

COELIAC UK'S RESEARCH CONFERENCE 2018

Coeliac disease past, present, future; a spectrum of gluten related conditions

Thursday, 15 March 2018





COELIAC DISEASE PAST, PRESENT, FUTURE; A SPECTRUM OF GLUTEN RELATED CONDITIONS

ROYAL COLLEGE OF PHYSICIANS

11 St Andrew's Place, Regent's Park, London, NW1 4LE

Chaired by Prof David Sanders, Royal Hallamshire Hospital and
University of Sheffield

10.00 **Arrival and networking – refreshments**

10.30 **Coeliac UK welcome – Chief Executive Sarah Sleet**

Session 1:

10.35 **Is porridge still on the menu? Clarifying the safety of oats in
coeliac disease**
Dr Jason Tye Din

11.00 **Spectrum of gluten related conditions**
Prof Knut Lundin

11.25 **Global perspective of coeliac disease with a focus on Asia**
Dr Govind Makharia

11.50 **So many patients, too little time; a dietetic led service**
Elaine Buchanan RD

12.15 **Lunch and poster exhibition**





Session 2:

- 13.30 **The psychology of coeliac disease and gluten free diet adherence**
Dr Kirby Sainsbury
- 13.55 **Dermatitis herpetiformis; skin manifestation of coeliac disease**
Dr Teaa Salmi
- 14.20 **The Environmental Determinants of Diabetes in the Young; The TEDDY study with a focus on paediatric coeliac disease**
Prof Daniel Agardh
- 14.45 **Break – refreshments**

Session 3:

- 15.15 **Top ten research priorities in coeliac disease**
Prof David Sanders
- 15.40 **Gluten related neurological conditions and patient case study**
Prof Marios Hadjivassiliou / TBC
- 16.05 **Follow up of adult coeliac disease to prevent further complications and patient case study**
Prof Chris Mulder/Prof David Sanders
- 16.30 **Chair's closing remarks and presentation of poster prize**
- 16.35 **CLOSE**

This event has been kindly sponsored by Biomedal, Dr Schär, Regenerus Laboratories.





SARAH SLEET

Chief Executive of Coeliac UK

Welcome

The experience of living with coeliac disease today could not be more different to that of 20, or even 10, years ago. Awareness of coeliac disease is higher than ever before. We have better, more accurate tests for diagnosis. Labelling of foods has revolutionised gluten free choice in shops and restaurants. Undoubtedly, the work of the charity and its tens of thousands of supporters was critical to achieving change, not least the £2m investment in medical research over the last decade.

So, as we celebrate Coeliac UK's 50th anniversary, you might think that the need for change is less urgent and will only be of marginal benefit. Nothing could be further from the truth.

Today we welcome you to our Research Conference, an event to bring healthcare professionals and researchers together to hear about the latest research on coeliac disease and the evolving spectrum of gluten related conditions. We proudly launch the top ten research priorities for

coeliac disease from our Priority Setting Partnership and our £5m Research Fund Appeal to provide the launch pad for a new era of research breakthroughs. We encourage you to join us on this journey to find answers for people whose lives who are affected by gluten.

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PROF DAVID SANDERS

Consultant Gastroenterologist,
Royal Hallamshire Hospital,
and Professor of Gastroenterology,
University of Sheffield,
Sheffield, UK

Professor David S Sanders is a consultant gastroenterologist and a professor of gastroenterology at the Royal Hallamshire Hospital & the University of Sheffield. He has published >300 peer reviewed papers (H-score >50). He is internationally recognised for his work in coeliac disease, gastrostomy feeding and small bowel endoscopy. His other research interests include pancreatic exocrine insufficiency, irritable bowel syndrome and gastrointestinal bleeding.

In 2010 he received a European Rising Star Award and a Cuthbertson Medal in 2011 (UK Nutrition Society). In 2017 he received the most prestigious award of the Swedish Gastroenterology Society (Bengt Ihre Award). His clinical work with patients who have coeliac disease has resulted in him being awarded the Coeliac UK Healthcare Professional of the Year Award (2010) & the inaugural Complete Nutrition Coeliac Health Care Professional Award (2013). He is fortunate to work as part of the Sheffield Gastroenterology

Team, which has been recognised for its standards of care. The Small Bowel Endoscopy Service won one of the inaugural British Society of Gastroenterology National GI Care awards (2011) & the Medipex award (2013). In 2012 the Percutaneous Endoscopic Gastrostomy team won both Health Service Journal primary care and integrated clinical care awards. In 2014 the Hallamshire Gastroenterology team, won one of the SAGE (Shire Awards for Gastrointestinal Excellence) awards for their primary care and GI bleed unit services. Professor Sanders has chaired both the British Society of Gastroenterology (BSG) Small Bowel and Nutrition Section (2006-2012) & the BSG Audit Committee (2010-2013).

He is the current Chair of the Coeliac UK Health Advisory Council, BSG Council Member and President of the International Society for the Study of Coeliac Disease (ISSCD).

www.profdavidsanders.co.uk





DR JASON TYE DIN

Laboratory Head, Walter and Eliza Hall Institute of Medical Research, Victoria, Australia

Biography

Jason Tye-Din MBBS, FRACP, PhD is a medical graduate of the University of Melbourne, Australia and completed gastroenterology training at the Royal Melbourne Hospital. He has practiced medicine since 1996, and for the last 15 years has combined coeliac disease research with patient care. His PhD examined immune responses to gluten in coeliac disease which led to the development of an immunotherapy now in clinical trials.

He heads the Coeliac Research Lab at the Walter and Eliza Hall Institute where his interests are understanding the genetic and immune basis for coeliac disease and improving the health and quality of life of patients. He runs a coeliac clinic at the Royal Melbourne Hospital managing gluten and other food related issues. He chairs the Medical Advisory Committee of Coeliac Australia and works closely with them to promote medical education and public awareness. Jason is the recipient of a Coeliac UK research grant.

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IS PORRIDGE STILL ON THE MENU? CLARIFYING THE SAFETY OF OATS IN COELIAC DISEASE

Historically, oats were regarded as unsafe for people with coeliac disease and were excluded from the gluten free diet. Subsequent studies have countered this view by showing that most people with coeliac disease can safely consume gluten free oats. However, for some people, abnormal immune responses and symptoms can be triggered by oats. What does this mean? Are your patients at risk? This presentation will discuss the place of oats in coeliac disease, including their potential health benefits and our current research to resolve the question of their safety.





PROF KNUT LUNDIN

Professor of Medicine and Head of Clinical Education, Faculty of Medicine, University of Oslo, Norway

Biography

Knut E A Lundin is Professor of Medicine and Head of Clinical Education, Faculty of Medicine, University of Oslo, Norway.

He is further a consultant gastroenterologist at the endoscopy unit at Oslo University Hospital, Rikshospitalet. He completed his scientific training at the Institute of Immunology with a MD degree in cellular immunology in 1990. He has, since the mid 1980s, worked together with Professor Ludvig M Sollid on the immunobiology and clinical aspects of the small intestine with particular focus on coeliac disease.

His highest ranking scientific achievement was published in 1993 when gluten specific T cells from the small intestine of coeliac disease patients were reported. This powerful tool was, in the years to come, used to define the gluten peptide antigens driving the disease. In recent years focus has also been paid to non coeliac gluten sensitivity. Other clinical and scientific areas

involve “regular” and “complicated” coeliac disease, refractory coeliac disease, inflammatory bowel disease and other GI disorders in a tertiary referral hospital setting. He has training in all aspects of diagnostic and therapeutic endoscopy. Together with Professor Sollid he arranged the 14th International Coeliac Disease Symposium in Oslo in 2011.

He was involved in the founding of the International Society for the Study of Celiac Disease in 2011 and the European Society for Study of Coeliac Disease in 2015 and holds a board position in both societies. He has published nearly 200 papers as original papers, reviews and book chapters and has been cited in > 10,000 other publications.

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SPECTRUM OF GLUTEN RELATED CONDITIONS

Coeliac disease is a common autoimmune condition affecting around one in 100 people. It is caused by an abnormal immune response to gluten, in people who have the associated HLA-DQ phenotype. Classical gastrointestinal symptoms include diarrhoea, bloating, constipation, abdominal pain but people may also have blistering rashes due to dermatitis herpetiformis, the skin manifestation of coeliac disease and/or gluten related neurological conditions such as gluten ataxia, neuropathy or encephalopathy. A spectrum of gluten related conditions is evolving.

