Low incidence of reactive arthritis in children following a salmonella outbreak

M Rudwaleit, S Richter, J Braun, J Sieper

Abstract

Objectives—To assess the incidence of reactive arthritis (ReA) in an outbreak of salmonella infection in a large cohort of children in Germany.

Methods—A few days after the salmonella outbreak all parents of affected children and all pediatricians and general practitioners in the region were provided with detailed information about the possibility of ReA. Six weeks after the outbreak a telephone call was made to all general practitioners and pediatricians to identify patients with ReA. Ten weeks after the outbreak a questionnaire assessing symptoms of ReA was mailed to all parents, and after a period of 4 months pediatricians and general practitioners were contacted again to search for additional unreported cases of ReA.

Results—Of the 286 children (age range 11 months to 9 years) with diarrhoea and stool cultures positive for *Salmonella enteritidis* lysotype 8/7, not a single case of arthritis was reported over the 4 month period. However, six children (2%) had arthralgia of various duration (1 day to 6 weeks) with a single recurrence in one child. The joint pattern was oligoarticular and lower limb joints (knee/ankle) were affected exclusively.

Conclusion—The incidence of ReA after salmonella infection in children appears to be very low which may be related to differences in the immune response between children and adults.

(Ann Rheum Dis 2001;60:1055–1057)

Reactive arthritis (ReA) following outbreaks of enteric infections with *Salmonella* is well recognised and occurs in 6–15% of the infected population. In those outbreaks where both adults and children are affected, it appears that ReA occurs less often in children than in adults.

At the end of January 1998 a large outbreak of *Salmonella enteritidis* occurred in Storkow, a small town 60 km south east of Berlin, Germany. The outbreak was caused by vanilla cream dessert contaminated with *S. enteritidis* lysotype 8/7. The affected children all attended nurseries, kindergartens, and primary schools. Two days after the outbreak the regional health authorities were contacted to assess prospectively the incidence of ReA in this large cohort.

Patients and methods

In all, 286 children with positive stool cultures were reported to the regional health authorities. A few days after the outbreak the regional health authorities were asked to deliver detailed information to the parents of all affected children about the possibility of developing ReA days to weeks after the onset of diarrhoea. The same information was handed out to all pediatricians and general practitioners in the region. Medical help and advice in cases of suspected musculoskeletal symptoms were offered to the affected families.

Since no case of arthritis was reported directly to us during the following 6 weeks, we contacted all general practitioners and pediatricians in the region by telephone to identify patients with ReA. Ten weeks after the outbreak a questionnaire on the severity of enteritis, joint symptoms, joint distribution, enthesitis, and extra-articular symptoms suggestive of ReA was mailed to all parents of affected children through the regional health authorities.

Four months after the outbreak all pediatricians and general practitioners in the region were contacted again by one of us (MR) to identify further cases of possible ReA which had not been reported to us before but which had, in the meantime, sought medical help from the local doctor.

Results

ENTERITIS

Two hundred and eighty six children (age range 11 months to 9 years) with diarrhoea and stool cultures positive for *S. enteritidis* were reported to the regional health authorities. The only strain isolated from stool cultures in this outbreak was *S. enteritidis* lysotype 8/7. The severity of the enteritis required admission to hospital for 3–7 days in seven children. Four of the seven hospitalised children and virtually all of the other affected children with enteritis were managed without antibiotics.

ARTHRITIS AND ARTHRALGIA

None of the children admitted to hospital for enteritis suffered from joint symptoms during the hospital stay. Six children (2%) presented to two local pediatricians with arthralgia of...
The precise number of children and adults is not given in the publication (total n=418) and had to be calculated from a figure.3

The definition of ReA varies according to the authors’ opinion.5

Where possible, the number of infected and subsequently assessed persons is given.2

20 di

less likely to cause arthritis. In Germany about

strain (S enteritides) which may be

related to a lower susceptibility to ReA in

young children in general, or to the bacterial

related to a lower susceptibility to ReA in

this cohort of children is not clear but may be

simply because no adults were a

pare children and adults in this outbreak

Take place can also be excluded since the

problems are unlikely explanations, given the

Communications).3

icke, Reference Centre for Salmonella Infec-

tions, Wernigerode, Germany; personal com-

munication).3

The reason for the low incidence of ReA in

chronic arthritis and enthesopathy reported by the

parents.

