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MAJOR ARTICLE

Increasing Rates of Invasive Group A Streptococcal Disease in Alberta, Canada; 2003–2017

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Background. We present an analysis of increasing rates of invasive group A streptococci (iGAS) over a 15-year period in Alberta, Canada.

Methods. From 2003 to 2017, the *emm* type of iGAS isolates was identified from patients with iGAS disease in Alberta. Demographic, clinical, and risk factor data were collected.

Results. A total of 3551 cases of iGAS were identified in Alberta by isolation of a GAS isolate from a sterile site. The age-standardized incidence rates of iGAS increased from 4.24/100 000 in 2003 to 10.24 in 2017. Rates (SD) were highest in those age <1 (9.69) years and 60+ (11.15) years; 57.79% of the cases were male. Commonly identified risk factors included diabetes, hepatitis C, non-surgical wounds, addiction, alcohol abuse, drug use, and homelessness. The overall age-standardized case fatality rate was 5.11%. The most common clinical presentation was septicemia/bacteremia (41.84%), followed by cellulitis (17.25%). The top 4 *emm* types from 2003–2017 were *emm*1, 28, 59, and 12. In 2017, the top 4 *emm* types (*emm*1, 74, 101, and 59) accounted for 46.60% of cases.

Conclusions. The incidence of iGAS disease in Alberta, Canada, has increased from 2003 to 2017. This increase has been driven not by a single *emm* type, but rather what has been observed is a collection of common and emerging *emm* types associated with disease. In addition, it is also likely that societal factors are playing important roles in this increase as risk factors associated with marginalized populations (addiction, alcohol abuse, and drug use) were found to have increased during the survey period.

Keywords. Alberta; Canada; *emm* type; Group A streptococci; high incidence.

Group A streptococci (GAS) or *Streptococcus pyogenes* are Gram-positive, catalase-negative bacteria. Group A streptococci cause a variety of diseases in humans, including pharyngitis, skin and soft tissue infections, rheumatic fever, rheumatic heart disease, and the severe invasive diseases necrotizing fasciitis and streptococcal toxic shock syndrome [1–7]. GAS bacteria are a global pathogen causing an estimated 1.8 million new severe disease infections annually; however, this estimate is likely an underestimation as some countries have reported increases in rates of GAS disease, notably those with low to middle incomes [1, 8, 9]. To understand the epidemiology of GAS, GAS infections can be tracked via variability in the *emm* gene sequence that encodes the M protein [10]. There are currently >250 different *emm* types and >90 sequence types based on the nucleotide variability in the 5' end of the *emm* gene (ftp://ftp.cdc.gov/pub/infectious_diseases/biotech/tsemm/).

Currently no GAS vaccine exists that is in routine use; however, there has been renewed interest in development of potential GAS vaccines, many of which are M protein based [11, 12]. Due to variability in the M protein, it is important to understand the prevalent circulating M/*emm* types in a population and the incidence and epidemiology of invasive GAS (iGAS) in a region. This information aids in determining the need and type of potential future vaccines that are M protein based.

We previously reported rates of iGAS for the province of Alberta for the years 2000 to 2002, along with M types [13]. Here, we provide an update of iGAS rates in Alberta and *emm* types, clinical presentations, and risk factors from 2003 to 2017 (a 15-year period).

METHODS

Demographics and Clinical Data Collection

All cases used in the data analysis were from Alberta residents only. The population of Alberta in 2003 was 3 182 852, and in 2017, the population was 4 286 144, constituting 11.68% of the Canadian population for 2017 [14]. In Alberta, many infectious diseases including iGAS are listed as notifiable diseases, requiring reporting to the provincial Ministry of Health under the Public Health Act (https://open.alberta.ca/publications/streptococcal-disease-group-a-invasive) [15]. The notification process is to facilitate contact tracing by public health nurses, thereby allowing prophylaxis procedures to be followed if necessary. Data from both confirmed and probable cases were collected.

Received 16 April 2018; editorial decision 16 July 2018; accepted 19 July 2018.

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DOI: 10.1093/ofid/ofy177

Confirmed iGAS cases were defined as the identification of GAS from any normally sterile site including blood, CSF, brain, other sterile organs, deep tissues, joints, etc. (https://open.alberta.ca/publications/streptococcal-disease-group-a-invasive). Probable iGAS cases were defined as severe invasive disease in the absence of another etiology with isolation of GAS from a nonsterile site.

