Chapter 1

Introductory Chapter: Pertussis - Disease, Control and Challenges

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1. Introduction

Since that the smallpox vaccine became available in the late eighteenth century, a significant number of diseases were gradually being controlled by vaccines, which are currently considered the most successful and cost-effective intervention in public health [1]. Recent data from Gavi - the Vaccine Alliance [2] in a survey for 10 immunopreventable diseases in 41 developing countries, indicate vaccines will prevent 36 million deaths between 2016 and 2030. The impact of vaccination extends from "saving lives" to socioeconomic aspects, in a line of cause and effect between health and social productivity. After almost 70 years, vaccination around the world ended up exerting selective pressure in the microbial environment, so it is now virtually impossible to know how it would be like if the vaccines had not been introduced.

However, the control of microorganisms by the vaccines may lead the population to the false impression that pathogens responsible for devastating epidemics in the past centuries are definitively extinguished. As a consequence, the refusal of vaccines, for religious or philosophical questions, or even for discredit on the effectiveness and safety of these products is becoming a growing concern. This change in population behavior, fueled by the relatively recent technology allowing for almost instantaneous dissemination of information, whether true or false, has been observed in several countries, with a consequent increase in the number of cases and deaths related to infections that can be controlled by vaccines, as has been happening in relation to measles and whooping cough, in a very worrying way.

In this book, we propose some approaches about interrelationships between vaccine strategies and microbial epidemiology, taking as reference the whooping cough, an endemic disease with significant morbidity and mortality and of indisputable importance in public health.

The major causative agent of pertussis, *Bordetella pertussis*, was first isolated in 1906 by Bordet and Gengou [3], and throughout that century, endemic and epidemic episodes of the disease were recorded [4].

In 1933, a vaccine which conferred a certain degree of protection was described, a suspension of killed *B. pertussis* cells [5]. In that decade and in the next, several whole cell pertussis preparations have been described and used in both prevention and treatment of the disease, with some efficacy [6]. In 1947, the Kendrick protection test was described, with intracerebral challenge in mice that is until now recommended by the WHO as an assay of potency of whole cell pertussis vaccines and the only one that showed correlation with protection in children [7]. Immunization against pertussis is part of the childhood immunization schedule and in some countries it is also recommended in booster doses for adolescents and adults [8]. Whole cell pertussis vaccines (wP), composed of inactivated suspensions of partially detoxified *B. pertussis*, have been used in vaccination programs for 60 years with proven efficacy, combined with tetanus and diphtheria toxoids adsorbed on aluminum salts as adjuvants [9]. The introduction of these vaccines in the 1950s–1960s led to a dramatic reduction of more than 90% in the incidence and mortality caused by the disease in the industrialized world [10].

Adverse reactions related to them led to development of acellular pertussis vaccines (aP), containing purified antigenic components of *B. pertussis*. These preparations are effective and less reactogenic [11], and they have replaced the (wP) in several countries in the last two decades. However, their cost of production is much higher, making prohibitive their introduction in developing countries. Preliminary clinical trials in the 1990s comparing bacterial triple vaccines formulated with diphtheria (D) and tetanus (T) toxoids combined with whole cell pertussis component (DTwP) or acellular pertussis component (DTaP), suggested similar efficacy and immunogenicity [12–16]. More recent data showed that pertussis is not adequately controlled, and epidemic outbreaks are occurring even in countries with high vaccination coverage, making the resurgence of the disease a worldwide problem [17–19].

This increase in the incidence is certainly related to multiple factors. The improved diagnostic testing, which would lead to an increase in reported cases; the decrease in vaccine efficacy and faster loss of immunity could certainly contribute to this scenario [20].

Besides that, the introduction of the aP vaccines which appear to require earlier and more frequent booster doses for disease control, suggest a shorter period of effective immunity [21]. A recent study in a systematic review and meta-analysis of published studies comparing the efficacy of wP and aP within 3 years after the 3-dose primary series concluded that the protection against the disease was lower for aP vaccines than for the wP, with efficacy of 84% and 94%, respectively [22]. The study, comparing the duration of immunity conferred by childhood vaccination scheme using 3–5 doses of DTaP, suggested that for each year after the last dose of DTaP, the disease probability would be increased 1.33 times. Assuming 85% of vaccine efficacy it was estimated that only 10% of the vaccinated children had persistence of pertussis immunity for a period of 8.5 years after the last dose [22].

Broadly speaking, aP vaccines are considered safer, but there is a currently consensus that they also require more frequent booster doses, given that they confer protective immunity for a shorter

period than that elicited by wP, besides not preventing colonization and transmission after challenge [23]. Recent WHO reports confirm that wP and aP are equivalent in disease prevention in the first year of life, but that there is in fact a more rapid loss of immunity conferred by aPs [24].

In this sense, alternative pertussis vaccines have been suggested, including a live attenuated pertussis vaccine [25] and a whole cell pertussis vaccine with reduced content of endotoxin [26]. Although with efficient and safe alternatives for prevention, pertussis is still the most frequent and lethal immunopreventable disease. New vaccine options, combined with strategic actions in immunization programs, are still essential for disease control and the spread of the microorganism in the target populations.

The following chapters will focus on different aspects of the pertussis host-pathogen interrelationship. Important epidemiological aspects that may contribute to the diagnosis of the microorganism and treatment of the disease will be addressed. Current vaccine proposals, the current disease control situation and future challenges will be discussed. In this sense, it will be approached the modern vaccination strategies that aim to focus children under one year of age, mainly on the group up to 6 months, still with incomplete vaccination schedule, acquiring the infection from adults and adolescents of their conviviality. Vaccination of the mother during pregnancy a strategy that has been successfully adopted for the protection of the newborn; the currently used vaccines and the influence of high vaccination coverage strategies in the incidence of the disease should be also discussed.

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