Epidemiology of *Salmonella typhimurium* O:4–12 Infection in Norway
Evidence of Transmission from an Avian Wildlife Reservoir

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In 1987, a nationwide outbreak of *Salmonella typhimurium* O:4–12 infection traced to contaminated chocolate bars occurred in Norway. In the 5 years after the outbreak, elevated numbers of sporadic cases caused by the epidemic strain of *Salmonella* were detected, followed by a decline in subsequent years. To characterize the epidemiology of this infection, the authors analyzed information concerning all sporadic cases reported in Norway from 1966 to 1996. Of the 153 patients infected by the outbreak strain, 43% were less than 5 years of age, and only three persons had acquired the infection abroad. In contrast, 46% of the cases attributable to other *S. typhimurium* O:4–12 variants and 90% of the total number of *Salmonella* infections were related to foreign travel. A distinct seasonality was observed: 76% of the cases appeared between January and April. At the same time of year, the epidemic strain was regularly encountered as the etiologic agent of fatal salmonellosis among wild passerine birds, suggesting an epidemiologic link between the avian and human cases. The strain was rarely isolated from other sources. From 1990 to 1992, the authors conducted a prospective case-control study of sporadic indigenous infections to identify risk factors and obtain guidance for preventive efforts. Forty-one case-patients, each matched by age, sex, and geographic area with two population controls, were enrolled. In conditional logistic regression analysis, the following environmental factors were independently related to an increased risk of infection: drinking untreated water, having direct contact with wild birds or their droppings, and eating snow, sand, or soil. Cases were also more likely than controls to report having antecedent or concurrent medical disorders. Forty-six percent of the study patients were hospitalized for their salmonellosis.

Bacteria belonging to the genus *Salmonella* are acknowledged pathogens of considerable medical and economic interest throughout the world (1–3). *Salmonellae* are important causal agents of acute enteritis in humans, and they affect a wide range of warm- and cold-blooded animals (4, 5). Salmonellosis in humans and animals is usually due to consumption of contaminated food or water. Secondary spread may occur directly via the fecal-oral route of transmission (4, 5). In most industrialized countries, including Norway, *Salmonella enterica* serovar *typhimurium* (S. *typhimurium*) is the second most common agent of human salmonellosis, surpassed only by *Salmonella enteritidis*, which has become the dominant serovar during the past decade (1, 6).

In 1987, a nationwide outbreak of *S. typhimurium* infection, which probably involved thousands of persons and precipitated 349 culture-confirmed cases, occurred in Norway (7). Epidemiologic and bacteriologic investigations identified chocolate bars produced by a Norwegian company as the vehicle of transmission, and suggested that the epidemic strain originated from an avian wildlife reservoir (7, 8). The bacterial isolates recovered from patients and chocolate products during the outbreak exhibited the antigenic factors O:4–12 and shared a number of distinguishing properties, including a characteristic plasmid profile and a rare phage lysis pattern (U277) (8). In the years following the outbreak, the number of reported cases caused by this strain increased considerably from a low baseline level in pre-outbreak years. No recognized outbreaks, changes in surveillance techniques, or alterations in culture methods explained the increase. In 1990, a prospective case-control study of sporadic infections was launched to identify factors responsible

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Abbreviations: NIPH, National Institute of Public Health; OR, odds ratio.

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for the increasing number of cases and to obtain guidance for preventive efforts.

This report describes the epidemiologic progression of the epidemic strain in Norway, notes the environmental risk factors identified by the case-control study, and describes clinical aspects of the disease.

**MATERIALS AND METHODS**

**Descriptive epidemiology**

**Human cases.** The occurrence of *S. typhimurium* as a cause of human illness was ascertained using the records of the National Salmonella Reference Laboratory at the National Institute of Public Health (NIPH), where all clinical bacterial isolates of *Salmonella* species recovered by the medical microbiologic laboratories in Norway have been collected since the late 1940s. When they were received at the NIPH, all isolates were serotyped and characterized biochemically according to standard procedures (9), as outlined previously (8). Plasmid profile analysis and phage typing of selected isolates was done as described elsewhere (8). All sporadic cases of *S. typhimurium* O:4–12 infection recorded from 1966 to 1996 were selected, and a comparative epidemiologic analysis of two different groups of bacterial variants was performed: 1) variant 1, which comprised isolates showing the same characteristic plasmid profile and biochemical properties as the epidemic strain seen in 1987 (8), and 2) all other variants combined. Epidemiologic information (age, geographic affiliation, and travel to foreign countries prior to illness onset) was obtained from the patient registration forms which followed the stool samples to the laboratories. Attempts were also made to identify isolates of variant 1 obtained prior to 1966 in our strain collection.

