

Hot Topics in Gastroenterology

Wednesday 13th November 2013 • The Institute of Physics, 76 Portland Place, London, UK

Anne Holdoway, BSc RD MBDA, Specialist Dietitian - Independent Practitioner/Freelance Dietitian, reports on the joint GSG/Dr Schar study day

With an excellent line-up of speakers and a range of topical subjects the audience were in for an exceptional educational event, the highlights of which are brought to you in this article.

Non-coeliac Gluten Sensitivity – An update

Professor David Sanders, Professor of Gastroenterology and a Consultant Gastroenterologist, Royal Hallamshire Hospital and the University of Sheffield

Professor Sanders gave an enlightening presentation on non-coeliac gluten sensitivity (NCGS), a new and evolving area in which dietitians have a key role to play.

Professor Sanders highlighted the one per cent prevalence of coeliac disease (CD) in the adult population. He went on to describe how the number of patients consuming a gluten-free diet seems greatly out of proportion to the projected number of patients with CD. In the USA, for example, marketers have estimated that 15 to 25 per cent of consumers want gluten-free (GF) foods. Professor Sanders highlighted the growing need to manage patients complaining of gluten-related symptoms in the absence of diagnostic markers for CD, such as negative coeliac serology and normal duodenal biopsies. In a UK population survey, in 2013, 13 per cent of patients reported symptoms related to gluten, 3.7 per cent were on a GF diet, doctor diagnosed CD stood at 0.8 per cent. These figures allow us to estimate the numbers of patients who may respond to gluten exclusion. Whilst previously these patients posed a clinical dilemma, evidence is beginning to emerge that gluten exclusion is a viable option in these patients and can relieve presenting gastrointestinal symptoms and other manifestations, such as fatigue, headaches and 'foginess'.

Professor Sanders posed the uncertainty in treatment, i.e. whether it is the withdrawal of gluten that benefits patients or

whether the withdrawal of gluten inadvertently reduces the ingestion of wheat fructans, which interplay with gut microbiota, gas production and fermentation. Current evidence to support the withdrawal of fermentable carbohydrates (FODMAPs) for IBS suggests that there may be overlap with a gluten-free diet. Professor Sanders concluded that in IBS a skilled dietitian, with knowledge of gluten and FODMAPs, offers the capacity to tease out the response to gluten/FODMAPs and help individuals determine whether they are gluten sensitive or intolerant of fermentable carbohydrates.

Key messages:

- It is essential to diagnose or exclude CD prior to commencing a GF diet for the management of NCGS
- IgE wheat allergy should be excluded
- Consider treating the coeliac like or coeliac 'lite' group with a gluten-free diet
- Consider a wheat free diet or low FODMAP® diet
- Bear in mind that the public are choosing a GF diet irrespective of medical advice (self-reporting of symptoms may be a cue)
- An effective biomarker will facilitate understanding, diagnosis and management of NCGS
- The medical community is on a learning curve. NCGS is a newly recognised clinical entity for which we do not yet fully understand the natural course or pathophysiology. Dietitians are key to diagnosing and managing NCGS.

Key references: Aziz A, et al (2012). Does gluten sensitivity exist in the absence of coeliac disease. *BMJ*; 345: e7907 doi: 10.1136/bmj.e7907 • Hogg Koollars S, Sanders DS, Rostami K (2011). Gluten sensitivity a new condition in the spectrum of gluten disorders. *Complete Nutrition*; 11(3): 53-55.

Non-Gut Manifestations of Coeliac Disease and Gluten Sensitivity

Professor Marios Hadjivassiliou, Consultant Neurologist, Royal Hallamshire Hospital Sheffield

Based on his lifelong research, Professor Hadjivassiliou provided the audience with considerable insights into the neurological manifestations of gluten sensitivity and CD.

Professor Hadjivassiliou described how initial research into the neurological symptoms of CD suggested that symptoms were caused by vitamin deficiency. He went on to illustrate how recent research has revealed that the symptoms are autoimmune related. He outlined the range of neurological manifestations associated with CD and gluten sensitivity encountered in his specialist clinic over many years; the most common being ataxia and neuropathy (gluten ataxia existed in 20% all patients with ataxias, 25% among patients with sporadic ataxias). Using patient stories he illustrated the symptoms in ataxia due to cerebellar damage: loss of balance, walking, specific eye movements observed in the absence of gut symptoms. He went on to describe the most common form of neuropathy in CD; sensorimotor axonal peripheral neuropathy where both the motor and sensory nerves are affected resulting in loss of feeling, difficulty using limbs, tingling, numbness, burning and pain.

