Summary of Key Points

WHO Position Paper on Vaccines against Pertussis September 2015

World Health Organization

Background

- Pertussis (whooping cough), caused by the bacterium *Bordetella pertussis*, was one of the most common childhood disease world wide before vaccines became widely available
- In developing countries, the average case fatality rate (CFR) for pertussis has been estimated at almost 4% in infants aged <1 year and at 1% in children aged 1–4 years
- Large scale vaccination programmes were associated with a steep decline in the number of pertussis cases and deaths in children
- Despite high vaccination coverage (in 2014, 86% coverage with 3 doses of a pertussis containing vaccine), pertussis remains endemic in all countries and continues to be a public health concern

Disease and Distribution

- Following an incubation period of 9–10 days, patients develop catarrhal symptoms, including cough with characteristic “whoop”
  - Cough is particularly severe at night and frequently followed by vomiting
  - In very young infants, pertussis may initially present as apnoea and cyanosis
  - In previously immunized adolescents and adults, a persistent cough may be the only manifestation, without the characteristic “whoop”
- A shift in distribution towards older age groups has been reported in some high income countries, particularly where aP vaccines have replaced wP vaccines for primary series. This shift may be due to:
  - Increased recognition and surveillance including
  - More sensitive laboratory testing
  - Waning of vaccine-derived protection
  - Reduced boosting of immunity by circulating *B. pertussis*

Pertussis Vaccines

- Two types of pertussis vaccines are available:
  - Whole-cell (wP) vaccines based on killed *B. pertussis* organisms
  - Acellular (aP) vaccines based on one or more highly purified individual pertussis antigens
- The wP vaccines were introduced in mid-20th century and included in the Expanded Programme on Immunization since 1974
- Many high-income countries have replaced wP with aP vaccines as a means of decreasing the reactogenicity of the vaccine
- Pertussis vaccines are produced as combinations with other antigens; no stand-alone pertussis vaccines are currently available

Whole Cell Pertussis Vaccines Immunogenicity, Efficacy and Effectiveness

- Different wP vaccines may have different antigenic content and methods of production and control, leading to variations in immune responses
- Data from a systematic review showed that pooled efficacy of wP vaccine against pertussis disease in children was 78%, but varied significantly among vaccines. Effectiveness is highest against the most severe forms of the disease
- An updated systematic review indicates that 3p schedules of wP given in infancy are effective against pertussis disease in the first 5 years of life

Acellular Pertussis Vaccines Immunogenicity, Efficacy and Effectiveness

- Vaccines differ not only in the number (and concentration of the antigen components, but also with regard to the bacterial clone used in production, methods of purification and detoxification, adjuvants, and the use of preservatives

- Although some systematic reviews have favoured multi-component aP vaccines over vaccines with 1 or 2 aP components, taken together with the experience of vaccine use in countries, evidence is not sufficient to establish any significant difference in vaccine effectiveness of aP vaccines with differing numbers of components

- A systematic review that included 49 randomized controlled trials and 3 cohort studies indicated absolute efficacies ranging from (67% to 84%).

Comparison of the effectiveness of wP-containing and aP-containing vaccines

- Studies to date indicate that aP vaccines are more effective than low-efficacy wP vaccines (wP vaccines shown to be suboptimal are no longer in use), but may be less effective than the highest-efficacy wP vaccines
- Recent modelling studies as well as data from a baboon model of pertussis suggest faster waning of protection with aP primary series and limited impact on infection and transmission
- Although the reasons for the resurgence of pertussis in a number of countries were found to be complex and varied by country, the shorter duration of protection and probable lower impact of aP vaccines on infection and transmission are likely to play critical roles

Effectiveness of incomplete schedules with wP or aP vaccines

- Observational studies have consistently shown around 50% protection against severe pertussis in infancy following a single dose of either wP or aP pertussis vaccine, and that 2 doses offer at least 80% protection
- However, as the evidence is consistent with incremental protection after each additional dose, it is essential to complete a full primary series to obtain the full protective effects conferred by pertussis vaccine
- Subsequent boosters have been shown to extend the duration of protection against pertussis