QUESTIONNAIRE

The response rate to the questionnaire was poor (less than 20%). The six children with

arthralgia already known to us from our
telephone calls 6 weeks after the outbreak were

among the responders. A further contact with all

paediatricians and general practitioners in the

region 4 months after the outbreak did not

reveal any further cases of possible ReA.

Discussion

In this large cohort of 286 children affected by

salmonella food poisoning only six children

(2%) developed oligoarticular arthralgia of

short duration. Not a single case of frank

arthritis was reported. Various efforts were

undertaken to deliver information to and

obtain information from all parents and
doctors at several time points, making it

unlikely that clinically relevant cases were

missed. Likewise, according to the regional

health authorities and local doctors, visits of

parents and children to doctors outside the

region can be excluded.

The reason for the low incidence of ReA in

this cohort of children is not clear but may be

related to a lower susceptibility to ReA in

young children in general, or to the bacterial

strain (S enteritides lysotype 8/7) which may be

less likely to cause arthritis. In Germany about

20 different strains of S enteritides are isolated
each year from stool cultures, 15 of which

occur in frequencies higher than 0.2% of all

outbreaks. The most common lysotype is S

enteritides lysotype 4/6 which accounts for

70–80% of all salmonella infections, followed

by lysotype 8/7 which accounts for 5% of all

infections, and the lysotypes 6/6 and 21/1

which each account for 3–5% of all infections.

Thus, the strain S enteritides lysotype 8/7

isolated in this outbreak is a common strain in

Germany. These strains are not known to differ

in their clinical manifestations. Furthermore,

there are no data on differences between the

strains in their ability to cause arthritis (B Ger-
icke, Reference Centre for Salmonella Infec-
tions, Wernigerode, Germany; personal com-

munication).

Underreporting of cases or methodological

problems are unlikely explanations, given the

extent of the efforts made to identify patients

with ReA in this cohort. A particularly low fre-

quency of HLA-B27 in the region where the

outbreak took place can also be excluded since

the area of the outbreak is located just 60 km

outside Berlin which has an HLA-B27 preva-

lence of 0.3%.3

From the literature it appears that, in

general, children are less susceptible to ReA (or

joint symptoms) after enteric infections than

adults (table 1) and joint symptoms are often

milder in children than in adults.1–4 6–12 It is

noteworthy that in all the salmonella outbreaks

which affected both adults and children, the

incidence of ReA was always lower in children

than in adults.1–4 6–12 Although we could not com-
pare children and adults in this outbreak

simply because no adults were affected, our

data confirm earlier reports on the generally

low incidence of ReA in children. The reduced

susceptibility to ReA of children compared

with adults cannot be accounted for by genetic

factors. Methodological difficulties in assessing

ReA in children or in recognising very mild

forms of ReA which were otherwise unnoticed,

may contribute to the difference between chil-

dren and adults. However, if the difference is

found to exist, it may well relate to differences

in the immune systems of children and

adults—for example, viral infections such as

the Epstein Barr virus cause no or only mild

symptoms in children but usually have a much

more severe clinical picture and often a

prolonged course in adults. The immune

Table 1 Incidence of reactive arthritis (ReA) among children (<16 years) and adults (≥16 years) following Salmonella infection: summary of epidemiological studies

<table>
<thead>
<tr>
<th>Total number of children infected</th>
<th>Total number of adults infected</th>
<th>Children with ReA/joint complaints (%)</th>
<th>Adults with ReA/joint complaints (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>286†</td>
<td>330</td>
<td></td>
<td>3.9</td>
<td>Hakansson et al (1975)†</td>
</tr>
<tr>
<td>260‡</td>
<td>212</td>
<td>0.5</td>
<td>3.3</td>
<td>Eastmond (1983)‡</td>
</tr>
<tr>
<td>–</td>
<td>83</td>
<td>0.5</td>
<td>7.3</td>
<td>Thomson et al (1992)†</td>
</tr>
<tr>
<td>–</td>
<td>115</td>
<td>2.6</td>
<td>7.2</td>
<td>Locht et al (1993)†</td>
</tr>
<tr>
<td>–</td>
<td>84</td>
<td>2.6</td>
<td>13.3</td>
<td>Thomson et al (1994)†</td>
</tr>
<tr>
<td>155</td>
<td>91</td>
<td>2.6</td>
<td>13.2</td>
<td>Matilla et al (1994)†</td>
</tr>
<tr>
<td>–</td>
<td>411</td>
<td>6.6</td>
<td>6.6</td>
<td>Thomson et al (1999)†</td>
</tr>
<tr>
<td>–</td>
<td>38</td>
<td>8.0</td>
<td>12</td>
<td>Matilla et al (1998)†</td>
</tr>
<tr>
<td>286</td>
<td>–</td>
<td>2.1**</td>
<td>–</td>
<td>Present study</td>
</tr>
</tbody>
</table>

