30. *Escherichia coli* K51 and K93 capsular polysaccharides are cross-reactive with the Group A capsular polysaccharide of *Neisseria meningitidis*: immunochemical, structural and epidemiological studies

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Serum antibodies to the capsular polysaccharide (CPS) of *Neisseria meningitidis*, as well as to other encapsulated bacterial pathogens, confer immunity to invasive diseases caused by these organisms. There is an age-related development of meningococcus Group A (GrA) CPS antibodies. During infancy and childhood when placentally-acquired antibodies have declined and adult levels have not yet developed, the attack rate of GrA meningitidis is highest. GrA diseases have a different epidemiological pattern than the other two major pathogenic Groups of meningococci (B and C). GrA diseases occur annually with high frequency in central Africa. In other parts of the world, GrA diseases occur as epidemics lasting one or two years. Yet, in both endemic and epidemic situations, asymptomatic carriage of GrA organisms is low, ranging about three percent.

In the U.S., GrA organisms have been only rarely detected either in patients or in asymptomatic carriers during the past 30 years. Despite the absence or low carriage rate of the homologous organism, most adults in these countries have protective levels of GrA CPS antibodies. An important antigenic stimulus for CPS antibodies, including those of GrA, has been postulated to be asymptomatic carriage of cross-reacting bacteria of the respiratory and or the gastrointestinal tract. To-date, two strains of bacteria have been reported to cross-react with the GrA CPS; a *Bacillus pumilis* species, strain Sh17, and a non-groupable *Streptococcus faecium*.

The structure of the GrA CPS has been shown to be a pseudo-randomly 0-acetylated, 1-6 linked linear homopolymer of 2-acetamido-2-deoxy-D-mannose-6-phosphate. A similar structure has been detected in *B. pumilis*. *B. pumilis* and *S. faecium* are not common inhabitants of the human flora and it is unlikely that these bacteria are major stimuli for the widely prevalent GrA CPS antibo-
dies. Two cross-reactive \textit{B. pumilis} strains, however, were detected in stool cultures of skid row inhabitants of the Pacific Northwest (personal communication) during an outbreak of GrA meningitis.

Eleven \textit{Escherichia coli} strains, cross-reactive with the capsular polysaccharide (CPS) of \textit{Neisseria meningitidis} Group A (GrA), were detected among 645 stool isolates from healthy families in Cairo, Egypt. Ten of these strains were of the 0107:K93:H27 or 0107:K93:SP serotypes and may be considered as descendants of a single bacterium or as a clone. The remaining cross-reactive strain was of the 07:K51:H18 serotype. All 11 strains did not produce enterotoxins and were not enteroinvasive. The purified CPS of these \textit{E. coli} strains as well as a polysaccharide from \textit{B. pumilis}, strain Sh17, precipitated with equine GrA (H49) antiserum. A partial identity between the \textit{E. coli} K93, K51 and Sh17 PS and the GrA CPS was observed by double immunodiffusion when reacted against the H49 antiserum. Four K93 strains and one K51 strain were found among 320 \textit{E. coli} strains from patients at the Clinical Center, NIH, and three K93 strains were found in 105 stool samples from children in Copenhagen. The data from these three surveys suggest that these cross-reactive \textit{E. coli} are common organisms and could serve as a stimulus for 'natural' GrA CPS antibodies.

Quantitative precipitin analysis showed that K51, K93 and Sh17 PS precipitated 25\%, 50\%, and 59\% of H49 antibodies, respectively. Absorption of H49 antiserum with the GrA CPS removed its precipitating activity with the \textit{E. coli} K93, K51, and Sh17 PS. Absorption of H49 antiserum with either K51 CPS or Sh17 PS removed the homologous cross-reactivity only, whereas, K93 CPS absorbed both K93 and K51 reactivities. Antibodies, raised by intravenous injection of formalinized \textit{E. coli} K93 or K51 cells into rabbits, precipitated with GrA CPS and were bactericidal against GrA meningococci.

The K93 CPS has the following repeating unit: $\rightarrow 3\rightarrow\alpha\text{-Gal}f(1\rightarrow4)\beta\text{-GlcUAp}(1\rightarrow$ and is acetylated at 0–5 and 0–6 of the galactosyl unit. The K51 CPS is a polymer with a $\rightarrow 3\rightarrow\text{GlcNAc}l(P04\rightarrow$ repeating unit and is acetylated at 0–6. The cross-reaction between the \textit{E. coli} K93, and the GrA CPS, a randomly \textit{O}-acetylated polymer of $\rightarrow 6\rightarrow\text{ManNac}l(P04\rightarrow$, was unexpected since these two CPS are compositionally so dissimilar.