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Clonal characteristics of invasive *Neisseria meningitidis* following initiation of an A + C vaccination program in China, 2005–2012

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Summary *Objectives:* To reveal the population structure of invasive *Neisseria meningitidis* isolates after the initiation of an A + C vaccination program in China.
Methods: Multilocus sequence typing (MLST) and PorA typing were used to characterize 238 invasive *N. meningitidis* isolates collected in China between 2005 and 2012.
Results: During this period, sequence type (ST)-5, ST-4821 and ST-11 complexes were dominant among serogroups A, C and W, accounting for 100%, 98.5% and 100% of each serogroup, respectively. P1.20,9, P1.7-2,14 and P1.5,2 were the dominant *PorA* types of serogroups A, C and W, respectively. Serogroup B showed high genetic diversity with two dominant lineages: ST-4821 complex and ST-5662 subgroup.
Conclusions: The population of 238 invasive *N. meningitidis* isolates was primarily composed of a select group of recognized hypervirulent lineages. Among these clonal complexes, ST-7 serogroup A and ST-11 serogroup W are distributed globally, and other three clones exist only in China.
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Introduction

Neisseria meningitidis remains a leading cause of bacterial meningitis and septicemia throughout the world, and most cases of meningococcal disease are caused by serogroups A, B, C, Y and W.[1] In the 20th Century, over 95% of meningococcal disease cases in China were caused by serogroup A *N. meningitidis*, and reported annual disease incidence reached up to 400 cases per 100,000 inhabitants.[2] Following the initiation of a national immunization program using a serogroup A polysaccharide-based vaccine in early 1980s, only sporadic cases were reported in the following two decades. However, during 2003—2004, a new hyperinvasive lineage (ST-4821 serogroup C) was identified in China.[3] This lineage spread nationwide and caused several outbreaks of serogroup C meningococcal disease in 2004—2005 and an increase in the number of serogroup C cases over the next few years.[4] In 2005 a national vaccination program, using a polysaccharide-based A + C vaccine was initiated to replace the serogroup A polysaccharide-based vaccine.

To better understand the population structure of invasive *N. meningitidis* isolates after the initiation of an A + C vaccination program in China, we used multilocus sequence typing (MLST) and PorA typing to characterize invasive isolates collected in China over the 8 years, between 2005 and 2012, following the initiation of the A + C vaccination program.

Materials and methods

Bacterial isolates and serogroups

The tested isolates in this study were received by the Nationally Active, Laboratory-based Surveillance Network as part of the routine disease surveillance between 2005 and 2012 and came from 27 provinces in China (Table 1). All 27 provinces have laboratories that routinely collect pathogenic *N. meningitidis* isolates and were requested to send isolates to the central laboratory in Chinese Center for Disease Control and Prevention (China CDC) for surveillance and research. During 2005—2012, a total of 348 laboratory-confirmed meningococcal diseases were reported and 238 (68.4%) invasive *N. meningitidis* isolates were sent to the central laboratory. During 2005—2012, the incidences of meningococcal disease in China were lower than 0.2 cases/100,000 inhabitants, with 185—2698 cases reported each year. These tested isolates represented 3.17% of reported meningococcal diseases. The serogroup distribution of the 348 laboratory-confirmed meningococcal diseases was 47.1% serogroup C ($n = 164$), 35.3% serogroup A ($n = 123$), 12.9% serogroup B ($n = 45$), 4.0% serogroup W ($n = 14$), 0.3% serogroup X ($n = 1$), and 0.3% nongroupable ($n = 1$). The 238 isolates which sent to the central laboratory in China CDC, accounting for 79.9% of serogroup C ($n = 131$), 52.0% of serogroup A ($n = 64$), 64.4% of serogroup B ($n = 29$), 85.7% of serogroup W ($n = 12$), 100.0% of serogroup X ($n = 1$) and nongroupable

Table 1 Number of *N. meningitidis* used in this study according to province and year.

	2005	2006	2007	2008	2009	2010	2011	2012	Total
Anhui	11	15	5		5		1	3	43
Beijing	4	3	3		4				14
Chongqing	1								1
Fujian	1	3	3						7
Gansu	1			1		1			3
Guangdong	9	5	1	3	3	6	5	4	36
Guangxi	1			1			2		4
Guizhou	1		1			2			4
Hebei	2				1			1	4
Henan	1							1	2
Heilongjiang						2			2
Hubei		1	5		2	2	2	1	13
Hunan				1				2	3
Jilin		2	1						3
Jiangsu	13	3			1	4	3		24
Jiangxi	1	2	2	5					10
Liaoning			1	1		3			5
Ningxia			1						1
Qinghai	3								3
Shandong	2	3	1			4	2	1	13
Shanxi	1								1
Shanghai	3	6	11			1	4		25
Sichuan	1	1		1					3
Tianjin	2								2
Xinjiang			1		1				2
Zhejiang	4	7	1				1		13
Total	62	51	37	13	17	25	20	13	238

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