



Editorial

Pertussis Vaccine in COPD and Asthma: An Old Acquaintance Is Back

Vacuna de la tosferina en EPOC y asma: vuelve una vieja conocida



Whooping cough is a highly contagious disease, caused by bacterium *Bordetella pertussis* (BP), that presents vague symptoms due to which only 1% of cases can be diagnosed.¹ Although it is a pathology that mainly affects children, adults also can get it, though in their case its diagnosis is more difficult since it presents non-specific symptoms such as a prolonged cough or, a milder one, in those who were previously vaccinated in their childhood.² In addition, the number of cases is more frequent than reported and the proportion has been increasing. The adults aged 65–74 and ≥ 75 years old have a higher risk of pertussis-related hospitalizations than adults aged 45–64 years, up to 4–6 times higher.^{3,4}

If we take into account that pertussis is a highly infectious disease that occurs with periodic outbreaks every 3–5 years and that neither natural immunity, which disappears at 4–20 years, nor the vaccination in childhood, which is effective within 4–12 years after the last dose, provide lifelong immunity, then the question arises whether vaccination in adults is necessary? In this sense, the recommendation could go beyond a booster dose at the age of 65 or earlier, since its immunogenicity and safety profile are good, a dTpa vaccination every 10 years would be advisable.⁵ Despite the increase of the countries adhering to the strategy of a single booster dose, several states, including Belgium, Italy, Luxembourg, Norway, San Marino, the USA and Canada, have already opted for the vaccination every 10 years.

On the other hand, we find data that establish an efficacy rate of the vaccine of around 50% in adults, which is decreasing after 65 years.⁶ Although it is true that it can decrease in old age, it still confers a level of protection that is comparable, as it is often reported, to other vaccines, for example, against influenza. The same study also reflects the short protection conferred by the vaccine between 5 and 6 years,⁶ so that the repetition of vaccination every 10 years could not ensure a full protection between doses. Furthermore, although the vaccine has been shown to be safe, it is known that the greater the number of doses of tetanus vaccine, the stronger Arthus-type in situ reactions are. Could these reactions make patients refuse dTpa vaccination?

In relation to chronic obstructive pulmonary disease (COPD), and in the absence of more exhaustive studies, we know that some researches have shown an increased risk of BP infection in patients with COPD, and that the probability of being hospitalized is also higher in these patients, regardless of the time of observation.^{7,8} Moreover, the findings of a study evaluating severe BP infections in several states in the USA showed that 14.5% of patients aged 21–64

years and 26.8% of ≥ 65 -year-old patients who were hospitalized for whooping cough also developed COPD, which means that the subjacent COPD may contribute to the clinical severity of pertussis infections.⁹ However, the results of several studies have not been able to clearly associate the seroprevalence of BP with the severity of COPD, but colonization by BP could serve as a potential risk factor for its development. On the other hand, we can affirm that patients with whooping cough and COPD accumulate significantly more medical care costs than patients without COPD.⁸

Therefore, if we realize that COPD increases susceptibility to infectious agents that, in turn, can cause exacerbations in these patients, and that protection against whooping cough is not lifelong, unless a booster shot is given, we can postulate that COPD patients are especially prone to pertussis infections. Apart from this, it is also possible to pose a hypothesis on a type of vicious circle, where COPD could favour the onset of BP infection, and where the infection itself favours the progression of COPD. The pertussis booster shot would probably be the main tool to break this cycle.

The Center for Disease Control and Prevention (CDC) already suggests vaccination for adults every 10 years.¹⁰ The most important COPD management guidelines, and the Spanish COPD Guide (GesEPOC) recommend evaluating vaccination with dTpa, and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guide also advises vaccination in adult patients with this pathology who were not vaccinated in adolescence.^{11,12} In the future, and with more studies with solid results, these guidelines will have to rethink their recommendations and approach those of the CDC.

With regard to asthma the evidence is less solid and it also requires more prospective, multicenter studies with a sufficient sample size. Although some data suggest that they are patients at special risk for BP infection, the similarity of the symptoms of both diseases determines a high rate of infradiagnosis.¹³ The relationship between BP and asthma also appears to be bidirectional. On the one hand, pertussis could favour the incidence and severity of asthma, and on the other, pre-existing asthma would favour the incidence and severity of pertussis.