**Nonhuman isolates.** Information on nonhuman isolates of *S. typhimurium* O:4–12 was obtained from the files at the National Veterinary Institute, which has isolated and recorded salmonellae from wild and domestic birds and mammals and animal feed since the early 1950s. During the study period, several hundred samples were analyzed annually; less than 5 percent were from wild birds. Additional information was obtained from the NIPH reference laboratory, which receives all *Salmonella* isolates from food, feed, animals, and the environment for verification and typing. Isolates were serotyped, characterized biochemically, and subjected to plasmid profile analysis as described above.

**Case-control study**

**Cases and controls.** The prospective case-control study was conducted from January 1990 through June 1992. We defined a case-patient as someone with acute enteritis who: 1) had a culture-confirmed infection with *S. typhimurium*, variant 1, 2) was diagnosed at one of the medical microbiologic laboratories in Norway during the study period, and 3) had not traveled abroad in the 2 weeks before the onset of illness. If stool specimens from more than one member of a household yielded *S. typhimurium* or if the case was part of a recognized outbreak, only the first identified case-patient was enrolled. All bacterial isolates were verified at the NIPH.

Whenever a case was identified, a letter was mailed to the patient’s physician to request informed consent from the patient for participation in the study. Once enrolled, each case-patient was matched by age, sex, and geographic area with two controls selected from Norsk Folkeregister, a government registry of all Norwegian residents which is updated on a quarterly basis. Matching was accomplished by selecting persons from the registry who were closest in age to the case and who lived in the same municipality or an adjacent one. The cases and their controls were rarely more than 2 weeks apart in age. Criteria for exclusion of potential controls were: a history of *Salmonella* infection, diarrhea or abdominal pain with fever during the preceding month, or travel abroad during the previous 2 weeks. If a person declined to be interviewed, additional controls were identified until two agreed to participate.

**Interviews.** Cases and controls were interviewed via telephone by trained interviewers from the NIPH, using a structured questionnaire. With few exceptions, each case/control set of participants was questioned by the same person. The interviewers were not blinded to the case/control status of enrollees. If an enrollee was under 15 years of age, a parent was interviewed. Case-patients were questioned about the 2-week period before onset of their illness. Four patients could not specify a date of illness onset. These persons were questioned about the 2 weeks before the positive stool sample was submitted. The median interval between illness onset (or sample date) and interview was 34 days (mean = 44 days; range, 15–170). In order to reduce recall bias, controls were queried about the 2-week period before the interview. A median of 14 days elapsed between the control interview and the case interview (mean = 28 days; range, 5–469).

**Questionnaire.** The questionnaire covered personal and demographic data, travel abroad, medical history, use of medications, and exposure to potential risk factors, including drinking water source and consumption and contact with wild-living, captive, and domestic animals. Detailed information on contact...
with wild birds was requested. Precise information on drinking water quality was provided by local food control authorities. Case-patients were also interviewed about the duration of their illness, hospitalization, and time lost from work or school. If the patient was a child, we recorded how many days a parent or guardian had to stay home with the child while he/she was sick.

Statistical analyses

Descriptive epidemiology. Univariate analyses of descriptive epidemiologic data were carried out with the computer program Epi Info (version 6.0; Centers for Disease Control and Prevention, Atlanta, Georgia). For dichotomous variables, the significance of differences between groups was assessed using the chi-squared test; Fisher's exact test was used when an expected cell value was less than five. Continuous variables were analyzed using either Student's t test or the Mann-Whitney U test, as appropriate.

Case-control study. Univariate analyses of dichotomous variables from the case-control study were performed using the procedure for matched data sets in Epi Info. Conditional logistic regression was implemented for univariate analysis of continuous variables and for multivariate analysis using the computer program EGRET (version 0.26.04; Statistics and Epidemiology Research Corporation, Seattle, Washington). The results are expressed as matched odds ratios with 95 percent confidence intervals and two-tailed p values. Adjusted estimates of population attributable fractions based on the logistic regression model were calculated as suggested by Coughlin et al. (10), using the multivariable adjustment procedure for matched data provided by Bruzzi et al. (11).

