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Evaluating Household Transmission of Invasive Group A *Streptococcus* Disease in the United States Using Population-based Surveillance Data, 2013–2016

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Abstract

Using population-based surveillance data, we quantified the secondary invasive group A *Streptococcus* disease risk among household contacts. The disease risk in the 30 days postexposure to an index-case patient was highest among individuals aged ≥65 years, versus the annual background incidence of all ages.

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Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Keywords

group A *Streptococcus*; *Streptococcus pyogenes* ; epidemiology; surveillance; disease transmission

In the United States, ~93% of people with invasive group A *Streptococcus* (iGAS) infections are hospitalized and 12% die [1]. Transmission primarily occurs through direct person-to-person contact. Close household contacts of people with iGAS disease are at increased risk for developing disease following exposure to the index-case patient [2–7]. Since the Centers for Disease Control and Prevention's (CDC's) 2002 publication of public health guidelines for the control of iGAS disease among household contacts of people with iGAS infection [3], no additional US studies of household iGAS disease transmission have been conducted; only 5 population-based studies estimating risk have been published worldwide [2, 4–7].

Using previously described methods [7], we retrospectively reviewed active, population-based surveillance data to identify household iGAS disease clusters and update risk estimates of subsequent iGAS infections among household contacts.

METHODS

Surveillance for Invasive Group A *Streptococcus* Infections

Active Bacterial Core surveillance (ABCs), part of the CDC's Emerging Infections Programs network, operates in 10 US sites (https://www.cdc.gov/abcs/index.html). For each iGAS case, surveillance officers complete a standardized case report form that includes questions on demographics, residence at time of illness (eg, private residence, nursing home), and underlying medical conditions. Available GAS isolates are sent to the CDC for *emm* typing (https://www.cdc.gov/streplab/protocol-emm-type.html).

Identification of Invasive Group A *Streptococcus* Household Clusters

We reviewed all iGAS cases reported to ABCs in 2013–2016 that were from people living in private residences. We first defined a potential household cluster as ≥2 iGAS cases (regardless of *emm* type or isolate availability) in patients whose cultures were collected within 30 days of each other and who lived in the same zip code or county (if zip was missing). Surveillance officers next verified whether those individuals with GAS disease within a cluster had the same address and, if so, determined their relationship based on a database review. Potential household clusters occurring in persons living at the same private residence and caused by the same *emm* type were considered as confirmed household clusters. Among each household cluster, the case occurring in the first person with a positive GAS culture was considered the index case; remaining cases were considered secondary cases.

Statistical Analysis

We performed a descriptive analysis of iGAS cases within each household cluster and calculated the secondary attack rate (sAR) per 100 000 contacts (number of secondary cases among total household contacts) in the 30 days following exposure. We also represented

the sAR in the 30 days after exposure as cases per 100 000 person-years. Excluding index cases, we estimated the total number of household contacts among all iGAS patients in private residences, based on average household sizes for the patients' states, using US Census Bureau data (https://www.census.gov/quickfacts/fact/table/CT/HSD310216). Using the ABCs population as our denominator, we calculated the annual incidence of sporadic iGAS disease. We calculated the number needed to treat (NNT) with antibiotic prophylaxis to prevent 1 secondary iGAS disease case, assuming 100% adherence and chemoprophylaxis effectiveness.

We calculated sARs and NNTs for (1) household clusters with ≥3 days between the index and secondary cases of infection; and (2) household clusters with ≥1 secondary case of infection in a person aged ≥65 years. We chose the ≥3-day interval because this time interval may be necessary to identify, contact, and offer prophylaxis to household contacts. To calculate the total number of household contacts aged ≥65 years, we used 2010 [8] and 2018 Census data (https://www.census.gov/data/tables/2017/demo/families/cps-2017.html) to estimate the proportion of households including a person aged ≥65 years. We calculated a weighted average number of contacts aged ≥65 years for each reported iGAS case from a private residence by multiplying this proportion by the average household size for an individual aged ≥65 years, based on 2014 data from the US Bureau of Labor Statistics (https://www.bls.gov/opub/btn/volume-5/spending-patterns-of-older-americans.htm).

