An Investigation Into an Increase in Invasive Group A *Streptococcal* Disease Cases in Rhode Island

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INTRODUCTION

Group A *Streptococcus* (GAS), or *Streptococcus pyogenes,* is a bacteria that can cause a wide range of illnesses, including those that are mild (eg, strep throat) and those that are more severe (eg, bacteremia, necrotizing wound infections, and Streptococcus Toxic Shock Syndrome [STSS]). Invasive GAS disease (iGAS) occurs when GAS invades a normally sterile part of the body, such as the blood, deep muscle tissue, and lungs. These infections can be severe, difficult to treat and are associated with prolonged hospital stays and increased mortality.[1] Elevated risk for iGAS occurs among adults 65 years of age and older, persons with chronic or immunocompromising conditions, people who inject drugs, individuals experiencing homelessness, and residents of congregate care settings.[1]

Active Bacterial Core surveillance (ABCs) is a component of the U.S. Centers for Disease Control and Prevention's Emerging Infections Program and operates among geographically distributed sites in the United States. The ABCs provides national estimates of invasive disease for select pathogens, including iGAS. From 1995 to 2013, iGAS incidence at ABCs sites remained stable. After a temporary decline during the COVID-19 pandemic, incidence rose overall from 2014 to 2023.[2-5]

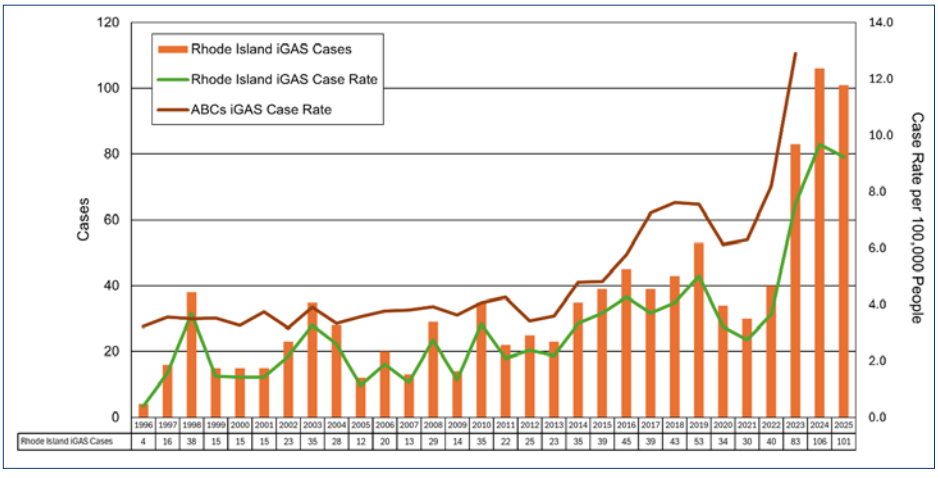
Over the past 20 years, Rhode Island has mirrored what has been observed by ABCs. From 1996 until 2014, iGAS incidence rates remained stable in Rhode Island, averaging 2.0 cases per 100,000. Between 2015 and 2019 cases began to increase, averaging 4.1 cases per 100,000 before decreasing to an average of 3.2 cases per 100,000 from 2020 to 2022 during the COVID-19 pandemic. From 2023 through 2025, the incidence rate of iGAS in Rhode Island drastically increased with an average incidence rate of 8.8 cases per 100,000. This was a 340% increase compared to the average incidence rate of the 19 years between 1996 and 2014 [**Figure 1**]. To investigate this increase, the Center for Acute Infectious Disease Epidemiology (CAIDE) performed enhanced surveillance for confirmed iGAS cases over an 8-month period and the Rhode Island State Health Laboratories (RISHL) performed whole genome sequencing of available *Streptococcus pyogenes* isolates from 2018 to 2025.

METHODS

Through regulation 216-RICR-30-05-01, cases of iGAS and STSS are reportable to the Rhode Island Department of Health and clinical laboratories must submit *Streptococcus pyogenes* isolates grown from sterile sites to the RISHL. A case was considered confirmed if *Streptococcus pyogenes* was isolated from a normally sterile site, such as blood, or if invasive disease was suspected. STSS cases were classified using the 2010 CDC STSS case definition. Confirmed iGAS cases with a specimen collected from November 1, 2023, to June 30, 2024, were included in the enhanced surveillance group for an in-depth medical record review. The 2023 ABCs Case Report Form was used to capture case demographics, hospitalization information, outcome of illness, pregnancy/postpartum status, congregate care associations, underlying health conditions and substance use. Microsoft Excel 365 was used for data storage and analysis.

