

LARGE OUTBREAKS OF *SALMONELLA* TYPHIMURIUM INFECTION IN DENMARK IN 2008

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An outbreak of *Salmonella* Typhimurium phage type U292 has been ongoing in Denmark since 1 April, with 1,054 cases registered until 23 October 2008. Extensive investigations including hypothesis-generating interviews, matched case-control studies, cohort studies in embedded outbreaks, shopping list analyses, analyses of food samples from patient's homes, trace-back analyses and extensive microbiological analysis of products have not provided clear indications of a specific source of infection but the main hypothesis is that the vehicle of the outbreak are different pork products. In addition to the large U292 outbreak, at least four other *S. Typhimurium* outbreaks (caused by phage types U288, DT120, DT3 and DT135) have been investigated in Denmark in 2008.

Introduction

The outbreak caused by *Salmonella enterica* serotype Typhimurium phage type U292 which was detected in April 2008 [1] is still ongoing and the source has not been found. The outbreak

includes 1,054 patients as of 23 October 2008, thus being the largest outbreak of salmonellosis in Denmark recorded since 1980 when the present surveillance system became active.

The total number of laboratory-confirmed infections with *S. Typhimurium* (phage type U292 and other phage types) was 1,652 as of 12 October 2008; at the same time in 2007 the cumulative annual number of *S. Typhimurium* infections was 285 (Figure 1). In comparison, the number of *Salmonella* Enteritidis infections registered up to this time of the year (i.e. end of week 41) was 557 in 2008, 473 in 2007 and 497 in 2006 [2]. The high number of *S. Typhimurium* infections in 2008 include several distinct outbreaks in addition to the U292 outbreak. This report gives a brief account of the present status of the investigations of the U292 outbreak and presents basic epidemiological facts of the other recent *S. Typhimurium* outbreaks.

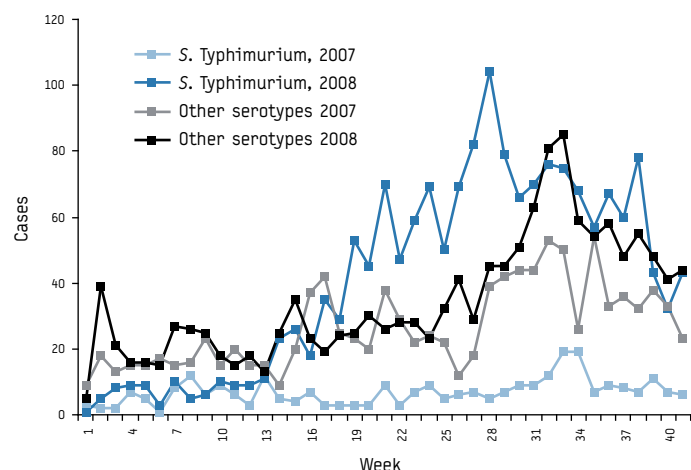
Methods

In Denmark clinical microbiology laboratories are required, within one week, to notify Statens Serum Institut (SSI) of findings of salmonella from patient samples. In addition strains are sent to the SSI and further characterised. Currently, all strains of serotype Typhimurium are subtyped using Multiple Loci Variable Number of Tandem Repeats Analysis (MLVA) as a means of detecting outbreaks [3]; furthermore *S. Typhimurium* strains are phage typed and tested for resistance, and selected strains are typed by Pulsed Field Gel Electrophoresis (PFGE). Clusters of patient-isolates with identical MLVA types are investigated as potential outbreaks. The case definition in the outbreaks described here is by MLVA type.

