2.3 Invasive Group A Streptococcal Disease

Summary

2013 total number of cases = 168
2013 crude incidence rate = 3.66 per 100,000 population

Notifications
In 2013, 168 cases of invasive group A streptococcal (iGAS) disease were notified, which corresponds with a rate of 3.66 iGAS cases per 100,000 population [95% confidence interval (CI): 3.13 – 4.26 per 100,000]. The 2013 iGAS rate was higher than in 2012 (3.66 versus 2.66 [95% CI: 2.21 – 3.17 per 100,000]). However, the increase is not considered to be statistically significant as the confidence intervals overlap.

The majority (n = 158; 94%) were classified as confirmed cases: patients with group A streptococcus (GAS; *Streptococcus pyogenes*), isolated from a sterile site. The remaining ten were classified as probable cases: patients with streptococcal toxic shock syndrome (STSS) or necrotising fasciitis and GAS isolated from a non-sterile site (e.g. throat, sputum, vagina).

Patient demographics
Of the 168 cases, 95 (57%) were male. The mean age of patients with iGAS was 41 years (range = 1 month – 93 years) and iGAS was more common in young children and older adults (Figure 1).

Geographic spread and seasonal variation
Table 1 displays the numbers and crude incidence rates (CIRs) of iGAS disease by HSE area from 2009 to 2013. While HSE East accounted for the highest number of reported cases in 2013 (n=67), HSE West had the highest CIR (4.27 per 100,000 population). In all HSE areas except the Midlands, both numbers of cases and CIRs increased. HSE Mid-West reported the largest annual increase (two-fold on 2012).

In 2013, the peak months were April (17 cases), May (26 cases) and July (18 cases). As in previous years, the peak period occurred during the first half of the year (Figure 2). Upon annual review of cumulative monthly data, the increase in notifications was first noted from April 2012 (Figure 3). Data presented here are based on the date the case was notified to public health, not on the date the case was first detected.

Isolate details
Of confirmed cases, GAS was isolated from a sterile site in 147, with a source site not reported for the remaining 11. GAS was isolated primarily from blood cultures (n=107; 73%), abscesses (n=15), deep tissue (n=9), joints

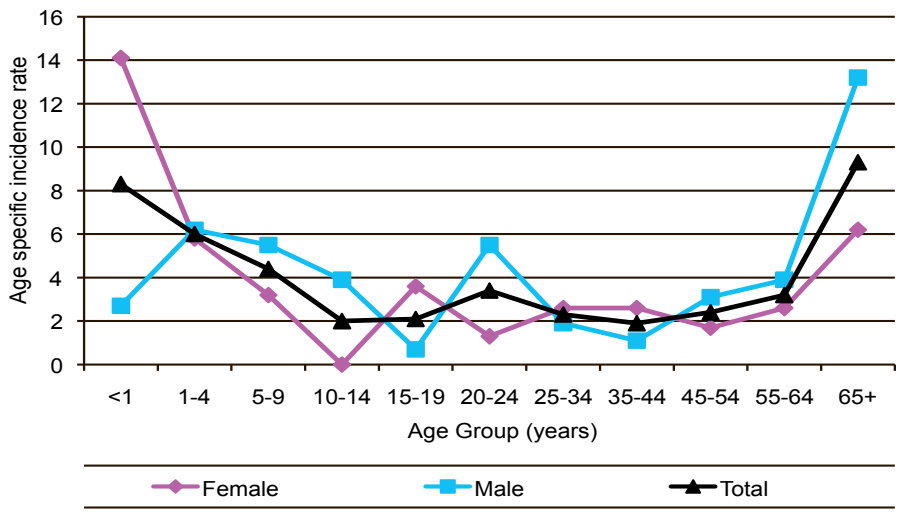

Figure 1. Age and sex specific rates of iGAS disease in 2013

(n=10), pleural fluid (n=3), peritoneal fluid (n=2) and cerebrospinal fluid (CSF) (n=1). For four cases, GAS was isolated from another sterile site in addition to blood: deep tissue (n=3) and joint (n=1).

For the 10 probable cases, GAS was isolated from non-sterile sites, including sputum, swabs and wound tissue.