Irritable bowel syndrome like symptoms, in response to wheat ingestion, are common in untreated coeliac disease but also reported by many others. However, in these cases, whether the reaction is due to gluten (ie non coeliac gluten sensitivity - NCGS), other wheat proteins, or FODMAPs (mostly fructans) alone or in combination, is highly debated and not clearly defined. In a recent randomised, double blind, placebo controlled crossover study of individuals with self reported NCGS, it was the fructans that induced symptoms, measured by the Gastrointestinal Symptom Rating Scale Irritable Bowel Syndrome. The absence of a clear biological mechanism of action and difficulties with the design and interpretation of research studies have plunged NCGS

into even deeper controversy. In the absence of clarity in its diagnosis, the epidemiology, prognosis, and therapeutic approaches to a patient who may be gluten sensitive remain to be determined. Adequate understanding of the issues surrounding the controversy and further research will slowly unravel the truth behind the problem.



DR GOVIND MAKHARIA

Professor, Department of Gastroenterology and Human Nutrition, All India Institute of Medical Sciences, New Delhi, India.

Biography

Dr Govind K Makharia received his training from the prestigious Postgraduate Institute of Medical Education and Research, Chandigarh. He has trained 48 fellows in gastroenterology and seven PhD students. Dr Makharia has published 186 articles in the indexed journals, 35 chapters for different books and edited a handbook on coeliac disease. He is a Board member of the International Society for the Study of Celiac Disease.

He was nominated as co-Chair of the global guidelines on Diet and the Gut and World Digestive Health Day 2016, World Gastroenterology Organisation. He has co-chaired the World Gastroenterology Organisation and Asia Pacific Association of Gastroenterology working party on celiac disease. He is a core member of the Asia Pacific working party on inflammatory bowel disease, and Asia Pacific colorectal cancer study group. He is presently the Secretary General of the Indian Society of Gastroenterology and a

coordinator of the national taskforce on inflammatory bowel disease.

Dr Makharia is also involved in the development of medical device innovation and is a co-inventor of a device for faecal incontinence. He has received many awards including BMJ, South East Asia research paper of the year award, Alkem Om Prakash Memorial award, Young Clinicians' Award (World Gastroenterology Organisation), Young Investigator Award (APAGE), Award of Achievement by OESO, and SR Naik Memorial award, and AIIMS Excellence Award. He also delivered the ISG-Zydus oration in 2017.

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GLOBAL PERSPECTIVE OF COELIAC DISEASE WITH A FOCUS ON ASIA

Until three decades ago, coeliac disease (CD) was considered to be an uncommon disease and limited to Western Europe. Initial studies of its prevalence in the general population came from European countries and estimated to affect about 1% of the European population. CD was subsequently reported in other parts of world with predominantly Caucasian populations such as North America, Australia and South American countries such as Brazil. Population based data on the prevalence of CD has also been reported from Middle Eastern Asia, India and a few African countries. The global epidemiology of CD continues to evolve with improvement in the diagnostic tests, simplification of the diagnostic criteria and an increased awareness of the disease.

We conducted a systematic review and meta-analysis of the global prevalence of CD and observed that the pooled global sero-prevalence is 1.4% (95% CI 1.1% to 1.7%) in 290,205 individuals based on a positive anti-tissue transglutaminase antibody and/or anti endomysial antibody test. The pooled global prevalence of biopsy confirmed CD is 0.7% (95% CI 0.5% to 0.9%) in 138,792 individuals. The abovementioned estimate may not be a true prevalence of CD as population based data are still not available from many countries with large populations such as

China, Indonesia, Pakistan, Nigeria, Bangladesh and Japan.

The Asian region is currently at the crossroads of the frontier of knowledge and awareness of CD. In many Asian nations, CD is still considered to be either non-existent or very rare. A notable exception is India, where CD has been well recognised, especially in northern India where three population based studies have revealed a prevalence of 0.6% - 1.04%. Initial reports from Malaysia, China, Japan and Singapore suggest the existence of CD in these countries. Although the absolute number of patients with CD at present is not very large, this number is expected to increase over the next few years/decades. It is thus appropriate that the medical community across Asia defines the extent of the problem and is prepared to handle the impending CD epidemic.





ELAINE BUCHANAN RD

Lead Paediatric Gastroenterology
Dietitian, Royal Hospital for
Children, Glasgow, UK

Biography

Elaine is a lead paediatric gastroenterology dietitian at the Royal Hospital for Children, Glasgow and also team lead within a department of 30 dietitians. She works within a large multidisciplinary clinical team including gastroenterologists, dietitians, clinical nurse specialists, pharmacy and clinical psychology and manages a large, varied caseload including; inflammatory bowel disease, coeliac disease, short bowel syndrome, liver disease and children on home parenteral nutrition.

Elaine is also the lead dietitian for the west of Scotland managed clinical network for paediatric gastroenterology ensuring equity of dietetic care across the west of Scotland. She has also been on the committee of the paediatric group of the BDA and the associates group of BSPGHAN.

Elaine has lectured extensively including paediatric group meetings, local BDA branch meetings, annual meeting of trainees and associate

members of BSPGHAN and SSPGHAN. She has also presented papers at ESPGHAN meetings and was one of two dietitians chosen to represent the associate members of BSPGHAN to lecture to dietitians in India.

Last year, Elaine was on the local organising committee of BSPGHAN and next year ESPGHAN will be in Glasgow and she is on the local organising committee.

Elaine has been involved in research and audit and has had numerous abstracts and papers published.

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SO MANY PATIENTS, TOO LITTLE TIME - A DIETETIC LED SERVICE

A dietetic led coeliac service for paediatric patients was established in 2007 at the Royal Hospital for Children in Glasgow. Previously all these patients were seen by paediatric gastroenterologists and there was no agreed pathway for managing their care. This included the frequency of review, the type and frequency of biochemical monitoring and the transition to adult care. Patients would attend a general gastroenterology clinic and dietetic review was inconsistent due to inadequate staffing. There was no dedicated dietetic clinic for these patients.

Following a successful business case, an additional dietitian was appointed and it was agreed with the consultants and also following patient consultation that dietitians would manage the service to coeliac patients. This entailed dietitians working at an advance level and required annual assessment and sign off by the clinical lead. Protocols, pathways and patient literature were agreed and initially a fortnightly clinic was established.

A database was developed to capture all patient details including referral reason, serology and ongoing management.

We now have a caseload of around 250 patients which is a 400% increase in patient numbers since we established the service just

over 10 years ago. There are two clinics a week for potential coeliac patients, newly diagnosed patients and follow up patients. Dietitians are responsible for referring patients for endoscopy, following through results and transitioning patients to adult services. There are six weekly meetings with the clinical lead to discuss all potential and follow up patients.

Recent developments include educational family days, study days for professionals in managing coeliac disease and the production of educational videos for families.





DR KIRBY SAINSBURY

Research Associate in Health Psychology at the Institute of Health and Society, Newcastle University, Newcastle, UK

Biography

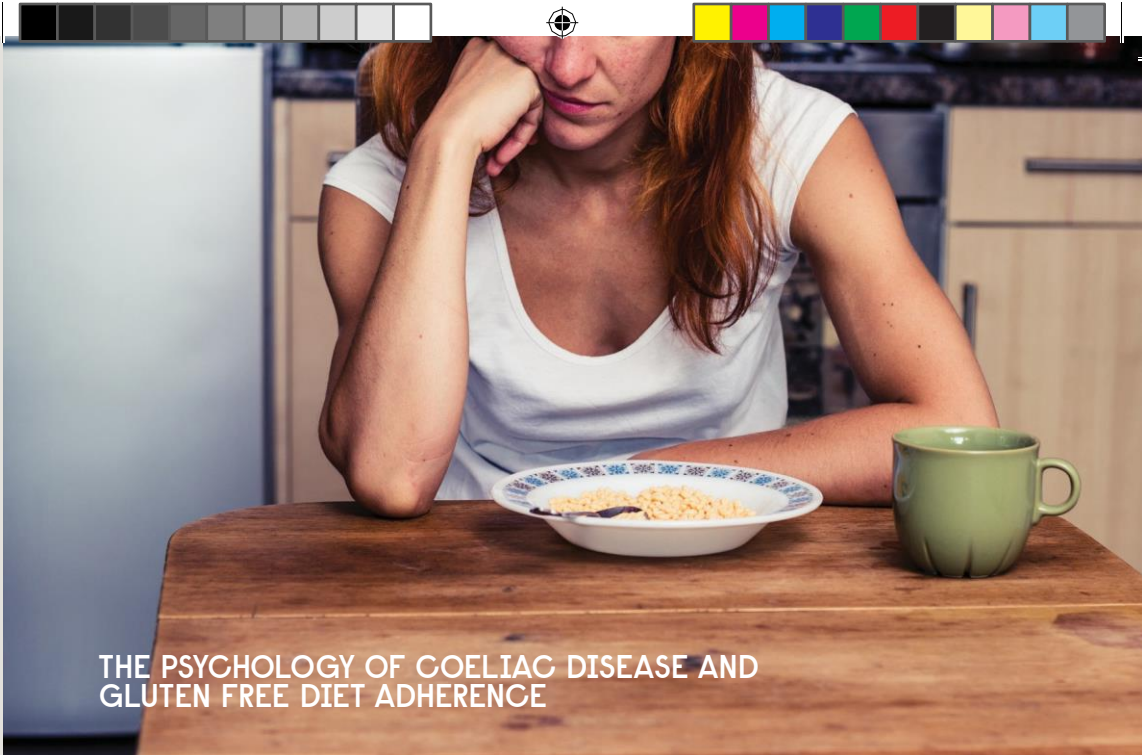
Dr Kirby Sainsbury has worked as a research associate in Health Psychology at the Institute of Health and Society, Newcastle University, since 2015. She is Editor of Health Psychology Update – the official journal of the British Psychological Society's Division of Health Psychology. She completed a Doctor of Clinical Psychology in 2011 and PhD in 2013 at the University of Sydney, Australia.

