(1) Submission ID#1539522

Meningococcal infection of differentiated primary nasal epithelial cells – influence of cell donor and bacterial strain on host-pathogen interactions

---

Author(s)

Daan Arends, n/a

PhD student

National Institute for Public Health and the Environment (RIVM)

Gerco Den Hartog, n/a

PI

National Institute for Public Health and the Environment (RIVM)

Debbie van Rooijen, n/a

Analist

National Institute for Public Health and the Environment (RIVM)

Janine Veldman-Wolf, n/a

Analist

National Institute for Public Health and the Environment (RIVM)

Esther Van Woudenbergh, n/a

PhD student

National Institute for Public Health and the Environment (RIVM)

Background

Neisseria menigitidis bacteria belonging to serogroup C (MenC) and Y (MenW), of clonal complex 11 (cc11) and other lineages are a major cause of invasive disease. Relatively little is known about the interaction of meningococci with the upper respiratory tract epithelium, while this interaction could explain the observed difference in invasiveness of specific serogroups and lineages.

Aim/Methods

To investigate the host-microbe interaction of invasive meningococci and primary nasal epithelial cells, we collected epithelial cells from the nose of seven donors. Primary epithelial cell cultures differentiated on an air-liquid interface for 6 weeks were infected with (1*105 CFU/0.33 cm2 insert) MenW, MenC or capsule null locus (cnl; not expressing capsule) strains. For MenW and MenC, an invasive isolate (cc11) and a laboratory strain (MenW: S-1975PHE, MenC: C11) were used. After infection, we determined bacterial adherence (CFU count), epithelial layer integrity (measuring transepithelial electrical resistance (TEER)) and the epithelial cytokine response (legendplex of basolateral medium).

Results

After two hours, bacterial adherence to epithelial cells was in the range of 0.01-30% of infection inoculum and depended on both the epithelial cell donor and meningococcal strain used. Most notable was the increased adherence of cnl meningococci. 24h post infection, cnl was no longer most abundant, because of differences in bacterial replication. The effect on epithelial integrity was also donor dependent. Infection caused a decrease in TEER in all strains 24 hours post-infection. TEER decrease was lowest in the cnl strain. Infection caused an increase of multiple cytokines (CCL20, IL-8, IL-1β). We observed no specific effect of serogroup or lineage on adherence, TEER or cytokine profile.

Conclusions

Strains specific differences in colonization kinetics were observed, but none specific to serogroup or lineage. Epithelial cell donor greatly affected response and kinetics, which could give insight into why people differ in susceptibility to and severity of disease. Similarity of the nasal epithelial cytokine response for all tested strains suggests a universal response to meningococci. This could have implications for vaccine strategies, as broad spectrum anti-meningococcal vaccine strategies might also displace non-virulent strains, while their presence could be beneficial for developing and maintaining immunological memory.