Inflammatory Bowel Disease

Inflammatory bowel diseases (IBD), is comprised of Crohn's disease (CD) and ulcerative colitis (UC) - two serious, chronic digestive diseases that affect five million people worldwide. Crohn's disease and ulcerative colitis directly affect the digestive system and cause chronic intestinal inflammation. Although both diseases have little impact on mortality, they have a substantial negative impact on the quality of life of affected individuals.

The prevalence of IBD is rising in Ireland and the developed world in general. These conditions are a major cause of sickness and suffering in young people and appear to be linked to increased sanitation of living environments. They are affected by diet, alcohol abuse, smoking and sedentary lifestyle with environment, genetics and intestinal bacterial flora all thought to play a part in their development.

Crohn's disease is a lifelong, relapsing and remitting disorder which may affect any part of the bowel. Patients often require expensive surgical operations as well as drug treatment. Smoking is known not only to increase the risk of developing Crohn's disease but also the risk of requiring initial and repeated surgery. Ulcerative colitis is usually treated by medication alone.

Inflammatory bowel disease is associated with an increased risk of colorectal cancer. Colorectal cancer is now one of the most common, but potentially preventable cancer among Europeans, with more than 400,000 new case per year in Europe.

Inflammation in ulcerative colitis is limited to the colon and rectum and is confined to the surface . Crohn's disease can involve any segment of the gastrointestinal (GI) tract from the mouth to the anus. In Crohn's disease the inflammation stretches across the wall of the intestine and sometimes into surrounding tissue. In some patients, IBD is associated with extra-intestinal manifestations involving the liver, skin, eyes and/or joints.

When their disease is active, patients usually present with persistent diarrhoea, abdominal pain and when the colon is affected, the passage of blood. Depending on disease severity and site, there may also be weight loss, anorexia and fatigue.

If you are experiencing these symptoms you should visit your General Practitioner who can arrange for further investigations.

UC and CD can present themselves either in an acute or chronic form and can be characterised by flare ups or exacerbations and periods of remission. The severity of symptoms, period of remission and length of flare up vary from person to person. The investigation of CD or UC by a doctor usually involves taking a history of symptoms from the patient followed by a general examination and a series of more specific analysis such as rectal, bowel and blood tests, along with x-rays and analysis of stool samples.

It can often take time to confirm a diagnosis of CD or UC as the symptoms of both are shared with quite a number of other diseases. It is therefore necessary to exclude other causes before a definite diagnosis can be made.

Conventional medical treatments for both types of IBD are corticosteroids and aminosalicylates. Nutritional therapy has a role for some patients with Crohn's disease, particularly children, as nutritional deficiencies are often present. Immunosuppression with a thiopurine (azathioprine or 6-mercaptopurine) is a widely used second-line therapy for resistant disease. Immunomodulatory medication, such as methotrexate, and more specifically targeted cytokine therapies, such as infliximab, a monoclonal antibody to tumour necrosis factor alpha (TNFα), are increasingly used in patients with resistant Crohn's disease.

Unfortunately, none of these drugs are universally effective and all can be associated with adverse effects. A range of new therapeutic targets are currently under investigation.

IBD Research at the Alimentary Pharmabiotic Centre

A central goal of the Alimentary Pharmabiotic Centre is the development of new therapeutic approaches for the treatment of infectious and inflammatory disease. The research activity within the Host Response core increases our understanding of the mechanisms that underpin immunological "tolerance" towards commensal bacteria which normally reside in the intestine and how a loss of "tolerance" can contribute to and exacerbate inflammatory disease. Core 2 investigates the cellular and molecular mechanisms underpinning host-flora interactions using *in vitro, ex vivo* and preclinical models. It is expected that the elucidation of key signalling pathways in intestinal epithelial cells, dendritic cells and Treg/Th17 cells will provide novel targets for proof of concept and validation studies in animal models and their application in human inflammatory disease states. While our goals and experimental strategy are primarily focused on mucosal inflammation and the molecular and cellular mechanisms that control inflammatory processes, these findings will be of direct relevance and interest to industry collaborators.