RESULTS

Descriptive epidemiology

Human cases. Over the 31-year period 1966–1996, 1,053 cases of S. typhimurium O:4–12 infection were recorded among 4.4 million Norwegians (1996 Norwegian census data (12)). Variant 1 was isolated from 502 patients, of whom 349 were associated with the 1987 outbreak, while the remaining 153 patients represented sporadic cases reported from 18 of Norway's 19 counties. The first patient with variant 1 infection appeared in 1971. Only two additional cases were detected during the 1970s (figure 1). The number increased slightly to 2–6 cases annually in the 1980s before the outbreak. In the years 1988–1993, elevated numbers of cases were detected (10–26 per year), followed by a significant decline in subsequent years. The distributions of the patients by age, sex, and season were similar in the years before and after the outbreak. Therefore, all data except those from 1987 were combined before further analysis.

The median age of the 153 patients with sporadic variant 1 infection was only 7 years (mean = 21 years; range, <1–88); 81 (52.9 percent) were less than 10 years of age, and 66 (43.1 percent) were younger than 5 years (figure 2). There was, however, a tendency toward a trimodal age distribution, with smaller peaks among elderly and young adults. In contrast, the 551 patients infected with other O:4–12 variants showed a median age of 28 years (mean = 30 years; range, <1–93), and only 17.0 percent (n = 93) were younger than 5 years. For all ages combined, 54.2 percent of the variant 1 patients were female, compared with 49.9 percent for other variants. For children under 5 years of age, the corresponding figures were 53.0 percent and 46.0 percent, respectively. Patients with variant 1 infection were less likely to have traveled abroad prior

FIGURE 1. Culture-confirmed human cases of infection with Salmonella typhimurium O:4–12, variant 1, Norway, 1966–1996. The number of cases is indicated above each bar.
to the onset of illness than were the remaining patients (odds ratio (OR) = 0.02, 95 percent confidence interval 0.01–0.08; \( p < 0.001 \)). Only three (2.0 percent) of the 153 variant 1 patients developed symptoms abroad or shortly after their return home, compared with 254 (46.1 percent) of the other patients. The seasonal distribution also differed substantially (figure 3). Whereas 75.8 percent of the cases of variant 1 infection were recorded during the first 4 months of the year, cases involving other strains showed a distinct peak in the summer and fall. This peak was equally evident among imported and domestically acquired cases (data not shown).

**Nonhuman isolates.** Of 278 nonhuman isolates of *S. typhimurium* O:4–12 collected during the years 1951–1989, 113 (40.6 percent) belonged to variant 1. The majority of these isolates (\( n = 89, 78.8 \) percent) were obtained from wild-living birds. Variant 1 was only exceptionally recovered from other sources, including a horse (\( n = 1 \)), a dog (\( n = 1 \)), a mouse (\( n = 1 \)), a monkey (\( n = 1 \)), a bird feeder (\( n = 1 \)), sewage (\( n = 3 \)), and chocolate (during the 1987 outbreak) (\( n = 16 \)). An additional 138 isolates of *S. typhimurium* O:4–12 which differed from variant 1 were recovered from wild birds. Of the 89 avian isolates of variant 1, 83 (93.3 percent) were isolated from sporadic cases and epizootic outbreaks of fatal salmonellosis among wild passerine birds. All isolates were recovered from
dead birds submitted to the Veterinary Institute by the general public; no systematic sampling of avian wildlife was attempted. Birds were submitted from 12 counties. The seasonality of the avian cases is presented in figure 3; 89.0 percent of these cases were recorded during the first 4 months of the year. Of the 89 avian isolates of variant 1, 66 (74.2 percent) were obtained from bullfinches (Pyrrhula pyrrhula), four (4.5 percent) were obtained from green finches (Carduelis chloris), and the remaining 19 were recovered from 18 other bird species. The first 10 isolates of variant 1 appeared in 1972, and variable numbers were detected between 1973 and 1989 (range, 0–27 isolates; median, 5).