Prior to 2008, Kirby had never heard of coeliac disease (CD). She and her sister were both diagnosed ten years ago, and this provided the impetus for her PhD topic, as she was in the process of specifying her research interests for her postgraduate application. Her PhD focused on the psychological characteristics associated with inadequate gluten free diet (GFD) adherence in adults with coeliac disease. This included the design of a theory based behaviour change intervention to improve GFD adherence, which, after

five years, remains the only published intervention for this purpose.

Since finishing her PhD, Kirby has continued to collaborate with researchers in this area and has successfully supervised several Masters' students on projects in CD and GFD adherence. She has published in a range of psychological and gastroenterological journals (including ten papers on GFD adherence), in the Australian Coeliac magazine, and presented at conferences in Australia, the UK, and across Europe. Her current research work is on weight loss maintenance in obesity and adherence to UV protection in the rare disease, xeroderma pigmentosum. She previously worked as a clinical psychologist, specialising in eating disorders, depression, and emotion regulation difficulties, in both private practice and hospital settings, in Australia.





THE PSYCHOLOGY OF COELIAC DISEASE AND GLUTEN FREE DIET ADHERENCE

Rates of strict gluten free diet (GFD) adherence are inadequate, and merely providing patients with information about treatment and the consequences of non-adherence is not always sufficient to ensure a favourable outcome. Patient behaviour is the single most important determinant of clinical outcome and remission in coeliac disease. In contrast to many other patient characteristics that may relate to GFD adherence (eg age of diagnosis, education, SES), behaviour is modifiable and represents a proximal and viable target for individual level interventions to improve adherence. Understanding the psychological factors associated with behaviour and adherence is therefore integral for supporting patients to improve their adherence, whether in one to one consultations or through the design of evidence based behaviour change interventions.

The aim of this presentation is to provide a broad overview of the psychology of coeliac disease and GFD adherence, with a specific focus on factors shown to narrow or explain the 'intention behaviour gap' – that is, why many adults with positive intentions or motivation to be strictly adherent fail to achieve this. Such factors include depression, coping skills, self regulation, confidence, the type of motivation, and psychological resources. Recommendations for improving adherence via targeting changes in these factors will also be discussed. The focus will be on research with adults with coeliac disease, although a brief summary of the comparable child/adolescent literature will be provided.



DR TEEA SALMI

MD, PhD, docent, Clinical Lecturer,
Dermatologist, Celiac Disease
Research Centre, University of
Tampere, Finland

Biography

Dr Salmi is a specialist in dermatology and allergology. She has worked as a clinical lecturer at the University of Tampere, Finland, since 2011, and completed university training for clinical lecturers in 2016. Dr Salmi is also a senior consultant at the department of dermatology, and a physician at the Wound Center, Tampere University Hospital. The Finnish Medical Association awarded her with a special competence in wound management.

Dr Salmi's research in coeliac disease started in 2000, she completed her PhD on improving coeliac disease diagnostics in 2006, and received the title of Docent in Dermatology and Allergology in 2016. She is currently the group leader of the dermatitis herpetiformis study group, Celiac Disease Research Center, Tampere, Finland. She supervises six PhD students, and current research themes include autoantibody reactions in dermatitis herpetiformis, the burden of dermatitis

herpetiformis, the health benefits and effects of a gluten free diet and the development of gluten tolerance in dermatitis herpetiformis.

Dr Salmi is a member of the scientific advisory board of the Finnish Coeliac Society. Also a member of the Regional Ethics Committee of Tampere University Hospital and a Board member and representative of Finland at the Nordic Dermatology Association.





DERMATITIS HERPETIFORMIS: SKIN MANIFESTATION OF COELIAC DISEASE

Dermatitis herpetiformis (DH) is a cutaneous manifestation of coeliac disease presenting with an itching and blistering rash predominantly on elbows, knees and buttocks. Coeliac disease and DH share the same triggering factor, gluten, and the equivalent HLA DQ2 and DQ8 haplotypes in chromosome 6, predispose to both coeliac disease and DH. Opposite to the increasing incidence of coeliac disease, the incidence of DH has been shown to decline, and recent evidence shows that approximately 1/8 of patients with coeliac disease have DH. Further, even though the vast majority of patients with coeliac disease are females, the incidence of DH is almost identical in females and in males. The highest incidence of DH occurs in females and males over 50 years of age.

When DH is suspected, the diagnosis must be confirmed by skin biopsy taken from perilesional skin where a granular IgA deposition may be found in the papillary dermis. The target for this IgA deposition is known to be transglutaminase (TG) 3. Small bowel biopsies are not necessary for the diagnosis, but if taken, approximately 75% of DH patients have villous atrophy and the remainder coeliac type inflammation, with an increase in the density of intraepithelial lymphocytes. Further, TG2 targeted coeliac autoantibodies are usually present in the serum at the time of

the DH diagnosis, but the sensitivity of serum coeliac autoantibodies is known to be lower in DH compared to coeliac disease and to correlate with the severity of small bowel mucosal damage. Further, the majority of DH patients have TG2 antibody deposits in the small bowel mucosa at the time of the diagnosis.

The mainstay of DH treatment is a strict, life long gluten free diet (GFD). However, a DH rash often responds rather slowly to a GFD, and hence DH patients with severe skin symptoms are additionally treated with dapsone medication, which alleviates the rash typically within a couple of days. DH patients have an increased risk of concomitant autoimmune disorders similar to patients with coeliac disease, and further, the risk for lymphoma is increased. However, strict adherence to a GFD lowers the risk for lymphoma.





PROF DANIEL AGARDH

MD, Associate Professor,
Department of Clinical Sciences,
Lund University, Malmö, Sweden

Biography

Daniel Agardh is an associate professor at the Unit of Diabetes and Celiac Disease, Department of Clinical Sciences, Lund University, and works clinically as a pediatric gastroenterologist at the Department of Pediatrics in Malmö and Lund, Sweden. The main focus of his research is to identify genetic and environmental factors that trigger coeliac disease in children followed in the longitudinal prospective birth cohort studies in the countries of Sweden and Ethiopia.

His research group is involved in several international collaborations and ongoing prevention trials in both coeliac disease and type 1 diabetes in Europe, the US and Ethiopia. Since 2007, he has been the co-chair of the Celiac Disease Committee in The Environmental Determinants of Diabetes in the Young (TEDDY) study. This longitudinal prospective observational study follows over 8000 children at genetic risk for type 1 diabetes and coeliac disease from

birth to 15 years of age at six clinical research sites located in Finland, Germany, Sweden and three states in the US. Several important findings have been published from the TEDDY cohort that relate environmental factors, such as gluten intake and gastrointestinal infections, to coeliac disease. The long term goal of his research is to find what triggers coeliac disease in order to evaluate new methods that prevent coeliac disease in early childhood.





THE ENVIRONMENTAL DETERMINANTS OF DIABETES IN THE YOUNG; THE TEDDY STUDY WITH A FOCUS ON PAEDIATRIC COELIAC DISEASE

Coeliac disease is a multifactorial disease caused by gluten in individuals carrying certain HLA genotypes. However, many questions on the aetiology are mainly unresolved. Although genetics and gluten are prerequisites for the disease to develop, it still remains unknown why not all individuals at genetic risk eating gluten develop coeliac disease. Infant feeding habits, such as time to gluten introduction and breastfeeding, have long been debated as important factors in coeliac disease. Other studies have demonstrated that mode of delivery, antibiotics and perinatal factors as well as changes in infants' microbiota may contribute to disease risk. More recently, studies indicate that a viral infection may trigger coeliac disease, but results are conflicting and vary between studies in different countries and populations.

