Temporal Clusters of *Salmonella* Serovars in Humans in Alberta, 1990-2001

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ABSTRACT

Background: Temporal clusters of salmonellosis are believed to occur but have not been quantitatively explored, thus, our objectives were to describe trends, seasonal patterns, and clusters of salmonellosis in humans in Alberta by examining isolates reported through passive surveillance systems.

Methods: Cases of salmonellosis reported through Notifiable Disease Records between January 1990 and December 2001 were obtained from Alberta Health and Wellness. Least squares regression was used to characterize the distribution (long-term trends and seasonal patterns) of isolates. A cluster detection test was used to determine if and when isolates of specific serovars aggregated in time, over and above the background distribution. Comparisons were made to temporal patterns in Alberta livestock and to known outbreaks in humans.

Results: *S. Typhimurium*, Enteritidis, Hadar, Heidelberg, and Thompson were the five most common serovars of the 9,188 isolates reported. The annual number of isolates was relatively stable over time, with a distinct summertime seasonal pattern. Clusters were observed in 23 of 32 serovars examined. More clusters occurred in September and October than in other months, and in 1998 through 2001 than in the early to mid-1990s. Also, more clusters were of short duration than long.

Interpretation: Short-duration clusters likely indicate a point source of infection, while long-duration clusters may indicate exposure to a persistent common source or the occurrence of secondary infections. A sharp increasing trend and a large cluster of *S. Heidelberg* may have public health implications. Surveillance activities focussed on similarities between common serovars, trends, and temporal clusters in humans and animals, and studies on factors associated with autumn clusters may be useful in preventing outbreaks in humans.

MeSH terms: Salmonella; cluster analysis; time factors; seasons; serotyping; humans; Alberta

La traduction du résumé se trouve à la fin de l'article.

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Foodborne illness caused by *Salmonella* represents an important public health problem in many parts of the world,¹ including health costs and economic losses to the food industry.² Exposure to particular foods or animals has been associated with human infection by specific serovars;³ outbreaks of *S. Enteritidis* were more often associated with eggs than were outbreaks due to other serovars.⁴ In 1997 and 1998, Alberta reported the largest number of foodborne, waterborne, or enteric disease outbreaks than any other Canadian province or territory (25/97 and 19/75 outbreaks, respectively), and *Salmonella* spp. were implicated in 43 and 26 of the total outbreaks in 1997 and 1998, respectively.⁵

Classifying *Salmonella* isolates by serovar may be used to follow trends³ and identify common isolates that cluster over time or space. Temporal clusters have been identified in *Salmonella* serovars in livestock in Alberta⁶ and California,⁷ but clustering has not been quantitatively explored in humans. Identifying clusters can provide information used to establish causes of disease and methods for control and prevention,⁸ thus, our objectives were to describe trends, seasonal patterns, and temporal clusters of salmonellosis in humans in Alberta, and make comparisons to temporal patterns of *Salmonella* in Alberta livestock⁶ and serovars implicated in outbreaks in humans in Alberta during a similar time period.

METHODS

Passive surveillance data from January 1990 to January 2002 were provided by Alberta Health and Wellness (AHW); laboratory data were merged with *Salmonella* disease reports to recover serovar information. A Notifiable Disease Record (NDR) number and the date the Regional Health Authority (RHA) reported the case to AHW were provided for each record; this was the date used for the temporal analysis. At the time of data collection, there were 17 RHAs in Alberta.

Salmonella taxonomy and nomenclature followed the scheme provided by the World Health Organization.⁹ Data manipulation was performed using Microsoft Excel 2000.¹⁰ Exclusion criteria were: 1) duplicate records (unless different serovars existed per NDR number); 2) records

where the RHA fell outside the range of 1 to 17; and 3) untyped isolates when two observations existed (one serotyped, one untyped) for an individual NDR number.