**Case-control study**

Forty-one case-patients and 82 matched controls were enrolled in the case-control study. During the study period, the NIPH noted 47 patients satisfying the criteria for a case. Thus, 87 percent of all eligible cases were enrolled. The median age of the 41 case-patients was 17 years (mean = 23.8 years; range, <1–77); 16 (39.0 percent) were less than 5 years of age. Twenty-three (56.1 percent) were female.

**Univariate analysis.** Drinking undisinfected water in the 2 weeks prior to onset of illness was associated with an increased risk of infection (OR = 3.5, \( p = 0.02 \)) (table 1). Only four of the 26 patients who had drunk untreated water had done so directly from a surface source. The results of the univariate analysis are presented in table 1.

### TABLE 1. Univariate analysis of selected risk factors for infection with *Salmonella typhimurium* 0:4-12, variant 1, Norway, 1990-1992

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No. of cases*</th>
<th>No. of controls*</th>
<th>Matched odds ratio</th>
<th>95% confidence interval</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drinking water supply and consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drinking undisinfected water</td>
<td>26/40</td>
<td>34/81</td>
<td>3.5</td>
<td>1.3–8.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Drinking water directly from a surface source†</td>
<td>4/40</td>
<td>6/82</td>
<td>1.3</td>
<td>0.4–4.8</td>
<td>0.91</td>
</tr>
<tr>
<td>Having an untreated water supply at home</td>
<td>25/41</td>
<td>27/82</td>
<td>12.5</td>
<td>2.5–83.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Having a private water supply at home</td>
<td>16/41</td>
<td>13/82</td>
<td>3.4</td>
<td>1.3–8.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Contact with wild birds</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feeding wild birds</td>
<td>9/39</td>
<td>13/80</td>
<td>1.6</td>
<td>0.6–4.2</td>
<td>0.54</td>
</tr>
<tr>
<td>Household members' feeding birds</td>
<td>21/37</td>
<td>34/81</td>
<td>2.3</td>
<td>0.9–6.0</td>
<td>0.11</td>
</tr>
<tr>
<td>Playing in an area with bird droppings</td>
<td>14/40</td>
<td>16/78</td>
<td>10.5</td>
<td>1.2–89.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Cleaning or removing bird droppings (A)</td>
<td>8/40</td>
<td>2/82</td>
<td>6.0</td>
<td>1.2–29.7</td>
<td>0.03</td>
</tr>
<tr>
<td>Tending/touching sick or dead birds (B)</td>
<td>4/39</td>
<td>2/82</td>
<td>7.0</td>
<td>0.7–68.1</td>
<td>0.15</td>
</tr>
<tr>
<td>Direct contact with birds or bird droppings (A or B)</td>
<td>10/39</td>
<td>3/82</td>
<td>9.5</td>
<td>2.0–44.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Contact with other animals</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dogs</td>
<td>16/38</td>
<td>42/81</td>
<td>0.7</td>
<td>0.3–1.5</td>
<td>0.39</td>
</tr>
<tr>
<td>Cats</td>
<td>19/39</td>
<td>33/80</td>
<td>1.5</td>
<td>0.7–3.6</td>
<td>0.44</td>
</tr>
<tr>
<td>Caged birds</td>
<td>1/40</td>
<td>8/80</td>
<td>0.2</td>
<td>0.02–1.9</td>
<td>0.21</td>
</tr>
<tr>
<td>Poultry</td>
<td>1/41</td>
<td>5/82</td>
<td>0.4</td>
<td>0.05–3.4</td>
<td>0.67</td>
</tr>
<tr>
<td>Cattle</td>
<td>1/40</td>
<td>3/82</td>
<td>0.7</td>
<td>0.1–6.4</td>
<td>0.86</td>
</tr>
<tr>
<td>Pigs</td>
<td>2/41</td>
<td>1/82</td>
<td>2.0</td>
<td>0.1–32.0</td>
<td>0.80</td>
</tr>
<tr>
<td>Wild-living mammals</td>
<td>1/41</td>
<td>1/82</td>
<td>2.0</td>
<td>0.1–32.0</td>
<td>0.80</td>
</tr>
<tr>
<td>Other animals</td>
<td>5/40</td>
<td>8/82</td>
<td>2.0</td>
<td>0.5–8.2</td>
<td>0.56</td>
</tr>
<tr>
<td>Miscellaneous factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eating snow, sand, or soil</td>
<td>8/34</td>
<td>12/79</td>
<td>11.0</td>
<td>1.3–36.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Attending day care or kindergarten</td>
<td>11/41</td>
<td>19/82</td>
<td>1.3</td>
<td>0.5–3.5</td>
<td>0.80</td>
</tr>
<tr>
<td>Living on or visiting a farm</td>
<td>8/40</td>
<td>13/82</td>
<td>1.3</td>
<td>0.5–5.3</td>
<td>0.80</td>
</tr>
<tr>
<td>Recent use of antimicrobial agents</td>
<td>8/38</td>
<td>7/82</td>
<td>2.0</td>
<td>0.6–7.0</td>
<td>0.46</td>
</tr>
<tr>
<td>Recent use of antibiotics</td>
<td>3/40</td>
<td>3/82</td>
<td>3.0</td>
<td>0.4–21.3</td>
<td>0.38</td>
</tr>
<tr>
<td>Using regular medications</td>
<td>12/40</td>
<td>8/82</td>
<td>5.8</td>
<td>1.8–18.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Recent history of gastrointestinal disorder</td>
<td>12/40</td>
<td>3/82</td>
<td>23.0</td>
<td>2.9–181.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nongastrointestinal medical conditions</td>
<td>13/40</td>
<td>9/82</td>
<td>3.1</td>
<td>1.3–7.6</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* No. of exposed individuals/total no. of respondents. Denominators exclude persons with missing values.
† For example, drinking from a lake, pond, brook, or river while hiking or camping.

