Bacterial colonization of the infantile bowel and the ileal pouch

with focus on *Escherichia coli*

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten:

I. Östblom AE, Bengtsson J, Barkman C, Öresland T, Börjesson L, Simrén M, Wold AE and Adlerberth I. **A longitudinal study of the ileal pouch microbiota using quantitatively culture.** *In manuscript*

II. Östblom AE, Adlerberth I, Wold AE and Nowrouzian FL. ***Escherichia coli* pathogenicity island-markers and capacity to persist in the infant's commensal microbiota.** *Submitted*

III. Östblom AE, Karami N, Nowrouzian FL, Adlerberth I, Lundstam U, and Wold AE. ***sfaD/E* and other virulence genes are enriched in *Eshcerichia coli* persisting in the ileal pouch microbiota.** *In manuscript*

IV. Nowrouzian FL, Östblom AE, Wold AE and Adlerberth I. **Phylogenetic group B2 *Escherichia coli* strains from the bowel microbiota of Pakistani infants carry few virulence genes and lack the capacity for long-term persistence.** *Clin Microbiol Infect* 2009; 15: 466–472

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Bacterial colonization of the infantile bowel and the ileal pouch

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Abstract

The colonic microbiota is a source of inflammatogenic and potentially pathogenic bacteria, but also a source of immune maturation signals to the infant. Here, we have investigated the normal colonic microbiota, with focus on *E. coli* in Swedish and Pakistani newborn infants, as well as the microbiota of the ileo-anal pouch in colectomized patients. The aim was to identify factors that contribute to long-term persistence of *E. coli* strains in the microbiota.

E. coli strains can be divided into four phylogenetic groups, of which most strains causing extraintestinal infections belong to the B2 group. These strains also carry an array of virulence-associated genes often located on chromosomal regions, termed pathogenicity-associated islands (PAIs). We have previously showed that B2 strains carrying certain adhesins and virulence markers have increased capacity to persist in the microbiota of Swedish infants.

Patients colectomized due to ulcerative colitis who received a continent pouch constructed from ileum were followed for 3 years with respect to adaptation of the microbiota. There was a gradual change in the microbiota, shown as a gradual rise in the ratio of anaerobic to facultative bacteria from 1:1 in ileostomal to 400:1 in the pouch after 3 years, which did not differ significantly from the ratio in normal colonic microbiota cultured in parallel (1000:1). The counts of facultative bacteria were considerably higher in the pouch content than in control faeces during the first year after connecting the pouch to faecal flow. *Klebsiella* and *E. coli* were very common in ileostomal samples but *Klebsiella* isolation rate isolation rate declined drastically, while *E. coli* stayed high in the pouch. Among anaerobic bacteria, bifidobacteria isolation rates increased rapidly over time reaching 88 % i.e. similar as in controls after 4 months, while *Bacteroides* did not reach the levels seen in controls until 10 months after closure. However, population levels of anaerobes in general, and bifidobacteria and *Bacteroides* in particular, remained considerably lower in pouch faeces than in control faeces.

E. coli capable of persisting in the gut microbiota of Swedish infants for >12 months carried a range of pathogenicity islands (e.g. PAI I, II_{CFT703}, $IV_{536,}$ $II_{J96,}$ and PAI_{usp}) while intermediate (1-11 m), or transient (< 3 w) colonizers had fewer of these traits. Although *E. coli* isolated from the ileal pouch most often belonged to phylogenetic group A ($p = 0.006$), group B2 strains were better at persisting and were more often found on biopsies, i.e. in the mucosa-adherent population. Long-term persisters also carried a range of virulence genes. Group B2 strains from pouches significantly more often carried the *sfaD/E* gene, than did B2 strains from the colon of healthy individuals.

In Pakistani infants, persistence in the bowel microbiota was associated with *papC* and *iutA*, but not B2 origin. Compared with B2 strains from Swedish infants, Pakistani B2 strains significantly less often carried several virulence genes (*fim H*, *papC*, *papG class III*, *sfaD/E*, *neuB*, *hlyA*) and the high pathogenicity island (PAI IV_{536}).

Our studies suggest that the bigger arsenal of virulence factor genes for extra-intestinal infections the longer *E. coli* can reside in the gut/pouch microbiota. However, different human populations differ in their *E. coli* composition and their traits favouring persistence in the gut microbiota.

Keywords: ileal pouch, intestinal microbiota, *E. coli*, persistence, virulence factor genes

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