#Where possible, the number of infected and subsequently assessed persons is given.

§The definition of ReA varies according to the authors’ opinion.

*The precise number of children and adults is not given in the publication (total n=418) and had to be calculated from a figure.9

**No case of arthritis was seen, all children had arthralgia only.

In this large cohort of 286 children affected by

salmonella food poisoning only six children

(2%) developed oligoarticular arthralgia of

short duration. Not a single case of frank

arthritis was reported. Various efforts were

undertaken to deliver information to and

obtain information from all parents and
doctors at several time points, making it

unlikely that clinically relevant cases were

missed. Likewise, according to the regional

health authorities and local doctors, visits of

parents and children to doctors outside the

region can be excluded.

The reason for the low incidence of ReA in

this cohort of children is not clear but may be

related to a lower susceptibility to ReA in

young children in general, or to the bacterial

strain (S enteritides) lysotype 8/7 which may be

less likely to cause arthritis. In Germany about

20 different strains of S enteritides are isolated
each year from stool cultures, 15 of which

occur in frequencies higher than 0.2% of all

outbreaks. The most common lysotype is S

enteritides lysotype 4/6 which accounts for

70–80% of all salmonella infections, followed

by lysotype 8/7 which accounts for 5% of all

infections, and the lysotypes 6/6 and 21/1

which each account for 3–5% of all infections.

Thus, the strain S enteritides lysotype 8/7

isolated in this outbreak is a common strain in

Germany. These strains are not known to differ

in their clinical manifestations. Furthermore,

there are no data on differences between the

strains in their ability to cause arthritis (B Ger-
icke, Reference Centre for Salmonella Infec-
tions, Wernigerode, Germany; personal com-

munication).

Underreporting of cases or methodological

problems are unlikely explanations, given the

extent of the efforts made to identify patients

with ReA in this cohort. A particularly low fre-

quency of HLA-B27 in the region where the

outbreak took place can also be excluded since

the area of the outbreak is located just 60 km

outside Berlin which has an HLA-B27 preva-

lence of 0.3%.3

From the literature it appears that, in

general, children are less susceptible to ReA (or

joint symptoms) after enteric infections than

adults (table 1) and joint symptoms are often

milder in children than in adults.1–4 6–12 It is

noteworthy that in all the salmonella outbreaks

which affected both adults and children, the

incidence of ReA was always lower in children

than in adults.1–4 6–12 Although we could not com-
pare children and adults in this outbreak

simply because no adults were affected, our

data confirm earlier reports on the generally

low incidence of ReA in children. The reduced

susceptibility to ReA of children compared

with adults cannot be accounted for by genetic

factors. Methodological difficulties in assessing

ReA in children or in recognising very mild

forms of ReA which were otherwise unnoticed,

may contribute to the difference between chil-

dren and adults. However, if the difference is

found to exist, it may well relate to differences

in the immune systems of children and

adults—for example, viral infections such as

the Epstein Barr virus cause no or only mild

symptoms in children but usually have a much

more severe clinical picture and often a

prolonged course in adults. The immune
system of children may be less educated or more "naive" and may, in general, also be less likely to mount an autoimmune response than that of adults. Alternatively, children might mount a more effective antimicrobial immune response resulting, in general, in an early, fast, and efficient elimination of bacteria.\textsuperscript{13}

We are grateful to Dr B Gericke, Reference Centre for Salmonella Infections, Robert-Koch-Institut, Wernigerode, Germany for providing epidemiological data on salmonella infections in Germany.

Low incidence of reactive arthritis in children following a salmonella outbreak

M Rudwaleit, S Richter, J Braun and J Sieper

Ann Rheum Dis 2001 60: 1055-1057
doi: 10.1136/ard.60.11.1055