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surface source during outdoor activities like hiking or camping. This exposure was not identified as an important risk factor (OR = 1.3, \( p = 0.91 \)). However, cases were more likely than controls to use untreated drinking water in their primary residence (OR = 12.5, \( p < 0.001 \)). More cases than controls received water from a private water supply—a well, borehole, or private waterworks (OR = 3.4, \( p = 0.008 \)). This type of water was invariably untreated.

Feeding wild-living birds or living in a household where other family members fed birds did not significantly increase the risk of infection (table 1). However, playing in an area where bird droppings were observed was associated with an increased risk (OR = 10.5, \( p = 0.04 \)). Case-patients were also more likely than controls to report having direct contact with wild birds or their droppings (OR = 9.5, \( p = 0.002 \)). Of the 10 patients who mentioned such exposure, six had cleaned a bird feeder or removed bird feces, while four had touched a dead bird, tended a sick bird, or both (table 1). Contact with other wild, captive, or domestic animals was not associated with an increased risk of infection. Case-patients were no more likely than controls to attend day care or kindergarten or to live on a farm. However, eating snow, sand, or soil was identified as a risk factor (OR = 11.0, \( p = 0.02 \)). Five of the eight patients for whom this exposure was reported had done so in the proximity of a bird feeder.

**Multivariate analysis.** In conditional logistic regression analysis, the following environmental factors were found to be independently associated with an increased risk of infection (table 2): drinking untreated water, having direct contact with wild birds or their droppings, and eating snow, sand, or soil. No significant first-order interactions were detected among the variables included in the analysis.

### Clinical impact data

Of the 41 patients enrolled in the case-control study, eight felt that their symptoms had not resolved at the time of the interview, while 30 patients no longer had symptoms related to salmonellosis (three were untreated). These 30 persons had been symptomatic for a mean of 11.0 days (median, 9 days; range, 2–38). A mean of 4.1 days were lost from work or school (median, 1.5 days; range, 0–38). Nineteen (46.3 percent) of the 41 case-patients were admitted to a hospital for a mean of 5.2 days (median, 4.5 days; range, 1–13). Hospitalization was no more common among patients under 5 years of age than in the remaining age groups (8/16 vs. 11/25, \( p = 0.71 \)). It was almost twice as common among males as among females (11/18 vs. 8/23), but this difference was not statistically significant (\( p = 0.10 \)). The mean duration of illness was greater among males than among females (14.4 days vs. 7.7 days, \( p = 0.02 \)).

Cases and controls did not differ significantly with respect to recent use of antimicrobial agents or antacids (table 1). However, more cases than controls used regular medications (OR = 5.8, \( p = 0.002 \)). The case-patients were also more likely to report a recent history of gastrointestinal disorder (OR = 23.0, \( p < 0.001 \)) or a nongastrointestinal chronic or protracted medical condition (OR = 3.1, \( p = 0.02 \)). (No controls were excluded from the study because of recent diarrheal illness.) Six of the 12 patients who reported gastrointestinal disorders had a history of chronic or recurrent diarrhea.