Least squares regression was performed using STATA 7.0¹¹ to characterize the overall distribution (long-term trends and seasonal patterns) of reported isolates. Year and month were treated as categorical independent variables, with January and 1990 as the referent categories. A significance level of 5% was set. Assumptions were evaluated using residual plots. Cluster detection software (SaTScan version 3.0)¹² was used to test the null hypothesis that isolates of *Salmonella* serovars are randomly distributed with respect to time. We used the Bernoulli model, where cases are contrasted with a control group. A case was defined as an isolate of a specific serovar, while the control group included all isolates except the serovar of interest during the same time period. The temporal scan statistic¹² identifies clusters of isolates beyond any background trends and seasonal patterns. Serovars were included in the cluster detection analysis if, during the study period, at least 30 isolates were reported, the serovar was implicated in an outbreak in Alberta (based on the literature), or a temporal cluster of the serovar was detected in Alberta livestock.⁶ January 2002 was included in the cluster detection analysis to provide a more accurate representation of cases occurring in December 2001 (this incorporated the lag between illness and recording of data). Dates were collapsed to a monthly basis, and 1- through 12-month scanning windows were used for cluster detection. For some serovars, a large cluster masked the presence of smaller clusters. Secondary clusters were detected by deleting the month(s) associated with the primary cluster from the case and control groups, then re-running the analysis.

RESULTS

Table I summarizes serovars isolated between January 1990 and December 2001 in decreasing order of frequency; serovars with fewer than 10 isolates were designated as "other". The 10 most common serovars accounted for 63% of all isolates. Gender was known in 9,168 (99.8%) of the cases, with equal submissions from both sexes.

TABLE I

Frequency and Percent of *Salmonella* Serovars in Humans, Reported Through the Notifiable Disease Records of Alberta Health and Wellness in Alberta, Canada, January 1990 - December 2001

Serovar	Frequency	Percent
Typhimurium	2241	24.4
Enteritidis	1225	13.3
Hadar	770	8.4
Heidelberg	610	6.6
Thompson	348	3.8
Infantis	165	1.8
Agona	146	1.6
Montevideo	109	1.2
Saintpaul	106	1.2
Newport	101	1.1
Java	94	1.0
Stanley	89	1.0
Mbandaka	65	0.7
Oranienburg	63	0.7
Meleagridis	58	0.6
Muenchen	55	0.6
Anatum	47	0.5
Virchow	45	0.5
Senftenberg	44	0.5
Typhimurium var. Copenhagen	43	0.5
Braenderup	41	0.5
Javiana	40	0.4
Blockley	37	0.4
Poona	37	0.4
Derby	35	0.4
Schwarzengrund	33	0.4
Berta	31	0.3
Panama	31	0.3
Brandenburg	26	0.3
Bovismorbificans	20	0.2
subsp. <i>arizonae</i> (IIIa)	19	0.2
Tennessee	19	0.2
Weltevreden	19	0.2
Sandiego	18	0.2
Bareilly	16	0.2
Ohio	16	0.2
Litchfield	15	0.2
Chester	13	0.1
Havana	13	0.1
Reading	13	0.1
Dublin	12	0.1
Glostrup	12	0.1
Rubislaw	12	0.1
Give	11	0.1
Haardt	11	0.1
Kentucky	11	0.1
Nienstedten	11	0.1
Emek	10	0.1
Muenster	10	0.1
Uganda	10	0.1
Other	276	2.9
Unknown	1886	20.5
Total	9188	100.0

There were 56 isolates registered in January 2002: *S. Agona* (1); *Blockley* (1); *California* (1); *Enteritidis* (3); *Hadar* (5); *Heidelberg* (4); *Infantis* (1); *Javiana* (1); *Muenchen* (1); *Newport* (1); *Oranienburg* (24); *Sandiego* (2); *Typhimurium* (9); *Weltevreden* (1); and 1 untyped serovar.

