Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Research Paper

J. Med. Sci., 4 (4): 307-311
October-December, 2004

Pertussis Vaccination: Current Status and Recent Developments

Yasmeen Faiz Kazi

Pertussis or whooping cough is a communicable disease of early childhood but persons of all ages are susceptible. Until recently this disease was protected by use of Whole Cell Vaccines (WCV), which have been used world wide for more than 50 years. However, undesirable effects attributed to these vaccines led to the development of acellular component vaccines for pertussis. Safety data from several studies show that the acellular vaccines are better-tolerated then whole-cell vaccines and have shown to be efficacious in preventing pertussis. The adverse reaction such as seizers and convulsion are more frequent after whole-cell vaccines where as after acellular vaccines these symptoms are obvious only after 4th and 5th dose although are not harmful, do not cause long-term neurological damage or allergy and are self-limiting. Vaccine types, immunization schedules, compliance and age are not uniform in many parts of the globe. Parents and health-care workers need to be given full information regarding risks and efficacy of pertussis vaccination.

Key words: Vaccine, pertussis, DTP, DTaP, side effects

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued four times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Dr. Yasmeen Faiz Kazi
Diagnostic and Research Center
Department of Microbiology
Shah Abdul Latif University
Khairpur, Sindh, Pakistan

Tel: 92 792 552012
Fax: 92 792 9280060
E-mail: yfkazi@yahoo.com

ANSInet
Asian Network for Scientific Information

Diagnostic and Research Center, Department of Microbiology, Shah Abdul Latif University, Khairpur, Sindh, Pakistan

INTRODUCTION

Whooping cough or pertussis is a non-invasive, highly communicable acute infection of the ciliated cells of the upper respiratory tract and affects mainly infants and young children. It is caused by the bacterium *Bordetella pertussis*. Transmission is usually due to droplet infection from infected carriers and the attack rate may be high, when individuals are exposed within a closed environment[1]. Symptoms of pertussis include a cough lasting 14 or more days usually accompanied by a gasping sound or inspiration 'whoop' after the prolonged coughing spells. Children sometime vomit or choke and have difficulty in breathing during a coughing paroxysm. Occasionally, infants die from the disease[2,3]. It has been estimated that the vast majority of the world's unvaccinated children acquire the infection by the age of five years and life- threatening cases occur mostly in very young children (under six months)[4,5]. However, persons of all ages are susceptible and although outbreaks in adults are uncommon, there is increasing evidence that adults serve as an important reservoir of infection[5].

The global burden of pertussis is approximately 45 million cases and 409 000 deaths per year, with highest incidence rates and major risk of deaths and complications occurring in developing countries[6]. In United States, 17 babies died of whooping cough in year 2000[7]. In England and Wales, around 80% of the bed-days in hospitals and 90% of the deaths due to pertussis occur in those too young to be immunized (<3 months of age)[8].

Effective whole-cell vaccines for whooping cough were developed in the 1940s[9]. Such vaccines ware composed of whole *Bordetella pertussis*. With few modifications, such conventional vaccines are still in general use as part of a trivalent vaccine; Diphtheria Tetanus Pertussis (DTP) containing diphtheria and tetanus toxoids and aluminum adjuvant. Current global coverage levels of 82% using three doses of DTP avert approximately 760 000 deaths each year and whole- cell pertussis vaccines have been shown to be efficacious in past and recent clinical trials[10]. However, a high frequency of adverse reactions and a temporal relationship with serious neurological events have been observed following administration of these vaccines[11,12]. In some Western countries the concern about these reactions (local reaction, fever, drowsiness, irritability, convulsions seizers and prolonged high-pitched crying) led to a sharp decrease in vaccine acceptance and reappearance of pertussis epidemics[13,14]. However, after much deliberation and analysis, it now seems to be generally accepted that the benefits provided by the whole- cell vaccines are greater than the risks. In the UK, for example, the uptake rate of whole-cell pertussis vaccine has returned to its former level[15].

Among other post- vaccine side effects like sudden and unexpected episodes of loss of tone, unresponsiveness and colour change, known as hypotonic-hyporesponsive (HHE) have been reported[16]. Although the HHE episodes uncommonly affect infants and children after vaccination there has been renewed interest in the adverse event in the light of community concerns regarding vaccine safety. However, it appears that there are no long-term sequelae or neurological damage. From the record of 700,000 children, DTP vaccine was associated with an increased risk of seizures only on the days it was administered and the frequency where the number was as low as 6-9 seizures per 100000 children (http://dailynews.yahoo.com/htx/abc/20010830/vaccines 010829_1html). It was concluded that the children who have had an HHE could be revaccinated[16].

