Added Value of the *emm*-Cluster Typing System to Analyze Group A *Streptococcus* Epidemiology in High-Income Settings

To the Editor—A new *emm*-cluster typing system has been recently proposed for group A *Streptococcus* (GAS) [1]. This system classifies most of the 223 *emm* types [2] into 48 functional *emm* clusters containing closely related M proteins that share structural properties. *emm* clusters help to predict the virulence potential of any GAS isolate by ascribing M protein binding attributes to *emm* types belonging to the same *emm* cluster [1, 3]. This system correlates with M protein vaccine antigen content and serves as a framework to investigate immunologic cross-protection between *emm* types [1, 4, 5]. *emm* clusters have been used to analyze the epidemiology of GAS in the Pacific region, which is characterized by high GAS disease burden and a great variety of circulating *emm* types [6, 7]. The *emm*-cluster system identified epidemiologic similarities across the Pacific region and highlighted vaccine target priorities [8].

We applied the *emm*-cluster system to GAS epidemiology in a high-income setting by analyzing prospective surveillance data for GAS pharyngitis in North America, 2000–2007 [9]. A total of 56 and 33 different *emm* types were recovered from 7040 US and 1434 Canadian GAS

Table 1. Frequencies of *emm* Types and *emm* Clusters Among 7040 Group A *Streptococcus* Isolates Recovered From Pharyngitis in the United States

			% of Isolates	
emm Type	*emm* Cluster	No.	All Isolates	15 Most Frequent *emm* Types
2, 8, 22, 28, 73, 77, 89, 102, 114	E4[a]	1912	27.16	26.68
1, 163	A-C3[a]	1252	17.78	17.76
12	A-C4[a]	1236	17.56	17.56
4, 60, 78	E1[a]	696	9.89	9.62
3	A-C5[a]	614	8.72	8.72
11, 48, 63, 75, 94, 177	E6[a]	429	6.09	5.87
6	M6[a]	393	5.58	5.58
9, 44, 49, 58, 82, 87, 103, 118, 219	E3[a]	350	4.97	3.85
5	M5[a]	106	1.51	1.51
33, 41, 43, 53, 70, 83, 101, 119	D4	17	0.24	
18	M18[a]	14	0.20	
62, 68, 76, 92, 96, 110, 117	E2[a]	12	0.17	
170, 205	E5	4	0.06	
14	M14	1	0.01	
57	M57	1	0.01	
74	M74	1	0.01	
234	M234	1	0.01	
236	M236	1	0.01	
		7040	100.00	97.15

The *emm*-type data originate from a previous study [9]. The 15 most frequent *emm* types are underlined.
[a] Stands for the *emm* cluster in common with the Canadian collection (1434 isolates).

isolates, respectively. In contrast with the Pacific region, the 15 most prevalent *emm* types accounted for 97.1% and 96.9% of GAS pharyngeal isolates, respectively, indicating that only a relative minority of *emm* types are responsible for most pharyngitis in North America.

By deducing the *emm*-cluster allocation from the *emm*-typing results [1], we observed that the 56 US *emm* types belonged to 18 *emm* clusters (Table 1), whereas the 33 Canadian *emm* types belonged to 14 *emm* clusters (data not shown). Eleven *emm* clusters were responsible for the majority of cases in both countries (99.6% and 98.7%, respectively) (Table 1). *emm* types 1 and 12 were the 2 most common *emm* types in the United States (17.8% and 17.6%, respectively) [9], but did not belong to the most common *emm* cluster; rather, *emm* cluster E4 (notably including the frequent *emm* types 2, 22, 28, 77, and 89) was more common (27.2%). Furthermore, we observed that 8 of the 56 *emm* types belonged to *emm* cluster D4, although representing only a small number of isolates (17 of 7040), a surprising result given that *emm* cluster D4 is associated with skin rather than pharyngeal infections [1]. Finally, *emm* cluster E2, which includes 15 *emm* types, was nearly completely absent from North America (0.2%–0.5% of isolates), whereas it was the most frequent *emm* cluster in New Caledonia (21% of isolates), suggesting that some *emm* clusters are restricted to defined geographical areas.

As shown here, and in the study in New Caledonia, application of the *emm*-cluster system to both tropical and nontropical settings improves our understanding of complex GAS epidemiology. This new system helps to refine clinically meaningful questions such as tissue tropism and the immune response to GAS infections in all settings worldwide.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

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