Typing data, based on sequencing of the *emm* genes that encode the M protein (the major virulence factor), were available on 140 isolates submitted from 30 laboratories: *emm*-types 1 (n=41; 29%), 3 (n=33; 24%), 89 (n=13; 9%) and 28 (n=8; 6%) comprised 69% of all the isolates typed. Twenty-one other *emm*-types (each represented by four isolates or less) were also detected. Of the 28 patients with STSS for whom *emm*-typing was undertaken, nine GAS isolates belonged to *emm*1 (32%) and nine to *emm*3 (32%).

Enhanced surveillance data

Enhanced data were provided for 155 (92%) of the 168 iGAS cases, which is higher than in 2012 (87%, 106 of 122 cases). The source laboratory could be ascertained for all cases. As in previous years, there was wide variation in completeness of enhanced data reporting. Table 2 summarises characteristics of iGAS cases in Ireland from 2008 to 2013.

Clinical details

Clinical presentation data were provided for 141 cases (84%). As in previous years, bacteraemia (n=111 cases, including cases where bacteraemia was not specifically stated but GAS was isolated from blood) and cellulitis (n=45) were the commonest presentations, followed by STSS (n=32; eight of which were implied based on the information provided on the clinical presentation), pneumonia (n=24), necrotising fasciitis (n=10), septic arthritis (n=10), puerperal sepsis (n=6), peritonitis (n=4), myositis (n=3), erysipelas (n=3) and meningitis (n=3). Note that an iGAS case could have more than one clinical manifestation of infection.

Risk factors

Risk factor data were provided for 140 iGAS cases (83%). Risk factors included; presence of skin or wound lesions (n=55), age ≥65 years (n=50), malignancy (n=23), diabetes mellitus (n=16), steroid use (n=11), alcoholism (n=6), childbirth (n=6), injecting drug use

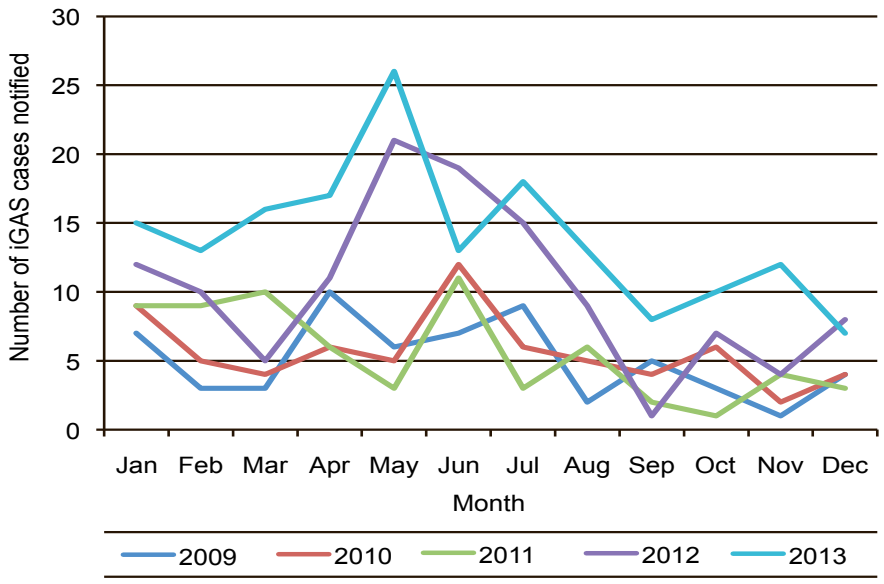

Figure 2. Monthly distribution of iGAS cases, 2009-2013

Table 1. Numbers (n) and Crude Incidence Rates (CIRs) per 100,000 population of iGAS disease by HSE Area (2009-2013)