The median number of isolates per month was 61 with interquartile ranges of 48 and 76. The annual number of reported isolates appeared to be fairly stable over the study period (Figure 1), except for 1995 and 1996, which had significantly fewer isolates than 1990. A summertime seasonal peak was apparent (Figure 1); July, August

and September had significantly more isolates than January, while December had significantly fewer isolates.

The distributions of the five most common serovars are illustrated in Figure 2. *S. Typhimurium*, *Heidelberg* and *Thompson* demonstrated consistent seasonal patterns with increased numbers in June or July to October each year, except for a peak of *S. Thompson* isolates in December of one year.

Thirty-two different serovars fulfilled the inclusion criteria for the cluster detection analysis; five of these were analyzed for the presence of secondary clusters. Twenty-seven temporal clusters (including sec-

Figure 1. Distribution of the total number of *Salmonella* isolates reported from humans in Alberta, Canada between January 1990 and December 2001 (N=9,188)

A 5-month rolling average of the number of isolates is presented.

ondary clusters) were detected at the 5% level, and here we report on significant clusters associated with the 20 most common serovars (Table II). Details include when the cluster occurred, scanning window size, number of cases and controls in the cluster period, relative risks, and p-values; where possible, only clusters associated with the narrowest (1- or 2-month) and widest (12-month) scanning windows are shown. For some serovars (e.g., *S. Infantis*), as the scanning window widened, cluster duration lengthened, whereas for others (e.g., *S. Montevideo*), the cluster did not enlarge. For still others (e.g., *S. Hadar*), clustering at two different time periods was noted depending on the scanning window used. Examination of narrow scanning windows showed that more clusters occurred in September and October than in other months, and in 1998 through 2001 than in the early to mid-1990s. When wide windows were examined, more clusters were of short duration than long.

DISCUSSION

While census data indicate that the population increased in Alberta between 1991

and 2001,^{13,14} the annual number of *Salmonella* isolates reported remained fairly stable. However, given our objectives to identify temporal patterns of salmonellosis, one weakness of utilizing passive surveillance data is the lack of a true denominator. Hence, differentiation between a change in the percentage of samples submitted that were culture positive, versus a change in the number of isolates due to reporting patterns,¹⁵ was not possible. Additional biases and uncertainties may include the moderate percentage of untyped isolates, changes in laboratory techniques over time,⁷ culturing techniques without 100% sensitivity,⁷ and the inability to exclude multiple samples from an individual³ due to confidentiality. Notwithstanding these limitations, since salmonellosis is a federal notifiable disease, isolates captured through passive surveillance systems reveal serovars that are commonly isolated.

The reason for the lower number of isolates in 1995 and 1996 remains unclear. A temporary increased level of public awareness in preventing food-related illness, or changes in reporting or surveillance in the province during that time period may account for this finding.

The increasing trend in *S. Enteritidis* infections was unlikely due to consumption of chicken products produced in Alberta, as *S. Enteritidis* was rarely isolated from non-human sources in the province.⁶ Investigations into identifying the source of *S. Enteritidis* infections may include examining phagetypes associated with human and non-human isolates, travel history of human cases, food and other exposure histories of the cases, prospective multilevel studies of the poultry industry, as well as identifying the proportion of eggs produced in the province versus the proportion imported into the province.

One key objective was to determine if *Salmonella* serovars tend to cluster temporally, and to describe the nature of those clusters. A cluster was defined as isolates of a serovar that aggregated together in time, beyond chance occurrence. Examination of the widest scanning window (12 months) for each significant cluster showed that many were of short duration only; 17 of 27 clusters spanned 3 months or less. Ten clusters were of longer duration (4-12 months), and in almost all of these, the cluster was detected with a 1-month window, then increased in size and duration as the window enlarged. Nine clusters were associated with recognized human outbreaks (Table III). We compared characteristics of these clusters to information gathered from the outbreak investigations, and from this, certain patterns emerged. Short-duration clusters likely indicate a point source of infection, such as a single food item (e.g., alfalfa sprouts in the *S. Java* outbreak), a contaminated water source, or direct animal-to-person contact (e.g., petting zoo). Long-duration clusters may indicate exposure to a persistent common source such as a non-food item (e.g., pig ear pet treats in the *S. Infantis* outbreak), or secondary infection.