There are multiple population based studies that have investigated risk factors associated with coeliac disease. The Environmental Determinants of the Diabetes in the Young, the TEDDY study, is to date the largest ongoing prospective observational study involving six clinical centres located in four different countries. The goal of TEDDY is to explore environmental differences in type 1 diabetes and coeliac disease across diverse populations and ethnic groups and in children. Over 8000 children with higher risk genes for type 1 diabetes and coeliac disease are prospectively followed from birth to 15 years of age. This presentation gives an overview of the most important findings of TEDDY in terms of triggers for coeliac disease in genetically predisposed children.





THE PRIORITY SETTING PARTNERSHIP (PSP) ON GOELIAC DISEASE

In 2017 Coeliac UK teamed up with the James Lind Alliance, experts in priority setting partnerships (PSP), bringing patients, their carers and healthcare professionals together to agree a top ten list of research priorities.

Since May 2017, the PSP has undertaken a number of stages, including:

- a survey for participants to submit their questions about coeliac disease which may be answered by further research (this includes the other immune conditions caused by gluten eg dermatitis herpetiformis and gluten ataxia)
- categorisation of the submitted questions by an information specialist and Steering Group
- a check of the evidence base to ensure the research hasn't already been completed
- a second survey to rank the research questions and provide a targeted list to take to a workshop.
- a one day workshop involving patients, their carers and healthcare professionals to discuss and agree a top ten list of priorities.



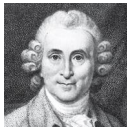
Today, Coeliac UK announces the top ten research priorities for coeliac disease. These priorities will focus the charity's research funding and help direct its agenda going forwards. Many thanks to all those who participated in our surveys, attended the final workshop, and dedicated their time to the Steering Group.

PSP lead: Dr Heidi Urwin
Clinical Lead: Professor David Sanders

PSP Co-ordinator: Katie Stokes
James Lind Advisor: Maryrose Tarpey
Information Specialist: Ann Daly
Steering Group: Manpreet Bains¹, Brian Barnes¹, Andrea Gibbons¹, Debbie Lane², Dr Debbie Bell^{2,3}, Dr David Bellamy^{1,2,3}, Abi Freedman³, Dr Peter Gillett³, Professor Marios Hadjivassiliou³, Veronica Mitchell³, Katherine Page^{1,3} and Dr Gerry Robins³.

(¹patient, ²parent/carer, ³healthcare professional)

Thanks also to the key partners involved in the PSP for coeliac disease:



James Lind Alliance

Priority Setting Partnerships



British Society of Paediatric Gastroenterology Hepatology and Nutrition



Ataxia UK





PROF MARIOS HADJIVASSILIOU

Consultant Neurologist, Royal
Hallamshire Hospital,
Sheffield, UK

Biography

Professor Marios Hadjivassiliou is a consultant neurologist with an interest in the neurological manifestations of systemic disease, the ataxias and peripheral neuropathies. His primary research is in the neurological manifestations of gluten related diseases, an area that he studied initially for his MD thesis and which has become the focus of his research career for the last 25 years.

His pioneering research has led to the definition of previously unrecognised disease entities including gluten ataxia and gluten neuropathy. He has published extensively on the subject in high impact journals including three first author papers in the Lancet. He runs weekly clinics for patients with neurological problems related to gluten sensitivity and a weekly ataxia clinic, receiving referrals from all over the UK and internationally. He is the director of the Sheffield Ataxia Centre, accredited by Ataxia UK as an Ataxia Centre of Excellence,

one of only three in the UK, and is a founding member of the Sheffield Institute of Gluten Related Diseases (SIGReD). He is a member of the Medical and Health Advisory Boards for Ataxia UK and Coeliac UK. He is the Deputy Academic Director and Theme Lead for Neuroinflammation in the Academic Department for Neurosciences, Sheffield, UK.





GLUTEN RELATED NEUROLOGICAL DYSFUNCTION

The presentation will cover the latest research on the neurological manifestations of gluten related diseases. The aim is to familiarise health professionals with the commonest neurological manifestations in an attempt to increase awareness and aid diagnosis. Data presented will be based on 1000 patients with gluten sensitivity/CD with neurological manifestations clinically assessed over the last 25 years at the Sheffield Institute for Gluten Related Diseases (SIGRED).

Given that at least half of patients with neurological presentations due to gluten sensitivity do not have enteropathy, diagnostic biomarkers aside of transglutaminase 2 and endomysium antibodies become extremely important yet they are not readily available. In addition the level of such antibodies differs between the “classic” CD and patients presenting with neurological manifestations, so adjustments need to be made. New biomarkers such as TG6 antibodies will also be discussed. The presentation will propose the concept of a spectrum within which there are patients presenting with “classic” CD easily diagnosed and treated early, thus protected from future development of extraintestinal manifestations versus those patients who primarily have neurological manifestations and thus remain undiagnosed until they present to a neurologist often

with a fixed neurological deficit. Even at that late stage of presenting with ataxia or neuropathy, screening for CD and gluten sensitivity is not always performed. The presentation will also cover relevant aspects of the pathophysiology that may explain why we observe such diverse manifestations.





PROF CHRIS MULDER

Hepatogastroenterologist, VU
Medical Center, Amsterdam,
Netherlands

Biography

Professor Mulder has been working in the VU Medical Center since 2002 as an hepatogastroenterologist and Head of Department. He aims to deliver high quality, sustainable services for a wide range of patients as well as safe patient care. In 2017, Gerd Bouma took over his position as Head of Department.

Chris Mulder has been contributing to coeliac research since 1984, mainly in the area of clinical and translational research. Initially his research focused on (neonatal) meningitis (PhD 1984). During his training in Amsterdam, he focused on IBD, especially 5-ASA/AZA treatments. Then he became interested in the underdiagnosis of coeliac disease in the Netherlands. In 1992, he started screening with sugar absorption tests to diagnose coeliacs. Because serology was not sensitive enough he focused on updating the Marsh criteria and implementation in clinical practice. With Cisca Wijmenga, genome wide screening was initiated and in 2000,

prospective evaluation of patients with refractory coeliac disease was started, resulting in clinical validation of T-cell flow in daily practice. He has trained over 50 gastroenterologists, mentored 45 PhD graduates and published over 500 papers in English. He is an honorary member of the South African, Romanian and Czech societies of gastroenterology and an honorary and distinguished fellow of the Royal College of Physicians. Since 2001, he started drug rediscovery for Thioguanine (Thiosix®) with 5000 Dutch IBD patients on this drug, as an alternative for AZA/6MP.





FOLLOW UP OF ADULT COELIAC DISEASE PATIENTS TO PREVENT FURTHER COMPLICATIONS

Coeliac disease (CD) is quite common in screening studies with a prevalence of around 1 in 100 people and it is readily treatable with a life long strict gluten free diet (GFD). Most patients report clinical improvement within weeks however, mucosal recovery may last years after the start of a GFD. CD requires a long term follow up plan to maintain excellent health and to prevent complications from occurring.

Maintaining a strict GFD is difficult and has both financial and quality of life implications. The evidence for follow up management is lacking in current literature and therefore is based on expert opinion.

Histological normalisation takes around 2 - 5 years, especially in patients who are asymptomatic or do not have the classical symptoms. It helps patients and their relatives to be properly informed about the condition, the 'dos and don'ts' and the risk of untreated CD to increase knowledge and encourage self empowerment of patients.

Amongst the many guidelines for coeliac follow up there is a lack of clarity regarding 'what, who and when'.

Rates of mucosal healing are highly variable. The majority of our patients diagnosed after the age of 40 - 45 years have slow normalising

histological recovery. Our major problem is whether re-biopsies indeed change the clinical outcomes in the majority of patients.

Since 2001, we divided our patients with ongoing symptoms and a lack of response to the GFD, into two types based on the absence (type I) or presence (type II) of an, usually clonal, intraepithelial lymphocyte population with aberrant phenotype. Enteropathy associated T cell lymphoma is such an infrequent complication that the majority of gastroenterologists may never see it amongst the population of coeliac patients they diagnose and follow up.

A life-long GFD improves health and the quality of life in a vast majority of patients with CD, even in those with minimal symptoms.





THANK YOU TO OUR SPONSORS

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ABSTRACT COMPETITION

Entries to the Coeliac UK Research Conference 2018 poster competition.

There is a £500 prize for the best abstract. The lead author may use the prize money to help pay towards attendance at an international event to increase dissemination of their research. The winner of our poster competition will be announced at the end of the conference.

**£500 PRIZE FOR
THE BEST ABSTRACT**



CHANGES IN THE TESTING FOR AND INCIDENCE OF COELIAC DISEASE IN THE UK 2005 - 2015

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Abstract

Introduction

Over many previous decades the incidence of coeliac disease has been increasing almost everywhere in the world where it has been measured. However there has been a suggestion that in the last five years that incidence has plateaued or even declined.

