

LETTERS TO THE EDITOR

Epidemiology supports oral contraceptives as a risk factor in Crohn's disease

EDITOR.—A recent clinical alert (*Gut* 1999;44:311-12) commented on a study of risk factors for relapse in Crohn's disease.¹ The author concluded that, unlike the established association with smoking, the link with oral contraceptive use is still controversial. To contribute to this discussion, I have investigated temporal trends in age and sex specific disease incidence and correlated them with the chronology of oral contraceptive use.

The birth control pill was first introduced in 1960 and soon became widely accepted; 10 million American women were taking it by 1973.² Concerns about side effects prompted further research, and by the mid-1970s most women taking were taking oral contraceptive pills containing 50 µg or less of oestrogen—a considerable decrease from the 100-150 µg in the pills of the 1960s.

Most epidemiological studies of Crohn's disease (especially those from the USA) have shown a rapid rise in the incidence of disease between the early 1960s and early 1970s, followed by a plateau phase in the 1980s.³ In my analysis I have used the only two American studies^{4,5} for which detailed age and sex incidence distributions were available and correlated them to American data on oral contraceptive use.

Without investigating the incidence trends in a group of 20-29 year old women (these are the most likely users of oral contraceptives), a correlation between the introduction and adoption of oral contraceptives and overall incidence trends of Crohn's disease would not be sufficient to establish oral contraceptive use as a risk factor. From 1964, both studies showed that there was a striking increase in incidence among the 20-29 year old age group, and an increased female to male incidence ratio. Unpublished data from

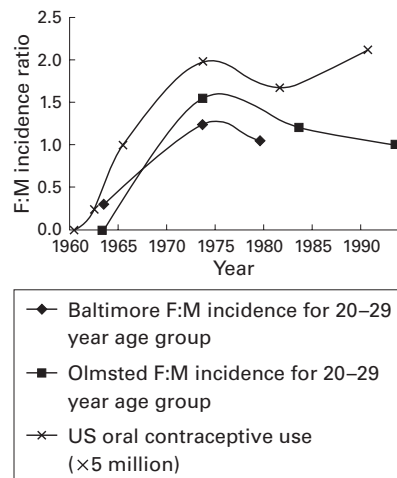


Figure 1 Trends in the use of oral contraceptives and incidence of Crohn's disease as a female to male ratio in the 20-29 year age group.

the Olmsted County study⁵ showed a crude incidence of 26.8 cases per 100 000 person years for this age group in women between 1964 and 1973. This is the highest incidence among all age and sex groups in the entire study period (1940-93), and the highest incidence rise between consecutive time periods. The incidence rise in men for the same period was much less dramatic and the crude rate for the same age group was 17.2. Data for Baltimore showed⁴ a 9.46-fold incidence increase for women aged 20-29 between the 1960-3 and 1973 surveys, and only a 2.33 increase for men of the same age group. Again, this jump in female incidence is the most abrupt and the highest incidence among all age and sex groups in all periods. Consistent with the introduction of oral contraceptives with a lower oestrogen content, incidence studies of Crohn's disease reported lessening of predominance in women aged 20-29 from the mid-1970s. Figure 1 shows changing female to male incidence ratio for this age group corresponding to oral contraceptive use.

Although detailed data on incidence and oral contraceptive use were not available, we used two European studies as controls,^{6,7} and, in the period 1960-5, both had the highest female to male incidence ratio, which corresponded to the rise in the USA.

The above epidemiological findings are concordant with Timmer and colleagues' study¹ and support their explanation that previous use of oral contraceptives is more strongly associated with relapse in Crohn's disease than current use. The change in oestrogen content of oral contraceptives may account for the contradictory findings of a link between oral contraceptive use and Crohn's disease, in studies published in the past 15 years.

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- 5 Loftus EV Jr, Silverstein MD, Sandborn WJ, et al. Crohn's disease in Olmsted County, Minnesota, 1940-1993: incidence, prevalence, and survival. *Gastroenterology* 1998;114:1161-8.
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The role of psychological and biological factors in postinfective gut dysfunction

EDITOR.—We read with interest the paper by Gwee *et al* (*Gut* 1999;44:400-406) which described the role of psychological and biological factors in postinfective irritable bowel syndrome (IBS). However, these authors did not study fructose or lactose malabsorption in relation to duodenal function. Carbohydrate malabsorption syndromes—

for example, fructose and/or lactose malabsorption, are frequently linked to IBS.¹ Patients with fructose malabsorption often have a clear history of postinfective onset of their symptoms, as Gwee and colleagues found in patients with IBS.

We have shown an association between carbohydrate malabsorption syndromes and early signs of mental depression^{2,3}; similarly, Gwee *et al* found significant links between anxiety, depression, and somatisation scores in patients with IBS. Our data suggest that non-absorbed carbohydrates interfere with tryptophan metabolism, which may explain the development of anxiety, mental depression, and other signs of serotonin deficiency.⁴ Furthermore, most of our patients were diagnosed as having IBS before a diagnosis of carbohydrate malabsorption syndrome was made. Preliminary data indicate that the symptoms of patients with IBS improved on a diet that did not include the malabsorbed carbohydrate; we also observed improved depression scores that meant that there was no further need for psychotherapeutic intervention.

In conclusion, we feel that many patients with IBS may have a carbohydrate malabsorption syndrome and may, therefore, develop signs of psychiatric illness. Thus, we suggest that all studies performed on patients with IBS should exclude minor forms of malabsorption syndromes.

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- 1 Rumessen JJ. Functional bowel disease: malabsorption and abdominal distress after ingestion of fructose, sorbitol, and fructose-sorbitol mixtures. *Gastroenterology* 1988;95:694-700.
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Reply

EDITOR.—I would like to thank Dr Ledochowski and colleagues for their interest in our paper, and for presenting evidence of a possible association between fructose or lactose malabsorption and mental depression. They suggest that psychological symptoms in patients with IBS may be due to carbohydrate malabsorption, caused by the interaction between malabsorbed sugars and the amino acid tryptophan. In contrast, we proposed that psychopathology predisposes to the development of IBS. We observed that neurotic traits, life events occurring before an attack of gastroenteritis, and psychological state at the time of the infection, all seemed to predict which patients would develop IBS.

I would not deny that events in the gut may influence state of mind. Research from our department, and others, has indicated that meals rich in fat induce feelings of calmness,