



## Seroprevalence of pertussis amongst healthcare professionals in Spain<sup>☆</sup>



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### ABSTRACT

**Introduction:** This multi-center, hospital-based observational study determined the seroprevalence of pertussis antibodies amongst healthcare professionals from three different hospitals in Spain to ascertain the health status of professionals attending to susceptible groups who are at risk of contracting and transmitting pertussis.

**Methods:** Medical professionals from three hospitals in Spain were recruited for this study (NCT01706224). Serum samples from subjects were assessed for anti-pertussis antibodies by ELISA. The percentage of subjects positive for anti-pertussis antibodies were determined by age-strata, gender, vaccination status, professional level (physicians, nurses, ancillary nurses and midwives), hospital department, number of working years, numbers of hours spent with the patient as well as number of children in the household.

**Results:** Overall, 31.2% of subjects were seropositive; 3.3% of these healthcare professionals had ELISA values indicative of current or recent infection. There were no significant differences in terms of pertussis prevalence with respect to age, gender, hospital department, profession, number of working years and number of hours spent with patients. These levels of seronegativity amongst healthcare workers further strengthen the rationale for vaccination amongst this specific population against pertussis.

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**Abbreviations:** ACIP, Advisory Committee on Immunization Practices; *B. pertussis*, *Bordetella pertussis*; CHUAC, Complejo Hospitalario Universitario, A Coruña; CI, confidence interval; ELISA, Enzyme Linked Immunosorbent Assay; HUdB, Hospital Universitario de Bellvitge, Barcelona; HUPdH, Hospital Universitario Puerta de Hierro, Madrid; IgG, Immunoglobulin G; PT, pertussis toxin; OD, optical density; Tdap, Tetanus-Diphtheria-acellular Pertussis vaccine.

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### 1. Introduction

Pertussis, caused by *Bordetella pertussis* (*B. pertussis*) is a highly contagious respiratory disease, primarily affecting infants and young children and it is estimated that, worldwide, pertussis results in over 16 million cases and 195,000 deaths annually [1,2].

Primary pertussis vaccination has been implemented in the National Immunization Programs of most countries and developed countries have high coverage rates for infants [3].

In Spain, universal vaccination with the whole-cell pertussis vaccine combined with tetanus and diphtheria vaccine was introduced in 1965, with vaccine coverage reaching 94% in 1997, and pertussis became a notifiable disease in 1982 [3]. Between 1982 and 1999, morbidity due to pertussis decreased by 95% and from

then on it has remained stable. In 2000, the annual incidence of pertussis was less than 1.5 cases per 100,000 persons [4]; however, by 2011, pertussis incidence reached 5.52 cases per 100,000 persons [5] with over 40% of cases being infants under one year, adolescents representing more than 14.6%, and adults representing 12.4% [4,6].

While the introduction of pertussis vaccination has greatly reduced the incidence and mortality due to whooping cough in infants, it has however been reported that waning of pertussis immunity occurs 4–12 years after vaccination or 4–20 years after natural infection [7–9].

Previous studies have shown that adolescents and adults serve as a major reservoir of pertussis infection which has led to an increase in the incidence of pertussis over the last 30 years in this population, particularly in the United States and Europe [9,10].

Within the general population, healthcare professionals form an important subset as they may act as vectors facilitating the transmission of pertussis amongst their patients, especially in immunosuppressed individuals. At the hospital level, the transmission of pertussis may occur between visitors and patients and between healthcare personnel and patients, or vice versa [11–14].

Given the risk of transmission to the most vulnerable populations in the hospitals (newborns, premature babies, etc.) [11–13], several countries have recommended vaccination to healthcare workers. Indeed, several nosocomial outbreaks have been reported involving health professionals showing how real the risk is and for this reason [6,11–15], several countries emphasize the importance of vaccination against pertussis amongst healthcare personnel, especially in Pediatric and Obstetric Departments.

According to the World Health Organization, a single dose of Tetanus-Diphtheria-acellular Pertussis (Tdap) vaccine is recommended for healthcare personnel who have not previously received Tdap as an adult and who have direct patient contact. In order to reduce the transmission of pertussis amongst children in whom the illness might be associated with serious complications, vaccination against pertussis has been recommended in Spain since 2004 for medical professionals caring for premature infants and those requiring hospitalization [16], and since 2011 for all members of staff working in Pediatric and Obstetric Departments [17]. The following are the recommendations of the Advisory Committee on Immunization Practices (ACIP) in 2011: Regardless of age, healthcare personnel should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap and regardless of the time since their most recent tetanus-diphtheria vaccination [18].

