Clinical and epidemiological picture of *B pertussis* and *B parapertussis* infections after introduction of acellular pertussis vaccines

J G Liese, C Renner, S Stojanov, B H Belohradsky, The Munich Vaccine Study Group

ORIGINAL ARTICLE

Pertussis is a highly communicable, vaccine preventable disease, which causes significant morbidity in unvaccinated individuals. In Germany, the general recommendation for pertussis vaccination was discontinued in 1975 because of concerns regarding the safety of whole cell pertussis vaccines. Vaccination coverage rates subsequently dropped from 50–60% to approximately 15% and, as a consequence, pertussis has become one of the most frequent endemic infections in German infants and children, with an estimated incidence of 180 cases per 100 000 per year. Pertussis infant vaccination was generally recommended again in 1991, but vaccination coverage only increased rapidly after the licensure of acellular pertussis (acP) vaccines in 1994. This was due, firstly, to the better acceptance of the less reactogenic acP vaccines, and secondly, to the availability of acP vaccines in combination with other childhood vaccines. A survey of vaccination coverage in 1999 found a pertussis vaccination coverage of 91% in a German infant population for the first three doses given at 2, 3, and 4 months of age. Another survey in 2001/2002 found a pertussis vaccination coverage in former West Germany of 27% in 12–17 year old adolescents compared to 61% in 7–11 year olds and 83% in 2–6 year old children, documenting the change from a predominantly non-vaccinated population to a population with high pertussis vaccination coverage over the course of about 10 years.

An ongoing pertussis vaccine, long term efficacy study permitted us to introduce prospective long term surveillance in a highly vaccinated population of children between 3 and 8 years of age in German paediatric practices. Our objective was to determine the incidence and to describe the clinical spectrum of *B pertussis* and *B parapertussis* disease in this population after the introduction of acP vaccines. In addition, we investigated whether we could find an increase in *B parapertussis* infections in a situation involving questionable or, at the most, a low efficacy of licensed acP vaccines against *B parapertussis*.²

**Methods:** Prospective surveillance for *B pertussis* and *B parapertussis* in 14 144 toddlers. Pertussis vaccination coverage was 86%, either with acP (75%) or whole cell pertussis (wcP) vaccine (11%). All children presenting with cough for more than seven days were examined for *B pertussis* and *B parapertussis* by culture, PCR, and serology (for cough duration ≥ 21 days).

**Results:** There were 180 *Bordetella* infections; 116 (64%) were caused by *B pertussis* and 64 (36%) by *B parapertussis*. Incidence rates were 4.8 and 2.8 per 1000 person-years, respectively. Paroxysmal cough, post-tussive whooping, and vomiting ≥ 21 days was found in 53%, 22%, and 8% of all *B pertussis* cases and in 22%, 5%, and 0% of all *B parapertussis* cases, respectively. A total of 81/116 (70%) *B pertussis* cases and 56/64 (87.5%) *B parapertussis* cases had received at least one dose of pertussis vaccine. Typical pertussis with paroxysmal cough ≥ 21 days was present in 29/35 (83%) unvaccinated *B pertussis* cases, in contrast to 33/81 (41%) vaccinated *B pertussis* cases.

**Conclusion:** Following the increase of pertussis vaccination coverage, we observed a relative increase of *B parapertussis* cases in comparison to *B pertussis* cases. In vaccinated children *B pertussis* disease frequently presented as a mild disease, clinically difficult to distinguish from diseases associated with coughing caused by *B parapertussis* and other viral or bacterial infections.

