allowed to undertake all endoscopic procedures in the field of conventional endoscopy. A recent editorial from Dewitt¹ asks, "Is there anything now we can't do?" with double balloon enteroscopy. We would ask, "Is there anything now we *can* do?"

We encountered the case in our early experience of double balloon enteroscopy, and only a diagnostic endoscope was available in Taiwan. Because of our limited experience in the use of double balloon enteroscopy and the lack of suitable haemostasis equipment, a discussion with the patient was held and it was determined that he preferred the option of surgical resection of the polyp.

At present, we are capable of diagnosing various small intestinal diseases with the use of double balloon enteroscopy. However, we still need more experience to improve our technique for treating the lesions found and managing the associated complications. More studies are required to show the effectiveness and safety of therapeutic double balloon enteroscopy compared with traditional methods.

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Remission and relapse of Crohn's disease following autologous haematopoietic stem cell transplantation for non-Hodgkin's lymphoma

Autologous haematopoietic stem cell transplantation (HSCT) for Crohn's disease has been described by Oyama and co-workers as producing remission in 11 of 12 patients with refractory Crohn's disease after a median follow up of 18.5 months.¹ They postulated that autologous HSCT was useful for refractory Crohn's disease. We report the case of a 32 year old woman with biopsy proven Crohn's disease diagnosed when she was 16 years old. Her mother also suffered from Crohn's disease. She developed a K11 positive anaplastic non-Hodgkin's lymphoma (NHL) three years later, treated successfully with ablative CHOP chemotherapy and autologous HSCT, inducing remission for the past 12 years (and she remains in remission on no treatment). As a consequence of her autologous HSCT she also went into long term remission from her Crohn's disease, but relapsed after eight years. She was a smoker, but was on no maintenance treatment for Crohn's disease in this eight year period. She developed abdominal pain and bloody diarrhoea and underwent a colonoscopy, and a biopsy proved the recurrence of her colonic Crohn's disease. She was treated with corticosteroids and 5-aminosalicylates, which induced temporary remission. However, she subsequently had two relapses over the past two years, with diarrhoea, histologically proven erythema nodosum, and seronegative arthropathy. She was treated with reducing courses of corticosteroids with

prompt resolution of her symptoms. There is no evidence of relapse from her NHL, and long term treatment with immunosuppressive agents or infliximab is under consideration but has been deferred because of a small increased risk of lymphoma associated with these agents (though it is not known whether this is attributable to Crohn's disease, immunosuppression alone, or a combination of the two²). Genotyping revealed no *CARD15* mutations (R702W, G908R, and L1007fs).

Our case is the longest reported "follow up" of autologous HSCT in Crohn's disease and raises some interesting questions with regard to the long term efficacy of autologous HSCT for Crohn's disease, as our patient appeared to be in complete long term remission and was apparently "cured" of her Crohn's disease for eight years before relapsing. We postulate that the autologous HSCT led to ablation of "activated" T cells for a prolonged period (resetting the immune system) but that her genetic predisposition (positive family history), allied to other environmental factors (smoking), subsequently led to her disease relapse. This is in keeping with the current hypothesis of the aetiopathogenesis of Crohn's disease and suggests that autologous HSCT not provide a long term "cure" for this disorder. Allogenic HSCT may be more appropriate,³ albeit at a much greater risk of treatment related complications such as graft versus host disease. This is further supported by the results of allogenic HSCT for Crohn's disease, where the only relapse occurred in a patient who developed a mixed donor-host haematopoietic chimerism following allogenic HSCT.⁴ Furthermore, in the study by Oyama and co-workers, there were two relapses in the short term and only two patients achieved treatment-free remission for more than three years.⁵

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Activated innate immune system in irritable bowel syndrome?