The occurrence of large clusters (i.e., 10 or more isolates) may be related to the pathogenicity of the serovar, infective dose within the contaminated food product, geographical distribution and how commonly the product is eaten, type of product (e.g., alfalfa sprouts) and difficulty in destroying *Salmonella* by washing,¹⁶ source of the pathogen, and endemicity of the serovar (e.g., *S. Typhimurium*). Large clusters have important health and economic consequences in a population.

Examination of the narrowest scanning window (1 or 2 months) showed that more clusters occurred in September and October than in other months. These clusters developed over and above the increased numbers of isolates that occurred in the summer months and may have resulted from secondary transmission from summertime cases or from continuing sources consistent with the regular late summer peak.

The greatest number of clusters occurred in 1998 to 2001. Improvements in serotyping capabilities and reporting of isolates may have accounted for this finding. Also, changes in the epidemiology of food-borne disease, such as new food vehicles (e.g., produce), consumer demands, global marketplace changes, or widely-distributed foods,¹⁷ may allow for multiple persons to become infected with the same serovar in the same time period.

Bacteriophage typing of serovars from outbreaks in Canada revealed that contaminated food products of poultry and bovine origin were frequently identified as the source of human salmonellosis,¹⁸ thus, we compared serovars found in Alberta livestock⁶ with those in our study. Four of the top five serovars were the same, and long-term trends of *S. Typhimurium* (humans, chickens, cattle and pigs), Hadar (humans and chickens), and Heidelberg (humans and chickens) were comparable. Similarities between the most common serovars from human and non-human sources,¹⁸⁻²¹ and trends in those serovars,^{18,20,22} have been noted, suggesting that animals may be the source of common *Salmonella* infections in the human population.

A marked seasonal pattern was evident for all serovars combined, with peaks in July to September each year. Similar seasonal characteristics have been noted.^{3,21} While animals may provide an ongoing source of *Salmonella*, and infection trends in animal hosts have been suggested as one reason for seasonal patterns in humans,³ seasonal patterns were not observed in non-human isolates in Alberta.⁶

Two large clusters of *S. Heidelberg* (1998/1999 and 2001) combined with a sharp increase in isolates since 1997 indicate that this serovar has become more prevalent in Alberta. Of interest, the trends and temporal clusters of *S. Heidelberg* iso-

Figure 2. Distribution of the number of *Salmonella* a) *Typhimurium*, b) *Enteritidis*, c) *Hadar*, d) *Heidelberg*, and e) *Thompson* isolates reported in humans in Alberta, Canada between January 1990 and December 2001

Arrow position and width indicate timing and duration of clusters, respectively.

lates from chickens in Alberta were similar.⁶ Two outbreak investigations have linked *S. Heidelberg* in chicken products with illness in humans.^{23,24} The annual per capita consumption of chicken and eggs increased in Canada in the 1990s,²⁵ illustrating the potential for increased human exposure to this serovar. Thus, identifying the source and transmission of *S. Heidelberg* in chickens, and investigating the importance of chicken products as a source for human salmonellosis, may have positive public health implications.

Additionally, a cluster of *S. Typhimurium* var. Copenhagen in chickens (8 isolates between February and November 2000)⁶ occurred just prior to the cluster in humans, suggesting a possible association between human illness and exposure to chicken products. As there

were few *S. Typhimurium* var. Copenhagen isolates from chickens and humans over the 12-year period, the close timing of these clusters would be consistent with a cause-and-effect relationship.

