations that recommended *"promoting the progressive decrease of the age of immunisation so that the vaccine will be administered to pre-adolescent girls 11-12 years of age with the purpose of increasing coverage, facilitating the work of healthcare professionals, and decreasing the incidence of mass psychogenic responses"*[25].

When it comes to **meningococcal group C** immunisation, the 3-dose immunisation scheme proposed by the Ministry-CISNS (2 months, 12 months, 12 years) raises some questions. First of all, it does not adhere to the data sheets of the vaccines approved in Spain, which indicate that children younger than 12 months need to be given 2 doses separated by an interval of at least two months[26]. Furthermore, starting immunisation at 3 months of age[27-28] rather than at 2 months, followed by a dose at 12 months, is more immunogenic, and

therefore in principle a preferable option. Last of all, not every autonomous community in Spain has followed the same procedures for catch-up immunisations nor has had the same vaccine coverage rates[29], so the herd immunity against group C meningococcus can vary from one autonomous community to another. This fact, along with the absence of seroprevalence studies, makes us consider that other immunisation schemes may be preferable in our area of influence (4 months, 12 months, 12 years / 2, 4, 12 months, 12 years).

Final considerations

January 2014 approaching, we are unlikely to see a unified immunisation schedule across autonomous communities, as some of them might not adjust to all of its guidelines. Will Galicia discontinue routine immunisation against pneumococcus? Will Navarra, Ceuta and Melilla stop immunising against varicella in the second year of life? Will Asturias, Catalonia, Ceuta, Navarra, and the Basque Country defer immunisation against HPV to 14 years of age? Will the Balearic Islands, Basque Country, the Canary Islands, Catalonia, Ceuta, Melilla, Murcia, Navarra, and La Rioja change their hepatitis B immunisation schedule? Will Ceuta, Melilla, and Madrid discontinue the Tdap vaccine at 14 years to replace it with Td? In time we will see whether the immunisation schedule eventually becomes homogenous in Spain, but at present there are serious doubts in this regard.

With the implementation of this unified schedule starting in 2014 we will miss a historic opportunity to achieve an optimal and up-to-date schedule fitting the social, public health, and epidemiological reality of the country. The general feeling among healthcare professionals and the public is one of powerlessness and frustration, and that a country that had enviable vaccine coverage rates and which set an example in this field deserved better. It would appear obvious that most of the decisions made by the Ministry in developing this immunisation schedule were based on economic reasons, with the purpose of cutting costs in immunisations the fast and easy way, at the expense of the most defenceless among us (the children). It is known that immunisations represent a very small expense in the total budget of the National Healthcare System. It is estimated that in the 2009-2012 period the average spending of the National Healthcare

System in public bids for vaccine procurement was of about 211 million euro per year, while in the same period it spent approximately 11,405 million euro a year in Social Security prescriptions. The healthcare authorities, especially those in Public Health, have reason to be proud when they speak of what has been achieved with immunisations, the impact they have had in public health, and the efficiency of the vaccines, yet they have resigned for many years to being the "second class citizen" in health, as they not only have to make do with a paltry provision out of the total healthcare budget for the country, but also when it is time to provide immunisations to all Spanish children under a unified schedule, this schedule turns out to be inadequate and to cover only the minimum immunisations.

Among other considerations, this would not be happening if in making these decisions the healthcare authorities took into account the technical recommendations of their own staff in the Advisory Committee of the Ministry and its Whitepaper on the Program and Register of Vaccinations, and the recommendations of scientific associations involved with and in charge of immunising the Spanish population, and most importantly, Spanish children.

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