Due to concerns about allergic side effects of DTP vaccine and about possible promotion of allergic diseases, incomplete vaccination rates in childhood have been reported[17]. When skin tests (prick and intradermal) were performed with DTP vaccines and with selected components of the vaccines in 30 children reporting reactions suggestive of allergy to these vaccines, immediate responses in skin tests were observed and antigen- specific IgE was detected in 10 children (33.3%). This suggest the diagnosis of immediate-type hypersensitivity to tetanus or diphtheria toxoids in ten children (33.3%), including four of the six children with anaphylaxis and six of the 16 children who had shown urticaria and angioedema. In the other 20 children, immediate, semi-late and late responses in skin tests and specific IgE determinations were negative. Booster immunizations with monovalent or bivalent vaccines in 14 of these children were well tolerated. These results suggest that most large local reactions and mild to moderately severe generalized skin reactions to multivalent vaccines are not allergic, but instead result from a nonspecific inflammatory reaction. However, toxoids may induce immediate-type hypersensitivity reactions in children and suggest that skin tests with vaccines and vaccine components and the determination of specific IgE against vaccine components, are of diagnostic value in children with anaphylaxis and immediate and accelerated urticaria and angioedema induced by booster injections of multivalent vaccines[18]. The risks of not vaccinating children, therefore, far outweigh the risk of allergy. Therefore, childhood vaccination remains an essential part of child health programs and should not be withheld, even from children predisposed for allergy.

A considerable effort has been expended to develop new vaccines, known as acellular pertussis vaccines (DTaP), composed of a number of purified bacterial antigens[19]. Acellular vaccines are better tolerated than whole-cell vaccines and have been shown to be efficacious in preventing pertussis in children[19-21].

In Japan, acellular vaccines were introduced in 1981[22] and are currently used in many developed countries during infant primary immunizations[21]. In United States acellular vaccines are licensed by the food and drug administration (http//: www.kidsource.com/kidsource/content/news/infant_vaccine8_1_96.html).

The introduction of booster doses of acellular vaccines at 4 years is expected to reduce morbidity and mortality from pertussis in the younger age groups by 40-100% and at 15 years by 100%[8].

According to a the Vaccine Adverse Events Reporting System database obtained from the Centers for Disease Control USA, statistically ($p<0.01$) higher rates of convulsions and death occur after whole-cell DTP vaccination than after DTaP and DT vaccination[11], showing, as do the previous findings of many other scientists, that acellular DTaP vaccine is much less reactogenic than is DTP vaccine (http//: www.kidsource.com/kidsource/content/news/infant_vaccine8_1_96.html).

However, DTaP vaccine is still more reactogenic than DT vaccine, probably because the pertussis component of most currently available acellular DPT vaccines contains toxoided pertussis toxin that has a significant rate of reversion to active toxin[11].

Despite the increased reactogenicity, particularly of the 4th and 5th doses, DTaP vaccines remain the preferred vaccines for preventing pertussis, diphtheria and tetanus among children because of the improved safety profile when compared with whole-cell pertussis vaccines[23-25]. In a recent study, the adverse reactions were attributed to the site of the injection of pertussis vaccine. Lower rates of adverse reactions were observed with both vaccines (DTP and DTaP) with ventrogluteal injection compared with anterolateral thigh injection and parental acceptability was greater in both the vaccines for ventrogluteal injection compared with anterolateral thigh injection[26].

In Switzerland, there are no special vaccination recommendations for premature and low-birth weight infants with respect to a particular target vaccination age. Incomplete and delayed vaccination bears the inherent risk of preventable infections. At the age of 4-5 year, the vaccination rates for diphtheria, tetanus, pertussis (DTaP) were similar in both pre-term and full-term infants. In both groups, the 4th dose of vaccine against DTP was far less frequently administered than the first three. The vaccination age in pre-term infants for most vaccinations was significantly higher than in age-matched full-term controls[9], although the immune response in pre-term and full- term children is different and it has been suggested that the 4th booster dose may be given earlier to the pre-term children as compared to full-term[27]. This was particularly obvious for the first dose of vaccine against DTP. In Belgium, through a survey conducted in 1999 it was noted that vaccine coverage was different in different parts of the country[28]. The main reasons for uneven and delayed vaccination may include insufficient information given to parents and health care workers.

