

## Letters to the Editor

### Invasive Meningococcal Disease Caused by *Neisseria meningitidis* Strains Expressing Both Serogroup Y and W-135 Antigenic Specificities<sup>∇</sup>

We read with interest of three *Neisseria meningitidis* strains recovered in Germany that reacted with commercial (Oxoid, Wesel, Germany) serogroup Y and serogroup W135 antisera (3). The molecular basis of this dual antigenic specificity has been determined to be due to a single amino acid change at position 310 in the EX<sub>7</sub>E motif of the capsule polymerase enzyme *synG* (also referred to as *siaD*<sub>Y</sub>) (from glycine to serine) or *synF* (*siaD*<sub>W-135</sub>) (from proline to serine) (2). Both studies confirmed our earlier report of such unusual strains causing invasive meningococcal disease (IMD) (10).

Here we report three other IMD cases caused by similar meningococcal strains in patients residing in an urban area of Alaska. These strains were collected by the Arctic Investigation Program, located in Anchorage, AK, which began statewide surveillance for IMD in 2000. The three cases of IMD reported here were identified through the interlaboratory quality control program implemented as part of the International Circumpolar Surveillance system established in 1999 to monitor infectious diseases of concern in the Arctic (11). Case 1 occurred in July 2006 in a 25-year-old female, while cases 2 and 3 occurred in August and October of 2008 in a male and a female infant less than 12 months old, respectively. There was no known epidemiological link between these cases. In all three cases the *N. meningitidis* strains were recovered from blood cultures. The serogroup of the isolates was determined by PCR (1, 7) and agglutination with specific rabbit antisera (BD Difco, Sparks, MD). Serotypes, serosubtypes, and PorB and PorA VR genotypes as well as multilocus sequence types (MLST) were determined using established methods as previously described (6). Sequencing of the *siaD* genes was accomplished by methods previously described (10).

All three isolates were identified as serogroup Y by genotyping using PCR but agglutinated in both anti-Y and anti-W135 antisera. The antigenic and genetic characteristics of these three isolates are summarized in Table 1.

It is striking to note that all three isolates have the same mutations in their capsule polymerase enzyme that involved incorporation of the amino acid serine into position 310 in

the EX<sub>7</sub>E motif, which apparently allows the isolates to assemble both glucose and galactose, together with sialic acid, into their capsular polysaccharide structure (2, 10). In addition, it is interesting to note that these three IMD isolates in Alaska have all the antigenic and genetic features characteristic of serogroup Y *N. meningitidis* strains (5, 8, 9).

Therefore, it is tempting to speculate that these unusual *N. meningitidis* strains may be derived from serogroup Y strains by acquiring a mutation in their capsule polymerase enzyme (G310S) to allow expression of this unique antigenic specificity. The emergence of these strains was coincident with the increase in serogroup Y strains in both the United States (4) and Canada (8), which may favor the argument that they were derived from serogroup Y meningococci.

In summary, surveillance of meningococcal disease with tests that can correctly identify these unusual isolates (2, 10) and MLST may help to determine the genetic background and molecular epidemiology of this group of meningococci.