RESULTS

Descriptive Analysis

From 2013–2016, ABCs identified 5416 cases of iGAS infection from people living in private residences. We identified 9 confirmed household clusters consisting of 1 index case and 1 secondary case and 2 possible clusters in which index and secondary cases occurred in residents of the same assisted living facility, but whose apartment numbers could not be confirmed. For all cases in each potential cluster in which persons resided at the same address, *emm* types were known and were identical. Characteristics of cases from confirmed and possible household clusters are described in Table 1. Approximately 0.2% (n = 9) of 5416 iGAS cases were secondary cases in confirmed household clusters. In confirmed household clusters, the median ages of patients with primary and secondary cases were 68 years and 67 years, respectively. The median interval between the index and secondary cases was 6 days (range: 0–30 days); 7 secondary cases occurred ≥3 days after the index cases and 8 occurred within 14 days. The most common relationships among confirmed clusters were spouses (n = 3 pairs) and parent/child pairs (n = 3). Chronic medical conditions and presenting clinical syndromes are shown in Table 1.

Attack Rate and Number Needed to Treat

The annual incidence of sporadic iGAS infections in ABCs during 2013–2016 was 4.0/100 000 population; among households with an iGAS case, the estimated sAR in the 30 days following the illness in the index case was 102/100 000 contacts (1240/100 000 person-years). Assuming 100% effective antibiotic prophylaxis, 1022 household contacts would

need to receive chemoprophylaxis in the 30 days after exposure to prevent 1 secondary case of iGAS disease.

Excluding secondary cases occurring <3 days following a primary case, the sAR in the 30 days after exposure to an index case was 79/100 000 contacts (964/100 000 person-years); the NNT to prevent a secondary case in the household was 1329. Among household clusters where the person with a secondary case was aged ≥65 years (5 of 9), the sAR in the 30 days following exposure to the index case was 339/100 000 contacts (4122/100 000 person-years) and the NNT was 303. The annual incidence of iGAS infections among persons aged ≥65 years in 2013–2016 was 8.6 cases/100 000 population.

DISCUSSION

We estimated the increase in the iGAS disease risk among household contacts, compared to the overall incidence of sporadic iGAS infection; most secondary cases occurred <2 weeks following the index patient's GAS culture. The resulting annual sAR was similar to the prospective US study conducted in 1997–1999 [4]. However, our current estimate is more robust. The previous study was conducted over 28 months at 4 ABCs sites, while this study was conducted over 48 months at 10 sites, allowing for the identification of more household clusters (1 cluster vs 9 clusters, respectively) and an estimation of the secondary disease risk among persons aged ≥65 years. The risk of a secondary iGAS infection was highest among those ≥65 years old, similar to other household transmission studies [7] and consistent with increased risks for sporadic iGAS disease and death among this age group [2].

The disease risk among household contacts in the United States was lower than those found in Canada, Australia, and the United Kingdom [2, 5–7] (see Supplementary Table); reasons for these differences are unclear. The risks in US studies were lower than those in other countries regardless of the methodological approach, suggesting a cause other than differing methodology for observed differences. Varying risks may be due to differences in GAS disease epidemiology between countries, possibly linked to household sizes or differences in frequencies of exposure to young children in homes: living with young children with GAS pharyngitis increases the risk of GAS infection among household members [9, 10]. Despite the increased risk of disease among household contacts, household transmission of an iGAS infection is relatively uncommon. Only 46 cases of subsequent infections were identified among >14 000 index cases across all studies.

Current US guidance does not recommend routine prophylaxis for household contacts, but provides a permissive recommendation to offer chemoprophylaxis to household members aged ≥65 years or with other risk factors for iGAS infection [3]. (Recommended antibiotic regimens include benzathine penicillin [intramuscular] and rifampin; azithromycin; clindamycin; and first-generation cephalosporins.) In the United Kingdom, prophylaxis is recommended for both mother and baby if either develops an iGAS infection in the neonatal period, due to an increased risk of disease in this subpopulation, and to the entire household if ≥2 iGAS cases occur in a 30-day period [11]. In Canada, prophylaxis is recommended for close contacts of confirmed severe cases who were exposed to the index patient during

the period from 7 days prior to symptom onset to 24 hours after the index patient initiates antibiotics [12].