**Methods**

**Study population**

A population based case-control study was carried out in Germany from February 1993 to May 1995 to determine the efficacy of Biken DTap vaccine. The study population consisted of 16 780 children born between December 1992 and June 1994, recruited in 63 paediatric practices. The children were vaccinated at the age of 3, 5, 7, and 15–24 months, either with Biken acP vaccine (received by 75%) or with a whole cell pertussis vaccine (received by 11% of the study population), or were not vaccinated against pertussis (14%) by decision of their parents or guardian. Pertussis vaccine catch up vaccinations were offered to study participants after licensure of acP vaccines for general infant vaccination in 1995. The data presented here refer to the period 1997 to 1999, when pertussis surveillance was reestablished in 45 of the initial 63 paediatric practices to determine the long term efficacy of the pertussis vaccines in the study population. The 45 practices had initially recruited 14 144 children into the study population, of which 11 087 (78%) were still regularly seen in the practice in 1997. In addition to the children of the original study population the surveillance for *Bordetella* spp. was extended to all other children of the same age group presenting in the participating paediatric practices.

The vaccination status of the study population was determined in a random sample of 479 children: 88 (18.4%) were vaccinated with wcP vaccine, 263 (59.9%) with acP vaccines, 13.4% with both wcP and acP vaccine (usually three wcP doses followed by a acP dose), and 8.3% were not vaccinated against pertussis. Children were between 3 and 8 years of age and were considered to be fully vaccinated if they...
Differences in symptoms and duration were evaluated with a Statistical analysis

Parents of children with laboratory confirmed bordetella cases were handed out diaries for a detailed daily infection. Seventy nine of the 116 infections (68%) were diagnosed either by PCR (5/42, 12%) or culture (38/42, 90%), whereas 22/64 B parapertussis cases (34%) were diagnosed by serology only.

A comparison between the symptoms of vaccinated B pertussis and vaccinated B parapertussis cases did not show significant differences with regard to the duration of any cough, but revealed significant differences with regard to the

**Table 1** Clinical symptoms in 116 children with B pertussis and 64 children with B parapertussis infection

<table>
<thead>
<tr>
<th>Symptom</th>
<th>B pertussis n=116 (64%)</th>
<th>B parapertussis n=64 (36%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough &gt;42 days</td>
<td>74 (64%)</td>
<td>24 (38%)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Paroxysmal cough</td>
<td>87 (75%)</td>
<td>39 (61%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Paroxysm &gt;21 days</td>
<td>62 (53%)</td>
<td>14 (22%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Whooping</td>
<td>63 (54%)</td>
<td>19 (30%)</td>
<td>0.0015</td>
</tr>
<tr>
<td>Whooping &gt;21 days</td>
<td>26 (22%)</td>
<td>3 (5%)</td>
<td>0.002</td>
</tr>
<tr>
<td>Vomiting</td>
<td>58 (50%)</td>
<td>16 (25%)</td>
<td>0.0011</td>
</tr>
<tr>
<td>Vomiting &gt;21 days</td>
<td>9 (8%)</td>
<td>0 (0%)</td>
<td>0.0276</td>
</tr>
</tbody>
</table>
occurrence and duration of paroxysmal cough and in post-tussive whooping. Thirty three of the 81 (41%) vaccinated *B pertussis* cases had more than seven days duration of paroxysmal cough in comparison to 14/57 (25%) of the vaccinated *B parapertussis* cases (p < 0.05). More than seven days duration of whooping was present in 33/81 (41%) of the vaccinated *B pertussis* and in 8/57 (14%) of the *B parapertussis* cases (p < 0.05).

In order to analyse the relation between age and clinical manifestation in both unvaccinated and vaccinated *B pertussis* cases, children were divided into a group aged <4.2 years and a group aged >4.2 years at the time of diagnosis of *Bordetella* spp. infection. No significant difference was found for cough duration and cough symptoms between vaccinated *B pertussis* cases of these two age groups. In unvaccinated *B pertussis* cases, however, children of the younger age group presented significantly more often with whooping of ≥7 days (p = 0.01) or ≥21 days (p = 0.009) and with vomiting of ≥21 days (p = 0.03). There was no significant difference in the duration of cough or paroxysmal cough.