He explained how a subgroup of patients with classic CD presentation might be susceptible to the development of neurological dysfunction if they continue to consume gluten and how the presence of gastrointestinal (GI) symptoms potentially

protect against neurological manifestations being overlooked as they are more likely to receive a diagnosis of CD and exclude gluten.

To improve diagnoses of neurological manifestations, Professor Hadjivassiliou emphasised the need to modify physicians' perceptions that gluten sensitivity is not solely a disease of the gut. The discovery of better markers of the extraintestinal manifestations, such as TG6 antibodies, may be helpful in overcoming outdated thinking. He concluded that removal of the immunological trigger (gluten) must be the basis of treatment of all manifestations and should be recommended to all patients once the diagnosis is properly made.

Key messages:

- CD may be initially defined after presentation with a neurological disorder
- In patients with ataxia and neuropathy, screening for CD should be considered, especially if a definitive cause for the neurological disorder is not obvious
- Further studies are needed to determine if neurological changes that have been attributed to the so-called 'gluten-sensitivity' in the absence of overt intestinal disease can be truly reversed with a gluten-free diet
- Neurologists and physicians should be aware that ataxia and neuropathy may be due to CD or gluten sensitivity
- Dietitians can play a role in promoting the awareness of gluten sensitivity and CD as a potential underlying cause of neurological problems.

Key references: Hadjivassiliou M, et al (2006). Neuropathy associated with gluten sensitivity. *J Neurol Neurosurg Psychiatry*; 77: 1262-1266. doi: 10.1136/jnnp.2006.093534 • Hadjivassiliou M, et al (2010). Gluten sensitivity: from gut to brain. *Lancet Neurol*; 9: 318-30.

Nutrition in IBD

Dr Peter Irving, Consultant Gastroenterologist, King's College London

Dr Irving provided an overview of our current knowledge regarding nutritional issues in inflammatory bowel disease (IBD), exploring the role of nutritional therapies in active disease but also summarising current knowledge on the role of microparticulates, organic foods, fish oils and industrial farming in the aetiology of IBD.

The National Audit on IBD, including patient responses, has highlighted the inadequate attention given to nutrition as a therapy and nutritionally related complications of IBD. Dr Irving reviewed current knowledge of enteral nutrition, both partial and sole source of nutrition as primary treatment and as adjunctive therapy in Crohn's disease, and outlined the benefits demonstrated in the use of elemental diets and polymeric diets in Crohn's disease for both acute flare up and the maintenance of remission in IBD.

Dr Irving acknowledged the role of the BDA in raising the profile of nutrition in the treatment and management of IBD and emphasised the role of the dietitian as an integral member of the team – assisting patients in adopting nutritional therapies, optimising adherence to feeding regimens and dealing with food exclusions.

The role of perioperative nutrition was highlighted along with the need to correct nutritional abnormalities, which can be often overlooked in patients with IBD but which may have significant consequences. Dr Irving concluded that nutritional therapy may have a central place in the hierarchy of treatment in IBD. He concluded that further research is critical in this area to better define the benefits of nutrition in IBD, notwithstanding that undertaking large, well designed, trials in this field is challenging and that many studies lack power and are subject to numerous drop outs, resulting in low number of patients completing studies.

Key messages (captured in the IBD Standards; A5 - Access to Nutritional Support and Therapy):

- Access to a dietitian should be available to all IBD patients
- All forms of nutritional therapy should be available to IBD patients, including exclusive liquid diet as therapy for Crohn's disease
- All patients with Crohn's disease should have the choice of receiving appropriately supported nutritional therapy as primary treatment
- Patients with complex nutritional needs, which may include enteral and parenteral feeding, must be able to access a full multidisciplinary nutrition support team for comprehensive assessment, management and advice.

Key reference: www.ibdstandards.org.uk

The Role of Pharmacy Supply Schemes for Gluten-Free Foods

Helen Fraser-Mayall, Nutrition & Dietetic Team Leader, West Cumberland Hospital, and Jean Foster, Patient Expert, Cumbria

Helen and Jean brought to life the challenges of dealing with a new diagnosis of CD and the minefield of information that patients have to cope with. Helen outlined the work undertaken by a multiprofessional steering group, which included Jean as the 'Patient Expert'. The aim was to overcome the barriers in obtaining gluten-free foods on prescription. The group also aimed to design a responsive service to newly diagnosed patients.