Likewise, the possibility of some relationship between BP vaccination and the prevalence of asthma has been raised, although the results are not conclusive and may be disputed, given that the small sample sizes and low response rates could bias the results. Some authors report that the patients who are correctly vaccinated (tetanus, diphtheria, poliomyelitis, haemophilus influenzae type B, hepatitis B and pertussis [TDPHiHeP]) have lower level of such dis-

eases as asthma, allergic rhinitis and atopic dermatitis after the first year of life.¹⁴ Other researchers point out that the sequence of administration of the doses of the DTP vaccine modifies the prevalence of asthma at the age of 7 years old, which is lower when the vaccine is delayed for some months. The decrease in the prevalence of asthma in children with delayed administration of 3 doses of DTP is 61%.¹⁵

The opposite view, that asthma can favour BP infection, has also been considered. Studies carried out in the adult population of the USA or Australia observed an increase in the prevalence of BP infection in asthmatics.^{4,8} These results agree with those reported by other authors where the prevalence of asthma in patients hospitalized for pertussis is 26% in adults and 44% in adolescents, clearly higher than the prevalence of asthma in the US population of these ages, which is 8% and 10% respectively.⁹

Pertussis has also been associated with greater baseline severity of asthma in stable phase, in which asthmatics with BP have more symptoms and poorer lung function than the ones without BP.¹⁶ Pertussis could also condition greater severity of asthma exacerbations, so it could lead to a longer duration of cough and more days of sleep disturbance.¹⁷

In summary, even though a more effective vaccine would be ideal, dTpa should be considered as an important intervention among public health strategies to prevent infectious respiratory morbidity in elderly people, so our recommendation is to use the vaccine against BP in patients with respiratory diseases at risk, such as COPD and asthma, in adulthood. In addition, it would be important to have more studies with robust results and that the main health guides and institutions include the vaccine in their recommendations and vaccination schedules.

Conflict of interest

F.V.-Á. has attended or participated in activities organized or financed by the pharmaceutical companies Amiral, AstraZeneca, Bial, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Esteve, Ferrer, Menarini, Novartis, Mundipharma, Orion, Pfizer, Teva and Zambon.

F.-J.G.-B. has received fees for scientific advice and/or for giving conferences and/or research grants from: ALK, Astra-Zeneca, Bial, Boehringer-Ingelheim, Chiesi, Gebro Pharma, GlaxoS-mithKline, Laboratorios Esteve, Menarini, Mundipharma, Novartis, Rovi, Roxall, Sanofi, Stallerge-nes-Greer and Teva.

P.J.B.-G. has received funding for attendance at Congresos y Jornadas de Vacunas, and participation as a speaker, from the pharmaceutical companies GlaxoSmithKline, Merck Sharp & Dohme, Sanofi Aventis, Pfizer and Seqirus.

F.V.-Á. and F.-J.G.-B. are part of the Editorial board of Open Respiratory Archives and declare that they have remained outside the evaluation and decision-making process in relation to this article.

References

1. Reported cases of selected vaccine-preventable diseases. World Health Organization (WHO); 2018. Available from: http://apps.who.int/immunization_monitoring/globalsummary/timeseries/tsincidencepertussis.html [accessed June 2021].
2. Moraga-Llop FA, Campins-Martí M. Pertussis vaccine. Reemergence of the disease and new vaccination strategies. *Enferm Infecc Microbiol Clin*. 2015;33:190–6.
3. Viney KA, McAnulty JM, Campbell-Lloyd S. EPIREVIEW. Pertussis in New South Wales, 1993–2005: the impact of vaccination policy on pertussis epidemiology. *N S W Public Health Bull*. 2007;18:55–61.