In a comparative study, 557 infants received either DTaP vaccine containing pertussis toxoid (PTd), Filamentous Hemagglutinin (FHA) and pertactin (PRN) or one of two commercially available DTP vaccines (Connaught or Laderle) at 2, 4 and 6 months of age. One month after the third immunization, IgG antibody values to pertussis PTd toxoid, FHA and PRN were significantly greater following DTaP than either of the DTPs ($p<0.05$). When reactions within 48 h after all three doses of vaccine were combined, fever (101^{0F}), moderate fussiness, moderate pain, swelling (10 mm reaction)and erythema (10 mm reaction) occurred less often after DTaP compared with DTP-Connaught ($p<0.001$). The same adverse events were also less after DTaP compared with DTP-Lederle ($p<0.05$), except for erythema. Thus the three-component DTaP vaccine produced fewer adverse events and greater antibody values to PT, FHA and PRN in comparison with either licensed DTP vaccine when given as the primary series[29].

Konda *et al.*[30] studied antibody responses to a-cellular pertussis vaccine (aP). They found that the ratio of individuals positive (=<10 ELISA U mL^{-1}) for anti-PT and anti-FHA antibodies at ages ranging from 0 to 3 years increased rapidly with the increase in the population vaccinated over three times with aP vaccine. However, the ratio of those positive for anti-PT antibody tended to decrease until 6-8 years of age and to increase again from 9 to 19 years among the vaccinated population, although the ratio of individuals positive for anti-FHA antibody remained constant at 80-100% in children and adolescents over 3-year-old. Moreover, positivity for anti-PT antibody was high (=>50 ELISA U mL^{-1}) in some serum samples collected from adolescents and young adults, suggesting recent symptomatic or asymptomatic infection with circulating *Bordetella pertussis*. On the other hand, 50-60% of infants <12 months of age were below the detection limit (1.0 ELISA U mL^{-1}) for anti-PT and anti-FHA antibodies and most early infants were not vaccinated against pertussis.

When serologic responses (IgG and IgA antibodies) to 4 *Bordetella pertussis* antigens were compared in adults after infection with serologic responses after vaccination, it was observed that after reaching peak levels, titers of antibody to pertussis toxin decreased more than did titers of antibodies to filamentous hemagglutinin, pertactinand fimbriae type 1 and type 2 in 28 months. Although studies of adults who have been vaccinated with acellular pertussis vaccines have had shorter follow-up periods than studies of adults with pertussis infection, the antibody decay patterns were similar in both groups[31].

Within the last decade, several countries such as Netherlands, the United States Finland and Italy[3,32] have reported an increased incidence of pertussis despite high vaccination coverage[3,17,32-34]. Resurgence in infant and adult pertussis cases observed in many countries after the introduction of vaccination is alarming. Antigenic differences between circulating strains of *B. pertussis* and vaccine strains, or changes in vaccine procedures, could be the cause of this resurgence. It has been suggested that antigenic variation may have occurred in isolates of *B. pertussis* that could have affected the efficacy of pertussis vaccines[3,35]. In a Dutch study, based on DNA fingerprinting it was found that vaccination has resulted in the selection of strains different in DNA type from the vaccine strains and it could be due to antigenic differences in the strains[36].

Genome analysis and antigen expression by vaccine strains used in Aventis Pasteur whole-cell pertussis vaccine were investigated from multiple lots stored since 1984. Despite lyophilisation of these strains for over 30 years, the genome was conserved and they still expressed the major toxins and adhesions. A study in mice confirmed that the vaccine lots were highly immunogenic and therefore, there was no evidence to suggest that many after years of production there has been any alteration in the quality of the French vaccine strains which quality has remained consistent since its introduction. This could explain its continued efficacy, effectiveness and the lack of epidemics in France[37].

Vaccination of infants with whole-cell vaccines has dramatically reduced the disease, complications and deaths from pertussis in infancy and early childhood. There is still a major public health challenge to deal with the morbidity and economic burden of pertussis illness in older children, adolescents and adults[8]. According to a recent study, the most economical would be to immunize adolescents 10-19 years of age, which would prevent 0.7-1.8 million pertussis cases and save $0.6- $1.6 billion over a decade. However routine adult booster vaccinations every decade would be more expensive and more difficult to implement. A recommendation for booster vaccinations every 10 years requires more information about duration of immunity, program costs, compliance and non-medical costs associated with pertussis[38].