#### REFERENCES

1. Borrow, R., H. Claus, U. Chaudhry, M. Guiver, E. B. Kaczmarski, M. Frosch, and A. J. Fox. 1998. *siaD* PCR ELISA for confirmation and identification of serogroup Y and W135 meningococcal infections. *FEMS Microbiol. Lett.* **159**:209–214.
2. Claus, H., K. Stummeyer, J. Batzilla, M. Muhlenhoff, and U. Vogel. 2008. Amino acid 310 determines the donor substrate specificity of serogroup W-135 and Y capsule polymerase of *Neisseria meningitidis*. *Mol. Microbiol.* **71**:960–971.
3. Claus, H., W. Matsunaga, and U. Vogel. 2010. Molecular discrimination between *Neisseria meningitidis* serogroups W-135 and Y based on the nucleotide recognition domain sequence of the capsule polymerase. *J. Clin. Microbiol.* **48**:3459–3460.
4. Harrison, L. H., K. A. Jolley, K. A. Shutt, J. W. Marsh, M. O'Leary, L. T. Sanza, M. C. J. Maiden, and the Maryland Emerging Infections Program. 2006. Antigenic shift and increased incidence of meningococcal disease. *J. Infect. Dis.* **193**:1266–1274.
5. Harrison, L. H., K. A. Shutt, S. E. Schmink, J. W. Marsh, B. H. Harcourt, X. Wang, A. M. Whitney, D. S. Stephens, A. A. Cohn, N. E. Messonnier, and L. W. Mayer. 2010. Population structure and capsular switching of invasive *Neisseria meningitidis* isolates in the pre-meningococcal conjugate vaccine era—United States, 2000–2005. *J. Infect. Dis.* **201**:1208–1224.
6. Law, D. K. S., M. Lorange, L. Ringuette, R. Dion, M. Giguere, A. M. Henderson, J. Stoltz, W. D. Zollinger, P. De Wals, and R. S. W. Tsang. 2006. Invasive meningococcal disease in Quebec, Canada, due to an emerging clone of ST-269 serogroup B meningococci with serotype antigen 17 and serosubtype antigen P1.19 (B:17:P1.19). *J. Clin. Microbiol.* **44**:2743–2749.
7. Mothershed, E. A., C. T. Sacchi, A. M. Whitney, O. A. Barnett, G. W. Ajello, S. Schmink, L. W. Mayer, M. Phelan, T. H. Taylor, Jr., S. A. Bernhardt, N. E. Rosenstein, and T. Popovic. 2004. Use of real-time PCR to resolve slide agglutination discrepancies in serogroup identification of *Neisseria meningitidis*. *J. Clin. Microbiol.* **42**:320–328.
8. Tsang, R. S. W., S. G. Squires, W. D. Zollinger, and F. E. Ashton. 2002. Distribution of serogroups of *Neisseria meningitidis* and antigenic characterization of serogroup Y meningococci in Canada, January 1, 1999 to June 30, 2001. *Can. J. Infect. Dis.* **13**:391–396.
9. Tsang, R. S. W., A. M. Henderson, M. L. Cameron, S. D. Tyler, S. Tyson, D. K. S. Law, J. Stoltz, and W. D. Zollinger. 2007. Genetic and antigenic analysis of invasive serogroup Y *Neisseria meningitidis* isolates collected from 1999 to 2003 in Canada. *J. Clin. Microbiol.* **45**:1753–1758.
10. Tsang, R. S. W., C. M. Tsai, A. M. Henderson, S. Tyler, D. K. S. Law, W. Zollinger, and F. Jamieson. 2008. Immunochemical studies and genetic

TABLE 1. Phenotypic and genetic characterization of Y/W135:2c:P1.5 *Neisseria meningitidis* strains<sup>a</sup> from Alaska

Strain	PorB VR type	PorA VR type	MLST typing
VR1	C	5–1	ST-1624
VR2	2c	10–4	(ST-167 clonal complex)
VR3	2bb	36–2	
VR4	Db		

<sup>a</sup> Strains from cases 1 to 3 appeared to be identical by phenotypic and genetic characterizations. The capsule polymerase enzyme EX<sub>7</sub>E motif amino acid composition for Y/W135:2c:P1.5 was EGFSYIFLE (the serine at position 310, believed to be important for donor substrate specificity, is highlighted in bold).

background of two *Neisseria meningitidis* isolates expressing unusual capsule polysaccharide antigens with specificities of both serogroup Y and W135. *Can. J. Microbiol.* **54**:229–234.

11. **Zulz, T., M. G. Bruce, and A. J. Parkinson.** 2009. International Circumpolar Surveillance: prevention and control of infectious diseases: 1999–2008. *Circumpolar Health Suppl.* **4**:13–30.

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