



Gastrointestinal Infections and the Risk of Inflammatory Bowel Disease in Twins and Siblings: Evidence Against the Hygiene Hypothesis

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Dear Sir,

We read with great interest the report by Dr Hannah Gordon and colleagues published in the June issue of *Digestive Diseases and Sciences* [1]. Their analysis of 91 twin pairs from the UK IBD Twin Registry showed that having experienced fewer episodes of infectious gastroenteritis compared with peers were protective factors against ulcerative colitis (UC). We congratulate our colleagues on their work, which provides new insights into the role of environmental factors in the development of inflammatory bowel disease (IBD).

Although classic twin studies are a valuable tool for disentangling common genetic and environmental factors for a given disease they have some well-described limitations [2]. In an alternative approach to control for confounders, we recently surveyed 1015 pairs of patients with IBD and their full siblings without IBD. Patients and their siblings as controls were eligible, if they had grown up in the same household and were still in contact with the same caregiver from childhood in order to verify answers in cases of doubt. [3]. Stimulated by the publication of the data from the UK Twin registry [1], we have now re-analyzed this dataset to confirm or refute the main results. Consistent with Gordon et al. [1], patients with IBD from our survey reported more hospitalizations for gastrointestinal infections before the age

of 18 than their matched siblings, both in UC (14.2% vs. 7.0%, $p < 0.001$) and in Crohn's disease (CD) (21.4% vs. 5.0%, $p < 0.001$). In addition, patients with UC reported to have more frequent intestinal worm infestations in childhood compared with their unaffected siblings (17.4% vs. 13.4%, $p = 0.03$), which was less consistent in CD (11.0% vs. 8.6%, $p = 0.09$). Use of household antibacterial disinfectants in the children's room, possibly reflecting parental concern about germs and infections, did not differ between patients who developed IBD and siblings of the same age who did not (9.2% vs. 8.2% in UC; $p = 0.39$; 10.0% vs. 10.4% in CD, $p = 0.73$).

Taken together, these data seem to be in contrast to the "hygiene hypothesis", which states that a lower microbial load due to improved hygiene measures in childhood contributes to an immunological imbalance in the gut and an increased incidence of IBD. This hypothesis remains an attractive concept to explain the pathogenesis of IBD, and the first publication investigating the association of hygiene and hay fever in the UK has been cited more than 6000 times [4]. However; pro and con arguments have been published and the concept continues to be controversial [5–7]. Assuming that cohort studies of twins and siblings largely exclude potential confounders such as rural environment, air pollution, income, and ethnicity, our analyses supports the observation that avoiding gastrointestinal infections in childhood may reduce the risk of developing IBD later in life.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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