HSE Area	2009		2010		2011		2012		2013	
	n	CIR	n	CIR	n	CIR	n	CIR	n	CIR
HSE-E	32	1.98	22	1.36	29	1.79	51	3.15	67	4.14
HSE-M	2	0.71	2	0.71	5	1.77	7	2.48	7	2.48
HSE-MW	5	1.32	6	1.58	6	1.58	8	2.11	16	4.22
HSE-NE	3	0.68	7	1.59	1	0.23	11	2.50	14	3.18
HSE-NW	1	0.39	8	3.10	2	0.77	5	1.94	6	2.32
HSE-SE	8	1.20	5	1.00	7	1.41	16	3.22	21	4.22
HSE-S	5	1.00	12	1.81	12	1.81	14	2.11	18	2.71
HSE-W	4	0.90	6	1.35	5	1.12	10	2.25	19	4.27
IRELAND	60	1.31	68	1.48	67	1.46	122	2.66	168	3.66

CIR for 2009 calculated using the 2006 census; CIRs for 2010-2013 calculated using the 2011 census

Change from previous reports: error in calculation of rates for HSE-SE and HSE-S for 2010-2012, corrected rates are highlighted in red

(IDU) (n=5), varicella infection (n=5) and non-steroidal anti-inflammatory drug (NSAID) use (n=4). Note that an iGAS case could have more than one risk factor. No risk factors were identified for 37 cases.

Among the patients with STSS, risk factor data were provided for 28 cases. Risk factors associated with iGAS disease and STSS included age ≥65 years (n=12), presence of skin or wound lesions (n=10), steroid use (n=7), alcoholism (n=4), diabetes mellitus (n=4), malignancy (n=4), IDU (n=3) and NSAID use (n=3). Note that cases could have one or more associated risk factors. No risk factors were identified for eight STSS cases.

Clinical management/Severity
Surgical intervention was required for 39 patients (aged 10 months – 86 years), which reflects an increase compared to 26 in 2012. This included six patients with STSS, three patients with necrotising fasciitis and three patients with both STSS and necrotising fasciitis.

Among patients requiring surgical intervention, risk factor data were provided for 36 cases. Risk factors included; skin and wound lesions (n=20), age ≥65 years (n=5), diabetes mellitus (n=3), malignancy (n=2), steroid use (n=2), IDU (n=1) and varicella (n=1). Note that an iGAS case requiring surgery could have more than one risk factor. No risk factors were identified for 14 patients.

Forty-four patients (aged 1 – 86 years) required intensive care unit (ICU) admission, which reflects an increase compared to 40 in 2012. This included 20 patients with STSS, four patients with necrotising fasciitis and three patients with both STSS and necrotising fasciitis.

Among patients admitted to an ICU, risk factor data were provided for 39. Risk factors included; age ≥65 years (n=16), skin and wound lesions (n=15), diabetes mellitus (n=4), malignancy (n=4), steroid use (n=4), childbirth (n=3), alcoholism (n=2), IDU (n=2) and NSAID use (n=1). Note that an iGAS case requiring ICU admission could have more than one risk factor. No risk factors were identified for ten patients. Length of ICU stay was provided for 27 cases. The median length of ICU stay was four days (range = 1 – 8).

Other epidemiological information
Five cases (including three with STSS) were reported as hospital-acquired (compared to three in 2012).

In 2013, two iGAS outbreaks were notified: one family outbreak and one hospital outbreak, both with two people ill (compared to just one family outbreak in 2012). There was one additional hospital GAS outbreak (non-invasive) reported in 2013.

Outcome
Outcome at seven-days following GAS isolation was reported for 107 cases:

- 89 were still alive
- 16 patients had died, where GAS was the main or contributory cause of death
- One additional patient had died, but GAS was not a cause of death

The seven-day case fatality rate (CFR) for iGAS disease was 15% in 2013, which is higher than in 2012 (12%). Of 32 STSS cases, outcome at seven-days was reported for 26. Of those, there were ten deaths due to GAS (CFR = 38%).