**DISCUSSION**

The results of this study are based on a long term surveillance of *Bordetella pertussis* and *parapertussis* disease during a widespread increase of acP vaccination coverage in a German population from about 20% before 1994 to about 90% in 1999 to 2001. The objectives were to determine the incidence, clinical spectrum, and relative frequency of *B pertussis* and *B parapertussis* disease in vaccinated and unvaccinated children.

It may be expected that in Germany, as in other countries with a high coverage of pertussis vaccination, clinically significant *B pertussis* infections will decrease in the paediatric population. In our study we observed a clear decrease in the incidence from 21.7 per 1000 person-years during 1993–95 to 4.8 per 1000 person-years during 1997–99. However, even in highly immunised populations, *B pertussis* and *B parapertussis* still continue to circulate and cause relevant cough disease. Because of the incomplete efficacy of acP vaccines, especially with regard to mild disease, further circulation and a shift of *B pertussis* infections to older age groups, to adolescents and adults can be expected, as has already been shown in other countries.

We observed a relative increase in the percentage of *B parapertussis* among all bordetella cases from 20% in the period 1993–95 to 36% in the period 1997–99. Since the larger part of *B pertussis* infections in this population might have been prevented by vaccination, this increase of *B parapertussis* infections may be both the effect of a decrease of *B pertussis* infections and a real increase in the incidence of *B parapertussis* infections. In contrast to the clear and expected decrease of *B pertussis* infections, the incidence of *B parapertussis* increased from 1.6 per 1000 person-years in 1993–95 to 2.8 per 1000 person-years in 1997–99.

We are confident that all symptomatic *B pertussis* infections were detected in both study periods, since prospective surveillance with a low trigger of any cough ≥7 days was used to initiate bordetella case investigations. However, the comparatively low sensitivity of *B parapertussis* PCR might have led to a certain underestimation of *B parapertussis* cases. If we consider the 77 Bordetella spp. cases diagnosed by culture alone, the ratio of *B pertussis* to *B parapertussis* was 51%:49%, compared to a ratio of 64%:36% when PCR and serology positive cases were also included.

Among bordetella infections, relative frequency rates of *B parapertussis* have been reported between 1% and 35%, and the rates in Germany during the time of low vaccination were between 2.1% and 25%. A Finnish study in a highly vaccinated population found a very similar distribution to ours, with about one third of laboratory confirmed bordetella infections being caused by *B parapertussis*. The protective role of pertussis vaccines against *B parapertussis* infections remains unclear. Whereas *B parapertussis* infections in Denmark decreased following the introduction of whole cell pertussis vaccination, the circulation was not seen to have decreased in former Czechoslovakia, despite the widespread use of whole cell pertussis vaccination.

A recent German study estimated the efficacy of the Lederle whole cell vaccine against *B parapertussis* to be 21% (95% CI: 45% to 56%), in contrast to a higher efficacy for the Lederle acP vaccine of 50% (95% CI: 5% to 74%). Other recent acP vaccine trials did not find efficacy of acP vaccines against *B parapertussis* infections. The high rate of pertussis vaccination among the *B parapertussis* cases in our study suggests only a very low or no efficacy against *B parapertussis* disease for the acP vaccines used. Formal efficacy analyses, using the method of a population based (“nested”) case-control study, will be provided at the end of this ongoing long term efficacy study.

The typical clinical picture of *B pertussis* whooping cough disease was found in almost all unvaccinated children, whereas the majority of vaccinated children had a significantly shorter cough duration and milder symptoms. This observation confirms data of the previously published efficacy study in the same population, where the Biken acP vaccine showed a significantly better efficacy against typical pertussis disease than against mild or less typical pertussis disease. The *B parapertussis* presented in general as a disease associated with milder symptoms of coughing. However, about one third of the children with *B parapertussis* infection had a disease presenting prolonged cough with typical whooping cough symptoms, as well as paroxysms, whooping, and vomiting. Other recent studies also confirmed that *B parapertussis* may cause symptoms similar to *B pertussis*. Therefore, clinical symptoms alone do not allow one to make a distinction between *B pertussis* and *B parapertussis* diseases, especially in populations with a high and sustained pertussis vaccination coverage. Further surveillance of *Bordetella* spp. in highly immunised populations is necessary in order to document changes in the epidemiology and clinical picture of bordetella infections and to target additional preventive measures.

