Tuberculin skin reactivity four years after neonatal BCG vaccination

were tuberculin positive. Altogether 251 of the 261 tuberculin positive results were grades 1 or 2 consistent with the BCG vaccination history. Ten had increased tuberculin reactions grade 3 or 4. Further investigation showed additional factors in these cases, such as household or non-household contact with tuberculosis.

All 10 of the children with grade 3 or 4 positive tests have been given chemoprophylaxis because of their contact history or after extended visits to the Indian subcontinent with strongly positive tests on return.

Discussion

This study shows a continuing high tuberculin positive rate at age 4 years in those who were shown to be tuberculin positive six to nine weeks after receiving their neonatal BCG. Crawshaw and Thompson also showed 19/22 (85%) of children to be tuberculin positive between 42 and 60 months. An appreciable proportion of children from the Indian subcontinent (80/103, 77.6%) were still tuberculin positive at age 12 when retested for the school programme. Our initial results showed a 97.3% rate of tuberculin positivity at six to nine weeks, and 93.6% of the neonates were tuberculin positive at six to nine weeks were still tuberculosis positive at age 4 years. Packe and Innes showed both a 95% positive tuberculin test rate after vaccination at age 3 months and a 65% overall protective effect. Hadfield et al showed a 97.8% positive rate after neonatal vaccination with a Dermostat injector. Thus three separate series found tuberculin positive rates between 95–97% after BCG vaccination in the first few months. This study supports earlier small studies showing a substantial tuberculin positive rates four to 12 years after vaccination. A negative tuberculin test does not mean that the vaccination is ineffective, however, as the degree of protection conferred on the individual is independent of the degree of tuberculin skin sensitivity induced.

This study in children already shown to have been tuberculin positive shortly after the initial vaccination refutes the findings of Grindulis et al. The explanation for the discrepancy between the results is that we were able to show an initial tuberculin response due to effective vaccination. As a quarter of the patients of Grindulis et al had no BCG scar, the likely explanation is not a failure of the vaccine but failure of the vaccination technique.


Association of high fever and short bacterial excretion after salmonellosis

A Sahib El-Radhi, Timo Rostila, Timo Vesikari

Infectious Diseases Teaching Unit,
University of Helsinki,
Finland
A Sahib El-Radhi

Epidemiological Department,
Aurora Hospital,
Helsinki, Finland
Timo Rostila

Department of Biomedical Sciences,
University of Tampere,
Finland
Timo Vesikari

Correspondence to:
Dr Timo Vesikari,
Department of Biomedical Sciences,
University of Tampere, PO Box 467,
SF-33101 Tampere, Finland.

Accepted 17 December 1991

Abstract

One hundred and two children with salmonella gastroenteritis were studied for factors affecting the length of convalescent bacterial excretion. There was a significant correlation between degree of fever and duration of excretion: a fever of ≥40°C had the shortest and no fever the longest duration of excretion. Fever therefore appears to have a favourable prognostic influence on the length of salmonella excretion.

Excretion of salmonella is an important public health problem that requires considerable attention and resources in countries with good hygienic standards. Factors associated with prolonged excretion of salmonella include malnutrition, use of antibiotics, young age, symptomatic infection, and infection with salmonella other than Salmonella typhimurium.

Accumulating evidence suggests that fever is beneficial to the infected host. A recent study of 125 children with salmonella gastroenteritis admitted consecutively to Ahmadi Hospital in Kuwait showed that children with a temperature greater than 40°C had a significantly shorter duration of bacterial excretion compared with afebrile children (AS El-Radhi, unpublished data). The aim of this study was to determine whether the same observation holds for Finnish children with salmonella gastroenteritis.

Patients and methods

The case records of all children who were hospitalised at the paediatric department of Aurora Hospital, Helsinki, Finland, with acute
gastroenteritis and a positive stool culture for non-typhoid salmonella were reviewed. The children were consecutive admissions with acute illness during a period of 17 years (January 1974 through December 1990). The study group consisted of 102 children (54 boys and 48 girls) aged less than 16 years (mean age 5-6 years; range 3 months–15.5 years). Children whose illness commenced in foreign countries or who were referred after the diagnosis had been established were not included. Temperature was recorded on admission and every four hours in the hospital. In children 5 years of age and under the temperature was measured rectally for three minutes and in older children axillary for seven minutes. Usually paracetamol 10 mg/kg every four hours was prescribed for fever above 38.5°C. None of the children received antibiotics specifically aimed at salmonella infection. Nine children received penicillin and six other children received various other antibiotics at the acute stage of illness. Routine investigations included a full blood count, measurement of concentrations of serum electrolytes, urea, and C reactive protein, and bacterial cultures from stool and urine. Blood culture was performed if clinically indicated. After discharge, a weekly stool specimen was submitted to the Epidemiological Department, City of Helsinki, until a bacteriological cure was achieved, defined as at least three successive negative cultures. The duration of excretion was assessed with the accuracy of one week.