Once iGAS isolates were initially identified by a diagnostic microbiology laboratory, Public Health officials were informed, and the clinical data were collected as per routine notifiable disease requirements by trained public health nurses using a notifiable disease reporting form [15]. These data were captured in the Communicable Disease Reporting System (CDRS), held at the Ministry of Health, Alberta. The definitions used to capture clinical presentation of disease are defined in the Alberta Health Notifiable Disease Manual [16]. Clinical data from CDRS were linked with laboratory data from the Provincial Laboratory for Public Health (ProvLAB) using a Unique Lifetime identifier for each patient. Case fatality rates (CFRs) were captured if the case had died at the time the notifiable disease report form was completed. All notifiable disease reports were completed within 30 days of the initial notification of an iGAS case.

iGAS Isolates and *emm* Typing

iGAS isolates are required to be submitted to ProvLAB for *emm* typing. The methodology used to type iGAS isolates from 2003 to September 2006 was via a previously described serological typing assay, and from October 2006 to 2017 by *emm* typing, which was done by DNA sequencing of the M serotype–specific region of the *emm* gene [13, 17, 18].

Statistical Analysis

Alberta population estimates from 2003–2017 were extracted from the online Interactive Health Data Application (IHDA) database [14]. We estimated incidence rates by year of diagnosis, age group, and health zone (of patient residence at the time of diagnosis) over the study period. Incidence rates were calculated for each characteristic as number of cases per 100 000 persons per year. The Cochran-Armitage trend test was used to test for linear trend of risk factors over time. Data were analyzed using SAS 9.3 (SAS Institute Inc., Cary, NC) and graphed using OriginLab software 2018 (OriginLab Corporation, Northampton, MA).

RESULTS

Incidence

From 2003 to 2017, there were 3551 cases of both confirmed and probable iGAS reported. Probable cases were 1.2% (43 cases). Table 1 shows that the incidence of iGAS in Alberta steadily increased over the 15 years surveyed. The overall age-standardized incidence was 4.24 in 2003 and increased to 10.24 in 2017. Increasing incidence rates over the 15 years surveyed are more evident in adults (age 20 years and older) than children (age 0–19 years) (Figure 1). Overall incidence was highest at the extremes of age, with individuals <1 year of age having an incidence of 9.69 and individuals' ≥60 years having an incidence of 11.15 (Figure 2).

Case Demographics, Clinical Presentation, and Risk Factor Analysis

Of the 3551 cases, gender was identified for 3549; 2051 cases (57.79%) were male. The mean age was 44.86 years. The overall age-standardized CFR was 5.11% (226 deaths/3551 cases) (Table 1). The year 2010 had the lowest percentage CFR (4.12%), and 2012 had the highest (8.85%) (Table 1). The CFR in males was 5.75%, and for females it was 7.21% (chi-square = 3.08; $P = .08$). The highest CFR occurred in those cases age ≥60 years (12.97%; 127 deaths) (Figure 2). The incidence was higher in males (7.20) than females

Table 1. Incidence (per 100 000), Number of Cases, Number of Deaths, and Case Fatality Rate of iGAS in Alberta, 2003–2017

Year	Crude Incidence, %	Age-Standardized[a] Incidence, %	No. Cases	No. Deaths	Crude CFR, %	Age-Standardized[a] CFR, %
2003	3.96	4.24	126	7	5.56	4.12
2004	4.38	4.63	142	10	7.04	6.12
2005	5.00	5.26	166	7	4.22	7.97
2006	5.58	5.93	191	10	5.24	4.20
2007	7.29	7.51	256	11	4.30	3.26
2008	6.15	6.33	221	9	4.07	3.73
2009	5.41	5.62	199	12	6.03	4.04
2010	4.77	4.98	178	7	3.93	3.39
2011	5.80	5.95	220	14	6.36	5.81
2012	6.29	6.41	244	25	10.25	8.85
2013	6.68	6.81	267	13	4.87	4.26
2014	6.45	6.61	265	19	7.17	5.92
2015	7.23	7.32	302	27	8.94	6.90
2016	7.91	7.94	335	22	6.57	4.95
2017	10.24	10.24	439	33	7.52	5.43
Total or avg	6.32 avg.	6.52 avg.	3551 total	226 total	6.36 avg.	5.11 avg.

