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## Papers

# Genetics versus environment in inflammatory bowel disease: results of a British twin study

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A genetic component to the cause of inflammatory bowel disease has been inferred from the increased risk among first degree relatives (5-20% cumulative incidence).<sup>1</sup> The only previous study of inflammatory bowel disease in twins used the Swedish twin registry and a register of hospital inpatients to identify 80 twin pairs.<sup>2</sup> The aim of our study was to determine the levels of concordance for inflammatory bowel disease in British twin pairs.

## Subjects, methods, and results

The National Association for Colitis and Crohn's Disease is a patient support group with about 16000 members with inflammatory bowel disease. All members were asked to complete and return a prepaid postcard if they had inflammatory bowel disease and were born as one of a twin pair. Those replying were sent a follow up questionnaire to obtain details of the member's diagnosis and twin. Zygosity was determined with a validated questionnaire.<sup>3</sup>

A report of inflammatory bowel disease in a proband's twin was confirmed by contacting the twin. All self reported diagnoses of inflammatory bowel disease were confirmed by contacting the patient's hospital physician or surgeon. Concordance rates for inflammatory bowel disease were compared by using Fisher's exact and Mantel-Haenszel  $\chi^2$  tests.

Completed questionnaires were obtained for 150 twin pairs in which at least one member had inflammatory bowel disease. For six twin pairs it was not possible to determine zygosity; these were excluded from analysis. The mean age of the probands was 32 (SD 13) years, the mean duration of their illness was 10 (9) years, and the mean age until which the twins had lived in the same house was 20 (3) years. In total, 15 pairs of twins were concordant for inflammatory bowel disease.

In 14 cases the reported diagnosis of inflammatory bowel disease in a proband's twin was confirmed; in one case the twin had died. The nature of the inflammatory bowel disease in concordant twin pairs was the same in all pairs. We were able to validate the diagnosis of inflammatory bowel disease in 149/159 patients (94%); in only one case was the diagnosis refuted. In four cases the diagnosis of Crohn's disease was changed to ulcerative colitis and vice versa in three cases. For 10 patients it was not possible to contact their doctor, their notes were lost, or their doctor did not reply to our inquiries.

Concordance for inflammatory bowel disease in twin pairs

	Identical twin		Non-identical twin	
Proband's diagnosis	Disease	No disease	Disease	No disease
Crohn's disease	5	20	3	43

Ulcerative colitis	6	32	1	33
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Total	11	52	4	76

Concordance rates are shown in the table. There was no difference in the levels of concordance between those with Crohn's disease and those with ulcerative colitis after zygosity was controlled for ( $P=0.64$ ). Identical twins (11/63, 17%) of probands were significantly more likely to develop inflammatory bowel disease than non-identical twins (4/80, 5%); relative risk 3.49 (95% confidence interval 1.17 to 10.45;  $P=0.03$ ). There was no difference between concordant and non-concordant twins in age, duration of disease, and age until which twins had lived in the same house. In concordant twins the mean period between diagnoses was five (SD 5) years.

### Comment

As there is no twin registry in the United Kingdom it was necessary to obtain twin pairs by soliciting volunteers. This has the potential methodological problem known as the "rule of two thirds."<sup>4</sup> Two thirds of typical volunteer twin panels are monozygotic, which is the inverse of the normal ratio of two dizygotic pairs for each monozygotic pair. If the propensity to volunteer is associated with disease concordance then bias will result. In our study there was a preponderance of dizygotic twins (57%), which would suggest that this potential problem was avoided to a considerable degree; there was a similar proportion in the Swedish study (57.5%).<sup>2</sup>

In most cases zygosity in this study was determined from answers from one member of a twin pair; in all 14 twin pairs, when answers were obtained from both members the replies concurred with regard to zygosity. The error rate in determining zygosity has been shown to be similar whether one or both twins respond to the questions posed.<sup>5</sup>

In summary, identical twins are significantly more likely to be concordant for inflammatory bowel disease than non-identical twins. Nevertheless, even in identical twins the concordance was only 17%, which suggests that non-genetic--that is, environmental--causes are more important in the development of Crohn's disease and ulcerative colitis. This register of British twins with inflammatory bowel disease will be a valuable resource for future research.

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