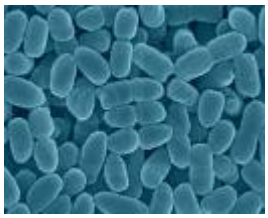
World Health Organization

Biologicals

Pertussis



B. pertussis

Pertussis (whooping cough) is caused by *Bordetella pertussis*, a small Gram-negative coccobacillus that infects the mucosal layers of the human respiratory tract. It is transmitted from infected to susceptible individuals through respiratory droplets. After an incubation phase of 7-10 days patients develop nose and throat inflammation and cough, and in the course of 1-2 weeks coughing spasms ending in the classical 'whoop' may occur. Bronchopneumonia, causing relatively high mortality, is the most prominent problem associated with pertussis.

Pertussis remains an important cause of infant death worldwide and continues to be a public health concern even in countries with high vaccination coverage. Maternal antibodies do not appear to protect neonates from severe pertussis, and even for individuals with vaccine-induced immunity, the initial antibody-mediated immune response to *B. pertussis* may minimize the toxic damage to both epithelial and immune cells, but it has limited impact on its subsequent circulation among non-immunized children and older individuals with waning immunity.

Following the introduction of pertussis vaccination during the 1950s – 1960s, a dramatic reduction (>90%) in pertussis incidence and mortality was observed in the industrialized world. Pertussis vaccine has thus been part of the WHO Expanded Program on Immunization since its inception in 1974.

Pertussis vaccines

Two forms of vaccine are in use, the whole-cell vaccine (wP), and the acellular vaccine (aP). Whole-cell pertussis vaccines were developed first and are suspensions of the entire *B. pertussis* organism that has been inactivated, usually with formalin. Most wP vaccines are available in combination with diphtheria (D) and tetanus (T) vaccines, contain aluminum salts as an adjuvant and, thiomersal as a preservative. Immunization with wP vaccines is effective and the vaccine is relatively inexpensive, but immunization has been frequently associated with minor adverse reactions such as redness and swelling at the site of injection, along with fever and agitation. Local reactions tend to increase with age and the number of injections; wP vaccines are therefore not recommended for immunization of adolescents and adults.

To address the adverse reactions observed with the whole-cell vaccines, aP vaccines were developed that contain purified components of B. pertussis such as inactivated pertussis toxin either alone or in

combination with other *B. pertussis* components such as filamentous haemagglutinin, fimbrial antigens and pertactin. As with the whole-cell vaccines, a wide variation exists between the bacterial clones used, the number and quantity of components, the methods of purification and inactivation, and the formulation, making direct clinical comparisons between vaccines difficult.

For the primary series of immunization, aP vaccines have no greater frequency of adverse events than controls, although in subsequent doses a higher rate of swelling has been observed leading to the use of vaccines with reduced antigen content for adolescents and adults. Although aP vaccines have gradually supplanted the use of wP vaccines in industrialized countries, the significantly higher development and production costs of aP vaccines result in prices that are much higher than that of a dose of wP vaccine. Given that the relative protective efficacy of the best wP and aP vaccines are comparable and the adverse events of both vaccines are relatively minor, wP vaccines remain the vaccine of choice in many developing countries.

DTP-containing multi-antigen vaccines (with Hep B, Hib, or IPV) are increasingly being used in national immunization campaigns.

Pertussis vaccine standardization

Written Standards

In that pertussis vaccines are commonly a component of the multivalent DTP combination vaccine, the WHO recommendations for the production and quality control of pertussis vaccines are found in the recommendations for DTP vaccine. The initial WHO recommendations on pertussis toxoid were formulated in 1963 and revised and incorporated into the DTP recommendations in 1978. In 1990 the recommendations for the combined vaccine were revised to reflect changes in the purification and potency measurements. The most recent revised WHO Recommendations for Pertussis Vaccines has been adopted by the ECBS in 2005 and published in TRS 941, 2007.

Whole cell pertussis vaccine

WHO recommendations on whole cell pertussis vaccine were first formulated in 1963 and revised and incorporated into recommendations for DTP in 1978. In 1989 the recommendations for the combined vaccine were revised to reflect changes in the purification and potency measurements. An amendment to these recommendations was made in 2003 to simplify the potency assays for the Diphtheria and Tetanus components but no changes were made to the requirements for pertussis. The most recent revised recommendations for whole cell pertussis vaccines were adopted by the ECBS in 2005. This revision should be considered as part of the revision of the overall requirements for DTP.

Recommendations for Whole Cell Pertussis Vaccine, Technical Report Series 941, 2007, Annex 6
pdf, 370kb

Recommendations for Diphtheria, Tetanus, Pertussis and Combined Vaccines, Amendment 2003, WHO Technical Report Series 927, 2005, Annex 5
pdf, 135kb

WHO Manual for Quality Control of Diphtheria, Tetanus and Pertussis Vaccines

Recommendations to assure the quality, safety and efficacy of DT-based combined vaccines, WHO Technical Report Series 980, Annex 6
pdf, 337kb
Replacement of Annex 2 of WHO Technical Report Series, No. 800

Acellular pertussis vaccine

Guidelines for the production and control of acellular pertussis component of monovalent and combined vaccines were adopted in 1996.

Recommendations to assure the quality, safety and efficacy of Acellular Pertussis Vaccines, Annex 4, Technical Report Series 979
pdf, 939kb
Replacement of Annex 2 of WHO TRS 878

Reference materials

WHO reference materials, including pertussis serotype 2 and 3 typing sera (anti-Bordetella pertussis fimbriae), anti-pertussis serum (mouse monoclonal), liquid purified pertussis toxin, lyophilized pertussis vaccine, acellular pertussis vaccine for potency assay by the modified Kendrick test, and opacity are available to qualified applicants:

International Reference Preparations Catalogue

Meeting reports

WHO Information Consultation on Acellular Pertussis, DTwP, Hepatitis B and Combination Vaccines - meeting report on acellular pertussis vaccine sessions, 9-13 November 2009, WHO, Geneva, Switzerland
pdf, 145kb

WHO Working Group meetings on revision of the Manual laboratory methods for testing DTP vaccines, Geneva, Switzerland, 20-21 July 2006 and 28-30 March 2007
pdf, 223kb

WHO Working Group meeting on Standardization of acellular pertussis vaccines: potency assay, Beijing, China, 7-9 November 2007
pdf, 278kb

WHO Working Group on standardization and control of acellular pertussis vaccines, St. Albans, United Kingdom, 16-17 March 2006
pdf, 144kb

Prequalified pertussis vaccines

Whole cell pertussis-containing vaccines (wP component of DTP) are prequalified for procurement by UN organizations. DTwP vaccines in combination with Hib and/or hepatitis B are also are prequalified for procurement by UN organizations.

Related information

WHO position paper on pertussis:
Global Advisory Committee on Vaccine Safety (DTP vaccines):
Immunization surveillance, assessment and monitoring:

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