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Consensus document on the approach to children with allergic reactions after vaccination or allergy to vaccine components

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Abstract Vaccinations are one of the main public health tools for the control of vaccine-preventable diseases. If a child is identified as having had an allergic reaction to a vaccine, subsequent immunisations will probably be suspended – with the risks such a decision implies. The incidence of severe allergic reactions is very low, ranging between 0.5 and 1 cases/100,000 doses. Rather than the vaccine antigens as such, the causes of allergic reactions to vaccines are often residual protein components of the manufacturing process such as gelatine or egg, and less commonly yeasts or latex. Most vaccine reactions are mild and circumscribed to the injection site; although in some cases severe anaphylactic reactions can be observed. If an immediate-type allergic reaction is suspected at vaccination, or if a child with allergy to some of the vaccine components is scheduled for vaccination, a correct diagnosis of the possible allergic process must be made. The usual vaccine components must be known in order to determine whether vaccination can be safely performed.

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Rationale and importance of the problem

Introduction

An update on allergic reactions to vaccines or their components should start by underscoring the importance of vaccines as one of the main public health tools for the control of vaccine-preventable diseases. With the exception of water potabilisation, vaccination is considered to be the health initiative that saves most lives each year. Vaccines made it possible to eradicate smallpox in 1979, and have considerably lessened the burden of a range of diseases which only a few decades ago were the cause of great morbidity–mortality. At present, both poliomyelitis and measles are in the process of elimination and eradication, and in our setting we no longer diagnose congenital rubella, neonatal tetanus or diphtheria, among other serious diseases, which have been the target of a systematic vaccination programme in Spain since 1975.

The main objective of vaccination programmes is to protect the vaccinated child, i.e., to prevent the vaccinated patient from suffering the disease against which he or she has been vaccinated. However, such programmes are even more ambitious and seek to immunise the largest possible number of susceptible individuals, with the aim of generating a collective protective environment encompassing the entire community. In some cases, the protective effect of the vaccine extends to non-vaccinated people, producing what is known as group (community) or herd immunity, as a result of limitation of the circulation of the microorganism within a community in which a large number of subjects have received protective vaccination.

If a child is presumed to have suffered an allergic reaction to a vaccine, the subsequent immunisations will probably be suspended, and the patient becomes part of the population of individuals susceptible to diseases against which he or she is no longer being vaccinated. It is therefore essential to establish a firm diagnosis of adverse reactions attributed to vaccines, and to confirm whether or not there is a direct relationship between the reaction and the vaccination.

In our approach to patients with suspected adverse reactions following vaccination, we must first answer the question of whether the signs or symptoms are directly related to administration of the vaccine. In this respect, immediate measures must be adopted and the allergic reaction must be adequately treated in that moment. We must then determine whether the adverse effect was an allergic reaction to the actual vaccine antigen or to any of the other components of the vaccine, since this will condition the future administration of doses of the same or of similar vaccines.[1]

An **adverse drug reaction (ADR)** is defined as a harmful and unintended effect occurring at doses normally used in humans for the prevention, diagnosis and treatment of diseases or for the modification of a physiological function (including both preventive and therapeutic vaccination). Adverse reactions to vaccines are highly varied and are generally mild (i.e., manifesting as a local reaction), although in exceptional cases they can be serious (of an anaphylactic type) or even fatal.[2]

Many adverse reactions have been attributed to vaccines in recent years, although in most cases without clear justification. For this reason, some countries have created organisms in charge of the vigilance and study of declared adverse reactions. Specifically, the VSD (Vaccine Safety Datalink, http://www.cdc.gov/vaccinesafety/activities/vsd.html) and the VAERS (Vaccine Adverse Event Reporting System, a system open to the public, with the possibility of access in Spanish, http://vaers.hhs.gov/spanishmain) has been established in the United States, while Canada has introduced the CAEFISS (Canadian Adverse Events Following Immunisation Surveillance System, http://www.phac-aspc.gc.ca/im/vs-sv/).

In Spain we have the **Spanish Pharmacovigilance System for Human Drugs** (*Sistema Español de Farmacovigilancia de medicamentos de uso Humano*, SEFV-H), which has been created with the main purpose of registering the suspected adverse drug reactions identified by health professionals or citizens. In each Spanish Autonomous Community (AC), a pharmacovigilance centre is in charge of evaluating and registering the adverse effects suspected to be caused by a medication in a common database known as the FEDRA. The Spanish Medicines Agency (*Agencia Española de Medicamentos y Productos Sanitarios*, AEMPS) acts as coordinator of the SEFV-H through the Division of Pharmacoepidemiology and Pharmacovigilance. The SEFV-H has a suspected adverse drug reaction reporting form that is designed to be completed whenever a possible adverse reaction to a vaccine is detected, known as the ''yellow card''. This form is used to register the patient information, the brand name and batch number of the administered vaccine, the date and place of vaccination, and a description of the observed reaction. The form must be forwarded to the pharmacovigilance centre of the Autonomous Community (the card comes with a pre-printed mailing address and requires no stamp or envelope). Different software applications used in the primary care setting, such as the OMI system, allow direct online yellow card reporting upon diagnosing an adverse drug reaction. Reporting can also be made on the website of the SEFV-H (http://www.aemps.gob.es/vigilancia/medicamentosUsoHumano/SEFV-H/NRA-SEFV-H/docs/notificaSospechas-RAM-profSanitarios.pdf).

Citizens can also report suspected adverse drug reactions using an online electronic form as a complement to patient reporting of adverse events to health professionals. The software system redirects the cases to each pharmacovigilance centre – the latter continuing to serve as interlocutor for the reporting party as has been the practice in the past.

In reporting adverse effects on the part of the SEFV-H, an *unexpected adverse reaction* is regarded as an adverse reaction not previously described or documented by the Summary of Product Characteristics (SPC) of the vaccine, while a *serious adverse reaction* (SAE) is a reaction that proves life-threatening, causes patient death or hospitalisation (or prolongs hospital stay), or results in persistent disability or congenital defects.

Specifically, in the case of vaccines, the SEFV-H further extends reporting to include so-called vaccination-linked adverse events (VLAEs), which comprise events related to failure to comply with the required storage temperature conditions of the vaccine, errors in preparation of the dose, or errors referred to the administration route.