Adult-type acellular pertussis vaccines are likely to be safe and confer effective protection against pertussis[23,24]. The benefits of pertussis vaccination still outweigh the risk and universal childhood pertussis vaccination should continue, as recommended by WHO[6,10].

REFERENCES

1. Mastrantonio, P., P. Spigaglia, H. van-Oirschot, H.G.J. vander Heide, K.P. Heuvelman, P. Stefanelli and F.R. Mooi, 1999. Antigenic variants in *Bordetella pertussis* strains isolated from vaccinated and unvaccinated children. Microbiology, 145: 2069-2075.
2. Heininger, U., W.J. Kleemann and J.D. Cherry, 2004. A controlled study of the relationship between *Bordetella pertussis* infections and sudden unexpected deaths among German infants. Pediatrics, 114: 9-15.
3. Mikelova, L.K., S.A. Halperin, D. Scheifele, B. Smith, E. Ford-Jones, W. Vaudry, T. Jadavji, B. Law and D. Moore, 2003. Predictors of death in infants hospitalized with pertussis: A case-control study of 16 pertussis deaths in Canada. J. Pediatr., 143: 576-81.
4. Muller, A.S., J. Leeuwenburg and D.S. Pratt, 1986. Pertussis: Epidemiology and Control, Bull, WHO, 64: 321-331.
5. Von Konig, C.H.W., S. Halperin, M. Riffelmann and N. Guiso, 2004. Pertussis of adults and infants. Lanc. Infect. Dis., 2: 744-750.
6. World Health Organization, 1998. Informal consultation on control of pertussis with whole cell and acellular vaccines, Geneva (18-19 May).
7. CDC, 2002. Morbidity and mortality. Weekly Report, 51: 616-618.
8. Edmunds, W.J., M. Brisson, A. Melegaro and N.J. Gay, 2002. The potential cost-effectiveness of acellular pertussis booster vaccination in England and Wales Vaccine, 20: 1316-1330.
9. Rappuoli, R., M. Pizza, A. Podda, D.M. Magistris and L. Nencioni, 1991. Towards third generation of vaccines. Trend. Biotech., 91: 232-238.
10. World Health Organization, 1999. Pertussis vaccines. WHO position paper. Weekly Epidemiology Record, 74: 137-144.
11. Geier, D.A. and M.R. Geier, 2002. An analysis of the occurrence of convulsions and death after childhood vaccination. Toxicol. Meth., 12: 71-78.
12. Golden, G.S., 1990. Pertussis vaccine and injury to the brain. J. Pediat, 116: 854-861.