Methods

We used the UK Clinical Practice Research Datalink and examined

the electronic health care records therein to estimate the European (2013 population) age standardised incidence of coeliac disease 2005 - 2015 and the corresponding rates of serological testing (anti-tissue transglutaminase (tTG) and endomysial antibody (EMA)) for the disease. We used Joinpoint analysis to examine changes in the rates of diagnosis and testing during this period.



Results

There were 8177 incident cases of coeliac diseases diagnosed among 45,539,211 million person years. Over the period 2005 - 2015 there was an increase in age standardised incidence from 2005 (14.6 per 100,000) until 2012 (20.3 per 100,000) and then a plateauing effect ($p < 0.05$). Serological testing increased and then decreased during the same period ($p < 0.05$).

plateaued and declined. The plateau in incidence is most likely to be a function of the corresponding decline in testing which in turn could be due to lack of resource, more targeted use of testing or that the threshold of clinically identifiable coeliac disease has been reached and a steady state incidence rate obtained.

Conclusions

Age standardised rates of diagnosis of coeliac disease and serological testing have, since 2011, respectively





BIOPSY AVOIDANCE STRATEGY IN ADULT COELIAC DISEASE

Authors

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Abstract

Introduction

Paediatric ESPGHAN guidelines support a diagnosis of coeliac disease (CD) when immunoglobulin-A anti-tissue transglutaminase antibody (IgA tTGA) titres are >10 times the upper limit of normal (ULN) and combined with supportive criteria. This study examines whether serological testing alone could be sufficient for diagnosis in adult patients, thus avoiding the need for duodenal biopsies.

Methods

We performed a prospective analysis of CD patients diagnosed in a university hospital. Symptoms of CD, villous atrophy (VA) on biopsy, IgA-endomysial (IgA-EMA) antibodies, tTGA and Human Leukocyte Antigen (HLA) genotype were used for analysis. We then compared the tTGA level against small bowel histology.



Results

CD patients (n = 443, 66.8% female, median age 41 years, range 15 - 84 years) were diagnosed between 2008 and 2016. 56.9% (n = 252, 95% CI = 52.12 - 61.53) had a tTGA value >10 times the ULN. 292 fulfilled ESPGHAN guidelines for features of malabsorption (diarrhoea = 157, weight loss = 45 and anaemia = 190). Of these symptomatic patients, 70.4% (n = 179, 95% CI = 64.86 - 76.08) had a tTGA value 10 times ULN. The proportion reaching the 10 x tTGA threshold was 55.4% (n = 87, 95% CI = 47.64 - 63.19) for diarrhoea, 60.0% (n = 27, 95% CI = 45.69 - 74.31) for weight loss, and 74.2% (n = 141, 95% CI = 67.99 - 80.43) for anaemia. Of the 151 patients who did not experience malabsorptive features, 49.0% met the 10 x ULN tTGA level (n = 74, 95% CI = 41.03 - 56.98). The sensitivity of tTG antibodies and EMA antibodies for predicting VA was 93.2% (95% CI = 90.89 - 95.57) and 90.7% respectively (95% CI = 88.05 - 93.44). Combined tTG and EMA antibodies the sensitivity was 98.6% (95% CI = 97.67 - 99.72). All patients had compatible HLA typing,

thereby failing to add any further diagnostic value.

Discussion

56.9% of patients would have been correctly diagnosed with CD and avoided a duodenal biopsy using an IgA tTGA threshold of >10 times the ULN. Symptoms and HLA typing did not add any supportive information. This study provides evidence that a biopsy avoidance strategy may be implemented into adult gastroenterological practice.





ADULT COELIAC DISEASE REMISSION ASSESSMENT: DOES A D1 BIOPSY INCREASE THE DETECTION OF VILLOUS ATROPHY?

Authors

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Abstract

Introduction

The duodenal bulb (D1) has been shown to be a sensitive site for detecting villous atrophy (VA) in newly diagnosed coeliac disease (CD), however there is a scarcity of data from those with established CD. In patients with established CD, we aim to establish whether D1 biopsies improved the identification of VA compared to biopsies from the second part of the duodenum (D2) alone.

Methods

Patients with established CD were prospectively recruited from the endoscopy department at the Royal Hallamshire Hospital between 2013 and 2017. These patients were undergoing repeat gastroscopy to assess dietary adherence. All patients underwent a gastroscopy, with one biopsy taken from the duodenal bulb and four from D2. Biopsies were classified according to Marsh criteria. We assessed concordance of histology between the D1 and D2 sites, and 95% confidence intervals were calculated for all results using a binominal distribution.




Results

Patients were recruited (n = 251, 70.5% female, age range 17 - 81 years, median age 53 years) having been on a gluten free diet for a median duration of six years. Concordant results: 35.1% (n = 88, 95% CI = 29.16 - 40.96) had normal duodenal biopsies in both D1 and D2; 32.3% (n = 81, 95% CI = 26.49 - 38.05) had VA in D1 and D2; 18.3% (n = 46, 95% CI = 13.54 - 23.11) had raised intra-epithelial lymphocytes (IELs) only in both D1 and D2. Disconcordant results: 4.4% (n = 11, 95% CI = 1.85 - 6.91) had VA in D1 but not D2; 2.4% (n = 6, 95% CI = 0.50 - 4.28) had raised IELs in D1 but normal histology in D2. 2.8% (n = 7, 95% CI = 0.75 - 4.83) had VA in D2 but normal histology in D1; 4.8% (n = 12, 95% CI = 2.14 - 7.42) had IELs in D2 but normal histology in D1.

Discussion

VA was confined to the duodenal bulb in 4.4% of patients with established CD. Thus a D1 biopsy in addition to distal duodenal biopsies increases the likelihood of detecting VA, although the significance of isolated VA in the bulb in patients on a gluten free diet is yet to be determined.



IS SEROLOGY PREDICTIVE OF PERSISTING VILLOUS ATROPHY IN PATIENTS WITH ESTABLISHED GOELIAC DISEASE?

Authors

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Abstract

Introduction

Recent work has suggested that an IgA tissue transglutaminase (tTG) <1.2 U/mL may predict mucosal healing in those with established coeliac disease (CD). This study examines whether a combination of serological markers may be used as a surrogate marker for the detection of villous atrophy (VA) in known CD patients.

Methods

We undertook a prospective analysis of known CD patients diagnosed in a university hospital. All patients

underwent a gastroscopy, with four biopsies taken from the second part of the duodenum, and one from the duodenal bulb. Serological markers were assessed at the time of endoscopy IgA tTG, IgA endomysial antibodies (EMA), IgA antigliadin antibodies (IgA AGA) and IgG antigliadin antibodies (IgG AGA), and their performances in isolation and in combination compared to histological outcomes.



Results

Patients (n = 107, 67.3% female, median age 53 years (20 - 81 years)) that were on a gluten free diet for a median duration of six years were included. The performance of the different serological markers to detect VA, both in isolation and in combination are shown in Table 1. The performance of tTGA using the previously used cut-off of <1.2u/ml produced a sensitivity of 38.5%, a specificity of 73.8%, a positive predictive value of 64.9% and a negative predictive value of 43.7% to detect VA.

Table 1 - Ability of serological markers to detect VA


	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)
tTGA	39.0 (29 - 48)	97.0 (89 - 99)	88.9 (64 - 98)	70.8 (61 - 81)
EMA	40.5 (26 - 57)	96.9 (88 - 99)	89.5 (65 - 98)	71.6 (61 - 80)
IgA AGA	47.5 (32 - 64)	95.5 (87 - 99)	86.4 (64 - 96)	75.3 (65 - 84)
IgG AGA	37.5 (23 - 54)	90.0 (80 - 96)	68.2 (45 - 85)	71.6 (61 - 80)
EMA + tTGA	33.3 (20 - 50)	98.5 (91 - 100)	93.3 (66 - 100)	30.4 (21 - 41)
IgA + IgG AGA	28.6 (16 - 45)	100 (93 - 100)	100 (70 - 100)	68.4 (58 - 77)
IgA or IgG AGA + EMA	28.6 (16 - 45)	100 (93 - 100)	100 (70 - 100)	68.4 (58 - 77)
IgA or IgG AGA + tTGA	31.0 (18 - 47)	100 (93 - 100)	100 (72 - 100)	69.1 (59 - 78)

PPV – positive predictive value
NPV – negative predictive value

Discussion

This study is the first study to evaluate the combination of serological markers to detect VA in patients with established CD. Our findings oppose recent work that serology may be used as a surrogate marker of mucosal healing in known CD.