The following measures of fever were considered in the analysis: temperature recorded on admission, the highest temperature recorded in hospital, and the highest mean temperature (usually a mean of four recordings) on any day in hospital.

**Results**

There was a weak but significant correlation between the age and the duration of bacterial excretion ($p<0.05$, $r=-0.21$), with younger patients having a longer duration of excretion.

The salmonella isolates consisted of 60 cases of *S. typhimurium*, 18 cases of *Salmonella enteritidis*, and 24 cases with other salmonellae. The mean (SD) duration of excretion was 5-4 (6-2) weeks for *S. typhimurium*, 3-8 (3-7) weeks for *S. enteritidis*, and 5-4 (13-6) weeks for other salmonellae; these differences were not significant ($p=0.3338$, analysis of variance using logarchimetric transformations of duration of excretion).

There was a significant association between the degree of temperature, whether on admission, highest ever, or the highest mean temperature on any day recorded in hospital, and the duration of excretion ($p=0.0004$, analysis of variance for each of the measures of fever).

Considering the degree of temperature on admission, the 102 patients were divided into four groups: (i) a temperature of $\geq 40^\circ$C ($n=15$), (ii) a temperature of 39–39.9°C ($n=22$), (iii) a temperature of 38–38.9°C ($n=44$), and (iv) no fever at presentation and a normal temperature during hospitalisation ($n=21$). When these groups were compared with each other for the length of bacterial excretion no difference was found between groups (ii) and (iii); these were pooled to make a group of 66 children with fever from 38–39.9°C. A comparison of the three remaining groups is presented in the table. The mean excretion time of salmonella was shortest in children who presented with fever of $\geq 40^\circ$C and longest in those who were afebrile at presentation.

No correlation was found between the leucocyte count or concentration of C reactive protein and the duration of bacterial excretion (data not shown).

**Discussion**

Several factors are known to influence the clinical course and the duration of bacterial excretion after salmonella gastroenteritis. In this study a tendency towards longer duration of excretion was seen in younger children; this finding is in agreement with other studies.

In our study a significant correlation was found between the duration of convalescent excretion and fever at the initial stage of illness. The shortest mean duration of excretion was found in children with high fever on admission and the longest was in afebrile children, including all four children who continued to excrete for longer than six months. Although the reason for this finding is not clear, there is evidence from human and animal studies suggesting that fever as a response to infection is beneficial to the infected host in accelerating the local inflammatory reaction and limiting the spread of infectious agents. Fever enhances cytokine production leading to a higher production of antibodies and cell proliferation aimed at combating the invading organisms.

In conclusion, our data suggest that fever may be a useful sign in children with salmonella gastroenteritis in predicting short duration of salmonella excretion after acute illness. Afebrile and young children may have a short and uncomplicated clinical course of illness but a prolonged bacterial excretion.

We thank Ms Tuula Pousa for statistical analysis.


**Fever on admission and duration of bacterial excretion after salmonella gastroenteritis in children**

<table>
<thead>
<tr>
<th>Degree of fever</th>
<th>No of children</th>
<th>Duration of salmonella excretion (weeks)</th>
<th>Range</th>
<th>Mean</th>
<th>Mean (SD) of log (1+x)</th>
<th>Mean (SD)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) $\geq 40^\circ$</td>
<td>15</td>
<td>0-10</td>
<td>0</td>
<td>1-2 (9-0)</td>
<td>0.381 (0.363)</td>
<td></td>
</tr>
<tr>
<td>(B) 38–39.9</td>
<td>66</td>
<td>0-18</td>
<td>11</td>
<td>4-1 (6-2)</td>
<td>0.585 (0.339)</td>
<td></td>
</tr>
<tr>
<td>(C) $\leq 37^\circ$</td>
<td>21</td>
<td>2-60</td>
<td>7</td>
<td>11-7 (15-1)</td>
<td>0.912 (0.383)</td>
<td></td>
</tr>
</tbody>
</table>

*F=13.70, p=0.0001, analysis of variance (log (1 + duration of excretion)).* Pairwise comparisons with Tukey-Cramer test: (A) v (B), $p=0.0160$; (B) v (C), $p=0.0011$; (A) v (C), $p=0.0001$. 

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Arch Dis Child 1992 67: 531-532
doi: 10.1136/adc.67.4.531

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