

Treating Crohn's Disease with Diet

Jenny Woolner, Freelance Gastroenterology Specialist Dietitian,
Spire Cambridge Lea Hospital, Impington, Cambridge

Introduction

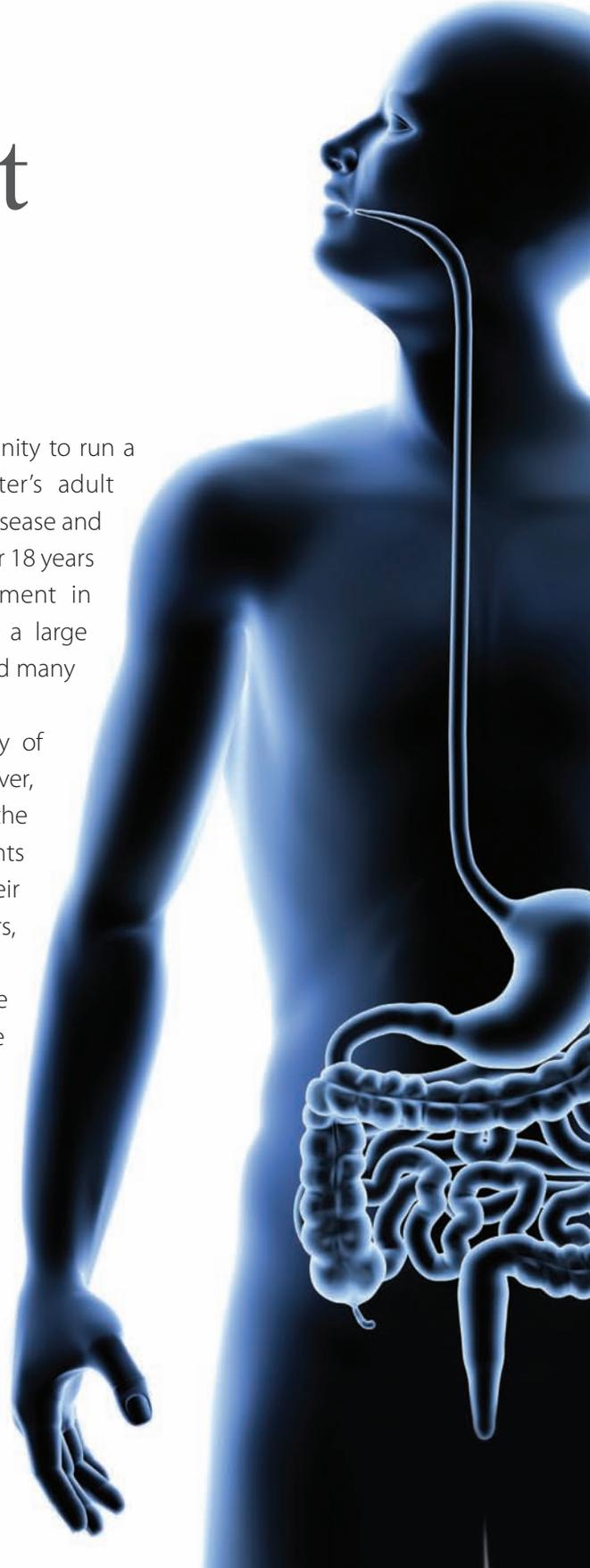
Starting up as a freelance dietitian 18 months ago gave me the opportunity to run a dietetic clinic in a private hospital alongside Professor John Hunter's adult gastroenterology clinic. The majority of patients I see suffer from Crohn's disease and irritable bowel syndrome. My interest in Crohn's disease stretches back over 18 years from earlier days working in the gastroenterology research department in Addenbrooke's Hospital where we saw excellent responses to diet in a large number of patients. However, it is a subject that attracts much debate and many gastroenterologists consider diet to be ineffective.

Immunosuppressive drugs provide a good response in the majority of patients, and are generally an easy treatment for a patient to take. However, many people with Crohn's disease are reluctant to take these drugs due to the possible serious side effects. This concern is more pressing for those patients that become drug dependent and, therefore, unable to reduce their medication to safer levels without a relapse of their condition. For others, drug therapy is simply ineffective.