Vaccine Safety

- Vaccination with wP vaccines is associated with minor local and systemic adverse events (1 in 2–10), such as local redness, swelling, induration, fever and agitation which increase with age
  - Prolonged crying and febrile convulsions are not uncommon (<1 in 100 vaccinations)
  - hypotonic–hyporesponsive episodes are uncommon (<1 in 1000–2000 vaccinations)
- The frequency of adverse events following aP vaccination does not differ from that observed in a placebo group, however after primary series, reactions tend to increase with each successive DTaP booster
- There is no association between pertussis vaccination and encephalopathy

WHO Position

- The main aim of pertussis vaccination is to reduce the risk of severe pertussis in infants and young children, due to the high morbidity and mortality caused by the disease in this age group.
- All children worldwide, including HIV-positive individuals, should be immunized against pertussis.
- Every country should seek to achieve early and timely vaccination initiated at 6 weeks and no later than 8 weeks of age, and maintain high coverage (≥90%) with at least 3 doses of assured quality pertussis vaccine at all levels (national and subnational)

WHO Position

- WHO recommends a 3-dose primary series, with the first dose administered at 6 weeks of age; subsequent doses should be given 4–8 weeks apart
- The series should be completed by 6 months of age; for those who have not completed the schedule, vaccine may be given later than 6 months of age, at the earliest opportunity
- For children whose vaccination series has been interrupted, the series should be resumed without repeating previous doses
- National programmes using alternate primary vaccination schedules with adequate surveillance should continue using these schedules and continue to monitor disease trends

WHO Position: Choice of Vaccine

- Protection against severe pertussis in infants and early childhood can be obtained with primary series of either wP or aP vaccine
- Available evidence indicates that there is more rapid waning of immunity, and possibly a reduced impact on transmission, with aP relative to wP vaccines.
- When considering a switch from wP to aP vaccines for the primary series, the overall goal of the programme needs to be considered
- A switch from wP to aP for primary infant immunization should only be considered if the additional periodic boosters or maternal immunization can be assured
- National programs currently using aP vaccine may continue but should consider the need for additional booster doses
- National programmes currently administering wP vaccines should continue with wP

WHO Position: Booster Dose

- A booster dose is recommended for children aged 1–6 years, preferably during the second year of life
- Only aP containing vaccines should be used for vaccination of persons aged over 7 years
- Although a booster dose in adolescence has been shown to decrease disease in adolescents, this is not generally recommended as a means of controlling disease in infants
- A decision to introduce an adolescent and/or adult booster dose should be taken after careful assessment of local epidemiology, contribution of adolescents as a source of infection in young infants, target groups, incidence and cost-effectiveness data

WHO Position: Additional strategies for preventing early infant mortality

- Vaccination of pregnant women is likely to be the most cost-effective additional strategy for preventing disease in infants too young to be vaccinated and appears to be more effective and favourable than cocooning

- National programmes may consider the vaccination of pregnant women with 1 dose of TdaP in the 2nd or 3rd trimester and at least 15 days before the end of pregnancy

- Cocooning may have an impact on disease prevention in some settings if high coverage can be achieved in a timely manner

WHO Position: Vaccinating Health Care Workers

- Health Care Workers should be prioritized in pertussis immunization programmes for adults
- Although there is as yet no evidence on the effectiveness this strategy, vaccination of Health Care Workers may be used to help prevent nosocomial transmission to infants within health-care settings if high coverage rates can be obtained
- Selected groups with direct contact with pregnant mothers and infant patients, such as staff working in maternity units or involved in neonatal and infant care, may be considered as priority groups for pertussis immunization

WHO Position: Interchangeability and Co-administration

- Changing between wP and aP vaccine groups is unlikely to interfere with the safety or immunogenicity
- Surveillance should be implemented in countries that introduce combinations of vaccines, especially when aP vaccines are used
- Data regarding simultaneous administration of the first 3 doses of DTaP or DTwP containing vaccines with other childhood vaccines indicate no interference with the response to any of these other antigens
  - When two injections are given concomitantly, they can be given in different limbs
  - When three injections are given, one injection should be administered in one limb and two injections in the other limb 2.5 cm apart

WHO Position: Surveillance

- Careful epidemiological surveillance of pertussis, particularly laboratory-confirmed disease, should be encouraged worldwide to monitor the disease burden and the impact of immunization.

- There is an urgent need to improve surveillance and assessment of disease burden particularly in low and middle income countries and to assess the impact of infant immunization, with particular focus on fatalities in infants <1 year of age and on hospital surveillance

For more information on the WHO Pertussis position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers

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