G76 Virulence Factors in Neisserial Meningococcemia

Wendy M. Gunther, MD, Office of the Chief Medical Examiner and Department of Legal Medicine, Virginia Commonwealth University, 830 Southampton Avenue, Suite 100, Norfolk, VA 23510-1046; Gregory Racszniak, MPhil, Eastern Virginia Medical School, 714 Woodis Avenue, Norfolk, VA 23510; Elizabeth L. Kinnison, MD, Office of the Chief Medical Examiner, 830 Southampton Avenue, Suite 100, Norfolk, VA 23510*

Attendees will review new research into factors that make neisserial meningitis fatal for one person, while subclinical for another. Virulence factors include microbial adaptations, such as adhesive pili, lipopolysaccharides, and opacity proteins (Opa); host factors include toll-like receptors, cytokines, mannose-binding proteins, and immunoglobulin G receptors.

All of pathologists deal with the impact of cases of fulminant neisserial meningitis on communities, but rarely do is there an opportunity to review the science which lies behind the current understanding of what makes one victim die, while another survives. This “snapshot” overview of what is understood about the genetics behind host and microbe virulence factors will update the medical community, and will allow physicians to go on following the science as results continue to come in, and perhaps point the way for tests in the future on meningitis cases.

A 13-year-old boy underwent a rapid progression, over a period of hours, from normal health to septic shock and death, while family members remained healthy and free of disease. At autopsy, despite grossly clear meninges, evidence of Waterhouse-Friderichsen syndrome led to the suspicion of meningitis. Microbial culture determined the agent to be Neisseria meningitidis. This child’s extreme susceptibility to the devastating effects of neisserial infection, while his family remained well, was likely due to the interplay of microbial virulence factors, with newly understood host factors. Newly understood microbial factors, recently described by functional genomics and microbiology research, include genes that play essential roles in the pathogenesis of meningococcemia. These are neisserial genes involved with quorum sensing, and with variation of surface antigens, such as adhesive pili, lipopolysaccharides, and opacity proteins (Opas). Regulation of expression of these genes is likely to underlie incomplete virulence among close patient contacts. However, the development of sepsis rather than an innocuous commensal relationship is not only a function of the microbe, but also of increased susceptibility of the host. A variety of gene products implicated in a diminished immune response to Neisseria meningitides include genetic polymorphisms in toll-like receptors, cytokines, mannose-binding proteins, and immunoglobulin G receptors on neutrophils, monocytes, and macrophages. This affords us an opportunity to review the recent research into the critical determinants of meningoccemia, from the aspect of both host and microbe.

Neisserial Meningitis, Virulence Factors, Host

 ** Presenting Author*