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EDITORIAL

Reemergence of pertussis: Strategies and challenges in its control in Spain

Reemergencia de la tosferina: estrategias y retos en su control en España

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Pertussis, a respiratory disease caused by *Bordetella pertussis*, continues to be a public health problem worldwide. Its resurgence has been particularly notable since the 1990s, despite the implemented vaccine policies and adequate vaccination coverages achieved. However, neither vaccination nor natural disease provide lasting immunity, and the duration of immunity is shorter in those vaccinated with acellular vaccine, which is less effective compared to the whole-cell vaccine. The vaccination coverage in Spain in 2023 exceeded 95% for the first 3 doses, but dropped to 88.6% for the dose given at age 6 years, and the coverage for this last dose is below 80% in in 5 autonomous communities.[1]

Since 2003, the immunization schedule of the Asociación Española de Pediatría (Spanish Association of Pediatrics) recommends a booster dose in adolescents between ages 12 and 14 years in addition to the doses given at 2, 4 and 11 months and at 6 years. Some autonomous communities (Ceuta, Melilla and Madrid) included it in the routine immunization schedule but later discontinued its administration; only the Principality of Asturias has implemented the booster dose since 2015, which is given at age 13 years. In the European Union/European Economic Space, all countries but 6 (including Spain) recommend a dose between ages 10 and 16 years; in addition, 14 countries recommend an additional dose in adulthood and 8 countries administer a booster dose every 10 years.[2]

Severe complications of pertussis in infants under 3 months are rare since the implementation of vaccination against pertussis of pregnant women. This strategy was first implemented in Catalonia in February 2014 and was generalised to all of Spain in January 2016, reaching a coverage of 88.5% in 2023.[1] It has proven effective in reducing the incidence of pertussis in infants, providing antibodies that protect neonates until they can receive vaccines themselves.

In Spain, following the decrease in incidence of pertussis caused by the COVID-19 pandemic, we have witnessed an

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extraordinary surge in the last months of 2023 and in 2024,[3] chiefly in the form of school and household outbreaks around children aged 10–14 years, as has also been the trend in the rest of Europe.[2] In April 2024, the number of notified cases reached 9785, four times the total number of cases notified in 2023,[3] and it is estimated that the actual number of cases is at least three times the official number of reported cases. Severe cases and 4 deaths (2 infants and 2 elderly individuals with underlying disease) have been reported in 2024. The two deceased infants had been born preterm; in one case, the mother was not vaccinated during pregnancy, and in the other, the mother was vaccinated 5 days before delivery.[3]

The immunity achieved through acellular vaccines starts to wane 2–5 years after the last dose, so school-aged children and young adults are most affected during outbreaks after the dose given at 6 years. In addition, current acellular vaccines do not induce sterilizing immunity, which means that vaccinated individuals can become infected and transmit pertussis while remaining asymptomatic, thus contributing to the persistence of the disease in the population.

One of the most complex challenges is the evolution of antigens in *B. pertussis*, which adapts through strategies like antigenic shift or loss of expression of specific antigens included in the various vaccines. Since the introduction of acellular vaccines, there has been an increase in the prevalence of pertactin-deficient strains.[4] The selective pressure generated by vaccination has favoured the development of mutant strains that can evade the immune response.[5] Variations have also been identified in other antigenic components, such as the pertussis toxin, filamentous haemagglutinin and fimbrial serotypes.[6,7] These changes can affect the ability of current vaccines to induce an effective and lasting immunity. The variability in the expression of these antigens also complicates disease diagnosis and surveillance. Mutant strains exhibit changes in the genes that encode these antigens, resulting in the production of altered proteins or their complete absence. These antigenic changes also have a direct impact on the epidemiology of pertussis. Recent outbreaks, contrary to the trends observed until 2018, were attributed chiefly to the re-emerging circulation of pertactin-producing strains, which highlights the need of constant and adaptive surveillance. Outbreaks do not only affect unvaccinated or partially vaccinated children, but also adolescents and adults whose immunity has waned over time.

There are several aspects that need to be improved in the current vaccination strategy with the currently available vaccines. Coverage for the booster dose given at 6 years must increase in order to prolong immunity, and another booster dose should be given in the preadolescent age group (10–11 years). The purpose of this dose, in addition to individual protection in adolescence, is above all to reduce the burden placed on health care systems and public health by the development of outbreaks, which would reduce the associated direct and indirect costs. However, *B. pertussis* will continue to circulate and, in consequence, infection will shift to young adults and older individuals, so the need to revaccinate these groups should be considered so that, even if it has no impact on the spread of the infection, the individual is protected against the disease, prioritising vaccination in adults who belong to risk groups (with respiratory or cardiovascular diseases or immunosuppressed status). Another important strategy is occupational vaccination, that is, vaccination of individuals whose work puts them in contact with risk populations, such as health care professionals or the staff of nurseries, early education centres or day centres for the chronically ill.

Despite the substantial impact of vaccination worldwide for more than 8 decades in terms of the reduction of the morbidity and mortality associated with pertussis, this infectious disease continues to be a public health problem. Research into novel vaccines to not only prevent disease but also prevent infection and transmission of *B. pertussis* is essential to control it. Among the vaccines currently under development, the BPZE1,[8] which is administered intranasally and contains a live attenuated strain of *B. pertussis* has shown promising results in clinical trials. This vaccine could induce an effective mucosal immune response and reduce the transmission of infection. Other strategies are being tested, such as vaccines designed to include multiple antigens of *B. pertussis* or the development of new adjuvants that may induce a more robust and longer-lasting immune response. Case notification and surveillance also need to be improved to allow prompt identification of outbreaks and circulating strains.

The fight against pertussis requires a multidisciplinary approach including improvement of current vaccines and implementation of strategies of vaccination throughout the lifespan. In the meantime, as paediatricians, we play an essential role in educating parents about the importance of primary vaccination and booster doses. Achieving high vaccination coverage rates guarantees the highest possible protection currently achievable against this vaccine-preventable disease.

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