References

- 1 Tysk KC, Lindberg E, Järnerot G, Fluderus-Myrhed B. Ulcerative colitis and Crohn's disease in an unselected population of monozygotic and dizygotic twins. A study of heritability and the influence of smoking. 1988; **29**: 990–6.
- 2 Danforth DN, Scott JR. *Textbook of obstetrics and gynecology*. Philadelphia: Lipincott, 1986.

Reply

SIR,—We are grateful for the interest that Drs Zlotogora and Rachmilewitz have shown our twin study. They suggest that there is an increased risk for an individual born as a twin to be affected by Crohn's disease. This is based on their findings of four pairs of dizygotic twins within a population of 154 patients with Crohn's disease. None of these four pairs was concordant for the disease. Thus, in their study one of 39 Crohn's disease patients was a twin in contrast with one of 89 in the general population. These figures must, however, be interpreted with caution as their Crohn's disease population is small and risk of errors produced by chance must be fairly great.

Obviously Drs Zlotogora and Rachmilewitz find support for their hypothesis in our results as they comment on the high prevalence of Crohn's disease in the twin population in comparison with epidemiological data from Stockholm. We are presently performing an epidemiological study on inflammatory bowel disease within our catchment area. The preliminary data show that the prevalence for both ulcerative colitis and Crohn's disease is considerably higher than in Stockholm. Furthermore, the Stockholm data do not include ulcerative proctitis cases. Thus, epidemiological comparisons of this kind are like comparing apples and pears. In fact the prevalence data in our twin study were not included in the original version but were added on request by the referees in order to get an idea about selection bias. In our study only hospitalised patients could be traced which means that there is a good chance of identifying patients with Crohn's disease more easily while patients with ulcerative colitis can be lost as they are more often treated as outpatients. Our findings did indicate, however, that the selection bias was reasonable when comparing published prevalence figures from Sweden.

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Possible target for cystic fibrosis in the small intestinal epithelium

SIR,—We read with interest the paper by Taylor *et al*¹ reporting the failure of jejunal biopsies from children with cystic fibrosis to respond to secretagogues. Taylor and coworkers used the short circuit current approach to evaluate the ability of cAMP- and Ca²⁺-dependent substances to promote secretion. Secretagogues failed to have an effect in cystic fibrosis epithelium but the Ca²⁺-ionophore A23187 was reported to have a small effect. This led the authors to suggest that the defect lies beyond the step for cAMP generation and that a mechanism for raising intracellular Ca²⁺ might also be impaired. We have recently been studying the ionic channels present in small intestinal epithelial cells by the patch clamp technique and would like to comment on Taylor and colleagues' data in the light of our own data.

Necturus small intestine, is an established model for intestinal ion transport studies, with which direct evidence that the apical membrane of enterocytes possesses a cAMP-activated Cl[−] conductance has been obtained.² Chloride channels identified in isolated enterocytes by the patch clamp technique³ share many of the properties documented for the Cl[−] channels defectively regulated in cystic fibrosis airway epithelium.^{4,5} In cell attached membrane patches the channel is activated by an increase in cellular cAMP. Upon excision of the membrane patch silent channels could be irreversibly activated by strong (+120 mV) depolarisation. In excised, inside-out membrane patches bathed in symmetrical Cl[−]-rich solutions the chloride channels exhibit outward rectification, that is outward currents (chloride flowing from the extracellular to the cytoplasmic side) observed at depolarised potentials are significantly greater than inward currents recorded at corresponding hyperpolarising potentials. The small intestine Cl[−] channels are highly selective for anions (Br[−], F[−], I[−] and SCN[−], but not HCO₃[−] or gluconate, are permeant) over cations. Moreover, changing the Ca²⁺ concentration bathing the cytosolic patch surface was without effect upon channel behaviour. This is again consistent with results for Cl[−] channels originating from tracheal epithelium.⁴

The homology between the Necturus enterocyte Cl[−] channel and those of mammalian origin suggests that this channel may be the agent responsible for intestinal secretion reported by Taylor *et al*. If this were indeed the case then the conclusions drawn from their experiments with the calcium ionophore should be re-examined in view of the Ca²⁺-insensitivity of this channel. The possibility must be considered that the ionophore induced elevation of intracellular Ca²⁺ activates basolateral K⁺ channels, which are known to be Ca²⁺-activated.^{7,9} The result-