

Irritable Bowel Syndrome: Infections, Food and Stress

– Summary of talks presented at Alimentary Pharmabiotic Centre Public Forum for World Digestive Health Day 2011

Professor Eamonn Quigley, Professor of Medicine at UCC, Consultant Gastroenterologist at Cork University Hospital (CUH) and Principal Investigator at the APC spoke about “*Post-infectious IBS; what is it and who gets it?*”

IBS is defined by abdominal discomfort associated with altered bowel habits (American College Gastroenterology 2002). In a community survey of over 40,000 adults in eight European countries the overall prevalence was 11.5%, but only 2.8% had been diagnosed with IBS even though 9.6% had symptoms at the actual time of the survey. The symptoms reported included abdominal pain (88%), bloating (80%), trapped wind (66%), tiredness (60%), constipation (19%), diarrhoea (59%) and heartburn (47%) (Hungin AP. *Aliment Pharmacol Ther.* 2003;17(5):643-50).

Post-infectious IBS is IBS that develops following an episode of food-poisoning or other gastrointestinal (enteric) infections (usually water-borne). IBS-like symptoms were first linked to amoebiasis back in the 1940s and Chaudhary and Truelove, who coined the term “Irritable Colon Syndrome”, provided a clear description of post-infectious IBS as long ago as 1963. Since then, IBS has been linked to several outbreaks of bacterial gastroenteritis in the 1990s, related to such organisms as salmonella, shigella, campylobacter, as well as occurrences of multiple and unidentified organisms and non-bacterial agents such as giardia, amoeba and viruses, e.g. norovirus. Careful follow-up of large numbers of people following community outbreaks of gut infections has clearly defined the existence of post-infectious irritable bowel syndrome (PI-IBS). About 10% of people who have an episode of gastroenteritis will go on to develop PI-IBS.

Risk Factors for PI-IBS have been shown to include being female (3 times as common), suffering a severe gastroenteritis illness (2 weeks and more), depression and persistent inflammation in the gut wall.

Research exploring the pathology, genetics and immunology of this entity has thrown new light on IBS. Stress and infection have been shown to result in subtle changes in the bacterial flora in the intestine which, in turn, leads to an altered immune response. Increased levels of the pro-inflammatory cytokines interleukins 6 and 8 have been shown in the blood in IBS patients (Scully et al (2010) *Am J. Gastroenterology* 105(10) 2235-2243, and McKernan et al, (2011) *Aliment Pharmacol Ther.* 2011 May;33(9):1045-52). Enhanced expression of the toll-like receptor TLR4 have been observed in colon biopsies from patients with IBS and decreased levels of TLR7 and TLR8 (Brint et al. (2011) *Am J Gastroenterol.* 2011 Feb;106(2):329-36). TLRs are a family of receptors which recognise pathogens and are known to be involved in the translation of bacterial signals into anti-bacterial innate immune responses. Their results support the presence of an immune engagement between the bacterial population and the host in IBS; an interaction that involves innate immunity and could generate a low-grade inflammatory response. Putting the two together they provide an important link between the microbiota and the immune response in IBS.

Raised levels of interleukin 1 β and TNF α may explain symptoms beyond the gut e.g. in chronic fatigue syndrome, fibromyalgia and premenstrual syndrome.

This research may open new diagnostic and therapeutic avenues for IBS.

Professor Colin Hill, Professor of Microbial Food Safety at UCC and Principal Investigator at APC, discussed the concept of using beneficial bacteria to fight infection in the developing world. In his talk “*Enteric pathogens and infections; what’s new and what’s to do?*” Prof. Hill reminded us that infectious disease continues to claim the lives of almost 10 million children every year, 2 million of them from the scourge of diarrhoea and 3.5 million involving malnutrition. In addition to these deaths, diarrhoea and malnutrition create a deadly cycle of infectious disease which has lifelong consequences for the survivors in terms of life expectancy, intellectual capacity and even adult stature and work productivity. As an adult these consequences include a reduction of 10 years in lifespan, 10cm reduction in height and cognitive impairment seen as a reduction of 10 IQ points. Interventions such as provision of a nutrient-dense atole to 1-2yr old male children in Guatemala between 1966 and 1977 resulted in adults aged 25-42 years earning 46% more, while women supplemented as children had gains in schooling and reading comprehension (Guerrant et al, Nutrition Reviews 66;487-505,)

While providing clean water, appropriate vaccines and sanitary conditions remains the best way to combat disease in developing countries, using beneficial bacteria (often marketed as probiotics) to fight infection in the developing world is a novel additional strategy that might provide an economically viable, long-term strategy to help to break the disease cycle and improve the health and quality of life of some of the world’s most disadvantaged populations. Probiotics are live microbes which, when ingested, have a beneficial effect on the host. They have been shown to protect against infection, inflammation and atopic disease, and they can be delivered as capsules or in foods.