Abbreviations: CFR, case fatality rate; iGAS, invasive group A streptococci.

[a]Standardized to 2017 Alberta population estimates.

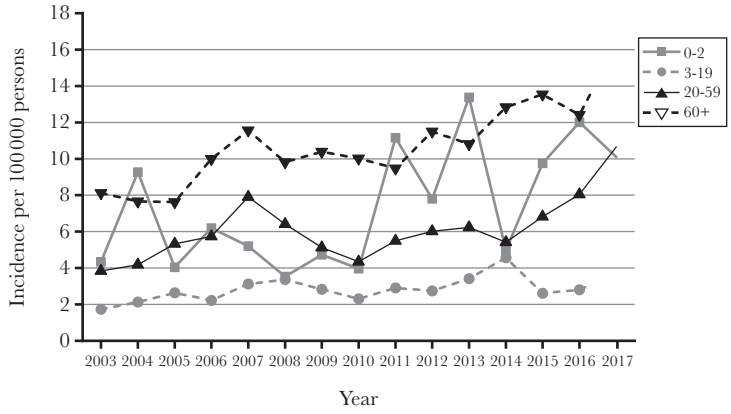

Figure 1. Incidence of iGAS by age in Alberta from 2003 to 2017.

(5.42) overall. The most common clinical diagnosis was septicemia/bacteremia, at >40% of cases, followed by the skin-associated infections cellulitis (17.25%) and soft tissue infection (12.31%) (Table 2). Table 3 shows risk factor data presented in 3-year periods. Diabetes, hepatitis C, nonsurgical wounds, addiction, alcohol abuse, drug use, and homelessness ($P < .05$) were commonly found risk factors that trended upward over the 15 years surveyed. No identified risk factor significantly trended downward (Table 3). Only 2.5% (87/3511) of the cases were classed as postpartum.

emm Types

M or *emm* type was captured for 3102 (87.36%) of the 3551 iGAS cases identified during the survey period. Of the 3102 typed isolates, 3053 had an identifiable M or *emm* type (49 isolates were serologically nontypable) (Table 4). No single *emm* type can be attributed to the increased incidence over the 15 years, but rather the increase appears to be associated with a variety of *emm* types that changed in prevalence from year to year. Sixty-five *emm* types were identified, of which the top 30 are shown in Table 4. The top 20 *emm* types accounted for approximately 90% of the circulating *emm* types causing iGAS disease. Of these 20 *emm* types, 14 are part of the 30 valent M type–based vaccine [19]. Of the 65 *emm* types identified, 3 *emm* types emerged, with higher rates in 2017 than the previous 14 years. These were *emm*74, 76, and 81. In addition, *emm*101 showed higher case numbers starting in 2015 than the years before.

With respect to overall numbers of cases, *emm*1, *emm*28, and *emm*59 accounted for more than one-third (34.33%) of all cases typed. The most common *emm* type was *emm*1, accounting for 19.28% of the total cases typed (Table 4). The percentage of *emm*1 typed cases compared with the overall typed case numbers by year ranged from a low of 9.43% (2006) to a high of 29.17% (2011). *emm*28 was the second most common *emm* type, with a high of 20.15% in 2004 and a low of 4.07% in 2009.

In the last year of the survey (2017), 32 different *emm* types were identified, with *emm*1 accounting for 20% (Table 4). The next most common *emm* types in order of prevalence for 2017 were 74 and 101, followed by 59. Together, these 4 *emm* types (1, 74, 101, and 59) accounted for 46.58% of the iGAS cases in 2017 (Figure 3 and Table 4). The 10 *emm* types (1, 74, 101, 59, 11, 28, 76, 81, 12, and 82) accounted for 316 cases or 77.07% of cases in 2017 (Figure 3).