THE RISING INCIDENCE OF CHILDHOOD COELIAC DISEASE – A 7 YEAR REGIONAL COHORT STUDY

Authors

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Institution

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Abstract

Introduction

The incidence of coeliac disease (CD) during childhood is rising in the United Kingdom, however many cases remain undetected as current prevalence is certainly not approaching 1%. CD may present with classic symptoms, detected following screening of at risk populations or during investigation of non specific symptoms if awareness levels are high. We have previously reported data from our region and have shown regional differences due to increased clinical awareness.

Aims and Objectives

To determine the incidence of childhood CD in Southeast Scotland over a 7 year period.

Subjects and Methods

We performed a retrospective cohort study of patients diagnosed with CD <16 years of age during 2010 - 2016, identified by direct laboratory notification of raised anti-tissue transglutaminase (anti-tTG) levels, endoscopy records and case notes. Annual incidence was calculated using population figures published by Scottish government and further classified by mode of presentation (classical/non classical symptoms as per Oslo criteria, or targeted screening) and method of diagnosis (biopsy/no biopsy). Poisson regression was used to calculate changes in incidence over time.



Results

382 children were diagnosed during the seven year period (31 diagnoses in 2010 and 85 in 2016 respectively) with a significant increase in incidence from 13.8 to 36.7 per 100,000 population.

Female to male ratio was consistent (2.2:1 throughout period). Median age at diagnosis was 8.3 years (IQR 5.1 - 12.3). Only 8% were identified through targeted screening, with the remainder presenting classically/non classically in equal proportion. Diagnosing CD without biopsy (as per European Society of Paediatric Gastroenterology Hepatology and Nutrition guidelines) began in our region in 2012, with 27% of total cases diagnosed with this strategy by 2016. 20% of diagnoses occurred in the least deprived 10%

of the population, as determined by national multiple deprivation scores by postcode.

Summary and conclusion

The incidence of coeliac disease in children and young people <16 years of age increased 2.5 fold during the seven year period from 2010 - 2016. A no biopsy strategy is becoming more common over time. To our knowledge the incidence of 36.7 per 100,000 in 2016, is the highest reported in the UK, whether in childhood or adult studies, and shows no signs of diminishing.



COELIAC DISEASE IN THE NO BIOPSY ERA: SCOPE TO DO FEWER SCOPES?

Authors

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Abstract

Introduction

The incidence of coeliac disease (CD) is increasing in many countries. ESPGHAN guidelines published in 2012 simplify the diagnostic process and reduce the need for biopsy to secure the diagnosis in symptomatic patients. This represented a significant shift in practice, requiring modifications throughout the multidisciplinary team.

Aims and Objectives

To assess compliance with ESPGHAN 2012 guidance and review individual cases in which new guidance was not followed.

Subjects and Methods

We performed a retrospective cohort study of patients diagnosed with CD in Southeast Scotland between

01.01.10 and 31.12.16. All raised anti-tissue transglutaminase (anti-tTG) levels are reported to the local lead for CD. We included two years of data collection prior to ESPGHAN guideline introduction, allowing analysis of a greater number of individual cases who had biopsy confirmed diagnosis, acting as a form of control group. Results were cross referenced with endoscopy lists and case notes. Data were collected on sex, age at diagnosis, presentation (classical/non-classical/identified by screening, as per Oslo criteria), initial anti-tTG and biopsy result. For those not biopsied, repeat anti-tTG and HLA-DQ type were recorded. Data were recorded using a specific proforma.



Results

382 (261 female) patients with CD were identified over this seven year period. Median age at diagnosis was 8.3 years (IQR 5.1-12.3). Increasing incidence was noted year on year. Since 2012, 177 patients met the criteria for no biopsy consideration. All had CD confirmed on further blood testing or biopsy. In total, since 2012, 44 patients have been diagnosed with no need for biopsy and in 2016, 23 of 43 (53.4%) eligible patients were diagnosed using the no biopsy strategy with the consultant doing a virtual consultation by telephone and sending informatics using e-communication. Diagnosis was confirmed by repeat anti-tTG and HLA-DQ2/8, performed on the day of the dietetic appointment, all within a month of the initial blood test.

Summary and conclusion

Our modified ESPGHAN 2012 strategy is a cost effective option for the NHS and allows quicker diagnosis for the patient. Confidence in this approach is increasing. This study confirms that all eligible patients in our region could have had a secure diagnosis made without a biopsy.

PATIENT AND PARENT SATISFACTION WITH CURRENT SERVICE FOR PAEDIATRIC PATIENTS WITH COELIAC DISEASE AT ST GEORGES HOSPITAL

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Abstract

Introduction

Currently paediatric patients with coeliac disease (CD) at St George's Hospital are followed up annually by the paediatric gastroenterologist and the paediatric gastroenterology dietitian at separate time points. BSPGHAN (2013) and NICE (2015) recommend annual review. Positive predictors of patient satisfaction have been reported to be that physicians spend ample time managing CD needs and having CD antibody levels checked yearly.

Method

The paediatric gastroenterology dietitian developed an online survey. Patients and parents were asked questions and given the opportunity to comment in their own words

about the current service. Contact was established with 31 parents of patients with CD and they were emailed with the link of the survey.





Results

Twenty one patients or parents of patients with CD completed the survey, a response rate of 67%. The vast majority of patients had been diagnosed with coeliac disease for over one year. Overall parents of patients were likely or extremely likely (76%) to recommend the service to a friend.

Discussion

The results of this study show that the satisfaction rates with the current service are high. Areas which require improvement are that blood results are available and discussed in line with clinic appointments and the reason for annual review appointments is clearly explained. Additionally 23% of responders reported that their doctor or dietetic reviews were not frequent enough and 10% did not feel that they had adequate access for advice

from the dietitian. A UK based study showed comparable high satisfaction ratings at a centre running a dietetic led clinic and a centre providing traditional follow up.

The service has now changed to a dietetic led clinic. A dietetic led clinic will strive to allow for adequate access to the dietitian and blood tests will be arranged prior to their appointment so that they can be discussed at the appointment. The frequency of follow up can be more regular if clinically indicated. A referral back to the paediatric gastroenterologist can be made if clinical input is required. This survey will be redistributed to patients and parents after the dietetic led clinic has been established for eighteen months to assess the satisfaction rates with the new service.



CO-PRODUCING A MODERN COELIAC DISEASE CLINICAL PATHWAY FOR SCOTLAND

Authors

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Abstract

Introduction

Around 1 in 100 people in Scotland have coeliac disease (CD), but there is an average of 13 years from first presentation to diagnosis, a reported point prevalence of 0.27%, and variation in access to the right clinicians, dietitians, to support with treatment, the gluten free diet. The Modern Outpatient Programme team led the co-production of a new coeliac disease clinical pathway to provide an improved approach to the diagnosis, treatment and review of CD in Scotland. The aim was to co-produce a standard approach to diagnosis, treatment and review of CD in Scotland.

Method

To gain as much co-assessment and design as possible Coeliac UK advertised nationally two events which were held in Dundee and Glasgow in September 2017. These events were held with Coeliac UK representatives and members of the Modern Outpatient Programme and aimed to explore peoples' experiences, gain insight into the variation and work together to identify the positives and negatives of current and future pathways. The tool used to explore views was adapted from the Kings Fund and now available from the Point of Care Foundation.

www.pointofcarefoundation.org.uk



Results


Nine people attended the Dundee event from various health boards in the east of Scotland. Thirteen people attended the Glasgow event from across Scotland. Both events were similar in their outputs for diagnosis, treatment, review and overall themes, although individuals did have varying experiences within and across health boards.

Key themes identified that there is variation in practice at each point of the patient journey across Scotland and the need for a coeliac disease clinical pathway has never been greater. Improvements in the provision of care at diagnosis, treatment and review have been identified and prioritised by patients.

Conclusion

The Modern Outpatient Programme will deliver on the priorities identified by patients by ensuring:

1. Development and publishing of a co-produced clinical pathway for coeliac disease
2. Development of training and awareness raising materials/ tools for coeliac disease in GP, gastroenterology, dietetics, community pharmacy and the public
3. Development of technology enabled care tools to support clinicians and patients manage care better
4. NHS Boards deliver more co-ordinated coeliac disease services
5. NHS Inform provide patient information and support
6. That the new pathway delivers better care at more efficient costs compared with the current pathway.



RAPID URINE HOME TEST FOR GLUTEN FREE DIET MONITORING

Authors

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Abstract

Introduction

To date, the only effective management of coeliac disease is adherence to a strict gluten free diet (GFD). However, there has been no reliable method to confirm adherence to a GFD or to ascertain whether the origin of acute symptoms in a coeliac patient may be related to gluten exposure. There is poor or no correlation of coeliac serology and dietary questionnaires with gut mucosa recovery. To address this need, we recently developed a lateral flow test to detect gluten immunogenic peptides (GIP) in urine samples, excreted after gluten consumption. Our study demonstrated that about 50% of coeliac patients following a GFD have GIP in urine and that there is a high correlation between GIP detection and gut mucosal damage. Our goal was to simplify the test so that it could be used at home and to validate the test, establishing its performance characteristics.