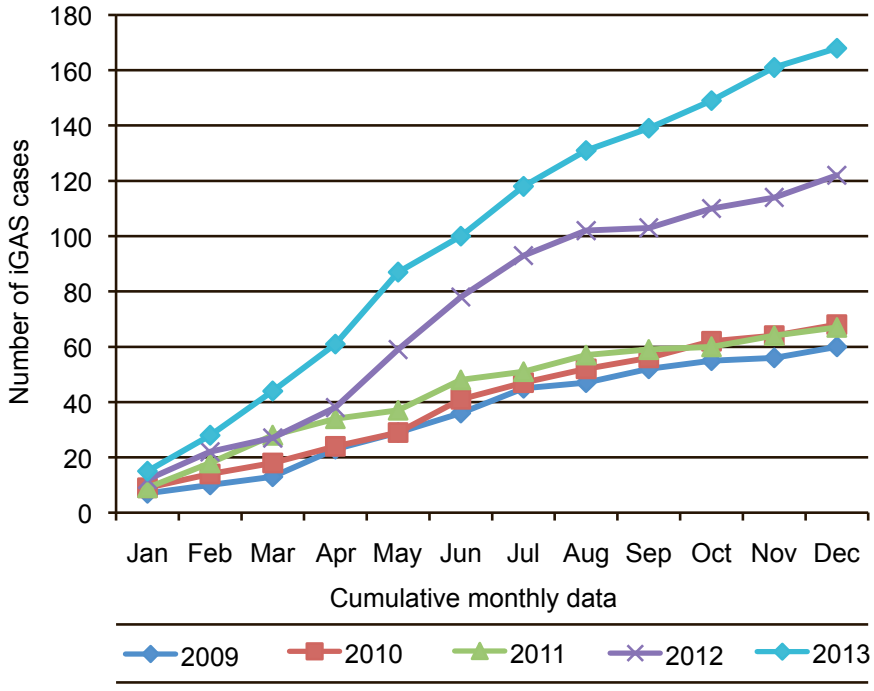

Figure 3. Cumulative monthly numbers of iGAS cases, 2009-2013.

Table 2. Characteristics of iGAS cases in Ireland (2008-2013).