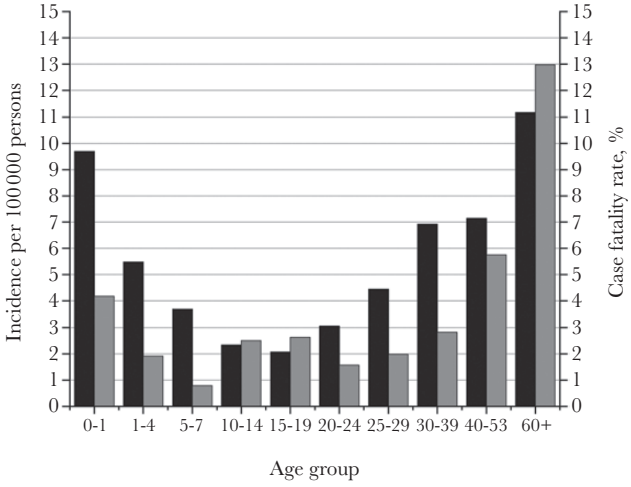

Figure 2. Incidence and case fatality rate by age for invasive group A streptococci cases from 2003 to 2017. Black bars correspond to incidence, and gray bars correspond to case fatality rate.

emm Type, *emm* Clusters, and Clinical Presentation

Table 5 shows the distribution of iGAS cases according to clade, *emm* type, *emm* cluster, and clinical presentation. The distribution of cases between clades X and Y is equal in case numbers, at 50% each. Four cluster types, A-C3, D4, E4, and E6, accounted for the majority of septicemia/bacteremia (71%), cellulitis (72%), soft tissue infections (70%), pneumonia (68.9%), and necrotizing fasciitis (77%) iGAS cases. For STSS, cluster types A-C3, A-C5, E4, and E6 were the most common, accounting for 72.4% of iGAS cases that occurred during the period surveyed.

Table 2. Number of Cases of iGAS in Alberta by Clinical Diagnosis, Deaths, and CFR[a]

System Affected	Clinical Presentation	No. Cases (%)	No. Deaths (CFR, %)
Blood/brain/sterile tissue	Septicemia/bacteremia	1889 (41.84)	118 (6.25)
	Toxic shock syndrome	254 (5.63)	55 (21.65)
	Meningitis	25 (0.55)	5 (20.00)
	Peritonitis	29 (0.64)	2 (6.90)
	Pericarditis	10 (0.22)	2 (30.00)
	Encephalitis	1 (0.02)	0 (0.00)
Skin/soft tissue	Cellulitis	779 (17.25)	22 (2.82)
	Soft tissue infection	556 (12.31)	13 (2.34)
	Necrotizing fasciitis	326 (7.22)	35 (10.74)
Respiratory	Pneumonia	341 (7.55)	31 (9.09)
	Epiglottitis	13 (0.29)	2 (15.38)
Bone	Joint	255 (5.65)	1 (0.40)
	Osteomyelitis	37 (0.82)	1 (2.76)
	Total	4515 (100)	

Abbreviations: CFR, case fatality rate; iGAS, invasive group A streptococci.

[a]Many cases had more than 1 clinical presentation.

Seasonality

Figure 4 displays the number of cases identified by month for each year surveyed. Presenting the 15 years surveyed as 1 calendar year shows that a peak in iGAS cases generally occurred in the winter months of January and December, with a low in the month of September (Figure 4).

DISCUSSION

We have provided a report on 15 years of iGAS disease in Alberta, Canada, during which incidence rose from 4.24 (2003) to 10.24 (2017). Recent surveillance from the Active Bacterial Core surveillance program (a program representing approximately 10% of the US population) also documented a rise in rates [20]. This program showed an incidence of 3.4 in 2012 rising to 5.8 in 2016, suggesting that increases in iGAS are occurring throughout North America [20].

In addition to the United States, the Public Health Agency of Canada has been reporting incidence of iGAS for Canada since 2000. In 2000, Canadian incidence was 2.81 climbing to 5.28 (2015, last reported year; http://disease.canada.ca/notifiable/charts?c=yl). Recently, the British Columbia Centre for Disease Control (BCCDC) released a report describing iGAS incidence in British Columbia at 8.4 in 2017 [21]. Based on these reports and our data, it is evident that iGAS rates in parts of North America have risen in the last decade.

