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Lifestyle, biomarkers and the risk of developing inflammatory bowel disease

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Abstract
Introduction: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is a chronic disease causing inflammation in the gut mucosa. The pathogenesis involves alteration in gut microbiota and in the intestinal barrier due to genetic factors, environmental exposure and dysregulation of the immune response. Several environmental risk factors and risk genes have been identified, but still, the pathogenesis is not fully understood.
Methods: Included papers are all case-control studies based on previously collected data stored with the biobank in Umeå, Sweden. Cases are individuals that participated in the Northern Sweden Health and Disease Study (NSHDS) at least one year before developing IBD. Information was available for all cases regarding age, time and place for inclusion in NSHDS, height and weight, sex and tobacco use. Part of the cases also had available data from a detailed food-frequency questionnaire. For each available case, controls matched for age, sex and time and place were selected. Analysed factors included tobacco use, with smoking and snuff use analysed separately), cotinine(a metabolite of nicotine), iron status (including ferritin, iron, transferrin and transferrin saturation), B-vitamins and tryptophan metabolites.
Results: Smoking was associated with an increased risk of developing IBD both based on questionnaire data and using cotinine as a marker for exposure. Snuff use was not associated with risk for developing IBD. A lower ferritin was associated with an increased risk of developing IBD, whereas no association was seen for other iron status analytes. When analysing iron deficiency based on ferritin and CRP, it was shown that iron deficiency was more common among men before onset of IBD, whereas no difference was seen for women. Active vitamin B6 was lower among cases compared to controls, as well as an index indicating functional B6 deficiency. Kynurenic acid and xanthurenic acid, both tryptophan metabolites with immunomodulatory properties, were lower among cases than controls. For CD only, picolinic acid was lower among cases later developing IBD.
Discussion: Smoking increases the risk of developing both UC and CD. Snuff use did not increase the risk for IBD, indicating that tobacco exposure is not the reason for increased IBD risk. Low ferritin indicates an early pathological process affecting iron storage unrelated to inflammation. Changes in vitamin B6 and tryptophan metabolites might indicate early pathological processes possibly related to gut microbiota changes.
To conclude, this dissertation shows that multiple differences between individuals later developing IBD and controls can be seen years before IBD diagnosis. Some of which give insight to early pathophysiology in IBD.

Keywords
Inflammatory bowel disease; ulcerative colitis; Crohn's disease; smoking; cotinine; iron deficiency; ferritin; pyridoxal-5-phosphate; kynurenine pathway.

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