	YEAR					
	2008	2009	2010	2011	2012	2013
Notifications						
Total iGAS cases notified	70	60	68	67	122	168
iGAS incidence rate per 100,000 population	1.65	1.31	1.48	1.46	2.66	3.66
Cases for which Enhanced data provided (%)*	*44 (63%)*	*44 (73%)*	*61 (90%)*	*60 (90%)*	*106 (87%)*	*155 (92%)*
Patient Demographics						
Male (%)	37 (53%)	34 (57%)	36 (53%)	28 (42%)	59 (48%)	95 (57%)
M:F ratio	1.12:1	1.31:1	1.13:1	0.72:1	0.94:1	1.31:1
Mean age	45	47	49	43	44	41
Median age	47	48	39	49	42	41
Age range	0-89	0-95	0-97	0-97	0-92	0-93
Paediatric cases (aged <18 years) (%)	16 (23%)	13 (22%)	10 (15%)	15 (22%)	28 (23%)	45 (27%)
Older cases (aged 65+ years) (%)	18 (26%)	21 (35%)	22 (32%)	22 (33%)	42 (34%)	50 (30%)
Clinical Presentation†						
Data on Clinical Presentation (%)	39 (56%)	42 (70%)	59 (87%)	58 (87%)	103 (84%)	141 (84%)
Streptococcal Toxic Shock-like Syndrome (STSS) without NF (%)	6 (15%)	3 (7%)	7 (12%)	4 (7%)	22 (21%)	28 (20%)
Necrotising fasciitis (NF) without STSS (%)	3 (8%)	1 (2%)	2 (3%)	1 (2%)	2 (2%)	6 (4%)
STSS and NF (%)	1 (3%)	4 (10%)	2 (3%)	2 (3%)	4 (4%)	4 (3%)
Bacteraemia with focal presentations (%)	23 (59%)	14 (33%)	27 (46%)	30 (52%)	42 (41%)	45 (32%)
Bacteraemia with no focal presentations (%)	3 (8%)	18 (43%)	20 (34%)	15 (26%)	21 (20%)	35 (25%)
Other focal presentations with no bacteraemia (%)	3 (8%)	2 (5%)	1 (2%)	6 (10%)	12 (12%)	23 (16%)
Bacteraemia (%)	33 (85%)	39 (93%)	55 (93%)	52 (90%)	80 (78%)	111 (75%)
Other focal presentations:						
Cellulitis (%)	17 (44%)	13 (31%)	22 (37%)	24 (41%)	41 (40%)	45 (32%)
STSS (%)	7 (18%)	7 (17%)	9 (15%)	6 (10%)	26 (25%)	32 (23%)
Pneumonia (%)	6 (15%)	2 (5%)	10 (17%)	8 (14%)	17 (17%)	24 (17%)
Septic arthritis (%)	6 (15%)	2 (5%)	2 (3%)	2 (3%)	7 (7%)	10 (7%)
Myositis (%)	2 (5%)	2 (5%)	2 (3%)	0 (0%)	4 (4%)	3 (2%)
Necrotising fasciitis (%)	4 (10%)	5 (12%)	4 (7%)	3 (5%)	6 (6%)	10 (7%)
Puerperal sepsis (%)	5 (13%)	2 (5%)	4 (7%)	5 (9%)	6 (4%)	6 (4%)
Peritonitis (%)	0 (0%)	0 (0%)	1 (2%)	3 (5%)	1 (1%)	4 (3%)
Erysipelas (%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)	3 (3%)	3 (2%)
Meninigtis (%)	2 (5%)	0 (0%)	2 (3%)	1 (2%)	3 (3%)	3 (2%)
Risk Factors†						
Data on Risk Factors (%)	37 (53%)	36 (60%)	49 (72%)	49 (73%)	98 (80%)	140 (83%)
Skin lesions/wounds (%)	15 (41%)	16 (44%)	16 (33%)	20 (41%)	34 (35%)	55 (39%)
Diabetes (%)	5 (14%)	3 (8%)	8 (16%)	7 (14%)	5 (5%)	16 (11%)
Varicella (%)	2 (5%)	2 (6%)	2 (4%)	2 (4%)	9 (9%)	5 (4%)
Malignancy (%)	3 (8%)	6 (17%)	6 (12%)	6 (12%)	10 (10%)	23 (16%)
Alcoholism (%)	1 (3%)	0 (0%)	3 (6%)	1 (2%)	5 (5%)	6 (4%)
Injecting drug user (%)	2 (5%)	3 (8%)	6 (12%)	3 (6%)	6 (6%)	5 (4%)
Steroid use (%)	4 (11%)	1 (3%)	2 (4%)	1 (2%)	8 (8%)	11 (8%)
Childbirth (%)	5 (14%)	2 (6%)	4 (8%)	5 (10%)	6 (6%)	6 (4%)
Non-steroid anti-inflammatory drug use (%)	3 (8%)	0 (0%)	6 (12%)	1 (2%)	2 (2%)	4 (3%)
No identified risk factor (%)	11 (30%)	10 (28%)	12 (24%)	12 (24%)	25 (26%)	47 (34%)
Outcome at 7 days						
Data on outcome at 7 days (%)	27 (39%)	30 (50%)	43 (63%)	43 (64%)	65 (53%)	107 (64%)
RIP/GAS main cause or contributory (%)	1 (4%)	2 (7%)	4 (9%)	5 (12%)	8 (12%)	16 (15%)
STSS cases: Data on outcome at 7 days (%)	6 (86%)	6 (86%)	8 (89%)	5 (83%)	17 (65%)	26 (81%)
STSS cases: RIP/GAS main cause or contributory (%)	1 (17%)	1 (17%)	2 (25%)	1 (20%)	6 (35%)	10 (38%)
Severity						
Data on Admission to ITU (%)	39 (56%)	40 (67%)	57 (84%)	57 (85%)	99 (81%)	152 (90%)
Admitted to ITU (%)	7 (18%)	16 (40%)	14 (25%)	11 (19%)	40 (40%)	44 (29%)
Data on Surgical Intervention (%)	32 (46%)	28 (47%)	49 (72%)	45 (67%)	86 (70%)	135 (80%)
Surgical Intervention Required (%)	9 (28%)	8 (29%)	12 (24%)	8 (18%)	26 (30%)	39 (29%)
Typing						
iGAS isolates that were typed (%)					109 (89%)	140 (83%)
*emm*1 (%)					53 (49%)	41 (29%)
*emm*3 (%)					4 (4%)	33 (24%)
*emm*12 (%)					10 (10%)	3 (3%)
*emm*28 (%)					8 (7%)	8 (6%)
*emm*89 (%)					4 (4%)	13 (9%)
Other*emm*-types (%)					30 (27%)	42 (29%)

* Degree of completion of enhanced surveillance forms varies from case to case: information may not be available on all variables/categories, thus calculations of percentages take into account only those cases for which data are provided

†Note: A patient may have more than one clinical presentation or risk factor

Of 39 cases requiring surgical intervention, outcome at seven-days was reported for 27. Of those, there were four deaths due to GAS (CFR = 15%).