Professor Hill used examples of research conducted in the Alimentary Pharmabiotic Centre in Cork to indicate the potential of this novel approach. In one study in pigs probiotic strains were shown to provide significant protection against incidence and duration of salmonellosis resulting in reduced clinical scores and higher weight gain (Casey et al., 2004 Lett. Applied Microbiol 39; 431-438 and Casey et al. 2007 Appl Environ Microbiol. 73;1858-1863).

The advantages of probiotics are that they are natural, could be delivered/produced locally, they *may* work through the immune system, resistance is less likely to develop and they could be combined with nutritional solutions such as oral rehydration. Challenges remain, not least the affordability of probiotics (average daily income in Sub Sahara is \$1.50). However, Professor Hill concluded that probiotics will prove a useful additional weapon in the fight to break the infection-malnutrition cycle of disease.

Dr Orla Craig, Cork University Hospital and researcher at the APC spoke about “*IBS, food and stress: new insights, new approaches.*” Dr Craig defined IBS as a disorder of the gut with abdominal pain and cramping, an abnormal bowel pattern (diarrhoea, constipation or both) and abdominal bloating. IBS is not life-threatening, doesn't cause permanent damage to the bowel and will not develop into a more serious condition. IBS affects 15-20% of the population, the majority will have mild symptoms but for those with more severe symptoms, day-to-day activities employment and quality of life may be affected. IBS is a functional disorder, which means that there are no structural or biochemical abnormalities and it often overlaps with other functional disorders such as chronic fatigue syndrome and fibromyalgia.

IBS may be caused by a combination of factors including those affecting the brain such as stress & emotion as well as food, bacteria and genetic factors. There are many misconceptions about IBS. While diet may play a role, IBS is not a food allergy and is not caused by eating wheat. A high fibre diet is not suitable for everyone with IBS, nor should everybody with IBS eliminate dairy products from their diet. Allergy testing is used to confirm or eliminate food allergies but is not generally useful in IBS. Keeping a food diary is the best way to detect other food intolerances/non-immune reactions to certain foods. A trial elimination of a suspect food may be warranted but if no improvement in symptoms is observed that food should be reintroduced. Unmonitored elimination diets may cause nutritional deficiencies.

A high-fibre diet improves overall health and increasing dietary fibre can improve abnormal bowel pattern in people with IBS, especially those with constipation. However, increasing fibre can make some people worse and a trial elimination of insoluble fibre (that found in bran and cereals) may be worthwhile in diarrhoea-predominant IBS.

Coeliac disease should be excluded in some people with IBS. In non-coeliacs a trial elimination of wheat- containing foods may be warranted but if no improvement in symptoms is observed wheat should be reintroduced.

Lactose intolerance is caused by a shortage of the lactase enzyme needed for digestion of dairy products. If a trial elimination of dairy products is attempted it is essential to supplement with calcium and vitamin D. If successful, yoghurt and some dairy products may be reintroduced. If not successful all dairy products should be reintroduced.

In general Dr Craig recommended minimising consumption of alcohol and caffeine, eating smaller meals more frequently, minimising intake of high-fat food, gradually increasing intake of fibre if constipated, and restricting intake of fructose and sorbitol. In some cases a trial elimination of wheat or dairy products may be warranted but recommended trying only one thing at a time and reintroducing the food if there was no improvement.

Symptoms of IBS are often worse at time of stress and higher rates of anxiety and depression are found in IBS (12 % in IBS patients versus 6 % in those without IBS). Traditional medications for IBS have included laxatives, antispasmodics and anti-diarrhoeals, however, low doses of anti-depressants have been found to be useful, even in the absence of depression. New drugs aim to act on the brain-gut axis and

affect serotonin and its receptors in the gut. Cognitive behavioural therapy and hypnotherapy have also been shown to be useful in those with severe symptoms.

About the Alimentary Pharmabiotic Centre

The Alimentary Pharmabiotic Centre, (APC; <http://apc.ucc.ie>) is a research centre funded by Science Foundation Ireland and industry partners. The APC, a partnership between University College Cork, Teagasc, the Irish Agriculture and Food Development Authority, and the Cork Institute of Technology, focuses on research in gastrointestinal health. Pharmabiotic is a neologism devised by the APC to represent any material (including molecules and microbes) originating from the gut ecosystem that can be exploited for a health benefit, and includes probiotics, prebiotics, metabolites, and potential new anti-microbials and anti-inflammatories. The independent international ratings agency Thomson Reuters Science Watch global analysis, recently ranked University College Cork at number 2 in the world for probiotics research, due primarily to publications from researchers in the Alimentary Pharmabiotic Centre (<http://sciencewatch.com/ana/st/probiotics/institution/>).