Acellular pertussis vaccines were safe and effective

Greco D, Salmaso S, Mastrantonio P, et al., and the Progetto Pertosse Working Group. ***A controlled trial of two acellular vaccines and one whole-cell vaccine against pertussis.*** *N Engl J Med. 1996 Feb 8;334:341-8.*

Objective
To compare the efficacy and safety among infants of 1 whole-cell and 2 acellular diphtheria-tetanus-pertussis (DTP) vaccines with DT alone.

Design
Randomised, double-blind, controlled trial.

Setting
62 public health clinics in Italy.

Patients
15 601 infants (50% boys) who were enrolled from September 1992 to September 1993. Exclusion criteria included a history of seizures or other central nervous system disease, serious congenital abnormalities, immunologic deficits, or failure to thrive. Follow-up beginning 1 month after the third dose was for a mean period of 17 months.

Intervention
Vaccines were given at 2, 4, and 6 months. Allocations were as follows: SmithKline acellular DTP vaccine (n = 4696), Biocine acellular DTP vaccine (n = 4672), whole-cell DTP vaccine (Connaught Laboratories) (n = 4678), and DT vaccine (Biocine) (n = 1555). 95% of the infants received all 3 doses.

Main outcome measures
Vaccine-related adverse events after each vaccination and occurrence of pertussis (illness with paroxysmal cough for ≥ 21 d plus culture or serologic confirmation of *Bordetella pertussis*).

Main results
Adverse events related to vaccination (local reactions; persistent crying; fever [$P < 0.001$]; and hypotonic, hyporesponsive episodes [$P < 0.01$]) were higher in the whole-cell DTP vaccine group. 330 cases of confirmed pertussis occurred in infants who received ≥ 1 dose of vaccine. Incidence rates for pertussis were 5.2% for the DT vaccine group, 3.5% for the whole-cell DTP vaccine group, 0.9% for the Biocine acellular DTP vaccine group, and 1.0% for the SmithKline acellular DTP vaccine group ($P < 0.003$ for all comparisons with DT). {Comparing the rates of pertussis in the DT and Biocine acellular DTP groups, the 4.3% absolute risk reduction (ARR) means that 23 infants (95% CI 18 to 31) would need to be treated with ≥ 1 dose of Biocine acellular DTP to prevent 1 additional case of pertussis; the relative risk reduction (RRR) was 82% (CI 74% to 88%). Comparing the rates of pertussis in the DT and SmithKline acellular DTP groups, the 4.2% ARR means that 24 infants (CI 18 to 32) would need to be given ≥ 1 dose of SmithKline acellular DTP vaccine to prevent 1 additional case of pertussis; the RRR was 81% (CI 73% to 87%).}*

Conclusion
Acellular DTP vaccines were safe and reduced the incidence of pertussis.

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*Numbers calculated from data in article.

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of pertussis in Italy and Sweden, or higher efficacy of other whole-cell vaccines used in the United States.

Acellular pertussis vaccines are safe and efficacious and should be recommended for infants and children. Several of the acellular vaccines may soon be licensed for routine use among infants in the United States. Immediate incorporation and acceptance of the routine preferred pertussis immunisation schedule will be tempered by the unavailability of acellular vaccines in combination with other vaccines. Until combination products become available, parents and providers will be faced with a choice between an extra injection, an extra visit, or vaccination with the existent combined whole-cell DTP-*Haemophilus influenzae* type b vaccines. More difficult issues for policy makers include making recommendations on interchangeability of acellular products for primary and reinforcing doses and recommending specific acellular products. Because the immunologic correlate of protection against pertussis is not known, the minimum number of vaccine doses required to induce protection has not been ascertained. Thus, it is not clear whether any vaccine can protect infants aged < 6 months who are incompletely immunised and at highest risk for pertussis and its complications. Because acellular vaccines vary in number, quantity, and constituent bacterial antigens and because some of these antigens function as attachment factors for *B. pertussis*, some vaccines may be more effective in preventing infection and interrupting transmission. Currently, the potential effect of these acellular vaccines on transmission of *B. pertussis* is not known.

Reliable surveillance for pertussis and extensive post-marketing studies are necessary to determine the risk for rare adverse events associated with acellular vaccines. Additionally, these studies will evaluate the effect of the vaccines on disease transmission, efficacy of mixed vaccine regimens, and efficacy of fewer doses of vaccine than are currently recommended in the United States.

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References

1. **Centers for Disease Control and Prevention.** MMWR. 1993;42:952-3, 959-60.
2. **Romanus V, Jonsell R, Bergquist SO.** Pediatr Infect Dis J. 1987;6:364-71.
3. **Noble GR, Bernier RH, Esber EC, et al.** JAMA. 1987;257:1351-6.
4. **Centers for Disease Control and Prevention.** MMWR. 1995;44:525-9.

Editor's note: A major impetus for (and funding of) these trials came from the United States, hence, the U.S. focus of this commentary. Our clinical selection panel, however, judged these results to be highly relevant to our readers throughout the world.

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