There is, therefore, a strong interest amongst patients to look at alternative treatments to drugs and, in particular, the role diet might play in altering disease state. If an individual is unable to access an interested gastroenterology team, the temptation is to self-treat or turn to unreliable sources of information. This carries the risk of a nutrient-deficient diet and weight loss. It is important, therefore, that patients expressing a desire to explore a dietary approach can be referred to a consultant and dietitian specialised in this area to receive expert advice and regular assessment of effectiveness.¹

Treatment involves three stages:

1. Exclusive enteral nutrition (EEN) used in place of immunosuppressive drugs to settle symptoms and induce remission of the disease
2. Food reintroduction programme commenced to transition from liquid feed to a varied solid food diet whilst maintaining remission
3. Foods that appeared to provoke symptoms initially are re-tested and the final diet assessed for nutritional completeness.



Stage 1: Exclusive Enteral Nutrition (EEN)

The efficacy of EEN has been demonstrated in a number of studies, with between 36 and 80 per cent remission.^{2,4} There has been much debate over the significance of formulations of enteral feed in Crohn's disease with the consensus now being that polymeric (whole protein) feeds are as effective as elemental (amino acid based) or semi-elemental (short chain peptide based) feeds.^{5,9} However, our experience of **elemental and semi-elemental diets** is that these are very effective, **providing remission rates of over 80 per cent** amongst compliant patients.^{10,11} Elemental and semi-elemental diets are therefore our treatment choice in clinic.

We ask patients to stay on the feed for two to three weeks, depending on how quickly their symptoms settle. All other foods and drinks except water are stopped. They are advised on the quantity of feed they need and instructed to build up to this over three days. The importance of sipping the feed throughout the day is stressed. These precautions are taken because the elemental diet has a high osmolarity, which can cause water to be drawn into the gut and lead to diarrhoea when first introduced. Semi-elemental diets may be better tolerated in some patients. Patients are also advised that they may notice initial headaches and light headedness and changes in stool appearance.¹

Stage 2: Reintroduction of food to maintain remission

LOFFLEX diet

The LOFFLEX diet stands for 'low fat, fibre limited, exclusion diet'. This is made up of foods that rarely cause problems amongst Crohn's patients and is usually followed for two weeks before reintroducing more troublesome foods. Fat and fibre are kept low initially because these foods are frequently problematic amongst Crohn's patients

and, therefore, need to be increased gradually to individual levels of tolerance. The LOFFLEX method is illustrated in **Figure 1**.

Elimination diet

Sometimes patients find their symptoms return when starting the LOFFLEX diet. This may be due to a previously undetected narrowing of the gut due to strictures and will require further investigation. However, occasionally it can be due to an intolerance of one or more of the 'safe' foods on the LOFFLEX diet or, simply, that a slower transition from liquid to solid diet suits the patient better. In such cases, we use an 'elimination' diet whereby foods are introduced one-by-one so that all foods are tested.

Stage 3: Food re-testing and nutritional assessment

Foods found to provoke symptoms are re-tested to check they have been correctly identified and, once the safe diet has been confidently established, nutritional adequacy is assessed.

Theory behind the effect of dietary manipulation in Crohn's disease

The cause of Crohn's disease is still not fully understood. We know that genetics, the immune system, gut flora and environmental factors all play a part.¹² A change in the metabolic activity of the bacteria in acute Crohn's disease has been described.^{13,14} Active disease is associated with the production of immunoglobulins directed against bacterial antigens, leading to inflammation of the gut mucosa.¹⁵ A model for the disease process could be thus: in genetically susceptible persons a change in the metabolic activity of the colonic flora provokes an attack by the body's immune system on these bacteria which leads to inflammation of the bowel.¹⁶ This attack may be modified by factors such as the host's normal gut flora, diet, female sex hormones, smoking, medications and possibly stress.

Medical treatments are generally targeted at suppressing the immune system, but is it possible to target treatment at a different level – at the bacteria themselves? Antibiotics can reduce symptoms of Crohn's disease¹⁷ but long or frequent courses of these would not be advisable.

Can diet have a significant effect on the gut flora?