Investigation of the U292 outbreak has been performed using a number of different methods which include the following: 1) Patient interviews performed using telephone-administered trawling questionnaires, focus group interview and home visits, the latter including recently conducted interviews of cases occurring at the Faroe Islands (which are part of the Danish kingdom). 2) Three separate matched case-control investigations with 29/83, 21/41 and 30/35 case/control sets respectively. 3) Investigations into point source sub outbreaks occurring among groups of people in closed settings, including two outbreaks where it was possible to perform cohort studies with 15/8 and 46/24 ill/healthy respondents respectively. 4) Two rounds of comparative analyses of patients'

FIGURE 1

Number of cases of *Salmonella* Typhimurium and other *Salmonella* serotypes registered by Statens Serum Institut in Denmark for 2007 and 2008, by week of submission of stool sample to the laboratory (weeks 1-41)



shopping lists obtained from supermarket computers with 126 cases invited out of whom data were collected for 41 cases. 5) Case-case analyses of interviewed *S. Typhimurium* cases of different phage types. 6) Early visits to homes of suspected *S. Typhimurium* patients in order to collect and analyse samples of food items which might have been eaten prior to onset of symptoms. 7) A large number of trace-back analyses of suspect food products, trade patterns and connections between herds in addition to geographical analyses. 8) Comparative molecular subtyping of patient-isolates with isolates obtained from food, animals and slaughterhouses in Denmark. 9) And finally, investigations, including sampling and microbiological analyses, into many domestic food production facilities and slaughterhouses of which some were selected based on epidemiological leads and some following a structured risk ranging approach.

Results

Outbreak of *S. Typhimurium* phage type U292

The first cases of the U292 outbreak reported onset of illness in February. Over the following three months the weekly number of cases increased and since May has stayed at the level of 30-60 cases per week (Figure 2). The age distribution is skewed towards younger age groups; the median age is 15 years. For comparison 70% of *S. Typhimurium* cases registered in previous years had been older than 15 years of age. The gender distribution is almost even, with 53% female cases. Cases have occurred in almost all parts of the country, but are not evenly distributed among the regions. Nine persons infected with the outbreak strain are known to have died; however, these patients had severe underlying illnesses. The strain is fully susceptible to all antibiotics in the test panel and does not appear to cause severe symptoms; the hospitalisation rate is between 15 and 20%.

Close to 500 cases have been interviewed as part of the different investigations. No vegetarians or persons specifically reporting never to eat pork have been identified in the course of these interviews. Judging by the names of patients, among those who have not been interviewed we have not been able to identify any persons originating from countries where people are predominantly

Muslim. The outbreak appears to be confined to Denmark; U292 is a rare phage type and clusters of cases have not been reported from other countries. Less than 10 cases (not counting 14 cases from the Faroe Islands) from outside of Denmark have been detected; they originated from Norway, Sweden and Canada and all, except one, had become infected while staying in Denmark for more than one week.

The analytical epidemiological investigations have largely been inconclusive and not been able to provide a clear indication of the source. Restaurant outbreaks or cases associated with canteens or similar facilities have not been detected, but four distinct embedded outbreaks are known and there are several occurrences of multiple cases within families. The outbreak strain has been found in pork from a major Danish slaughterhouse, in clinically ill calves or cows at three separate farms and at a broiler farm, in addition to food products of pork origin obtained from the home of a case family, but under circumstances that did not allow for epidemiological conclusions to be drawn. *S. Typhimurium* U292 with the same resistance pattern (fully susceptible) and same PFGE pattern (using XbaI), but with a MLVA type differing in two loci, has been found in a number of Danish pig herds within recent months.

Outbreaks of other *S. Typhimurium* phage types

In addition to the large U292 outbreak, at least four other *S. Typhimurium* outbreaks have been investigated in Denmark in 2008 (Figure 3). Outbreak 1 was caused by a strain of phage type U288. It comprised 37 cases and occurred from March to May. Cases were predominantly living near Denmark's second largest town, Århus, and epidemiological investigations showed a clear link to a group of kebab restaurants located in Århus. The precise mechanism of transmission of the infections was not found. U288 is a rare phage type in humans in Denmark, but is known to have been present for many years among pig herds in Denmark.