Drivers in Alberta responsible for increased incidence are not readily clear and are likely multifactorial. Contributors likely include a collection of various risk factors for iGAS disease. The

Table 3. Risk Factors for iGAS Disease in Alberta; 2003–2017

	2003–2005	2006–2008	2009–2011	2012–2014	2015–2017	
Risk Factor	n (%)	n (%)	n (%)	n (%)	n (%)	*P*[a]
Diabetes	13 (3.0)	57 (8.5)	79 (13.2)	111 (14.3)	193 (17.9)	<.001
Hepatitis C	16 (3.7)	68 (10.2)	49 (8.2)	43 (5.5)	106 (9.9)	.035
HIV	6 (1.4)	20 (3.0)	11 (1.8)	9 (1.2)	14 (1.3)	.109
Immunocompromised	14 (3.2)	60 (9.0)	50 (8.4)	74 (9.5)	81 (7.5)	.064
Postpartum	5 (1.2)	20 (3.0)	15 (2.5)	28 (3.6)	13 (1.2)	.513
Wound (nonsurgical)	25 (5.8)	167 (25.0)	159 (26.6)	149 (19.2)	208 (19.3)	.022
Wound (surgical)	10 (2.3)	32 (4.8)	30 (5.0)	46 (5.9)	58 (5.4)	.008
Addiction abuse	19 (4.4)	157 (23.5)	102 (17.1)	136 (17.5)	318 (29.6)	<.001
Alcohol abuse	10 (2.3)	93 (13.9)	75 (12.6)	99 (12.8)	178 (16.5)	<.001
Drug use	10 (2.3)	97 (14.5)	50 (8.4)	72 (9.3)	204 (19.0)	<.001
Homelessness	15 (3.5)	91 (13.6)	48 (8.0)	59 (7.6)	161 (15.0)	<.001
Total cases, n[b]	392	539	483	614	829	-

Years surveyed are divided into 3-year blocks.

Abbreviation: iGAS, invasive group A streptococci.

[a]The Cochrane Armitage trend test was used to calculate the *P* value.

[b]Many cases had more than 1 risk factor.

Table 4. Top 30 *emm* Types by Year and Number of Cases

	Year															
emm Type	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total
1	22	31	21	15	27	25	32	38	56	50	44	50	47	58	82	598
28	12	27	22	25	13	15	7	15	12	17	20	17	15	20	23	260
59	0	0	1	1	24	51	37	16	6	5	4	5	8	18	31	207
12	6	4	9	10	10	6	6	14	14	8	11	10	9	19	20	156
82	6	8	1	7	29	5	3	0	6	6	14	4	21	25	16	151
3	3	0	1	9	9	16	29	1	10	8	4	5	29	16	2	142
89	2	0	3	1	9	3	11	10	14	9	13	16	13	7	14	125
101	0	0	0	0	0	1	9	6	5	4	3	3	24	31	39	125
11	3	2	1	5	3	4	3	3	4	13	15	7	10	14	23	110
41	2	7	8	3	4	1	0	0	0	9	11	20	16	6	6	93
4	9	4	2	1	2	3	3	1	14	8	8	9	7	7	12	90
83	1	3	4	10	17	2	0	0	3	6	3	3	8	13	14	87
77	1	6	2	3	1	2	3	7	9	10	16	5	5	6	6	82
114	8	4	6	10	15	7	1	3	2	1	0	9	7	5	0	78
2	4	3	1	4	7	2	3	7	6	9	5	10	2	3	4	70
6	1	1	4	2	3	1	3	1	2	3	11	18	12	5	2	69
91	12	4	2	5	4	2	1	1	1	10	10	4	6	5	1	68
53	1	0	0	2	3	1	3	6	9	7	15	9	3	0	3	62
74	1	0	0	0	0	0	0	0	0	1	0	0	0	13	39	54
22	3	1	0	1	1	1	0	3	3	4	8	4	6	9	3	47
87	1	1	2	2	2	2	1	2	5	3	5	3	5	6	3	43
80	1	0	1	1	5	12	5	5	2	2	1	1	0	1	0	37
81	0	0	1	0	0	0	0	1	0	0	0	2	3	3	21	31
75	0	8	2	5	1	2	1	0	0	0	1	2	4	3	1	30
76	0	0	1	2	0	0	0	1	0	1	2	0	0	0	22	29
5	1	1	14	3	0	2	1	0	0	0	0	0	0	0	0	22
92	3	2	4	9	0	0	0	1	0	0	0	0	0	0	3	22
73	0	1	0	2	1	1	3	1	2	2	1	3	0	2	1	20
68	0	0	0	2	8	5	0	0	0	0	0	1	1	1	2	20
9	0	0	1	1	1	2	0	0	0	1	3	0	1	1	4	15
Others	3	5	3	9	7	8	7	10	7	12	6	8	5	10	13	113
NT	7	11	20	11	0	0	0	0	0	0	0	0	0	0	0	49
Total	113	134	137	161	206	182	172	153	192	209	234	228	267	307	410	3105

Abbreviation: NT, nontypable.