Methods

Urine samples (n = 254) from volunteers under different gluten exposure conditions were analysed with the simplified lateral flow test. The samples included:

Positive control first morning urine samples from healthy volunteers following a non-standardised gluten containing diet (GCD) who had ingested gluten in the previous 16 hours (n = 25). Each volunteer analysed their own sample.

Negative control random samples from coeliac patients on a reportedly strict GFD (n = 180). The samples were analysed in a central laboratory.

First morning samples from healthy subjects on a GFD after the administration of 0.5 g of gluten a day (2.5 - 5% of the gluten content of the average Western diet) ie a moderate gluten challenge (n = 49). The samples were analysed in a central laboratory.



Results

GIP were detected in all samples of volunteers on a GCD whereas no GIP were detected in 179 out of 180 samples from patients on a GFD. GIP were detected in 44 of the 49 samples collected from volunteers ingesting 0.5 g of gluten.


The diagnostic sensitivity of the test was 100% and the specificity 99%. The positive and negative predictive values were 96% and 100% respectively. The sensitivity for the detection of the ingestion of 0.5 g of gluten was 90%.

Discussion

The point of care / home test for GIP detection in urine is highly sensitive and specific to assess adherence to GFD and to detect dietary transgressions, with superior performance over other methods. These tests will enable monitoring of the GFD to subjects avoiding gluten.

Conflict of interest

Remedios Domínguez-Flores is an employee of Biomedal SL, Ángel Cebolla is the CEO of Biomedal SL and owns stock in Biomedal SL.



PROSPECTIVE STUDY OF A LOW FODMAP DIET IN PATIENTS WITH COELIAC DISEASE AND ONGOING FUNCTIONAL GUT SYMPTOMS

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Abstract

Introduction

Patients with coeliac disease (CD) symptoms usually respond to a gluten free diet (GFD). However, up to a quarter of adults with CD have persistent gastrointestinal (GI) symptoms despite strict adherence to a GFD and complete intestinal healing. Overlap between CD and irritable bowel syndrome (IBS) may explain this symptomology. Over the last decade there has been a renewed interest in dietary treatments in IBS particularly the low FODMAP diet (LFD) which temporally restricts fermentable carbohydrates. The aim of this prospective study was to investigate the efficacy of the LFD in patients with CD and IBS.

Methods

We conducted a prospective study of the LFD as an intervention in patients with treated CD and persisting IBS symptoms. All CD patients met the ROME IV criteria, had negative coeliac

serology and normal duodenal biopsy. All patients were reviewed by a specialist GI dietitian with experience in delivering the LFD. Symptom response was assessed using the validated Gastrointestinal Symptom Rating Scale (GSRS) from base line to follow up.




Results

Twenty four patients with a mean age of 44 years (SD = 15.2) met the inclusion criteria. Eight patients chose not to pursue treatment and two were unable to complete the minimum treatment period. 14 patients (n = 2 males) completed four weeks of a LFD. There were no differences in baseline demographics between patients who chose to participate in the study and those who did not, or who were unable to complete the study protocol ($p = 0.7$). Global symptom relief of gut symptoms was reported by 8/14 patients (57% $p = 0.007$). A subgroup analysis demonstrated a significant reduction

in both abdominal pain ($p = 0.001$) and distension ($p = 0.02$) respectively. There were no significant differences to anthropometric and biochemical features at follow up compared with baseline.

Conclusion

This is the first study to demonstrate that a LFD is an effective dietary treatment for patients with biopsy confirmed treated CD and ongoing GI symptomology. Such patients should be seen by a specialist dietitian to improve adherence, ensure nutritional adequacy and appropriate reintroduction of FODMAP containing foods.



IS THERE A ROLE FOR A GLUTEN FREE DIET IN 'LIFESTYLERS'? THE FIRST DOUBLE BLIND RANDOMISED STUDY

Authors

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Institution

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Abstract

Introduction

A gluten free diet (GFD) is essential in the management of coeliac disease, as well as several studies demonstrating its utility as a dietary therapy in patients with irritable bowel syndrome. The aim of this double blind placebo controlled study was to assess the role of a GFD in a healthy population who take a GFD as a lifestyle choice ('lifestylers').

Methods

Subjects were recruited via an advert, following exclusion criteria including coeliac disease. Following selection, subjects were commenced on a two week GFD following evaluation by a dietitian. Participants were then randomised to receive either organic gluten (Group A, Vital Gluten 14 g gluten protein/day) or gluten free

flour (Group B) in pre-made bags, over a two week period. These were sprinkled on their food twice daily. Gastrointestinal Symptom Rating Scale (GSRS) scores were assessed at baseline (following two weeks GFD) and after two weeks of randomisation. Data were analysed using SPSS version 22.



Results

Forty five subjects were identified with 28 participants recruited into the trial (Group A; n=14, Group B; n=14) following exclusion criteria. Median age was 36.5 years (range: 19-63) and 21 (75%) were female. There was no significant difference in baseline demographics between both groups ($p = 0.54$). Over a two week period there was no significant difference in gastrointestinal symptoms or fatigue in either group, as seen in Table 1.

Table 1 GSRs scores at baseline and following intervention

GSRs	Group A (Baseline)	Group A (End of Intervention)		Group B (Baseline)	Group B (End of Intervention)	
	Mean +/- SD	Mean +/- SD	Difference from Baseline (Paired T-test), p-value	Mean +/- SD	Mean +/- SD	Difference from Baseline (Paired T-test), p-value
Abdo Pain	2.50 +/- 1.40	2.14 +/- 1.70	0.504	2.35 +/- 1.33	2.07 +/- 0.99	0.486
Reflux	1.71 +/- 1.13	1.64 +/- 1.15	0.720	2.50 +/- 2.20	2.57 +/- 1.95	0.895
Indigestion	2.14 +/- 1.35	2.07 +/- 1.32	0.876	2.14 +/- 1.35	1.79 +/- 0.97	0.336
Diarrhoea	2.71 +/- 1.93	1.64 +/- 0.92	0.030	1.85 +/- 1.46	1.86 +/- 1.35	1.000
Constipation	2.50 +/- 1.82	2.46 +/- 1.81	0.697	1.92 +/- 1.54	2.50 +/- 1.65	0.179
Fatigue score	6.61 +/- 2.36	6.00 +/- 2.98	0.585	6.57 +/- 2.44	5.36 +/- 2.27	0.232

Discussion

This study demonstrates that gluten is unlikely to be the culprit agent for gastrointestinal symptoms or fatigue in healthy individuals. A GFD has no evidence base in individuals who do not have coeliac disease or IBS. The public should be discouraged from considering a GFD of their own volition.





DEVELOPING A NUTRIENT DATABASE OF GLUTEN FREE FOODS FOR THE COELIAC DIET AND NUTRITION SURVEY

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Abstract

Introduction

Coeliac disease is an autoimmune disease caused by an adverse reaction to gluten. The only available treatment is strict adherence to a gluten free diet for life. The National Diet and Nutrition Survey (NDNS) provides information about the diets of people in the UK, however people following a gluten free diet are not recognised within the data. The Coeliac Diet and Nutrition Survey (CDNS) aims to improve our understanding of the foods that make up a gluten free diet and the nutritional adequacy of the diet.

Participants of the CDNS will complete four 24h recalls of their food and drink intake (two weekend and two weekdays) using the online platform Intake24. Participants will also be asked to complete a survey to capture information on demographics, activity level and any other dietary requirements (eg lactose free diet, vegetarian diet). So far, over 5000 people have signed up to take part in the project.

Intake24 uses a nutrient database of over 1500 foods but like other nutrient databases such as McCance and Widdowson, lacks information on gluten free foods. Therefore, a nutrient database of gluten free foods had to be developed.

Methodology

Gluten free foods were compared with:

- Gluten containing equivalents
- Other brands of the same food (eg different gluten free breads)

This process led to the conclusion that gluten containing foods should not be used as a proxy for gluten free and that in many cases different brands of the same food should be included in the database rather than using an average.

Micronutrient information were theoretically estimated using a process previously described by Missbach et al. (2015) based on macronutrient information and ingredient lists available from manufacturer websites and food labels.




Discussion

Theoretical nutrient estimation is less costly than lab analysis and can be calculated rapidly from readily available information. To validate the data, lab analysis of selected gluten free food products will be carried out.