Identifying clusters has provided valuable information regarding the behaviour of salmonellosis in humans. While not all outbreaks are associated directly with foods of animal origin, surveillance programs that concurrently evaluate temporal trends and cluster detection of *Salmonella* serovars in animals may potentially benefit humans, as early detection may lead to control measures in animal industries that could theoretically reduce outbreaks of salmonellosis in humans, especially for serovars that are emerging or have become increasingly prevalent. Even if this technique identifies only a limited number of serovars, the ben-

TABLE II

Temporal Clusters of *Salmonella* Serovars Isolated from Humans in Alberta, Canada, January 1990 - January 2002

Serovar	Cluster (Start-Finish)*	Scanning Window (Months)	Cases	Controls	Relative Risk†	P-value
Enteritidis 1° cluster (n=1,228)‡	01/02-01/02	1-12	73	26	5.6	0.001
Enteritidis 2° cluster (n=1,155)	98/04-98/04	1-12	46	43	4.1	0.001
Hadar (n=775)	00/10-00/10	1	21	55	3.3	0.001
	92/08-92/09	2	40	153	2.5	0.001
	92/01-92/10	12	136	572	2.3	0.001
Heidelberg (n=614)	99/04-99/04	1	40	114	3.9	0.001
	99/03-99/04	2	49	155	3.6	0.001
	01/09-01/11	3	55	167	3.7	0.001
	01/09-01/12	4-8	64	195	3.7	0.001
	98/08-99/04	9	109	504	2.7	0.001
	98/08-99/05	10, 11	119	563	2.6	0.001
	98/08-99/07	12	135	692	2.5	0.001
Infantis (n=166)	99/10-99/10	1	8	59	6.6	0.002
	99/03-99/11	12	43	688	3.3	0.001
Java (n=94)	99/09-99/09	1	34	76	30.4	0.001
	99/08-99/10	12	44	221	16.3	0.001
Meleagridis (n=58)	97/10-97/10	1	19	62	37.4	0.001
	97/09-97/12	12	52	219	30.6	0.001
Montevideo (n=109)	00/08-00/08	1-12	7	87	6.3	0.023
Muenchen (n=56)	99/07-99/07	1	8	71	16.7	0.001
	99/06-99/07	12	12	133	13.7	0.001
Oranienburg (n=87)	02/01-02/01	1-12	24	32	45.5	0.001
Saintpaul (n=106)	95/11-95/11	1	3	15	14.5	0.040
	95/10-96/04	12	15	292	4.3	0.001
Senftenberg (n=44)	98/11-98/11	1-12	4	35	21.5	0.008
Stanley 1° cluster (n=89)	92/10-92/10	1-12	16	82	17.0	0.001
Stanley 2° cluster (n=73)	01/07-01/07	1	6	66	10.4	0.001
	01/06-01/11	12	24	434	6.6	0.001
Thompson 1° cluster (n=348)	97/04-97/04	1-12	38	59	10.4	0.001
Thompson 2° cluster (n=310)	00/06-00/06	1-12	32	68	9.4	0.001
Typhimurium 1° cluster (n=2,250)	91/10-91/10	1	46	55	1.9	0.002
	91/09-91/10	12	92	113	1.8	0.001
Typhimurium 2° cluster (n=2,158)	98/09-98/09	1	35	36	2.1	0.001
	98/08-99/02	12	156	253	1.6	0.001
Typhimurium var. Copenhagen (n=43)	01/09-01/09	1	10	71	26.5	0.001
	01/01-01/12	12	42	838	10.3	0.001

* Dates are reported as year/month

† The relative risk implies that, during the specified time period, the risk that a case is infected with the serovar of interest is "x" times higher than the case being infected with any other serovar

‡ Discrepancies between the number of cases for serovars listed in Tables I and II are due to the inclusion of January 2002 in the cluster detection analysis

TABLE III

Comparison of Temporal Clusters of *Salmonella* Serovars Isolated from Humans in Alberta, January 1990 - January 2002, and Reported Outbreaks in Alberta Described in the Literature

