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The Neisseria meningitidis urethritis clade: characterization of a “chimeric pathogen”

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Background
Unlike Neisseria gonorrhoeae (Ng), Neisseria meningitidis (Nm) is an atypical cause of urethritis. However, in 2015, a molecularly-linked cluster of urethritis cases was first reported in Columbus, Ohio, followed by outbreaks in other US states and globally, caused by a novel clade of non-groupable Nm within the hyper-virulent ST-11 clonal complex (the “NmNG urethritis clade” (NmUC)). Previous genetic characterization of these isolates revealed: 1) the acquisition of the Ng denitrification genetic loci, norB-aniA; 2) the expression of a unique factor H binding protein allele; 3) the loss of serogroup C capsule; and 4) the loss of intrinsic LOS sialylation. We hypothesized that acquisition of these characteristics might confer a survival advantage to clade strains during urogenital tract infection relative to Nm serogroup C (NmC).

Aim/Methods
NmUC, Ng, and NmC were comparatively evaluated in primary male urethral epithelial cell (UEC) infection studies.

Results
NmUC adherence to, invasion of, and survival within UECs was significantly decreased, but not completely inhibited, when host receptors known to mediate Ng or Nm interactions with epithelial cells were blocked. However, blocking complement protein factor H had no effect on UEC infection for any of the strains tested. Viable colony counts indicated that NmUC strains were approximately six times more invasive than Ng. Whereas clade strains survived and proliferated within UECs, Ng survival/replication was delayed/limited, and NmC strains did not survive to any appreciable degree. Thus, some of the mechanisms used by NmUC to infect UECs are shared with Ng, but mechanisms unique to the clade also mediate infection and allow adaptation to the urethral environment. For example, NmUC exhibited increased resistance to reactive oxygen species in vitro. Whereas, nitric oxide promoted Ng and clade survival during UEC infections, the presence or absence of nitric oxide had no effect on NmC. Finally, clade strains induced a distinct cytokine profile by UECs when compared to Ng or NmC.

Conclusions
The NmUC adapts to the urethral environment as a “chimeric pathogen”, displaying facets of Ng pathogenesis in addition to inducing host responses distinct from Ng and NmC.