Pertussis vaccines: WHO position paper - October 1, 2010
Grading of scientific evidence in support of key recommendations

Table II: Safety of pertussis vaccines

**Question:** What is the scientific evidence that wP and aP vaccines are safe with regard to serious adverse events?*

**Settings:** Global

**Conclusion:** The scientific evidence demonstrates that both wP and aP vaccines are safe with regard to serious adverse events. Further research is unlikely to change the estimated effect on health outcomes.

*For definition of serious adverse events, see [http://www.who.int/vaccines-documents/DocsPDF05/815.pdf](http://www.who.int/vaccines-documents/DocsPDF05/815.pdf)

<table>
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<tr>
<th>Quality Assessment</th>
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<tr>
<td>Safety of aP vaccines</td>
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<tr>
<td>6^1</td>
<td>RCT</td>
<td>No serious</td>
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^1 Number refers to RCTs comparing aP and wP, respectively, with appropriate controls (absolute safety). In addition, a large number of RCTs (and observational studies) compare the adverse events of wP and aP vaccines (relative safety).
The systematic review by Jefferson et al (2002) included 4 and 6 studies, respectively, on the safety of wP and aP vaccines. The review also included 19 RCTs that compared wP and aP vaccines with regard to adverse events.

**Absolute safety, serious adverse events:** As compared to the controls, there was no increased risk of invasive bacterial infections or death among those immunized with AP or wP in the studies by Greco D et al 1996, (study population 14.751); Gustafsson L et al 1996, (study population 9.829); Olin P et al 1997, (study population 82.892); Trollfors B et al 1995, (study population 3.450); Decker MD et al 1995, (study population 2.200); Black RE et al 1997, (study population 2.498); and Uberall MA et al 1997, (study population 10.271). Also, investigations by Greco D et al (1996); Gustafsson L et al (1996); Olin P et al (1997); Trollfors B et al (1995); Uberall MA et al (1997) did not find any cases of encephalitis or encephalopathia in children within the 3 first days of immunization with aP or wP vaccines.

**Absolute safety, less serious/mild adverse events:** wP vaccines were associated with significantly higher incidences of swelling and induration (odds ratio (OR) 11.67, 95% confidence interval (CI) 8.83-15.44), fever (OR for fever >39 degrees C 3.36, 95% CI 2.06-5.49) and crying for >2h (OR 4.72, 95% CI 2.94-7.59) than placebo or DT. Differences in incidence of hypotonic hyporesponsive episodes (HHE) and convulsions (febrile and afebrile) were not statistically significant.

Acellular pertussis vaccines did not cause a higher incidence of local signs, fever, convulsions, HHE or prolonged crying than placebo or DT.

**Relative safety:** Jefferson et al concluded that as compared with wP vaccines, all aP vaccines were associated with a lower incidence of local swelling and induration, and in most cases also with significantly less fever. Similarly, a Cochrane report by Tinnion ON et al in 2000 covering 45 RCTs on safety concluded that the adverse event profile of aP vaccines was considerably better than that of wP vaccines. More recently, a Cochrane review by Bar-On ES et al (2009) investigated the safety of administering combined DTP-HBV-HIB vaccine versus separately administered DTP-HBV and HIB vaccines. Nine studies with a total of 4932 participants were reviewed. In terms of serious adverse events there were no significant difference between DTPa-HBV-HIB combined and separate vaccines and DTPw-HBV-HIB combined and separate vaccines (RR 0.91, 95% CI 0.56 to 1.48). However, a significant increase in pain (RR 1.09, 95% CI 1.02 to 1.17) and redness (RR 1.09, 95% CI 1.00 to 1.19) was observed in the patients given the combination vaccine.

**References**