Serovar	Cluster (No. Cases)	Outbreak (No. Cases)	Location	Cause	References
Enteritidis (primary)	Feb 2001(73)	Feb-Mar 2001 (84)	Western Canada (mainly Alberta)	Mung bean sprouts	26
Enteritidis (secondary)	Apr 1998(46)	late Mar 1998 (>800)	Canada-wide	Commercial lunch pack product (cheese)	27
Heidelberg	Aug 1998-Jul 1999 (135)	Dec 1998 (130)	Canada	Turkey/ham	5,21
Infantis	Mar-Nov 1999 (43)	Dec 1998-Sep 1999	Canada-wide (initially in Alberta)	Pig ear dog treats	28
Java	Aug-Oct 1999 (44)	Aug-Sep 1999 (51)	Western Canada (mainly Alberta)	Alfalfa sprouts	29
Meleagridis	Sep-Dec 1997 (52)	Oct-Dec 1997(124)	Canada-wide (mainly Alberta)	Alfalfa sprouts	5,21,30
Muenchen	Jun-Jul 1999 (12)	Jun-Jul 1999 (>400)	US & Canada	Unpasteurized orange juice	31,32
Stanley (secondary)	Jun-Nov 2001 (24)	Jul-Sep 2001 (102)	Canada, Australia, & the UK	Imported peanuts	33-35
Thompson (primary)	Apr 1997(38)	Apr 1997(54)	Canada	Roast beef	5,21

efits to humans may be invaluable from both a health and economic viewpoint. Future studies could explore factors associated with seasonality of prevalence, including reasons for the occurrence of clusters in

the autumn beyond regular summertime peaks, as well as increasing public awareness of foodborne disease and appropriate hygiene during these periods of increased risk.

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RÉSUMÉ

Contexte : On estime qu'il se forme des grappes temporelles de cas de salmonellose qui n'ont pas encore fait l'objet d'études quantitatives. Aussi, notre étude visait à dégager les tendances, les schémas saisonniers et les grappes de la salmonellose chez les habitants de l'Alberta en examinant les isolats détectés par des systèmes de surveillance passive.

Méthodes : Après en avoir fait la demande, on a obtenu auprès du ministère de la santé et du mieux-être (*Ministry of Health and Wellness*) de l'Alberta les cas de salmonellose signalés et inscrits dans les documents relatifs aux maladies à déclaration obligatoire pour la période allant de janvier 1990 à décembre 2001. On a utilisé la technique de régression des carrés pour caractériser la distribution des isolats (de même que les tendances à long terme et les schémas saisonniers). Un test de détection des grappes a permis de déterminer la présence éventuelle d'isolats des sérovars particuliers agrégés et le moment de leur aggrégation, indépendamment de la distribution naturelle. L'analyse comparative a visé les schémas temporels du bétail albertain et les flambées connues chez les humains.

Résultats : *S. Typhimurium*, *Enteritidis*, *Hadar*, *Heidelberg* et *Thompson* représentaient les cinq sérovars les plus courants parmi les 9 188 signalés. Le nombre d'isolats signalés était relativement stable au cours des années même si on constatait une tendance distincte au cours de la saison estivale. On a observé la présence de grappes chez 23 des 32 sérovars examinés. On a relevé plus de grappes au cours des mois de septembre et d'octobre qu'au cours des autres mois et entre 1998 et 2001 que durant la période s'échelonnant du début au milieu des années 1990. En outre, davantage de grappes étaient de courte durée.

Interprétation : Les grappes de courte durée indiquent vraisemblablement une source ponctuelle d'infection tandis que celles de longue durée pourraient indiquer une exposition à une source constante et commune ou à la présence d'infections secondaires. Une nette tendance à la hausse et une grappe importante de cas de *S. Heidelberg* sont susceptibles d'avoir des répercussions sur la santé publique. Les activités de surveillance ont surtout visé les similitudes entre les sérovars, les tendances et les grappes temporelles communes chez les humains et les animaux. La réalisation d'études sur les facteurs rattachés aux grappes durant l'automne pourrait contribuer à prévenir les flambées chez les humains.