Helen outlined Jean's unique role in empowering patients to self-manage and help them come to terms with their diagnosis of a lifelong diet-dependent condition, reinforcing advice given by the dietitian. Helen and Jean described how, in conjunction with the Steering Group, they successfully streamlined the service to patients and switched the provision of gluten-free foods on prescription to a pharmacy-led scheme. This scheme has recouped financial

savings through reduced wastage and cost-effective prescribing of staples, maximised patient choice for staples and increased the responsiveness required to ensure the receipt of prescriptions. Helen described Jean as her 'walking oracle' in seeing CD through the patient lens. Equally Helen, who has CD herself, has found that this has enhanced her knowledge and understanding of the challenges faced when trying to adhere to a strict gluten-free diet.

Key messages:

- Expert patients have a key role to play in the design of services and supply of gluten-free foods
- Expert patients can support the role of the dietitian
- A multi-professional steering group has the capacity to streamline the provision of gluten-free foods in the community, producing savings that can be reinvested in service development and the provision of patient support.

Key reference: Community pharmacy supply of gluten-free foods - a toolkit for commissioners (2011). Available from: www.coeliac.org.uk/document-library/934-community-pharmacy-supply-of-gluten-free-foods-a-toolkit-for/

Dietitian-Led Gastroenterology Clinic in Primary Care – Reflections on implementation of the FODMAP approach in IBS patients

Marianne Williams, Specialist IBS and Allergy Dietitian

Marianne walked us through her experience of establishing the award winning 'Dietetic-Led Primary Care Gastroenterology Clinic', the first of its kind in the UK. Marianne presented the impact data developed in conjunction with Gastroenterologist Dr Emma Greig, which illustrated financial savings and improved outcomes. Analysis of referrals into secondary care identified potential savings in excess of £100,000 across two Trusts as a result of those with non-red flag symptoms being referred to the gastroenterology dietetic service. To date, the clinic has achieved a 78 per cent success rate in improving and alleviating IBS, with 63 per cent of positive responders using the Low FODMAP® Diet.

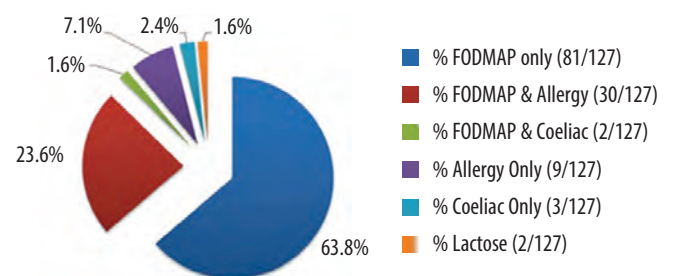
In essence, the service is commissioned as a service for primary care as an alternative to referral into secondary care, however, secondary care can refer into the service via the GP. Intractable IBS patients (no red flags) are referred to the specialist dietetic service. To date, >70 per cent of patients have improved and are discharged. Of the 30 per cent of patients who fail to improve, the GP refers to secondary care or CBT/hypnotherapy/medication.

Marianne asked: "Why not just set up an IBS clinic?" answering that patients seen may be managed through a whole host of approaches, including allergy, gluten sensitivity, low FODMAP® diet. **Figure 1** shows the various diets employed.

Key messages:

- There needs to be more integration between gastroenterology and allergy
- These are highly specialised areas of nutritional counselling and require experienced specialist dietitians to be delivering the service
- Specialist dietetic knowledge of the low FODMAP® diet, allergy and gluten related disorders is crucial for success.

Figure One: Various diets employed



Key references: Biesiekierski JR, et al (2013). No effects of gluten in patients with self-reported non-celiac gluten sensitivity after dietary reduction of fermentable, poorly absorbed, short-chain carbohydrates. *Gastroenterology*; 145: 320-328.e3.
 • Carroccio A, et al (2012). Non-Celiac Wheat Sensitivity Diagnosed by Double-Blind Placebo-Controlled Challenge: Exploring a New Clinical Entity. *Am J Gastroenterol*; 107: 1898-1906
 • Shepherd S, Gibson P (2006). Fructose malabsorption and symptoms of irritable bowel syndrome: guidelines for effective dietary management. *J Am Diet Assoc*; 106: 1631-1639
 • Tack GJ, et al (2010). The Spectrum of celiac disease. *Nat. Rev. Gastroenterol. Hepatol*; 7: 204-213
 • Volta U, De Giorgio R (2012). New Understanding of Gluten Sensitivity. *Nat. Rev. Gastroenterol. Hepatol*; 9: 295-299.
 Recommended course: MSc Food Allergy module at Southampton or Imperial.