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**Authors’ affiliations**

J G Liese, C Renner, S Stojanov, B H Belohradsky, University Childrens Hospital Munich, Ludwig-Maximilians-Universität, Lindwurmstr. 4, 80357 Munich, Germany

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**Table 2** Clinical symptoms of *B pertussis* infection in 81 pertussis vaccinated* children and 35 unvaccinated children

<table>
<thead>
<tr>
<th>Symptom</th>
<th>B pertussis vaccinated (n=81)</th>
<th>B pertussis unvaccinated (n=35)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough ≥21 days</td>
<td>74 (91%)</td>
<td>35 (100%)</td>
<td>0.1038</td>
</tr>
<tr>
<td>Paroxysmal cough</td>
<td>54 (67%)</td>
<td>33 (94%)</td>
<td>0.0023</td>
</tr>
<tr>
<td>Paroxysm ≥21 days</td>
<td>33 (41%)</td>
<td>29 (83%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Whooping</td>
<td>38 (47%)</td>
<td>25 (71%)</td>
<td>0.024</td>
</tr>
<tr>
<td>Whooping ≥21 days</td>
<td>11 (14%)</td>
<td>15 (43%)</td>
<td>0.0019</td>
</tr>
<tr>
<td>Vomiting</td>
<td>32 (40%)</td>
<td>26 (74%)</td>
<td>0.0012</td>
</tr>
<tr>
<td>Vomiting ≥21 days</td>
<td>3 (4%)</td>
<td>6 (17%)</td>
<td>0.0182</td>
</tr>
</tbody>
</table>

*p Pertussis vaccinated with either three (n=9) or four doses (n=72) of the following vaccines: wcP vaccine (n=8), acP vaccine (n=60), both wcP and acP vaccine (usually three wcP doses followed by an acP dose; n=13).
REFERENCES
1 Schmitz M, Wossick S, Schulte-Wissermann H, et al. Schaffung zur
2 Liese JG, Stojanov S, Belohradsky BH. [Pertussis vaccination with
acellular vaccines. Tolerance—effectiveness—current vaccination
vaccinations: a new approach to visualize vaccine uptake. Epidemiol
Impfstatus aus der Pilotphase des Kinder- und Jugendgesundheits surveys.
7 Heininger U, Stehr K, Christenson P, et al. Evidence of efficacy of the
Lederle/Toakeda acellular pertussis component diphtheria and tetanus
toxoids and pertussis vaccine but not the Lederle whole-cell component
diphtheria and tetanus toxoids and pertussis vaccine against Bordetella
8 Hoppe JE. Methods for isolation of Bordetella pertussis from patients
Erregerspezifisierung mittels Direktausstrich von Nasopharyngealabstrichen.
Monatschr Kinderheilkd 1994;142:967–70.
10 van der Zee A, Agterberg C, Peeters M, et al. Polymerase chain
reaction assay for pertussis: simultaneous detection and discrimination of
reaction (PCR) compared with conventional identification in culture for
detection of Bordetella pertussis in 7153 children. Clin Microbiol Infect
12 Schmid M, Enders G. Detection of Bordetella pertussis and Bordetella
parapertussis in clinical specimens by a semiautomated PCR-ELISA.
single-sample serological technique for diagnosing pertussis in
14 He Q, Viljanen MK, Arvilommi H, et al. Whooping cough caused by
Bordetella pertussis and Bordetella parapertussis in an immunized
15 Lautrop H. Epidemics of parapertussis. 20 years’ observations in
16 Borsko K, Simkovicova M. Studies on the circulation of Bordetella
pertussis and Bordetella parapertussis in populations of children. J Hyg
infection in children: epidemiology, clinical symptoms, and molecular
18 Heininger U, Stehr K, Schmitt-Grohe S, et al. Clinical characteristics of
illness caused by Bordetella parapertussis compared with illness caused