The RISHL performed whole genome sequencing (WGS) on all available banked *Streptococcus pyogenes* isolates

Figure 1. Twenty-year comparison of Rhode Island and active bacterial core iGAS case surveillance, 1996–2025*



collected from January 1, 2018, to December 31, 2025. Single-colony subcultures were plated on nonselective media and submitted for sequencing. Bacterial DNA was extracted using either New England Biolabs Monarch gDNA Purification Kit or Qiagen EZ1 DSP Virus Kit. Extracts were evaluated for purity and concentration; Zymo DNA Clean & Concentrator-5 Kit was used for additional DNA clean up as needed. Sequencing libraries were prepared using the Illumina DNA Prep Kit, standard protocol, modified for half-volume reactions. Libraries were indexed with compatible Illumina unique dual indexes and pooled. Libraries were sequenced on Illumina MiSeq, MiniSeq, or NextSeq 1000 using paired-end, 300-cycle chemistries. Fastq files were analyzed using *RISHL_Mixed_With_Emmtyping* on GalaxyTrakr, hosted by the U.S. Food and Drug Administration. This pipeline uses Trimmomatic (https://github.com/usadellab/Trimmomatic) for quality and adapter trimming, followed by MicroRunQC (https://github.com/estrain/MicroRunQC), which reports quality metrics and generates a de-novo assembly with SKESA (https://github.com/ncbi/SKESA). A Multi-Locus Species Type (MLST) is generated, utilizing the PubMLST reference set (https://github.com/tseemann/mlst). Identity is confirmed with KRAKEN2 (https://github.com/DerrickWood/kraken2) and *emm* type is determined with emmtyper (https://github.com/MDU-PHL/emmtyper). Suspected antimicrobial resistance genes are identified using AMRFinderPlus (https://github.com/ncbi/amr). Outputs of these analyses are then summarized for interpretation by laboratory personnel. Supplemental analyses for plasmid detection and phylogenetic comparison are carried out offline using PlasmidFinder (https://github.com/genomicepidemiology/plasmidfinder) and IQ-Tree (https://iqtree.github.io/), respectively.

RESULTS

From November 1, 2023, to June 30, 2024, 90 iGAS cases met the inclusion criteria for enhanced surveillance. **Table 1** summarizes the findings. Bacteremia was the most common disease (78.9%). This was followed by pneumonia (present in 13.3% of cases with either bacteremia or another site of disease), STSS (13.3%), and soft tissue necrosis, including necrotizing fasciitis (7.8%). The average length of hospital admission for cases was 7 days with a range of stay from 1 to 123 days. Of cases with a known outcome, 13 (15.3%) died. Cases identified with either STSS and/or soft tissue necrosis were more likely to die (50.0%) than cases without (9.7%).

Overall, 98.8 % of cases had an identified risk factor for invasive disease. The most common risk factors included being greater than or equal to 65 years of age (37.8%), having diabetes mellitus (32.2%) and either having a recent positive test for a respiratory virus (17.8%) or having a recent respiratory-like illness (11.1%). The Rhode Island Child and Adult Immunization Registry (RICAIR) was utilized to determine the influenza vaccination status of each case for the 2023–2024 flu season. Of the 90 cases, 37.7% received an influenza vaccination in the year prior to their iGAS illness onset date. This was slightly higher than Rhode Island's statewide influenza vaccination coverage (35.3%) for the 2023–2024 influenza season. Residents of long-term care facilities (LTCF) and assisted living residences (ALR) were also found to be

Table 1. Characteristics of iGAS Cases, Rhode Island, November 1, 2023 to June 30, 2024

Characteristic	Number of Cases (N= 90)	Percent of Cases
Age (Years)		
0–19	9	10.0
20–39	12	13.3
40–64	35	38.9
>=65	34	37.8
Sex		
Female	43	47.8
Male	47	52.2
Site of Disease*		
Bacteremia	71	78.9
Bacteremia with Pneumonia	8	8.9
Other Site of Focus	7	7.8
Other Site of Focus with Pneumonia	4	4.4
Streptococcal Toxic Shock Syndrome	12	13.3
Soft Tissue Necrosis, Including Necrotizing Fasciitis	7	7.8
Tenosynovitis	5	5.6
Cellulitis	30	33.3
Risk Factors*		
Diabetes Mellitus	29	32.2
Heart Disease, Chronic	7	7.8
Homelessness or Unsteady Housing	1	1.1
Recent Respiratory Illness	26	28.9
Immunosuppressed	5	5.6
Lung Disease, Chronic	9	10.0
Malignancy, Hematologic	4	4.4
Malignancy, Solid Organ	12	13.3
Obesity	6	6.7
Recent Surgery/Skin Trauma	17	18.9
Renal Failure, Chronic	7	7.8
Resident of Congregate Care Facility	10	11.1
Injecting Drug Use	5	5.6
Survived		
Yes	72	80.0
No	13	14.4
Unknown	5	5.6

*Cases may have had more than one site of disease and risk factor identified.