In 23 patient households, diarrhea or abdominal pain with fever was reported among other household members, either in the month before the patient became ill (seven households), in the month after (17 households), or on the same day as the patient (seven households). (In some households, members developed diarrhea both before and after the patient.) S. *typhimurium* was recovered from five family members (in different households), all of whom became ill after the patient.

### DISCUSSION

**Descriptive epidemiology**

*S. typhimurium* variant 1 infection appears to be domestically acquired in Norway, since only three of...
the patients had traveled outside the country prior to onset of symptoms. In contrast, during the study period, 90 percent of the total number of *Salmonella* infections were reported to be associated with foreign travel (13). Unlike most other *Salmonella* serovars, which have been successfully combated in Norway, *S. typhimurium* variant 1 has established an indigenous reservoir. The first recognized cases appeared in the human and avian populations only 1 year apart in the early 1970s. It is tempting to speculate that migratory birds were responsible for the initial introduction and subsequent establishment of a stable reservoir among avian fauna.

A slightly increased number of isolates was reported in the 5 years prior to the 1987 outbreak (figure 1). There is little doubt that this increase is attributable to the emergence of a more effective laboratory system and a growing awareness of *Salmonella* as a public health problem in Norway in the early 1980s. However, these factors are unlikely to have significantly affected isolation rates in subsequent years, although the possibility cannot be excluded that an increased sampling frequency in the months following the outbreak may have contributed to the elevated number of cases detected in 1988. The relatively high numbers of isolates observed from 1988 to 1993 may also reflect widespread environmental dissemination of the organism, a process which may have been initiated during the outbreak, when probably thousands of humans were infected and became fecal shedders of the bacterium. Apparently, failure of the organism to permanently occupy new ecologic niches and establish new, stable reservoirs led to its decline to a low baseline level in recent years. Such an epidemiologic succession is not unique. Similar histories of the introduction, emergence, and subsequent decline of new *Salmonella* serovars on a national scale have been reviewed by D'Aoust (2).

One striking feature of the patients with sporadic variant 1 infection was the dominance of infants and young children in the group. A closely similar age distribution was observed during the outbreak in 1987, when 49 percent of the reported cases were in children under 5 years of age, a finding which was explained by the low number of salmonellae found in the incriminated chocolate products (7). There is strong epidemiologic evidence that children are more susceptible to infection with low inocula of salmonellae than are persons in other age groups (5, 14). With this backdrop, the apparent predilection for young children observed in this study may not be unexpected, since the major risk factors identified were consumption of untreated water and fecal-oral contact with wild birds, both of which may result in low-dose exposure.

Infants with diarrhea may easily transmit salmonellae to other household members through the direct or indirect fecal-oral route. Diarrheal illness was commonly reported among members of case households, and the organism was isolated from diseased family members of five case-patients. Although this may well reflect transmission within the family, it may also represent exposure to a common source or selective recall of unrelated illnesses. Thus, it is difficult to draw conclusions about the risk of infection in other household members or the mode of transmission.

**Clinical impact**

Human infection with *S. typhimurium* variant 1 is notable for its severity. Almost half (46 percent) of the case-patients were admitted to a hospital, for a mean of 5 days. In comparison, 25 percent of *Yersinia enterocolitica* patients and 13 percent of *Campylobacter* patients enrolled in previous case-control studies in Norway were hospitalized (15, 16). The reported cases are only a small fraction of the total number of persons affected. It is likely, however, that the study patients represent the most severe cases, because participation in the study was limited to persons who sought medical attention and from whom a stool sample was collected.

Our data indicate that variant 1 infection is characterized by a predilection for people with antecedent or concurrent medical conditions. Underlying gastrointestinal and nongastrointestinal disorders, reported by 12 and 13 of the case-patients, respectively, have previously been shown to predispose people to *Salmonella* infection and to increase the severity of the disease (3, 4). Although it seems to be well documented that such persons represent a group at high risk for salmonellosis, it is also possible that physicians are more likely to have a stool sample cultured from patients with preceding illness when new symptoms develop, creating a detection bias.