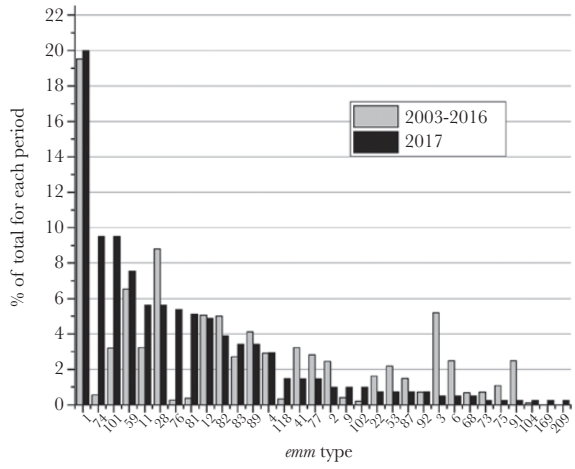

Figure 3. The percentage of each *emm* type identified in 2017 compared with the period 2003 to 2016. As 2017 had the highest incidence and is the most recent period surveyed, 2017 was compared with the past 14 years surveyed (2003–2016).

risk factors in Table 3 that trended upward over the 15 years surveyed for iGAS were diabetes, hepatitis C, nonsurgical wounds, drug abuse, alcohol abuse, addiction, and homelessness. These risk factors have been described as key players for patients with iGAS infections in other surveys [22–24]. For example, in the large *emm*59 outbreak that occurred in western Canada from 2006 to 2009, alcohol abuse, illicit drug use, and homelessness were considered significant risk factors [22].

It is interesting that the overall CFR in our survey of 6.36% is lower than reported in other surveys; however, this may be due to not following iGAS cases for a full 30 days after initial diagnosis. Lamagni et al. reported a CFR of 20% for 3422 cases in the United Kingdom [25]. Recently, Teatero et al. reported a CRF of 19% for iGAS infections with *emm*89 alone and 20% with *emm*1 in metropolitan Toronto from 2000 to 2014 using a definition of death within 30 days of positive culture [26]. Although the Toronto CFRs are *emm* type specific and not

Table 5. Distribution of GAS Isolates by *emm* and *emm* Cluster Type in Relation to Clinical Presentation