Table 2. Common predicted *emm* types identified, Rhode Island, 2018–2025

Predicted *EMM* Type	2018	2019	2020	2021	2022	2023	2024	2025	Total
*emm*1.0	9	11	1	1	6	25	39	5	97
*emm*3.1	0	0	0	0	0	6	19	2	27
*emm*11.0	1	0	1	0	1	4	4	10	21
*emm*12.0	3	2	1	0	3	13	1	0	23
*emm*49.0	0	1	1	0	0	0	1	13	16
emm77.0	3	1	5	3	0	2	1	1	16
*emm*81.0	0	0	0	1	8	1	0	0	10
*emm*82.0	0	0	1	1	0	2	1	16	21
*emm*89.0	5	4	2	1	1	8	7	5	33
*emm*92.0	0	0	0	1	4	9	7	2	23

at an increased risk for iGAS. Over the 8-month enhanced surveillance period, of the 10 cases residing in congregate settings prior to their illness onset, eight were determined to be residents of these facility types, leading to the identification of two outbreaks.

Of the 451 isolates submitted for sequencing, 429 were confirmed as GAS and successfully sequenced. Sequenced isolates passing acceptable quality metrics (429/451) were uploaded to NCBI BioProject PRJNA854046 and to Sequence Read Archive (SRA). WGS showed drastic changes to *emm* types and diversity from 2018–2025. **Table 2** summarizes these changes and highlights the predominant *emm* types circulating in Rhode Island.

DISCUSSION

The dramatic increase in iGAS cases since 2023 has had an impact on the health of Rhode Islanders. Although no single or combination of risk factors were identified as the cause of the increase, it was clear that having at least one risk factor put an individual at risk for acquiring a severe Group A *Streptococcus* infection. Residents of LTCFs or ALRs face higher risk due to increased age, underlying health conditions and congregate living. During the study period, eight iGAS cases were identified among residents of these facilities. Additional resident cases have been identified since June 30, 2024. Overall, in 2024–2025, 38 iGAS cases were associated with these facility types, leading to the identification of seven outbreaks.

WGS of GAS isolates, has established a robust phylogenetic framework, enabling the integration of genetic, phenotypic and epidemiologic data to support early outbreak detection and response. In addition, there is now a better understanding of the history of circulating strains in Rhode Island. Some *emm* types, such as 1 and 89, can be considered endemic and have been present in Rhode Island every year since at least 2018. Some *emm* types (eg, *emm*11), were rare pre-pandemic and now constitute a large subset of new cases. Other *emm* types (eg, *emm*12) were well represented pre/early pandemic but are virtually non-existent post-pandemic [**Table 2**]. The change in circulating *emm* types over the past 7 years has likely played a role in the increase in iGAS cases due to more severe strains being present in larger quantities.

During the 8-month enhanced surveillance period, 12 STSS cases were identified through medical record review. In total, 16 STSS cases were reported in 2024, representing a substantial increase compared with the prior decade (2014–2023), when fewer than two cases were reported annually. Several factors may explain this increase. Although STSS is a reportable condition at both the national level and in Rhode Island, requiring healthcare providers to report cases, the national case definition is based on specific clinical criteria. As a result, reporting to RIDOH depends on provider recognition and diagnosis of syndrome, which may have led to underreporting in prior years. Additionally, although many *emm* types can cause STSS, *emm* types 1 and 3 are often associated with STSS.[6] Of the 21 STSS cases identified from 2024–2025 with a known *emm* type, 61.9% were either *emm*1.0 or *emm*3.1.

The enhanced surveillance system implemented during the 8-month iGAS investigation was critical for identifying previously unreported STSS cases, and iGAS cases among residents of LTCFs and ALRs. The findings enabled timely infection prevention and control interventions to further transmission. Enhanced case investigation and WGS remain central to surveillance efforts and facilitated identification of an iGAS outbreak among individuals experiencing unstable housing in Rhode Island in December 2025. Although the increase in GAS activity represents an ongoing public health concern, strengthened surveillance capacity has improved early detection, guided targeted interventions and increased awareness among healthcare providers and the public.

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