**Case-control study**

Our finding that contact with wild birds or their feces was associated with an increased risk of infection is supported by veterinary investigations demonstrating the involvement of this organism in the etiology of fatal salmonellosis among wild passerine birds. Despite the fact that several hundred samples from animals, feed, and the environment were examined each year, variant 1 was almost exclusively recovered from wild birds. The possible epidemiologic link be-
tween human and avian salmonellosis is further substantiated by the fact that a majority of human as well as avian cases are reported between January and April (figure 3), a period when many people feed birds in their yards and gardens. Under the climatic conditions prevailing in Norway at that time of the year, starvation and cold stress make wildlife highly susceptible to infectious diseases. Although winter feeding undoubtedly saves the lives of many birds, it may also facilitate transmission of pathogens within and between bird species and to human beings. Activities related to bird-feeding, such as cleaning bird feeders, tending sick birds, and eating snow under bird feeders, were more frequently reported by case-patients than by controls in our study.

Bullfinches and green finches are the avian species most frequently associated with fatal salmonellosis in Norway. Both of these species frequent bird feeders, and dead birds are consequently easily observed, introducing a possible detection bias. The possibility exists that other species may be affected as well, and some may be healthy carriers. Wild-living birds may function as effective spreaders of disease through fecal contamination of the environment, including surface water. Drinking of undisinfected water, reported by 65 percent of case-patients, was independently associated with S. typhimurium infection. This finding is particularly striking considering how closely matched the cases and controls were. Since our study enrollees were matched by geographic area, we may have obtained an underestimate of the importance of water as a risk factor, because people living in the same area are likely to have the same drinking water supply or similar sources. Untreated water has also figured prominently in previous Norwegian epidemiologic studies as a vehicle of transmission for human and animal enteric infections (17–19). These observations are related to the frequent use of untreated surface water for human consumption and in animal husbandry in Norway. Surface waters are susceptible to contamination with runoff from rain or surrounding snow melt. Such runoff may become fecally contaminated by wild and domestic birds and mammals or by human activities. Even though the percentage of water samples contaminated may be small, the frequency with which untreated water is consumed in Norway may result in appreciable exposure. The attributable risk estimate indicated that consumption of untreated water is a major factor in variant 1 infection. While it is reasonable to assume that the association with untreated water was mainly due to contamination by wild birds, the possibility exists that carriage of the organism by other animal species, particularly humans, may have contributed to the presumed contamination of water supplies.

Limitations of this study

Although the associations between sporadic S. typhimurium infection and the exposures identified here are biologically plausible, the present study had several limitations. The long time which elapsed between illness onset and interview for some of the patients may have introduced recall bias, leading to underestimation for risk factors susceptible to recall problems. Likewise, possible geographic overmatching may have led to underestimation of factors closely related to geographic area, like drinking water quality, as discussed above. Moreover, the fact that case-patients and controls were questioned about different exposure periods (to reduce recall bias) may have resulted in overestimation of bird contacts as a risk factor, since this exposure is seasonal. An additional type of bias may have been introduced by the interviewers, who were aware of the case/control status of the enrollees. In addition, the study was limited to diagnosed cases. The pattern of risk factors and their relative importance may be different among nondiagnosed cases.

Finally, the results of the case-control study are not necessarily generalizable for the total period from 1966 to 1996. Although 87 percent of all eligible cases were enrolled, the study enrollees differed demographically from all sporadic cases identified during the 31-year study period (e.g., a median age of 17 years vs. 7 years).

Conclusion

While the number of reported sporadic cases of infection with S. typhimurium variant 1 is low, the medical consequences may be severe. The 1987 outbreak in Norway serves to illustrate the capacity of this organism to cause widespread disease, with substantial public health impact and serious economic effects on the food industry. The evidence that an extremely low infective dose is sufficient to cause disease (7), as well as the widespread distribution of the organism in the natural environment, underlines the need for continued vigilance and stringent control of salmonellae during food production. Our results strengthen the evidence that drinking water is a prominent vehicle for intestinal infection in Norway, and further emphasize the conclusion that increased attention should be paid to the health hazards associated with drinking of untreated water. The importance of taking proper hygienic precautions during contact with wild birds or their feces should also be impressed on the public.
REFERENCES


