

Letter to the Editor

Antisecretory Factor-induced Regression of Crohn's Disease in a Weak Responder to Conventional Pharmacological Treatment

To the Editor: A 38-year-old man with a 20-year history of Crohn's disease, who had previously undergone 2 sessions of colonic surgery (in 1985 and 1986) with removal of the transverse and descending part of colon with a remaining total colon length of about 50 cm. Those episodes were followed by an ileocecal resection (in 1988) with removal of about 10 cm of terminal ileum. He was admitted to our hospital in February 2001 due to a severe deterioration of his condition. Over the previous several years, he had been treated with corticosteroids, sulfalazine/5-ASA, metronidazole, immunosuppression, and infliximab. During 2000, the patient had suffered from progressive abdominal pain, weight loss (25% of his normal weight), and bloody stools (>15/day). Laboratory tests confirmed increased activity of Crohn's disease with B-hemoglobin 93 g/L (132-166), B-leukocyte counts 12.6×10^9 (4-10), B-platelets 395×10^9 (150-300), B-sedimentation rate 19 mm/hour (<13), S-C-reactive protein 64 mg/L (<5), S-albumin 27 g/L (40-51), S-haptoglobin 2.9 g/L (0.35-1.9) and S-orosomuroid 1.3 g/L (0.54-1.2). Colonoscopy revealed a discolored, dehausted, devitalized mucosa of the entire remaining large intestine and about 10 cm of terminal neo-ileum. No spontaneous bleeding was found, but after contact with the endoscope, small bleeding spots in the mucosa were noted in the region of ileo-colonic anastomosis. Small bowel radiography demonstrated a slight luminal reduction in the terminal part of neo-ileum. No scintigraphy examination was done at this moment. On the ward, the patient received total parenteral nutrition and high doses of intravenous betamethasone (4 mg twice daily in 14 days) with no clinical or laborative improvements.

At this time, the patient had a Crohn's Disease Activity Index (CDAI) of 623. Due to the severe clinical status, colonoscopy findings and failure of the intensive medical treatment, colectomy was suggested as a reasonable established alternative. After consideration, the patient declined the suggestion of surgery and asked for alternative medical treatment. He was then offered additional treatment with antisecretory factor (AF) in order to achieve a reduction in intestinal hyper secretion and in-

flammatory activity. Hence, the patient was initially given a diet based on egg yolk drinks (i.e., passive AF administration of 2 g freeze dried egg yolk, dissolved in 6 ml orange juice) (1), followed later by specially processed cereals (SPC) (i.e., active AF-induction) (2) as a complement to the traditional ongoing medication. The freeze-dried egg yolk displayed a verified high AF activity, determined by use of an *in vivo* rat assay (2,3). The egg yolk was given four times daily for 14 days. On day 4, finely grounded SPC (0.5 g/kg b.w./day) were given in addition. The finely grounded cereals were used in order to prevent overload or obstruct the inflamed intestine. The doses of unground SPC were initiated on day 10 and slowly increased to 1 g/kg b.w./day. The introduction of unground SPC was performed in parallel with termination of the egg yolk drinks and the finely grounded SPC. Normal feeding was parallel introduced on day 10. A rapid and significant decrease of average daily stools, from more than 15 down to 2-4 (Fig. 1), and recovery of the patient's general and gastrointestinal well-being, was recorded in response to the treatment (Fig. 2). After 2 weeks there was an increase in plasma AF-activity from 0.1 to 0.6 AF units. Further increase to 0.9 AF units was registered after 5 weeks, indicating active AF-induction as a response to SPC. Nine weeks after SPC introduction corticosteroid therapy was ended. At 16 weeks, the patient demonstrated a complete recovery of the weight loss combined with a normalization of the CDAI (reduced to 147). Furthermore, all laboratory parameters except B-hemoglobin (130 g/L) and S-albumin (37 g/L) were recovered at this time. The histological outcome of the colon biopsies demonstrates a remarkable and almost complete mucosal healing (Fig. 3), and normalization of AF reactivity determined by using immunohistochemical techniques previously described (4). Colonoscopy 4 months after SPC introduction displayed a mucosal reparative process of the entire large bowel with a vitalized light hyperemic mucosa and an overall view of healing in progress, including newly formed small capillaries in the mucosa, now resistant to bleeding after instrumental contact. For 16 months the patient was treated solely with SPC, combined with oc-

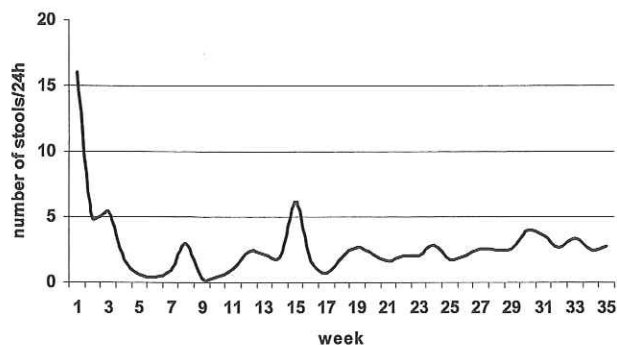


FIG. 1. Daily number of stools/24hour period (average/week).

casual codeine tablets. After this time, the SPC treatment was ended. After additional 9 months, the clinical and laborative recovery is maintained without any regular medication or SPC treatment.

