

Selected Summaries

Pertussis and its New Vaccines

Summary 1: [Bortolussi A R, Miller B, Ledwith M, Halperin S. *Clinical course of pertussis in immunized children. Pediatr Infect Dis f* 1995, 14: 870-874.]

Pertussis is an acute illness of respiratory tract characterized by progressive, repetitive and paroxysmal cough, whoop, post-tussive vomiting but mild systemic symptoms. However, it has been stated that this classical picture may not be seen in immunized children. This prospective study documented the clinical course of 103 children below 5 yrs age who were vaccinated with the usual killed vaccine but developed the disease confirmed by cultures from the nasopharyngeal secretions. The disease had a less severe and less protracted course in the immunized children. But, the typical catarrhal stage followed by the paroxysmal stage occurred in majority of the children. Persistent paroxysmal cough for >21 days was seen in 88% of the cases. Thus, though milder, the disease retains its classical clinical picture even in immunized children.

Summary 2: [Halperin SA, Mills E, Parreto L, Pin C, Eastwood Bf. *Acellular pertussis vaccine as a booster dose for seventeen to nineteen month-old children immunized with either whole cell or acellular pertussis vaccine at two, four and six months of age. Pediatr Infect Dis f* 1995,14:792-797.]

The safety and immunogenicity of an acellular pertussis vaccine (APV) as a booster at 17 to 19 months of age were

assessed in children immunized at 2,4 and 6 months of age with acellular or whole cell pertussis vaccine. In study I, 86 children primed with a five-component acellular vaccine combined with diphtheria and tetanus toxoids or with a whole cell pertussis-diphtheria-tetanus vaccine were boosted with the same vaccine. Local reactions (64% vs 93%) were less common after the fourth dose of acellular vaccine than after the fourth dose of the whole cell vaccine.

In study II, 96 children primed with either an acellular or whole cell pertussis vaccine were boosted with an acellular vaccine. Local adverse reactions after booster immunization with acellular vaccine were more common in children primed with acellular vaccine than those primed with whole cell vaccine (68% vs 33%; relative risk, 2.1). Antibody response to pertussis toxin, filamentous hemagglutinin and fimbriae were higher before and 1 month after the booster dose in children primed with the acellular vaccine.

Summary 3: [Trollfors B, Taranger J, Lagergard T, hind L, Sundh V, Zackrisson G, Lowe CU, Blakwelder W, Robbins JB. *A placebo-controlled trial of a pertussis toxoid vaccine. N EnglJMed* 1995,333:1045-1050.]

Although many whole-cell vaccines have been effective in preventing pertussis, these vaccines are difficult to standardize and can produce side effects. In Sweden, pertussis became endemic during the 1970s despite vaccination. Because of its limited efficacy, the Swedish-made whole-cell vaccine was withdrawn in 1979 and children in Sweden receive DT in place

of DPT. Accordingly, it was possible to perform a placebo controlled trial of a pertussis toxoid vaccine. Inclusion of a whole cell vaccine was considered undesirable because renewed licensure of a whole cell vaccine in Sweden was highly unlikely.

To evaluate the efficacy of an acellular vaccine consisting of pertussis toxin inactivated by hydrogen peroxide (pertussis toxoid), the authors conducted a randomized, double blind, placebo controlled trial in Sweden. Infants were vaccinated with either diphtheria and tetanus toxoids alone (DT toxoids, 1726 infants) or diphtheria, tetanus, and pertussis toxoids (DTP toxoids, 1724 infants) at 3, 5 and 12 months of age. There were no serious reactions. With the pertussis vaccine there were slightly more local reactions than with the DT toxoids alone, but the rates of post vaccination fever were the same. The main period of surveillance which began 30 days after the third vaccination, continued for a median of 17.5 months. There were 312 cases of pertussis (72 in the DTP toxoids group and 240 in the DT toxoids group) that met the clinical criterion (paroxysmal cough lasting >21 days) and laboratory criteria for pertussis as defined by the WHO. Thirty days after the third vaccination, 1670 recipients of DTP toxoids and 1665 recipients of DT toxoids remained at risk. The incidence of pertussis, according to the WHO definition, was 2.96 cases per 100 person years among the recipients of DTP toxoids and 10.32 cases per 100 person years among the recipients of DT toxoids, respectively. The efficacy of this acellular vaccine was 71% (95% confidence interval, 63 to 78%). The recipients of DTP toxoids who had pertussis had cough of shorter duration than the recipients of DT toxoids, and fewer had whooping and vomiting. The vaccine

efficacy after two doses was 55% (95% confidence interval, 12 to 78%). There was no evidence of decreasing efficacy with time after the third vaccination. In conclusion, a pertussis-toxoid vaccine was safe and immunogenic and reduced the incidence and severity of pertussis. Furthermore, recovery of the organism was reduced. It was concluded that pertussis toxoid is both essential and sufficient for the vaccination of children and adults. It is the simplest and thus theoretically the safest vaccine for pertussis.

Comments

Pertussis can occur in fully immunized children also and in them it is less severe.

Summary 1-suggests that there should be no difficulty in recognizing the clinical picture as the characteristic paroxysms of cough do occur even in these children.

A clinical diagnosis of whooping cough may not be difficult but strict criteria have to be followed for research purposes. The WHO meeting on case definition recommends a diagnosis of pertussis with a paroxysmal cough of 21 days or more and at least one of the following, a positive culture, a positive culture in a family member with onset of pertussis within 28 days before or after the onset of the episode studied, or a statistically significant increase in IgG antibodies against pertussis toxin or filamentous hemagglutinin. Culture of *B. pertussis* requires inoculation of nasopharyngeal mucus, obtained by dacron or calcium alginate swab, on special media (such as italic Bordet-Gengou) with incubation for 7 days. Because these media may not be routinely available, the laboratory should be informed when *B. pertussis* is suspected. This fastidious organism is most frequently recovered in

the catarrhal stage or early in the paroxysmal stage and is rarely found after the fourth week of illness. The difficulties in culturing this bacillus have forced the clinician to look for other diagnostic tests. Polymerase chain reaction is a potential candidate in this context.

Failure of the currently available killed vaccine to provide protection in all and the frequent side effects of the vaccine have encouraged many workers to continue their search for a better vaccine. Two such studies are summarized here. The acellular pertussis vaccine (APV) used in summary 2 is somewhat different from the toxoid vaccine used in Summary 3. The APV contained pertussis toxoid (PT) 10 or 20 mcg, filamentous hemagglutinin 5 mcg or 20 mcg, 3 mcg of 69-KDa membrane protein and 5 mcg of fimbriae 2 and 3 per dose. On the other hand, the

toxoid vaccine had 40 mcg of PT only per dose. Both the vaccines were used in combination with diphtheria and tetanus toxoids as is the standard practice. Both the vaccines appear to be effective and safe.

Mass vaccination with diphtheria toxoid has eliminated diphtheria from western countries even though the toxoid confers incomplete individual protection under endemic or epidemic conditions. The Summary 3 group is now investigating whether mass vaccination of children with pertussis toxoid will eliminate pertussis as happened in the case of diphtheria, another non invasive toxin mediated respiratory disease.

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