Pertussis vaccination in infancy and asthma or allergy in later childhood: birth cohort study

Anirban Maitra, Andrea Sherriff, Mansel Griffiths, John Henderson, Avon Longitudinal Study of Parents and Children Study Team

Some studies have shown a link between vaccination of infants with whole cell inactivated pertussis vaccine and the later development of asthma and atopy.\(^1\)\(^2\) A randomised controlled trial disagreed with these findings, but follow up was done until only 30 months of age.\(^3\) Our previous report of the lack of an association between pertussis vaccination and wheezing disorders was based on outcomes in early childhood.\(^4\) In this study we have examined the association between pertussis vaccination in infancy and asthma or atopy by age 7.5 years in a large, population-based birth cohort.

Participants, methods, and results

Participants were the 13 971 children who survived to 1 year in the Avon longitudinal study of parents and children. The study method has been described previously,\(^5\) and details can be found on the study website (www.cas.pacl.ac.uk). We obtained the vaccination status for each child from the child health surveillance database. We categorised children with regard to pertussis as fully vaccinated (completed a primary course of diphtheria and tetanus, and pertussis vaccination), partially vaccinated (completed a primary course of diphtheria and tetanus but did not receive pertussis vaccine) or non-vaccinated (no vaccinations). We excluded other combinations from analysis. We obtained three wheezing outcomes based on parental self-report questionnaire data: maternal education, maternal smoking during pregnancy, maternal history of asthma or eczema, maternal financial difficulties, damp housing, overcrowding, child’s ethnicity, number of siblings, contact with cats in the home, duration of breast feeding, and passive exposure to tobacco smoke; and, from medical records: birth weight, sex, gestational age, and maternal age at delivery. We used Pearson’s \(\chi^2\) (or Fisher’s exact test if the predicted number of subjects in any category was less than five) for our data analysis of univariable associations between vaccination status and possible confounders and principal outcomes. We used multivariable logistic regression models to evaluate associations between immunisation status and asthma and allergy outcomes while controlling for potential confounders.

Vaccination history was available for 13 810 children, of whom 13 109 (94.3%) were fully vaccinated, 446 did not have pertussis vaccination (340 non-vaccinated; 106 partially vaccinated), and 253 had some other combination. The table shows numbers of subjects with outcome data for each of the principal outcomes. The cumulative prevalence of asthma diagnosed by doctors was 20.3% (n = 1597) at 91 months. The prevalence of reported asthma at 69-81 months was 12.4% (n = 1024), reported wheeze with whistling at 69-81 months 9.8% (n = 788) and atopy at 7 years 20.5% (n = 1324). The table shows the adjusted and unadjusted odds ratios and 95% confidence intervals from logistic regressions for each of the principal outcomes. Although unadjusted analyses showed significant associations (asthma at 69-81 months: odds ratio 1.46, 95% confidence interval 1.31 to 1.63).
### Odds ratios with 95% confidence intervals for outcome variables according to pertussis vaccination status

<table>
<thead>
<tr>
<th>Outcome variable</th>
<th>Non-vaccinated*</th>
<th>Partially vaccinated†</th>
<th>Fully vaccinated‡</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma at age 69-81 months (1024/8240)</td>
<td>20.3 (14/69)</td>
<td>12.4 (98/8025)</td>
<td>1.00</td>
<td>0.05</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>8.2 (12/146)</td>
<td>9.0 (13/144)</td>
<td>15.6 (23/146)</td>
<td>15.2 (36/218)</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>3.3 (1/30)</td>
<td>1.36 (0.87 to 2.13)</td>
<td>0.98 (0.61 to 1.58)</td>
<td>0.1</td>
</tr>
<tr>
<td>Atopy at age 7 years (1324/8463)</td>
<td>1.00</td>
<td>0.94 (0.55 to 1.6)</td>
<td>0.55 (0.33 to 0.93)</td>
<td>0.1</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>9.8 (77/7902)</td>
<td>9.0 (13/144)</td>
<td>15.6 (23/146)</td>
<td>15.2 (36/218)</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>1.00</td>
<td>2.05 (0.8 to 5.3)</td>
<td>1.08 (0.68 to 1.99)</td>
<td>0.1</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>1.00</td>
<td>1.99 (0.82 to 4.4)</td>
<td>1.09 (0.62 to 1.94)</td>
<td>0.2</td>
</tr>
<tr>
<td>Prevalence in % (No/total)</td>
<td>1.00</td>
<td>0.94 (0.50 to 1.78)</td>
<td>0.94 (0.50 to 1.78)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