Antisecretory factor is a 43 kDa endogenous protein, capable of inhibiting intestinal secretion and inflammation. Increased AF-activity after intake of SPC has previously been documented in man and animals (2,5). AF can be administered passively by intake of egg-yolk drinks since egg yolk contains a high concentration of AF (1), or via breast feeding (3).

However, the exact biological mechanisms of action of AF remain to be described (3). Antisecretory factor in the gastrointestinal tract seems to be involved in the regulation of the fluid transport and able to decrease the inflammatory reaction in the mucosal tissue (3).

This patient's long-standing history of Crohn's disease activity, and gradually reduced response to various medications made a remission, as a response to the pharmacological treatment, less likely. This statement is strengthened by the patient's independence of further corticosteroid treatment after clinical remission. The positive clinical response in our patient suggests a ben-

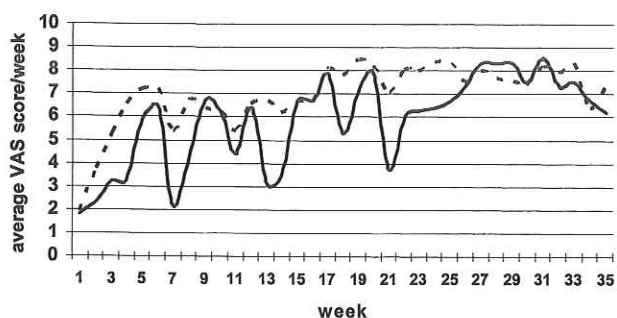


FIG. 2. The patient's experience of daily VAS score (average values) until 35 weeks (Visual Analogue Scale of 0–10, higher value means better clinical status) of his self estimated gastrointestinal discomfort (dotted line) and general well being (solid line). Registration began at the introduction of SPC (i.e., four days after admittance to hospital).

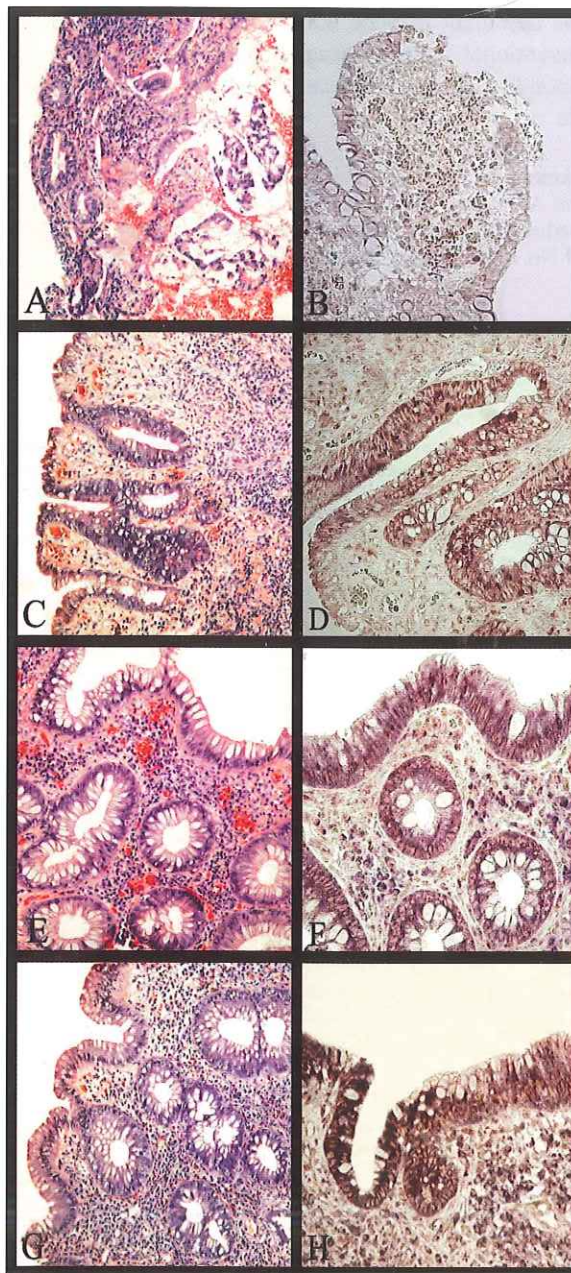


FIG. 3. Rectal biopsies, cryosectioned at 6 micron. Stained with hematoxylin/eosin (left panel) and immunostaining for antisecretory factor (AF) (right panel). A, B: At admittance. Severe destruction of the mucosa, with acute inflammation and hemorrhaging (A), and low AF immunoreactivity (B). C, D: After 6 days of treatment. Beginning of restoration of the epithelial lining, with persistent inflammation (C), and moderate AF immunoreactivity in the crypt epithelium (D). E, F: After 12 days of treatment. Normalization of the epithelium with well-developed Goblet cells (E), and distinct AF immunoreactivity in the epithelium and in lymphocyte-like cells in the lamina propria (F). G, H: Follow-up after 4 months. Similar histology (G) and AF immunoreactivity (H) as at 12 days.

eficial effect of AF therapy in severe Crohn's disease. This treatment may be considered as a complement to conventional medical treatment in patients with a non-responding disease in situations where surgery is unsuitable.

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