This analysis is subject to limitations. First, because this is a retrospective review of population-based surveillance data, we could not definitively identify the number of household contacts of each iGAS patient; the use of Census data may result in either an overestimation or underestimation of the risk of a secondary iGAS infection. However, when surveillance personnel directly contacted index patients in the prior US study to identify and count household contacts, the average number of household contacts was 1.4 (4), similar to our current study (1.6). We were unable to track household members who developed noninvasive GAS disease. For NNT calculations, we did not account for medication nonadherence and the unknown effectiveness of antibiotics in preventing iGAS infections in household contacts. Last, we did not estimate the risk of secondary infections in contacts in nonhousehold settings with an increased risk for iGAS disease (eg, homeless shelters, nursing homes) [13, 14].

CONCLUSION

Although the household transmission of iGAS disease is uncommon, we observed an increased risk of disease among household contacts in the 30 days following the index patient illness, especially in those ≥65 years old. Targeting recommendations for providing chemoprophylaxis to household contacts aged ≥65 years old should be considered when updating guidelines for public health responses to sporadic community iGAS infections.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Potential conflicts of interest.

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Table 1.

Confirmed and Possible Household Clusters of Invasive Group A *Streptococcus*, Active Bacterial Core Surveillance, 2013–2016

ABCs site	Sex	Age, years	Race	Relationship	Interval between cases, days	*emm* Type	Clinical Syndrome	Underlying Medical Conditions	Survived?
Site A	F	91	W	Mother	…	82	Cellulitis	Dementia	Y
	M	54	W	Son	5	82	Bacteremia	Smoker	Y
Site A	F	53	W	Wife	…	49	Cellulitis	Immunosuppressive therapy	Y
	M	53	U	Husband	30	49	Cellulitis	None	Y
Site A	F	36	W	Mother	…	101	Chorioamnionitis	None	Y
	F	0	W	Baby	0	101	Meningitis	None	Y
Site B	F	70	W	Daughter	…	3	Septic shock	Diabetes	Y
	M	95	W	Father	6	3	Pneumonia	CVA, CKD, CSD, diabetes	Y
Site C	F	24	B	Granddaughter	…	3	Abscess (parotid gland)	AIDS, asthma, drug use, smoker	Y
	F	72	B	Grandmother	6	3	Meningitis	ASCVD, CKD, diabetes	Y
Site D	M	42	W	Unknown relationship	…	1	Pneumonia	Smoker	Y
	M	48	W		0	1	Pneumonia	CRI, COPD	Y
Site E	F	78	U	Wife	…	92	Bacteremia	Asthma, obesity	Y
	M	82	U	Husband	11	92	Cellulitis	CVA, diabetes, CHF	Y
Site F	F	49	W	Fiancée	…	118	Bacteremia	Asthma, diabetes	N
	M	67	W	Fiancé	12	118	Abscess, septic shock	Alcohol abuse, CVA, diabetes, COPD, PVD, smoker	N
Site F	F	92	W	Mother	…	12	Pneumonia	Influenza	N
	F	69	W	Daughter	3	12	Pneumonia, septic shock	Diabetes, influenza	N
Site D[a] Possible cluster	M	92	U	Unknown relationship	…	89	Bacteremia	Solid organ malignancy	N
	M	89	W		25	89	Septic arthritis	CKD, dementia, diabetes, CHF, peripheral neuropathy	Y

ABCs site	Sex	Age, years	Race	Relationship	Interval between cases, days	*emm* Type	Clinical Syndrome	Underlying Medical Conditions	Survived?
Site D[a] Possible cluster	F	77	W	Unknown relationship	…	89	Cellulitis	CKD	Y
	F	85	W		6	89	Septic shock	CVA, Diabetes, Peripheral neuropathy	Y

Abbreviations: ABCs, Active Bacterial Core Surveillance; AIDS, acquired immunodeficiency syndrome; ASCVD, atherosclerotic cardiovascular disease; B, Black; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRI, chronic renal insufficiency; CSD, chronic skin breakdown; CVA, cerebrovascular accident; F, female; M, male; PVD, peripheral vascular disease; U, Unknown; W, White.

[a]Possible cluster: cases were in patients from same assisted living facility, but the patients' apartment numbers could not be confirmed.