

## CONCISE REPORTS

## Low incidence of reactive arthritis in children following a salmonella outbreak

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### 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 paediatricians 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 paediatricians 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 paediatricians 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.

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Reactive arthritis (ReA) following outbreaks of enteric infections with *Salmonella* is well recognised and occurs in 6–15% of the infected population.<sup>1</sup> In those outbreaks where both adults and children are affected, it appears that ReA occurs less often in children than in adults.<sup>1–4</sup>

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 paediatricians 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 paediatricians 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 paediatricians 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 paediatricians with arthralgia of

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

Total number of children infected#	Total number of adults infected#	Children with ReA/joint complaints (%)§	Adults with ReA/joint complaints (%)§	Reference
—	330	—	3.9	Hakansson <i>et al</i> (1975) <sup>6</sup>
206¶	212¶	0.5	3.3	Eastmond (1983) <sup>3</sup>
—	260	—	7.3	Inman <i>et al</i> (1988) <sup>7</sup>
—	83	—	7.2	Thomson <i>et al</i> (1992) <sup>8</sup>
—	113	—	15	Locht <i>et al</i> (1993) <sup>9</sup>
—	84	—	13.1	Thomson <i>et al</i> (1994) <sup>10</sup>
155	91	2.6	13.2	Mattila <i>et al</i> (1994) <sup>1</sup>
—	411	—	6.6	Thomson <i>et al</i> (1995) <sup>11</sup>
—	321	—	14*	Samuel <i>et al</i> (1995) <sup>12</sup>
38	153	8.0	12	Mattila <i>et al</i> (1998) <sup>4</sup>
286	—	2.1**	—	Present study

#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.<sup>3</sup>

\*Incidence as estimated by the authors.<sup>12</sup>

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

one or two joints without swelling or redness. These six patients were identified by telephone calls to the general practitioners and paediatricians 6 weeks after the outbreak. The joint pattern in these children was oligoarticular with one knee, both knees, or one knee and one ankle affected. The joint symptoms subsided in three children within 24–72 hours and in two children within 4 days and did not recur. In one child (aged 8 years) arthralgia of both knees occurred 7 days after onset of diarrhoea and subsided after 6 weeks with a single recurrence of another 3 weeks' duration as reported by the mother. No medical treatment was given in this case. Neither in these six children nor in any other children in the study were extra-articular manifestations associated with ReA such as eye inflammation or 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 enteritidis* lysotype 8/7) which may be less likely to cause arthritis. In Germany about 20 different strains of *S enteritidis* 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 enteritidis* 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 enteritidis* 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 Gericke, Reference Centre for Salmonella Infections, Wernigerode, Germany; personal communication).

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 frequency 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 prevalence of 9.3%.<sup>5</sup>

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.<sup>1–4 6–12</sup> 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.<sup>1 3 4</sup> Although we could not compare 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 children 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.<sup>13</sup>

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- 1 Mattila L, Leirisalo-Repo M, Koskimies S, Granfors K, Siitonen A. Reactive arthritis following an outbreak of Salmonella infection in Finland. *Br J Rheumatol* 1994;33:1136-41.
- 2 Lockie GN, Hunder GG. Reiter's syndrome in children. A case report and review. *Arthritis Rheum* 1971;14:767-72.
- 3 Eastmond CJ. Gram-negative bacteria and B27 disease. *Br J Rheumatol* 1983;22(suppl 2):67-74.
- 4 Mattila L, Leirisalo-Repo M, Pelkonen P, Koskimies S, Granfors K, Siitonen A. Reactive arthritis following an outbreak of Salmonella bovismorbificans infection. *J Infect* 1998;36:289-95.
- 5 Braun J, Bollow M, Remlinger G, Eggens U, Rudwaleit M, Distler A, et al. Prevalence of spondylarthropathies in HLA-B27 positive and negative blood donors. *Arthritis Rheum* 1998;41:58-67.
- 6 Hakansson U, Löw B, Eitrem R, Winblad S. HL-A27 and reactive arthritis in an outbreak of salmonellosis. *Tissue Antigens* 1975;6:366-7.
- 7 Inman RD, Johnston MH, Falk J, Helewa A. Postdysenteric reactive arthritis: a clinical and immunogenetic study following an outbreak of salmonella. *Arthritis Rheum* 1988;31:1377-83.
- 8 Thomson GTD, Chiu B, DeRubeis D, Falk J, Inman RD. Immunoepidemiology of post-Salmonella reactive arthritis in a cohort of women. *Clin Immunol Immunopathol* 1992; 64:227-32.
- 9 Locht H, Kihlström E, Lindström FD. Reactive arthritis after Salmonella among medical doctors: a study of an outbreak. *J Rheumatol* 1993;20:845-8.
- 10 Thomson GTD, Alfa M, Orr K, Thomson BRJ, Olson N. Secretory immune response and clinical sequelae of Salmonella infection in a point source cohort. *J Rheumatol* 1994;21:132-7.
- 11 Thomson GTD, DeRubeis DA, Hodge MA, Rajanayagam C, Inman RD. Post-Salmonella reactive arthritis: late clinical sequelae in a point source cohort. *Am J Med* 1995;98: 13-21.
- 12 Samuel MP, Zwillich SH, Thomson GTD, Alfa M, Orr KB, Brittain DC, et al. Fast food arthritis: a clinico-pathologic study of post-Salmonella reactive arthritis. *J Rheumatol* 1995;22:1947-52.
- 13 Sieper J, Braun J, Kingsley G. Report on the fourth international workshop on reactive arthritis. *Arthritis Rheum* 2000;43:720-34.

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