Different vaccination policies and programs are applied by the hospitals included in this study. Since 2009, a Tdap booster is offered to all healthcare professionals working with children at the Hospital Universitario Puerta de Hierro, Madrid (HUPdH). Three years ago, this has been extended to include all personnel. All healthcare professionals working at the Complejo Hospitalario Universitario, A Coruña (CHUAC) were offered a Tdap booster for the past 10 years. However, since 2011, vaccination is rigorously implemented amongst personnel working in pediatrics, obstetrics and emergency areas, and pregnant professionals working in clean areas, following outbreaks of severe cough. There is no systematic vaccination program in place for personnel at the Hospital Universitario de Bellvitge, Barcelona (HudB) as Department of Health does not provide the vaccine neither authorize its use for healthcare professionals.

Nonetheless, pertussis vaccination coverage ratios amongst healthcare personnel are still very low and many of these professionals are suspected to be susceptible [19].

The aim of this study was to determine the seroprevalence of pertussis antibodies amongst healthcare personnel in different hospital centers in Spain. This will help determine the current level of susceptibility of healthcare personnel to contract a

disease that could be transmitted to vulnerable groups at risk of suffering severe forms of the disease with a potential risk of fatal outcome.

## 2. Materials and methods

### 2.1. Study design and methods

This multi-center, hospital based seroprevalence study (NCT01706224) was carried out between 22 November 2012 and 28 May 2013, in three hospitals in Spain – HUPdH, CHUAC and HudB.

Healthcare personnel from different professional levels (physicians from different specialties, nurses, ancillary nurses and midwives) who were  $\geq 18$  years of age were eligible to be enrolled in the study. HUPdH and CHUAC had a population which included all four professional levels, while HudB excluded midwives. Based on data provided by the participating hospitals, distribution amongst the various healthcare groups was as follows: 30.3% ( $n=229$ ) physicians, 39.6% ( $n=300$ ) nurses, 26.7% ( $n=202$ ) ancillary nurses and 3.4% ( $n=26$ ) midwives.

Socio-demographic characteristics such as age, gender, data on pertussis vaccination, and infection history were collected. This information was collected exclusively during the interviews with the participants. The study was approved by each hospital's ethics committee, assessed by competent authorities and was conducted in accordance with Good Clinical Practice and the Declaration of Helsinki. Written informed consent was obtained from all participants who were enrolled.

### 2.2. Antibody assay

Serum samples were taken from all enrolled participants and stored at  $-20^{\circ}\text{C}$  until they were tested at the Instituto Valenciano de Microbiología (Valencia, Spain). Immunoglobulin G (IgG) antibodies to *B. pertussis* toxin (PT) were determined by a commercially available Enzyme Linked Immunosorbent Assay kit (ELISA, *PERTUSSCAN PT IgG*, Euro Diagnostica AB, Sweden).

The participant was considered seronegative if the anti-PT IgG levels were  $\leq 0.3$  optical density (OD), seropositive if the anti-PT IgG levels  $> 0.3$  OD. Participants with anti-PT antibody levels  $\geq 1.0$  OD were indicative of recent/current pertussis infection. These cut-off points were in accordance with the manufacturer guidelines. The assay detected an  $\text{OD} \geq 1.0$  with 98.1% sensitivity (95% confidence interval [CI] = 89.7–100%) and 97.2% specificity (95% CI = 92.0–99.4%), while the assay detected an  $\text{OD} \geq 1.5$  with 82.7% sensitivity (95% CI = 69.7–91.8%) and 99.1% specificity (95% CI = 94.9–100%) [20].

### 2.3. Statistical analysis

Analysis was performed on all participants who met the eligibility criteria. The target enrolment was 756 participants based on the assumption that anti-PT IgG was detected in 50% of healthcare personnel [21].

The prevalence of pertussis antibodies was assessed by age groups (18–24 years, 25–34 years, 35–44 years and  $\geq 45$  years), gender, professional level (physicians, nurses, ancillary nurses and midwives), type of hospital department (pediatrics, neonatology, obstetrics, internal medicine, surgery and other departments) the participant was working in, the percentage of labor time spent with patients ( $\leq 25\%$  of time,  $> 25\text{--}50\%$ ,  $> 50\text{--}75\%$  and  $> 75\%$ ) and duration of service of healthcare personnel in healthcare centers. The differences in the prevalence of pertussis antibodies based on classifications given above were calculated by the chi-square or Fisher's exact test.

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