The discovery of antimicrobial peptides has extended our knowledge of non-specific defence mechanisms. In addition to the

physical barrier, the intestinal epithelium contributes to host defence by producing antimicrobial peptides to limit access to enteric bacteria and other microorganisms.¹ The production of inducible antimicrobial peptides offers an initial rapid defence response of epithelial cells against invading microbes.²

Human β -defensin-2 (HBD-2) was the first inducible human antimicrobial protein discovered.³ It can be induced by probiotic microorganisms and pro-inflammatory cytokines.⁴ Recent results suggest that HBD-2 is expressed in active intestinal inflammation, especially in ulcerative colitis.⁵ Thus far, the expression of β -defensins has been quantified in the intestinal mucosa using the polymerase chain reaction procedure. Our aim was to evaluate faecal measurements of HBD-2 in patients with active ulcerative colitis, compared with irritable bowel syndrome as a non-inflammatory clinical control and with healthy controls. We expected that faecal HBD-2 levels would show a similar pattern to mucosal HBD-2 and thus be selectively increased in ulcerative colitis.

Faecal specimens were collected from 69 patients (22 with active ulcerative colitis, 24 with irritable bowel syndrome, and 23 healthy controls) (table 1). To avoid any influence of probiotics in our data, patients on probiotic drugs were excluded. Further exclusion criteria for the patients with irritable bowel syndrome were a raised C-reactive protein or leucocyte count and a history of infectious gastrointestinal disease or bacterial overgrowth over the previous six months. Disease status was addressed in all participating subjects by medical history and current symptoms. In addition, each patient with irritable bowel syndrome or ulcerative colitis underwent ileo-colonoscopy with histopathology. Faecal HBD-2 was measured by enzyme linked immunosorbent assay (Immundiagnostik, Bensheim, Germany) and reported as ng/g faeces. HBD-2 concentrations (mean (SD)) were 104.9 (62.9) ng/g in the active ulcerative colitis group, 72.9 (52.9) ng/g in the irritable bowel syndrome group, and 31.0 (15.4) ng/g in the healthy controls ($p < 0.0005$). Scheffé post hoc tests showed significant differences between healthy controls and the two patient groups (fig 1).

The results first imply that levels of HBD-2 are detectable in faeces and can be quantified. Second, as in mucosal specimens, HBD-2 levels are significantly raised in faeces in patients with ulcerative colitis compared with healthy controls. Finally, in contrast to our hypothesis,

Figure 1 HBD-2 levels in faeces.

Table 1 Sociodemographic, clinical, and laboratory characteristics of the patients

	UC	IBS	HC
Patients (n)	22	24	23
Male:female	9:13	5:19	10:13
Age (years) (mean (SD))	41.2 (11.7)	45.9 (13.5)	38.2 (7.1)
Age range (years)	21 to 68	15 to 69	25 to 48
Endoscopic/histological inflammation (n)			
No	0	24	
Yes	22	0	
CRP (n <1 mg/dl) (mean (SD), range)	1.2 (1.4), 0 to 3.9	0.3 (0.3), 0 to 0.9	
Leucocytes (n <10) (mean (SD), range)	7.2 (1.8), 4.3 to 11.9	6.1 (1.2), 4.3 to 9.6	

CRP, C-reactive protein; HC, healthy controls; IBS, irritable bowel syndrome; UC, ulcerative colitis.

faecal levels of HBD-2 were significantly raised in patients with irritable bowel syndrome compared with healthy controls and were similar to those in the patients with ulcerative colitis. These results suggest activation of the mucosal innate defence system towards a proinflammatory response in patients with irritable bowel syndrome, in the absence of macroscopic signs of inflammation.