Diagnosis and Monitoring of Patients with Coeliac Disease

Dr Lisa Sharkey, Senior Clinical Fellow, Cambridge University Hospitals NHS Foundation Trust

Dr Sharkey provided an overview of her extensive work contributing to the development of the Cambridge pathway for the diagnosis and monitoring of CD. Dr Sharkey outlined the difference in sensitivity and specificity of IgA EMA and TTG in research (95%) compared to 'real-life' EMA sensitivity – 78 per cent (Dickey 2000) IgA TTG sensitivity and specificity 90 per cent (Sheffield), IgA TTG sensitivity 84 per cent, specificity 96 per cent (Leuven). Given the added issue relating to IgA deficiency, Dr Sharkey confirmed biopsy remains the 'gold standard' using either the Marsh or Corazza grading system. Other causes of villous atrophy have to also be considered, including HIV, Giardia, Crohn's, Eosinophilic GE, SIBO, CVID, GVHD, malnutrition, radio/chemotherapy, drugs. Though not uniformly available, Dr Sharkey commented on novel methods and adjuncts to facilitate diagnosis, including gene expression profiling, I-FABP, REG 1a.

With regard to management, Dr Sharkey showed the variation in pathways from the American Guidelines, Mayo Clinic and NICE.

Dr Sharkey highlighted the limitations in relying on symptoms as a method of monitoring response, explaining that freedom of symptoms cannot be relied upon in all as they can be vague, can be due to other conditions, were never present in asymptomatic patients; plus Lahdeaho (2011) found one in five patients developed severe villous atrophy during gluten challenge but had no symptoms. **Table One** illustrates the pros and cons for follow-up biopsy.

Dr Sharkey concluded with an outline of the Cambridge pathway which includes an introductory group talk at diagnosis, a dual appointment (gastroenterologist and dietitian), dietetic review at two months, repeat biopsy

at nine to 12 months. If repeat biopsy shows expected response and villous recovery, patients are seen after two to three years and discharged to primary care. Those with persisting villous atrophy are seen for further investigations, including secondary dietetic advice and further repeat biopsies.

Key messages:

- First step in diagnosis is clinical suspicion (remember the iceberg)
- Serology performs better in studies than 'real-life'
- New pathways may exclude biopsy for diagnosis in some, e.g. children
- Serology performs poorly for follow-up
- Repeat biopsy on GFD facilitates stratification of patients for intensity of follow-up

Table One: Pros and Cons of Follow up Biopsy in CD

Pros	Cons
<ul style="list-style-type: none"> • Confirmation of mucosal 'healing' • Positive reinforcement • Early d/c of those doing well • Intensify interventions in those with persisting changes • Appropriate investigation of ongoing symptoms 	<ul style="list-style-type: none"> • Cost • Risk of invasive procedure • Not needed in everyone • No excess mortality

Key references: Lanzini A, et al (2009). Complete recovery of intestinal mucosa occurs very rarely in adult coeliac patients despite adherence to gluten-free diet *APT Aliment Pharmacol Ther*; 29: 1299–1308 - <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2036.2009.03992.x/pdf> (last accessed 30.11.2013). • Mahadev S, et al (2013). Is Dietetic Use associated with coeliac disease outcomes. *Nutrients*; 5: 1585–1594; doi:10.3390/nu5051585 - www.ncbi.nlm.nih.gov/pmc/articles/PMC3708338/pdf/nutrients-05-01585.pdf (last accessed 30.11.2013). • Lahdeaho ML, et al (2011). Small-bowel mucosal changes and antibody responses after low- and moderate-dose gluten challenge in coeliac disease. *BMC Gastroenterology*; 11: 129 - <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3240817/pdf/1471-230X-11-129.pdf> (last accessed 30.11.2013). • Lebowitz B, et al (2012). Diagnosis of Coeliac Disease. *Gastrointestinal Endoscopy Clinics of North America*; 22(4): 66 – 677. • Murch S, et al (2013). *Arch Dis Child*; 98: 806–811 - <http://adc.bmj.com/content/98/10/806.full.pdf> (last accessed 30.11.2013). • Murray JA, et al (2004). Effect of a gluten-free diet on gastrointestinal symptoms in coeliac disease. *Am J Clin Nutr*; 79(4): 669–673 - <http://ajcn.nutrition.org/content/79/4/669.full.pdf+html> (last accessed 30.11.2013). • Sharkey LM, et al (2013). Optimising delivery of care in coeliac disease - comparison of the benefits of repeat biopsy and serological follow-up *APT. Aliment Pharmacol Ther*; 38(10): 1278–91.