Bowel rest, reduced antigenicity of the diet and supplementation of nutrients may all have a role to play in the improvement of symptoms on an elemental diet.¹⁸⁻²³ However, it is the effect that an elemental diet has on bowel flora which is of particular interest. It has been shown that there is a reduction in bacterial dry weight of stools of over 50 per cent when compared before and after treatment with an elemental diet,²⁴ indicating a significant decrease in bacterial metabolic activity on this diet.

A study looking at immunoglobulin coating of faecal bacteria in patients with active Crohn's disease demonstrated a significant reduction in the percentage of faecal bacteria coated with IgG and IgM after two weeks treatment with elemental diet.²⁵ This implies that the immune reaction targeted towards the 'friendly' host bacteria seen in active Crohn's disease is turned off by treatment with elemental diet, thus allowing the inflamed gut to heal.

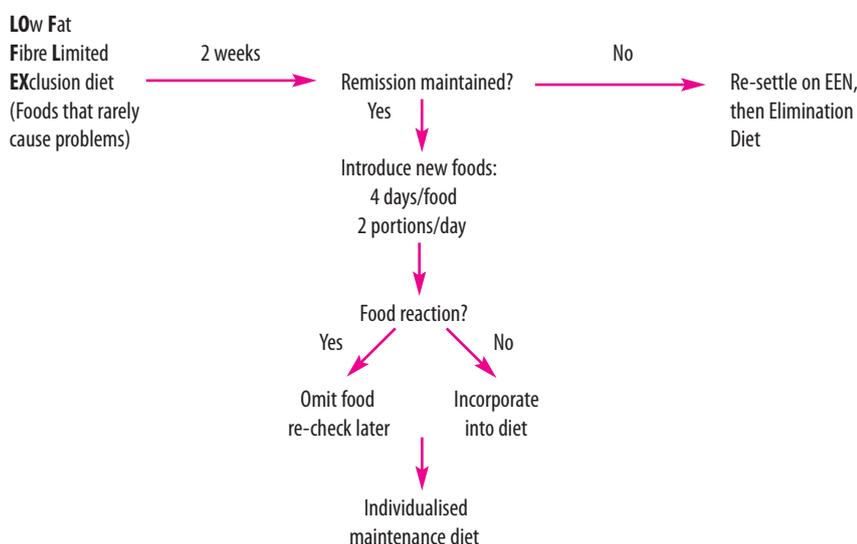
Specific dietary components may encourage the growth of subsets of the colonic flora.²⁶ It has been suggested that an alteration in bowel flora could be linked to a change in immune tolerance or that specific bacterial metabolites may be bioactive or toxic.²⁷ The hypothesis, therefore, is that when foods are reintroduced specific foods stimulate bacterial activity, re-triggering the immune attack and causing a return of symptoms.¹⁶ The foods that provoke reactions may differ from one individual to another due to differences in the gut flora.

Evaluation of dietary treatment

Whilst many gastroenterologists recognise the effectiveness of liquid feeds in inducing remission, it is how to maintain remission that proves problematic. Unfortunately there have been very few studies investigating this vital step. Returning to a normal diet leads to disappointing results with remission rates reported as being between nine and 58 per cent at 12 months.^{3,7,23,28} Remission rate at 12 months following steroid treatment has been reported as 36 to 50 per cent,^{29,30} and 31 to 35 per cent at two years.^{29,30}

The effect on long-term remission of the elimination diet compared to steroids was investigated in the East Anglian Trial.¹⁰ Thirty-eight per cent of patients receiving elemental diet followed by elimination diet were in remission at two years, compared to 21 per cent of patients receiving elemental diet followed by standard corticosteroid therapy. Eighteen per cent were non-compliant to dietary treatment and counted as treatment failures.

Figure 1: LOFFLEX Diet



A smaller trial compared the LOFFLEX diet to the elimination diet¹¹ and found remission rate at two years amongst compliant non-structured patients to be 56 per cent and 59 per cent respectively.