Clade (No. of Isolates; %)	*emm* Type(s) (No. of Isolates)	*emm* Cluster	No. (%) of Isolates by Clinical Infection											
			Sept/Bacterem	Cellulitis	Soft Tissue Infection	Pneum	NF	STSS	Joint	Osteo	Mening	Perito	Pericard	Epigl
X (1527; 50)	4 (90) (total 90 cases)	E1	55 (3.1)	16 (2.4)	14 (3.3)	7 (2.4)	5 (1.8)	7 (3.1)	8 (3.7)			2 (8.7)	1 (10.0)	
	27 (1), 66 (1), 68 (20), 76 (29), 90 (4), 92 (22), 104 (4), 106 (1) (total 82 cases)	E2	47 (2.6)	14 (2.1)	7 (1.7)	6 (2.1)	8 (2.9)	2 (0.9)	6 (2.7)			2 (8.7)		
	9 (15), 25 (3), 44/61 (14), 49 (3), 58 (14), 82 (151), 87 (43), 103 (1), 113 (1), 118 (15), 183 (3), 209 (1) (total 264 cases)	E3	148 (8.3)	70 (10.5)	49 (11.7)	19 (6.6)	15 (5.5)	15 (6.6)	22 (10.0)	3 (9.4)			1 (10.0)	1 (11.1)
	2 (70), 22 (47), 28 (260), 73 (20), 77 (82), 88 (1), 89 (125), 102 (9), 114 (78), 169 (1) (total 695 cases)	E4	405 (22.6)	129 (19.3)	96 (22.9)	48 (16.6)	56 (20.6)	40 (17.5)	54 (24.7)	6 (18.8)	3 (13.1)	7 (30.4)	4 (40.0)	1 (11.1)
	170 (1), 174 (4) (total 5 cases)	E5				1 (0.4)								
	11 (110), 48 (7), 59 (207), 75 (30), 81 (31), 94 (7), 182 (1) (total 393 cases)	E6	224 (12.5)	103 (15.4)	65 (15.5)	33 (11.4)	39 (14.3)	23 (10.0)	30 (13.7)	2 (6.3)	4 (17.5)	3 (13.0)		2 (22.2)
Y (1528; 50)	1 (598), 227 (2) (total 600 cases)	A-C3	355 (19.8)	99 (14.8)	61 (14.6)	86 (29.8)	77 (28.3)	83 (36.2)	30 (13.7)	5 (15.6)	8 (34.8)	6 (26.1)	2 (20.0)	4 (44.7)
	12 (156) (total 156 cases)	A-C4	97 (5.4)	27 (4.0)	16 (3.8)	22 (7.6)	13 (4.8)	11 (4.8)	9 (4.1)	3 (9.4)	1 (4.4)			
	3 (142) (total 142 cases)	A-C5	84 (4.7)	26 (3.9)	17 (4.1)	21 (7.3)	14 (5.1)	20 (8.7)	10 (4.6)	1 (3.1)	1 (4.4)	2 (8.7)	1 (10.0)	1 (11.1)
	100 (1), 115 (2) (total 3 cases)	D2	1 (0.1)	1 (0.2)					1 (0.5)	3 (9.4)				
	123 (2), 217 (1) (total 3 cases)	D3	1 (0.1)	1 (0.2)	1 (0.2)		1 (0.4)							
	33 (1), 41 (93), 43 (1), 53 (62), 64 (1), 80 (37), 83 (87), 91 (68), 101 (125), 223 (1) (total 476 cases)	D4	289 (16.1)	150 (22.5)	71 (17.0)	32 (11.1)	38 (14.0)	15 (6.6)	40 (18.3)	6 (18.8)	2 (8.7)	1 (4.3)		
	5 (22) (total 22 cases)	M5	7 (0.4)	2 (0.3)	2 (0.5)		2 (0.9)	1 (0.4)	1 (0.5)		1 (4.3)			
	6 (69) (total 69 cases)	M6	41 (2.9)	11 (1.6)	4 (1.0)	10 (3.5)	2 (0.9)	6 (2.6)	5 (2.3)	1 (3.1)	3 (13.0)			
	23 (1) (total 1 case)	M23	1 (0.1)											
	74 (54) (total 54 cases)	M74	36 (2.0)	19 (2.8)	16 (3.8)	4 (1.4)	2 (0.9)	6 (2.6)	2 (0.9)	2 (6.3)			1 (10.0)	
	122 (1) (total 1 case)	M122	1 (0.1)											
	218 (1) (total 1 case)	M218	1 (0.1)											
Outlier (1; 0.03)	111 (1) (total 1 case)	M111							1 (0.5)					
Total			1793	668	419	289	272	229	219	32	23	23	10	9

Abbreviations: Epigl, epliglottis; GAS, group A streptococci; Mening, meningitis; NF, necrotizing fasciitis; Osteo, osteomyelitis; Pericard, pericarditis; Perito, peritonitis; Pneum, pneumonia; Sept/bactem, septicemia/bacteremia; STSS, streptococcal toxic shock syndrome.

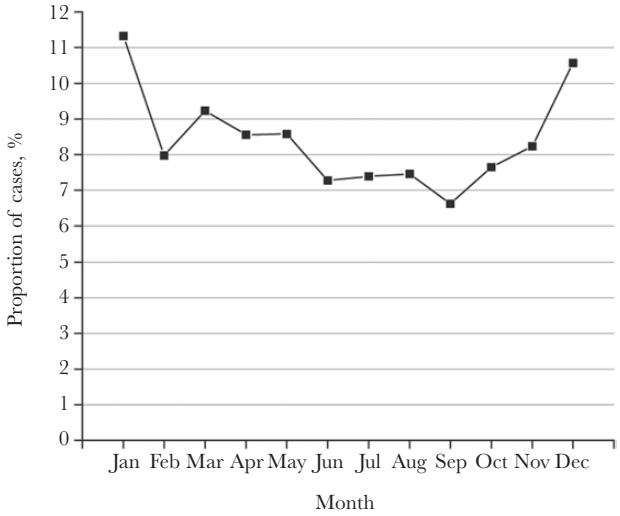

Figure 4. Invasive group A streptococci (iGAS) cases by month. The average proportion of cases by month expressed as a percentage of iGAS cases by month that occurred over the 15 years surveyed.

overall CFRs, CFRs of approximately 20% are similar to those reported in the United Kingdom [25]. A recent report from the BCCDC documented a CFR of 4% for 2017, similar to Alberta [21]. Alberta and British Columbia are neighboring provinces, suggesting that the similarly low CFR rates in Alberta are not inaccurate.