13. Cherry, J.D., P.A. Brunell, G.S. Golden and D.T. Karzon, 1988. Report of the task force on pertussis and pertussis immunization. Pediatrics, 81: 939-984.
14. Cherry, J.D., J. Gornbein, U. Heinin and K. Stehr, 1998. A search for serological correlates of immunity to *Bordetella pertussis* cough illness. Vaccine, 16: 1901-1906.
15. Parton, R., 1991. Review of biology of *Bordetella pertussis*. Biologicals, 27: 71-76.
16. Gold, M.S., 2002. Hypotonic-Hyporesponsive episodes following pertussis vaccination: A cause for concern? Drug Safety, 25: 85-90.
17. Grüber, C., L. Nilsson and B. Björkstén, 2001. Do early childhood immunizations influence the development of atopy and do they cause allergic reactions? Pediat. Aller. Immunol., 12: 296-311.
18. Ponvert, C., P. Scheinmann, C. Karila, V. Bakoe Bakonde, M. Le Bourgeois and J. de Blic, 2001. Allergy to multivalent vaccines in children: A study of 30 cases using immediate, semi-late and late responses in skin tests, specific antibody determinationsand challenge with monovalent and bivalent vaccines. Revue Francaise d' Alerg. Immun. Clini., 41: 701-711.
19. Edwards, K.M., M.D. Decker and E.A. Mortimer, 1999. Pertussis Vaccine. In: Plotkin, S.A. and Orenstein (Eds.) Vaccines, 3rd Ed. W.B Saunders Company, Philadelphia, Pa, pp: 293-344.
20. Jefferson, T., M. Rudin and C. DiPietrantonj, 2003.Systematic review of the effects of pertussis vaccines in children. Vaccine, 21: 18-24.
21. Olin, P., L. Gustafsson, L. Barreto, L. Hessel, T.C. Mast. A.V. Rie, H. Bogaerts and J. Storsaeter, 2003. Declining pertussis incidence in Sweden following the introduction of acellular pertussis vaccine. Vaccine, 21:2015-21.
22. Kimura, M. and H. Kuno-Saki, 1990. Developments in pertussis immunization in Japan. Lancet, 336: 30-32.
23. CDC, 1997. Pertussis vaccination: Use of acellular pertussis vaccines among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR, 46: 1-25.
24. CDC, 2002. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. Supplemental Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR, 46: 1-25.
25. Decker, M.D., K.M. Edwards and M.C. Steinhoff, 1996. Comparison of 13 acellular pertussis vaccines: Adverse reactions. Pediatrics, pp: 557-66.
26. Cook, I.F.and J. Murtagh, 2003. Comparative reactogenicity and parental acceptability of pertussis vaccines administered into the ventrogluteal area and anterolateral thigh in children aged 2, 4, 6 and 18 months. Vaccine, 21: 3330-3334.
27. Esposito, S., G. Faldella, A. Giammanco, S. Bosis, O. Friscia, M. Cleici and N. Principi, 2002. Diphtheria Tetanus, tricomponent acellular pertussis and hepatitis B vaccine in pre-term Infants. Vaccine, 20: 2982-2932.
28. Vellinga, A., A.M. Deporter and P. VanDamme, 2002. Vaccination coverage estimates by cluster sampling survey of children (18-24 months) in Flanders, Belgium. Acta Pediat., 9: 599-603.
29. Bernstein, H.H., E.P. Rothstein, M.E. Pichichero, J.L. Green, K.S. Reisinger, M.M. Blatter, J. Halpern, A.M. Arbeter, D.I. Bernstein, V. Smith, S.S Long, H. Rathfon and D.S. Krause, 1995. Reactogenicity and immunogenicity of a three-component acellular pertussis vaccine administered as the primary series to 2, 4 and 6 month old infants in the United States Vaccine, 13: 1631-1635.
30. Konda, T., K. Kamachi, M. Iwaki and Y. Matsunaga, 2002. Distribution of pertussis antibodies among different age groups in Japan. Vaccine, 20: 1711-1717.
31. Heininger, U., J.D. Cherry and K. Stehr, 2004. Serologic response and antibody-titer decay in adults with pertussis. Clin. Infect. Dis., 38: 591-594.
32. Mooi, F.R., Q. He, H. Van Oirshcot and J. Mertsola, 1999. Variation in the *Bordetella pertussis* virulence factors pertussis and pertactin in vaccine strains and clinical isolates in Finland. Infect. Immun., 67: 3133-3134.
33. Andrews, R., A. Herceg and C. Roberts, 1997. Pertussis notification in Australia 1991 to 1997. Commun. Dis., 21: 15-148.
34. Bass, J.W. and R.R. Wittler, 1994. Return of epidemic pertussis in the USJ. Pediat. Infect. Dis. 13: 343-345.
35. Long, S.S., C.J. Welkon and J.L. Clark, 1990. Wide spread silent transmission of pertussis in families: Antibody correlates with infection and symptomatology. J. Infect. Dis., 161: 480-486.
36. Van der Zee, A., S. Vernooij and M. Peeters *et al.*, 1996. Dynamics of the population structure of *Bordetella pertussis* as measured by IS1002-associated restriction fragment length polymorphism: comparison of pre- and post-vaccination strains and global distribution. Microbiology, 142: 3479-3485.
37. Njamkepo, E., F. Rimlinger, S. Thiberge and N. Guiso, 2002. Thirty-five years' experience with the whole-cell pertussis vaccine in France: Vaccine strains analysis and immunogenicity. Vaccine, 20: 1290-1294.
38. Purdy, K.W., J.W. Hay, M.F. Botteman and J.I. Ward, 2004. Evaluation of strategies for use of acellular pertussis vaccine in adolescents and adults: A Cost-benefit analysis. Clin. Infect. Dis., 39: 20-28.