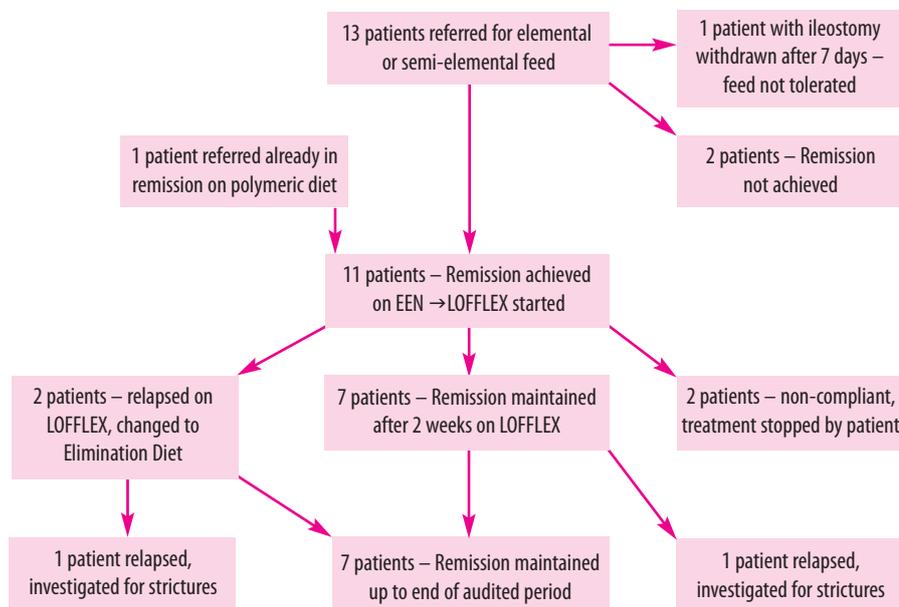
The ability to sustain the remission achieved with the liquid feed makes diet a far more attractive treatment choice for the gastroenterologist to consider. However, the dietetic involvement in supporting the patient through this process is considerable.

Auditing treatment outcome

A lack of recent studies makes auditing of treatment outcome for this group of patients a particularly important part of clinical practice. Over the period of 18 months, from September 2010 to February 2012, a total of 23 patients were referred to me for dietary advice, nine of whom were already established on maintenance diets. Thirteen were

started on EEN and one was referred who was already established on a polymeric diet. Their progress is shown in Figure 2. Eleven patients (78%) responded to EEN. One of these with terminal ileal involvement required a change from an elemental to semi-elemental diet and the addition of cholestyramine before remission was achieved. Of the 11 starting maintenance diets, seven (64%) remained in remission up to the end of the audited period. This represents 50 per cent of the total who started on EEN. As some of the patients have only recently started treatment it would be too early to conclude on the success rate of treatment. However, the initial progress is encouraging and in line with results expected from published studies. Progress will be continually updated and data extended as new patients are referred. This should provide interesting information on treatment outcomes in relation to disease location, length of diagnosis, and medical and drug history.

Figure 2: Treatment Outcomes



Other considerations

It is important to have a flexible and adaptive approach to treating individuals, both in terms of dietary advice and in consideration of other treatments that can be used in conjunction. Diet may provide additional benefit to the patient when used alongside remission maintenance drugs, such as 5ASAs and azathioprine, where these are not able to fully control symptoms alone.

It is often assumed that bowel symptoms that do not settle or that reappear can only be due to persistence of inflammation in the gut. There is the risk that treatment with diet is abandoned too early for this reason when there may be another explanation for the symptoms. For example, functional bowel disorders can exist alongside Crohn's disease. We have found that a number of patients' symptoms have been related to stress or anxiety leading to air swallowing, or have been

musculo-skeletal in origin. Referral to a physiotherapist specialised in these areas has corrected these problems. Likewise, some bowel symptoms may be related to the menstrual cycle and investigations by a gynaecologist may be warranted. It is also important to consider the impact of other drugs that a patient may be taking. In particular, the non-steroidal anti-inflammatory drugs such as Diclofenac used to treat arthritis, a common complication of Crohn's disease, can block the production of cyto-protective prostaglandins and can therefore be damaging to the bowel wall.³¹

Our current understanding of the impact of dietary manipulation on gut flora and Crohn's disease is limited. Elemental and semi-elemental diets have been shown to be effective at inducing disease remission. It is hoped that further research will allow improvements in managing long-term remission by dietary means, enabling it to become a treatment accessible to a wider number of patients.



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