The three other outbreaks were not geographically restricted. Outbreak 2 was caused by a strain of phage type DT120. There

FIGURE 2

Cases of *Salmonella Typhimurium* U292, with the outbreak MLVA type, by week of submission of stool sample to the laboratory, Denmark 2008, (n=1,054 as of 23 October)

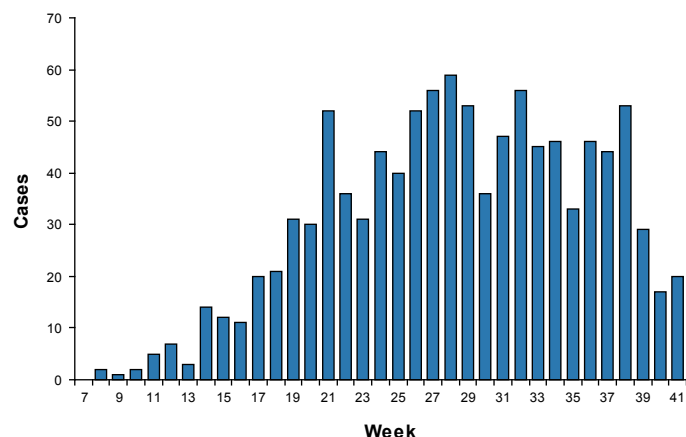
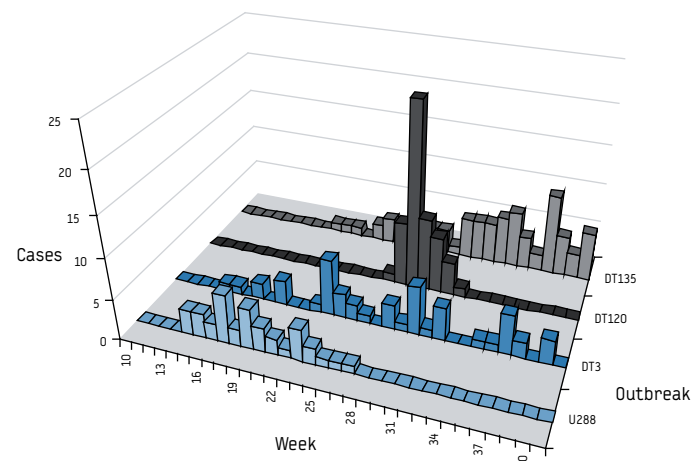


FIGURE 3

Registered cases of *Salmonella Typhimurium* associated with four different outbreaks (U288, DT120, DT3 and DT135), by week of submission of stool sample to the laboratory, Denmark 2008 (n=214, as of 12 October)



were 55 cases predominantly in June and July. As a side-result of investigations into the U292 outbreak, a Danish-produced smoked ham collected from the refrigerator of a case was found positive for this outbreak strain and hence it is believed that this outbreak was caused by consumption of products of the same brand.

Outbreak 3 is caused by a strain of which the majority of isolates have been found to be of phage type 3. Low numbers of cases have been detected since the beginning of the year and are still occurring; currently a total of 50 cases have been registered. A clear hypothesis as to the source of this outbreak does not exist.

Outbreak 4 caused by a strain of phage type DT135 is ongoing. Up to now 77 cases have been registered, predominantly since June. This outbreak shares a number of the epidemiological characteristics of the U292 outbreak. Investigations into this outbreak are ongoing.

Conclusions

The results of the investigations into the U292 outbreak indicate that the outbreak is not caused by a single type of food vehicle. The main working hypothesis continues to be that the outbreak originates from pigs, but it should be stressed that an association with pork or pork products has not been proved and that other hypotheses are also being actively investigated.

Circumstantial evidence pointing towards pork as the source of the U292 outbreak include: Very high exposure to pork among interviewed cases, apparent absence of cases that would refrain from eating pork out of religious beliefs or vegetarianism, findings of the outbreak strain in pork and of closely related strains in domestic pig herds and the lack of strong competing hypotheses. A number of large salmonella outbreaks in Denmark have previously been associated with pork [4-8], however, except for one instance, case-control studies have failed to provide evidence for these links [6].

Among the non-U292 outbreaks, the one caused by *S. Typhimurium* DT120 was likely to be associated with Danish produced salted, smoked and cooked ham. It is possible that some of the increased numbers of infections with *S. Typhimurium* observed in Denmark, including the currently ongoing outbreak of *S. Typhimurium* DT135, are also associated with consumption of pork or pork products, which would point to the same general food safety problem. However, due to lack of clear evidence more definite conclusions leading to possible control measures are not possible at this stage of the investigations.

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