With respect to *emm* types, the data show that *emm* types rose and fell in prevalence over the 15 years surveyed; therefore, no single *emm* type can account for the overall rise in incidence. It is important to note that the rise in the case numbers associated with various *emm* types was especially evident in 2017. *emm* types 1, 74, 101, and 59 accounted for close to 50% of the cases typed in 2017. Previous investigators have shown the emergence of a virulent M1 clone that has disseminated worldwide starting in the 1990s [27]. Although a worldwide virulent M1 strain likely contributes to increases for this *emm* type, it is unlikely the only reason for the increase in *emm*1 seen, especially for 2017. It is likely that the increase is multifactorial, involving both the GAS strain and the affected population having significant risk factors for the disease.

The second most common *emm* types in 2017 were *emm*74 and *emm*101. Data from the Centers for Disease Control and Prevention's Active Bacterial Core surveillance program (2010–2016) show that *emm*74 was documented once from a case in Maryland in 2010 and that *emm*101 has not been documented [20]. Although *emm*74 increases were not evident in the United States in the years surveyed, increases in *emm*74 have been reported in Ontario and other parts of Canada recently [28].

*emm*101 was first identified in Alberta in 2009, with the highest number of cases in 2017. In Canada, Athey et al. documented *emm*101 as 1 of the 6 most prevalent *emm* types from 2011 to 2013, identified from cases in Thunder Bay, Ontario [23]. The recent BCCDC report for 2017 listed *emm*101 as the third most common *emm* type in British Columbia, at 11% [21].

Increased rates of *emm*59 cases in Canada were first described in 2006, and since this outbreak, increased rates of *emm*59 cases have been reported in the United States (MT, WY, AZ, NM) [22, 29, 30]. In the description of the *emm*59 outbreak in Canada, *emm*59 cases were associated with alcohol abuse, illicit drug use, and homelessness [22]. Based on the risk factors described in this report, which are similar to the risk factors for the *emm*59 outbreak in 2006–2009, it would not be surprising to see *emm*59 case numbers rise again.

Potential GAS vaccines have focused on M protein as a vaccine component. For 1 vaccine, investigators used the variable portion of the M protein and incorporated 30 M types in 1 formulation [19]. Multivalent vaccines have the potential problem that M types can change over time, resulting in lack of coverage for specific circulating *emm* types. This could potentially be addressed through development of *emm* cluster–based vaccines as there is a limited number of cluster types, in comparison with the number of *emm* types [31]. In our survey, a breakdown of *emm* types by cluster type suggests that a vaccine for Alberta should encompass members of 5 cluster types, A-C3, D4, E3, E4, and E6, out of the 19 cluster types identified. These 5 cluster types constitute close to 80% of the *emm* types that were identified in our survey.

Although this survey provides important information regarding iGAS disease in Alberta, there are limitations. The described survey is retrospective and not prospective. A retrospective study does not allow investigators to go back to cases and interview patients for information that may not have been collected at the onset. Also, a passive surveillance system was used to collect the data; therefore, the possibility exists that cases may not have been reported. Another limitation is that not all cases had a GAS isolate for typing (87% were typed). However, having close to 90% of isolates *emm*-typed over a 15-year period still provides useful information regarding circulating *emm* types.

In summary, rates of iGAS disease in Alberta, Canada, have risen since 2003, reaching >10/100 000 in 2017. No single *emm* type alone can be attributed to the higher rates but rather a collection of common and new emerging *emm* types are evident. Another driver contributing is likely the growing number of marginalized and homeless people.

Acknowledgments

The authors would like to thank the clinical diagnostic microbiology laboratories in Alberta for identifying iGAS isolates and submitting them to the ProvLAB for *emm* typing.

Potential conflicts of interest. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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