Of 44 cases admitted to ICU, outcome at seven-days was reported for 32. Of those, there were ten deaths due to GAS (CFR = 31%). One additional patient died, but GAS was not a cause of death.

Antimicrobial susceptibility
In 2013, antimicrobial susceptibility data were reported on 126 GAS isolates (103 from blood and 23 from other specimens) by 20 laboratories via the European Antimicrobial Resistance Surveillance Network (EARS-Net). All isolates tested were susceptible to penicillin (n=110) and vancomycin (n=88). Resistance to erythromycin was reported in five (5%) of 104 isolates, to clindamycin in one (2%) of 51 isolates and to tetracycline in three (7%) of 43 isolates.

CONCLUSION

In 2013, 168 cases of iGAS infection were notified in Ireland, the highest annual number reported to date, representing an increase of 38% on 2012 (n=122). The CIR increased from 2.66 (2012) to 3.66 per 100,000 (2013), but this was not found to be statistically significant.

iGAS is a potentially life-threatening disease. In 2013, the CFR was 15% for all iGAS infections and even higher for patients admitted to ICU (31%) or presenting with STSS (38%). In 2012 and 2013, more patients presented with STSS than in previous years: 26 and 32 cases, respectively, compared with 6-9 cases in each of the previous four years.

emm-typing was undertaken on a national basis for the first time in 2012, with the establishment of a GAS typing service by the Epidemiology and Molecular Biology Unit (EMBU) at the Children's University Hospital, Temple St. In 2013, two *emm* types, *emm*1 and *emm*3 (together representing 74 of 140 isolates), comprised 53% of all isolates typed, compared with just one *emm* type, *emm*1 (53 of 109 isolates), which comprised 49% of all isolates in 2012. Certain *emm* types, including *emm*1 and *emm*3, are associated with STSS, and STSS in turn is strongly associated with increased mortality. The changes observed in the predominant *emm* types in circulation in just one year and in the clinical presentations over the last couple of years highlight the dynamic nature of iGAS infection.

Ongoing surveillance is essential, specifically completion of the enhanced data questionnaire, to gain a greater understanding of iGAS, to enable early detection of clusters/outbreaks, to ensure prompt implementation of infection prevention and control precautions and appropriate management of contacts. Epidemiological typing as provided by EMBU is another vital element to increase insight into GAS infection in Ireland, as certain *emm* types are associated with greater morbidity and mortality.

Antimicrobial susceptibility data confirm that iGAS remains susceptible to penicillin and that penicillin should continue to be the treatment of choice for iGAS.

HPSC thanks participating microbiology laboratories and public health departments for their ongoing contribution to the iGAS enhanced surveillance scheme.

All microbiology laboratories are encouraged:

- to return enhanced iGAS surveillance forms for every patient with iGAS
- to submit all iGAS isolates to the Epidemiology and Molecular Biology Unit (EMBU), Children's University Hospital, Temple St for *emm*-typing
- to submit antimicrobial susceptibility data on all iGAS cases along with EARS-Net quarterly returns

The enhanced surveillance form can be downloaded from the HPSC web site at:
http://www.hpsc.ie/hpsc/A-Z/Other/GroupAStreptococcalDiseaseGAS/SurveillanceForms/

Further information on iGAS disease in Ireland, including factsheets for patients and contacts, national guidelines and a new quarterly report, is available at: http://www.ndsc.ie/hpsc/A-Z/Other/GroupAStreptococcalDiseaseGAS/

The figures presented in this summary are based on data extracted from the Computerised Infectious Diseases Reporting (CIDR) System on **21st July 2014.**