4. Liu BC, McIntyre P, Kaldor JM, Quinn HE, Ridda I, Banks E. Pertussis in older adults: prospective study of risk factors and morbidity. *Clin Infect Dis*. 2012;55:1450–6.
5. González-Barcala FJ, Villar-Alvarez F, Martín-Torres F. Tosferina en el adulto: el enemigo visible. *Arch Bronconeumol*. 2021. <http://dx.doi.org/10.1016/j.arbres.2021.06.008>. Epub ahead of print.
6. Liu BC, He WQ, Newall AT, Quinn HE, Bartlett M, Hayden A, et al. Effectiveness of Acellular Pertussis Vaccine in Older Adults: Nested Matched Case-control Study. *Clin Infect Dis*. 2020;71:340–50.
7. Bonhoeffer J, Bär G, Riffelmann M, Solèr M, Heininger U. The role of *Bordetella* infections in patients with acute exacerbation of chronic bronchitis. *Infection*. 2005;33:13–7.
8. Buck PO, Meyers JL, Gordon LD, Parikh R, Kurosky SK, Davis KL. Economic burden of diagnosed pertussis among individuals with asthma or chronic obstructive pulmonary disease in the USA: an analysis of administrative claims. *Epidemiol Infect*. 2017;145:2109–21.
9. Mbayei SA, Faulkner A, Miner C, Edge K, Cruz V, Peña SA, et al. Severe pertussis infections in the United States, 2011–2015. *Clin Infect Dis*. 2018. <http://dx.doi.org/10.1093/cid/ciy889>.
10. Havers FP, Moro PL, Hunter P, Hariri S, Bernstein H. Use of Tetanus Toxoid, Reduced Diphtheria Toxoid, and Acellular Pertussis Vaccines: Updated Recommendations of the Advisory Committee on Immunization Practices - United States, 2019. *Morb Mortal Wkly Rep*. 2020;69:77–83.
11. Miravittles M, Calle M, Molina J, Almagro P, Gómez JT, Trigueros JA, et al. Spanish COPD Guidelines (GesEPOC) 2021: Updated Pharmacological treatment of stable COPD. *Arch Bronconeumol (Engl Ed)*. 2022;58:69–81.
12. Global Initiative for Chronic Obstructive Lung Disease Global Strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2021 report. Accedido noviembre 2020. Disponible en: <https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.0-16Nov20.WMV.pdf>.
13. Kandeil W, Atanasov P, Avramioti D, Fu J, Demarteau N, Li X. The burden of pertussis in older adults: what is the role of vaccination? A systematic literature review. *Expert Rev Vaccines*. 2019;18:439–55.
14. Schlaud M, Schmitz R, Poethko-Müller C, Kuhnert R. Vaccinations in the first year of life and risk of atopic disease - Results from the KiGGS study. *Vaccine*. 2017;35:5156–62.
15. McDonald KL, Huq SI, Lix LM, Becker AB, Kozyrskyj AL. Delay in diphtheria, pertussis, tetanus vaccination is associated with a reduced risk of childhood asthma. *J Allergy Clin Immunol*. 2008;121:626–31.
16. Harju TH, Leinonen M, Nokso-Koivisto J, Korhonen T, Rätty R, He Q, et al. Pathogenic bacteria and viruses in induced sputum or pharyngeal secretions of adults with stable asthma. *Thorax*. 2006;61:579–84.
17. De Serres G, Shadmani R, Duval B, Boulianne N, Déry P, Douville Fradet M, et al. Morbidity of pertussis in adolescents and adults. *J Infect Dis*. 2000;182:174–9.

Felipe Villar-Álvarez^{a,b,c,*,1},
Francisco-Javier González-Barcala^{c,d,e,f},
Pedro José Bernal-González^g

^a Pulmonology Department, IIS Fundación Jiménez Díaz, Madrid, Spain

^b Universidad Autónoma of Madrid, Madrid, Spain

^c CIBER Enfermedades Respiratorias, Instituto de Salud Carlos III, Madrid, Spain

^d Pulmonology Department, Hospital Clínico Universitario de Santiago de Compostela, Spain

^e Department of Medicine, Universidad of Santiago of Compostela, Spain

^f Research Group – Translational Research In Airway Diseases (TRIAD) – Fundación Instituto de Investigación Sanitaria de Santiago de Compostela (FIDIS), Spain

^g Head Manager Immunisation Programme, Health Department, Comunidad Autónoma de la Región de Murcia, Spain

* Corresponding author.

E-mail address: fvillarleon@yahoo.es (F. Villar-Álvarez).

¹ Twitter: @fvillarleon.