Inflammatory conditions of the gastrointestinal tract—including inflammatory bowel disease and acute gastrointestinal infections—are associated with disturbed intestinal motor function and decreased sensory thresholds.⁶ These sensorimotor abnormalities are not necessarily related to an overt inflammatory reaction as they can occur even when inflammation is minimal and is restricted to the mucosa.⁶ Thus altered sensory and motor function accompanied by the development of symptoms suggestive of irritable bowel syndrome has been observed in patients with quiescent ulcerative colitis.⁷ First support for a possible involvement of intestinal inflammation in irritable bowel syndrome was based on observations of increased numbers of mast cells in the muscularis externa⁸ or a significant increase in lamina propria immune cells in the colonic mucosa of affected patients,⁹ and has been under discussion since. Nonetheless, the general consensus is that irritable bowel syndrome is a non-inflammatory disease.

In conclusion, this is the first study to present preliminary data on faecal HBD-2 levels in patients with irritable bowel syndrome, ulcerative colitis, and healthy controls. In contrast to our hypotheses, our findings support a proinflammatory response of the mucosal innate defence system in irritable bowel syndrome. The functional significance of these findings remains to be elucidated.

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Is there an association between coeliac disease and irritable bowel syndrome?

We read with interest the study by van der Wouden *et al* (*Gut* 2007;56:444–5). The authors describe their experience of investigating patients with irritable bowel syndrome (IBS) fulfilling the Rome II criteria) for coeliac disease. They tested 152 patients with IBS using IgA endomysial antibodies and total IgA level or duodenal biopsy; 36 patients were subsequently biopsied but there were no cases of coeliac disease diagnosed (prevalence 0%: 95% confidence interval, 0% to 4%). They concluded that the prevalence of coeliac disease in patients with IBS is low and that screening may be ineffective.

We feel cautious about accepting these results as definitive proof of no relation between these two common conditions. Their study has some methodological limitations. First, the referral pattern appears to be significantly different from that seen in the United Kingdom, with approximately 55 patients being assessed for IBS symptoms per year by three physicians. Does this suggest that IBS is not a condition commonly referred to secondary care in the Netherlands? Perhaps primary care physicians have already investigated patients for coeliac disease before referral? Second, assuming the accepted population prevalence for coeliac disease is 1%, then with a sample size of 152 (11 patients were not serologically tested or biopsied) there is only a 21.4% power to detect a threefold difference (assuming a significance level of 0.05). Thus this study is underpowered. Third, endomysial antibody (EMA) negative coeliac disease is well recognised. The use of EMA in isolation may lower the detection sensitivity and with only 22% of their patients (36/163) having a duodenal biopsy, it is possible that some cases of coeliac disease could have been missed. Fourth, importantly, there are several studies examining this issue (table 1), not all of which were cited by the authors in their report. These international studies suggest that the prevalence of coeliac disease in cohorts of patients with IBS is higher than in the general population.

Table 1 Studies of coeliac disease in cohorts of patients with irritable bowel syndrome

Report	Country	n	Setting	Criteria	Serology	Biopsy	Prevalence	Outcome
Sanders ¹	UK	300	Secondary care	Rome II	AGA, EMA	Yes	4.7%	Better on GFD
Sanders ²	UK	123	Primary care	Rome II	AGA, EMA	Yes	3.3%	Better on GFD
Shahbazkhani ³	Iran	105	Secondary care	Rome II	AGA, EMA	Yes	11.4%	Better on GFD
Fasano ⁴	USA	5073	Mixed	Symptom group	AGA, EMA, TTG	Yes	Chronic diarrhoea (n = 1848), 3.85% Abdominal pain (n = 1695), 3.23% Constipation (n = 1530), 2.6%	NR
Holt ⁵	UK	138	Primary care	Rome I	AGA, EMA	No	0.7%	NR
Locke ⁶	USA	50	Primary care	Manning	tTG	No	0%	NR
Hin ⁷	UK	132	Primary care	NR	EMA	Yes	0%	NR
Catassi ⁸	USA	22	Primary care	NR	EMA, tTG	Yes	31.8%	NR

AGA, antigliadin antibodies; EMA, endomysial antibodies; GFD, gluten-free diet; NR, not reported; tTG, tissue transglutaminase antibodies.