*No primary vaccinations, including pertussis.
†Diphtheria and tetanus ≥3 doses and no pertussis.
‡Triple (diphtheria, tetanus, and pertussis) vaccine ≥3 doses.

69-81 months, P = 0.05; doctor diagnosed asthma, 91 months, P = 0.005), it should be noted that, because of small numbers in some groups, the confidence intervals were wide and the results did not support the hypothesis. When we adjusted for potential confounding factors we detected no significant associations (P = 0.1-0.8).

### Comment

These findings confirm and extend our previous observations of the lack of an independent association between pertussis vaccination in infancy with inactivated, whole cell vaccine and the subsequent development of asthma or atopy during later childhood.

Acknowledgments: We thank the mothers and children who took part and the midwives for their cooperation and help in recruitment. The whole ALSPAC study team comprises interviewers, computer technicians, laboratory technicians, clerical workers, research scientists, volunteers, and managers who continue to make the study possible. The ALSPAC study is part of the European Longitudinal Study of Parents and Children initiated by the World Health Organization.

Contributors: MG had the original idea. AM, AS, JH did the analysis. All authors contributed to the interpretation of the data. AM wrote the paper. JH will act as guarantor.

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### Corrections and clarifications

**British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary**

An error occurred in the order of the reference list in this Education and Debate article by Bryan Williams et al (13 March, pp 634-40). Reference 8 in the published version (Williams et al) should have been reference 3, and the references published as 3 (Kamay et al) and 7 (O’Brien et al) in the reference list should then have been renumbered and become references 4 to 8. The two references cited in the footnote to table 1 should be renumbered as 6 (European Society of Hypertension-European Society of Cardiology) and 7 (WHO-International Society of Hypertension); but the other references cited in the text of the article are correct. The pdf (but not the HTML) version on bmj.com has been amended.

Recent developments in secondary prevention and cardiac rehabilitation after acute myocardial infarction

As a result of technology problems, some amendments from the authors did not make it into this clinical review by Hasnain Dalal and colleagues (20 March, pp 693-7). In box 2, we should have added the website address for SEARCH (the study of additional reductions in cholesterol and homocysteine): www.ctsu.ox.ac.uk/projects/search.shtml. And the penultimate sentence of the subsection “Angiotensin converting enzyme inhibitors” should have said that rates of revascularisation (not rates of readmission for heart failure) were reduced in patients who took ramipril.

Obituary: Leonard (“Johnny”) Walker

Our weekly quest to squeeze in as many obituaries as possible led to the last minute deletion of an important sentence from this obituary (BMJ 2003;326:1291). We omitted to say “Christianity was an abiding passion and his faith directed his life.” We have apologised to Dr Walker’s wife.

### Is Dad mad, doctor?

I had just put away the pleural aspiration kit and labelled the samples, and had returned to the patient, whose family had now arrived, to check that he was comfortable.

One of the adult children greeted me with the question, “Do you think Dad’s mad, doctor?”

“Mad?” I was a little bemused as to where this had come from.

“Yes, He said you are going to send off the fluid from his lungs for psychology.”

After a few puzzled moments, the penny dropped: “No, not psychology, cytology.”

James S Dawson, senior house officer, Queen’s Medical Centre, Nottingham.

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**Competing interests:** None declared.

**Ethical approval:** Avon Longitudinal Study of Parents and Children Ethics and Law Committee.

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