POSTCARD FROM THE ROAD

Shoeshone

On impulse I asked the lady having her shoes shined how much the boy was charging. Around 50p ($0.75
or £0.75) seemed good—cheap enough to afford while travelling on a tight budget, expensive enough to feel like
there were two sides to the deal. The box on which he made me put my foot was roughly made but contained the tools he
needed—soap, wax, polish, cloths, and brushes—to give my shoes a shine they’d not had since I first bought them.

About halfway through the shine I realised that I was breaking a UN convention. Forget that I was paying what was
locally a good sum of money for the work. Forget that I was going to give him a pen too—big deal: have you ever met a
doctor who needs another pen? Forget also that the money from my job would have gone towards the rental, lease, or
purchase of his kit, moving him cent by cent closer to the
prospect of owning his own chair and stool, with the pride, self
respect, and status that this would give him.

The fact was that this was a child of about 11 years, kneel-
ing before me, dirtying his hands with polish so that I might be
able to see my face in my shoes. The UN convention states, in article 19, that children should be protected from exploita-
tion. At 11 years old pretty much any true work is

This was the first time I’d overty—or knowingly—flaunted
an international convention. But thinking about it I realised
that covertly we flaunt this particular article on a daily basis.
This happens every time we buy an item from an unknown
source in a country which is itself unwilling or unable to
abide by the convention. Looked at another way, our very way
of life depends on exploitation. How else could we buy some-
thing as complex as a television for a mere few hundred
pounds, or as simple as a T-shirt for less than ten? The worker,
being paid a few dollars a day, is likely either to be a child, or
an adult earning so little that there is no prospect of sending
his or her own children to school. There is a direct link
between the price we pay for the goods and the fact that the
worker requires his or her own children to work as well.

We feel justifiably pleased—maybe even smug—about our
own laws which aim to protect children. This is comparable to
the smugness we felt in the days of empire, when we pointed
out to less enlightened nations that we didn’t use slaves. Well,
not in Britain we didn’t, because we had plenty working for us
all over the rest of the Empire and beyond. We owe our current
place towards the top of the developed world hierarchy to that
exploitation, and we maintain our place there in a manner
which is only slightly less exploitative.

The developing world—some parts more than others—is
developing as a consequence of the efforts of its workforce,
often employed under extraordinarily competitive conditions
by companies who will move production from country to
country to secure the lowest price—or, depending on your
view, the highest efficiency. In some of these countries the
underage workforce is an important contributor to that
efficiency. Our position—the UN’s position—is very threaten-
ing to the economic growth of these countries. After all, they
say, badly paraphrasing Gandhi, that not every country can be
a Britain, with an entire India to plunder and exploit. They
have to create their economic growth from within, using what
they regard as their own strengths—which often means their
underage workforce.

At the heart of it, however, I cannot find fault in the UN
convention. I’ll continue to feel guilty until my shoes are
scuffed again. Then perhaps I’ll forget a bit, in the same way
that I can deny the source of my prosperity when I’m back at
home and can no longer see the polish blackened hands of the
shoeshine boy. But a part of me will recognise that for too
much of my life I live in the wrong half of another quote from
Gandhi: “Earth has enough to satisfy the need of all the
people, but not for satisfying the greed of some”.

Later that evening in the same square the band set up and
began to play. Lovers kissed and middle class families walked
with their children, pausing sometimes to allow another child
to play. Lovers kissed and middle class families walked
with their children, pausing sometimes to allow another child
to play.

I D Wacogne

Ian Wacogne is a consultant in general paediatrics
Birmingham Children’s Hospital, UK
Shoeshine

I D Wacogne

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