The Role of GI Microbiota in Health and Disease

Professor Kevin Whelan, King's College London

Professor Whelan provided a comprehensive overview of the gastrointestinal microbiota in health and disease, with specific reference to our knowledge preceding and in the presence of Crohn's disease and IBS, postulating a role of the microbiota in the pathogenesis of these conditions.

Professor Whelan expertly illustrated how the microbiota are a complex ecosystem in each human hosting at least 160 different bacterial strains. Our understanding of their role is rapidly expanding as a result of molecular microbiological techniques that accurately characterise composition and diversity along with technology that measures metabolic activity. Considerable research has been undertaken in relation to the microbiota and its modification in patients with GI disorders. Using the knowledge we have from studies in Crohn's and IBS, Professor Whelan explained how such knowledge might impact on the pathogenesis, including how intestinal dendritic cell function might be influenced by the composition of the microbiota in Crohn's disease.

Professor Whelan also explored the pathogenesis of IBS after gastroenteritis, highlighting studies that illustrate a range of effects including altered luminal microbiota in IBS, altered mucosal microbiota, increased gut fermentation arising in IBS and evidence that the gastrointestinal immune system is activated in IBS.

Professor Whelan concluded that healthy humans and patients experience a number of issues that may alter their microbiota (disease, antibiotics and inflammation). Microbiota modifying therapies, such as probiotics and prebiotics, offer promise and have been used with varying efficacy in the management of these disorders.

Key messages:

- The microbiota vary between individuals, vary through the lifespan and are affected by diet, drugs and disease
- Crohn's disease is associated with altered microbiota, inducing physiological and clinically important changes
- IBS is associated with an altered microbiota, fermentation and immune function
- Studies to date pave the way for approaches to modify the microbiota... some of which have been tested.

Key references: Benjamin, et al (2012). Smokers with active Crohn's disease have a clinically relevant dysbiosis of the gastrointestinal microbiota *Inflamm Bowel Disease*; 18 (6): 1092–1100. • Flint HJ, et al (2012). The role of the gut microbiota in nutrition and health. *Nature Reviews Gastroenterology and Hepatology*; 9: 577–589. • Hedin C, et al (2007). Evidence for the use of probiotics and prebiotics in inflammatory bowel disease: a review of clinical trials. *Proc Nutr Soc*; 66(3): 307–15. • King TS, et al (1998). Abnormal colonic fermentation in irritable bowel syndrome. *Lancet*; 352: 1187–1189. • Marshall JK, et al (2010). Irritable bowel syndrome: Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery. *Gut*; 59: 605–611. • Parkes, et al (2008). *Am J Gastro*; 103: 1557–1567. • Parkes, et al (2012). Neuro Gastro Motility; 24: 213–214. • Power SE, et al (2013). Intestinal microbiota, diet and health. *Brit J Nutr*; DOI: <http://dx.doi.org/10.1017/S0007114513002560>. • Silk DBA, et al (2009). Clinical trial: the effects of a trans-galactooligosaccharide prebiotic on faecal microbiota and symptoms in irritable bowel syndrome. *Alim Pharm Ther*; 29: 508–518. • Whelan K (2011). Probiotics and prebiotics in the management of irritable bowel syndrome: a review of recent clinical trials and systematic reviews. *Current Opinion in Clinical Nutrition*; 14(6): 581–587.

This day provided an excellent overview of hot topics in nutrition and gastroenterology. An array of take-home messages reinforced the important role of the dietitian with specialist knowledge to gastroenterology. This field of dietetics provides a promising future for dietitians in transforming lives, managing symptoms and teaching self-management strategies for conditions which can be hugely debilitating when not managed effectively. Thank you to Dr Schar and the Gastroenterology Specialist Group (GSG) of the BDA for a superb event.