The final database provides an estimation of 59 macro- and micronutrients contained in more than 200 gluten free food products. The database is now available on Intake24, ready for the first stage of the CDNS, launched March, 2018.





COST, AVAILABILITY AND NUTRITIONAL COMPOSITION COMPARISON BETWEEN GLUTEN FREE AND GLUTEN CONTAINING FOOD STAPLES PROVIDED BY FOOD OUTLETS AND INTERNET FOOD DELIVERY SERVICES BETWEEN TWO AREAS OF LONDON WITH DIFFERING UK DEPRIVATION INDICES

Authors

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Abstract

Introduction

The study aim is to compare the cost, availability and nutritional composition of manufactured gluten free (GF) products with their gluten containing (GC) counterparts, provided by food retailers (physical stores and online) between two areas of a London with distinctly contrasting deprivation indices.

Methods

A cross-sectional survey of 26 food categories was conducted in May 2017, data was collected on the cost, availability and nutritional composition of GF and GC foods. Food categories included traditionally wheat based and everyday foods usually containing gluten. Fifty physical stores were surveyed (10 in each

category); convenience stores, budget supermarkets, regular supermarkets, quality supermarkets and health food shops. In addition, online retailers of manufactured GF products which offered a delivery service to the areas under study were also included.




Results

A third of all stores surveyed did not stock any traditionally wheat based manufactured GF items, this comprised of budget supermarkets and convenience stores. The availability of GF foods across the two regions were similar, with products surveyed from the 'everyday foods' category found to be particularly poor. The online GF food suppliers superseded all the physical stores in the number of manufactured GF items available. However, over half the GF items were more expensive in online stores than in regular supermarkets. In fact, 74% of GF foods surveyed were more expensive than their GC counterparts, including food staples such as GF bread and bread rolls were 294 - 449% more expensive than the GC counterparts ($p < 0.001$), plain flour 94% ($p = 0.006$) and flaked cereals 93% more expensive ($p < 0.001$). Nutritional composition comparison revealed higher calorie, fat and saturated fat and lesser protein content for surveyed manufactured GF products.

Discussion

Availability of manufactured GF products remains poor, especially in convenience stores and budget supermarkets, serving those from poor socio-economic cohorts, the elderly and physically disabled. The stores where availability has improved from previous published findings are associated with the greatest additional cost. The inferior comparative nutritional quality of manufactured GF products emphasises need for those on a medically indicated GFD to be advised and monitored by adequately trained health professionals and also provides evidence towards dispelling false claims that removing gluten from the diet has health benefits.



SUBJECTIVE EXPERIENCES OF POST DIAGNOSIS WEIGHT CHANGE IN ADULTS WITH COELIAC DISEASE: RELATIONSHIPS WITH BMI, WEIGHT LOSS INTENTIONS, AND BODY IMAGE

Authors

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Abstract

Introduction

Although weight loss pre-diagnosis and weight gain post diagnosis are common in coeliac disease (CD), little research has focused on the subjective experiences of weight change or their relationship with BMI, weight loss intentions, and body image in this population. For those attempting weight loss, little is known about the strategies used, or barriers encountered, while balancing weight loss with a gluten free diet (GFD). The aim of this study was to fill these gaps.

Methods

In an online cross-sectional survey, 447 adults with CD completed measures of BMI before diagnosis, direction of any weight change following diagnosis, weight change interpretation (positive or negative), current BMI, body image, weight loss intentions, strategies, and barriers. Data analysis involved descriptives and a hierarchical multiple linear regression to predict current BMI.



Results

Weight spanned all BMI categories before CD diagnosis and current overweight/obesity was common. Most previously underweight participants gained weight post diagnosis and were currently healthy or overweight. Many participants with a healthy BMI pre-diagnosis also gained weight. Initial BMI and post diagnosis weight change were related to current BMI in the expected directions. A more negative interpretation of weight change and poorer body image were related to higher BMI, although their influence was reduced when weight history was accounted for. Weight change interpretations also influenced current weight loss intentions, and 50% of adults were currently trying to lose weight. A higher current BMI, weight gain following diagnosis, a more negative interpretation of post diagnosis weight change, and poorer body image were all related to current weight loss intentions. Weight loss strategies were consistent with those

reported by the general population. Barriers unique to the GFD included the high fat and sugar content in gluten free replacement products.

Discussion

Weight changes prior to, and following, diagnosis (once commencing the GFD) are important determinants of later weight status in adults with CD, and the interpretations of post diagnosis weight changes impact upon body image and weight loss intentions. Consequently, continued dietary and weight support from the point of diagnosis, including ways to ensure success of any weight loss efforts while maintaining GFD adherence, are of paramount importance to ensure the achievement and maintenance of a healthy BMI and improved body image. Current weight loss intentions were common, therefore, interventions targeting weight loss are warranted to effectively support adults with CD.



THE BODY IMAGE OF FEMALES WITH COELIAC DISEASE

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Abstract

Introduction

Commencement of a gluten free diet (GFD) has been associated with weight gain in some patients. Qualitative research indicates that this weight gain may be interpreted negatively and provoke body image concerns in some adults with coeliac disease (CD). Negative body image is high in adults with inflammatory bowel disease, a similar gastrointestinal illness, and is associated with increased symptoms and poor psychological health. Comparable relationships have not been researched in adults with CD. The aim of this study was to examine the body image of a sample of adults with CD and to determine

any associations between body image, psychological characteristics (depression, anxiety, quality of life), disease factors (GFD adherence and symptoms), and post diagnosis weight change.

Methods

Females (n = 471) with a self reported CD diagnosis completed online measures of weight characteristics (eg current weight and height, weight change following diagnosis, interpretation of weight changes), GFD adherence, CD symptoms, positive and negative body image, depression, anxiety, and quality of life (QOL). Correlations and multiple regression analyses were conducted to determine the predictors of both positive and negative body image.



Results

Negative interpretation of weight changes following diagnosis, irrespective of the direction of weight change (ie increase or decrease), predicted high negative and low positive body image. Lower BMI, lower depression, better GFD adherence, and decreased CD symptoms were associated with higher positive body image. The opposite was true for negative body image but GFD adherence was non significant. Although correlated, anxiety and QOL were not significant predictors of either positive or negative body image, when other variables were in the model.

Discussion

This study provides novel insights into how weight changes following a GFD can negatively impact female adults with CD, and how disease and

psychological variables relate to body image. The association between GFD adherence and positive, but not negative, body image suggests that positive body image interventions at diagnosis may be a unique way of improving GFD adherence and overall health in patients.



TRANSGLUTAMINASE 2 RELEASE IN THE INNATE IMMUNE RESPONSE

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Abstract

Introduction

Transglutaminase 2 (TG2) mediated stabilisation of extracellular protein assemblies has a pivotal function in tissue repair. However, aberrant TG2 activity has been linked to autoimmunity. TG2 is secreted via an unconventional and enigmatic mechanism, however active, extracellular TG2 is a requirement for the development of autoimmunity, for example in response to gluten in coeliac disease. Our group has shown that TG2 export is linked to purinergic signalling, and implicated P2X7 receptor activation. P2X7R has several activation states; ATP stimulation causes ion channel opening, allowing membrane depolarisation and Ca²⁺ entry into the cell. Prolonged stimulation

leads to 'large membrane pore' activity. Here, we investigate how mechanically cells export TG2 and control its subsequent activation. Investigating this process will unravel a novel secretory pathway, which could be crucial in the development of gluten related disorders.

Methods

P2X7R was stably expressed in HEK293 cells. TG2 and thioredoxin externalisation was assessed by Western blotting of conditioned medium. Myeloid precursors were isolated from human blood and differentiated using GM-CSF. TG2 expression was induced in THP-1 cells by stimulation of activation/maturation using phorbol ester (TPA).




Results

Our work implicates P2X7R pore formation in TG2 export. We have investigated this in HEK293 cells stably expressing P2X7R. To confirm the transferability of our findings in this cell model to the innate immune response, human peripheral blood monocytes were differentiated into M1 macrophages and P2X7R mediated TG2 export assessed. We have also investigated TG2 export in THP-1 monocyte cell line. In both of these cell types, we found differences in TG2 secretion in comparison to HEK293 cells. TG2 secreted by primary macrophages and THP-1 cells is a processed form, the secretion of which is dependent on caspase-1 activity. We have also assessed the export of thioredoxin, a TG2 activator, which reverses oxidative inactivation that occurs in the extracellular milieu.

Discussion

We show that P2X7R induced membrane pore activity directly correlates with TG2 export. Cells of the innate immune system secrete a processed form of TG2, which could be the disease relevant form. Thioredoxin is co-secreted with TG2 but is not required for TG2 externalisation. This begins to identify components of a mechanism for unconventional protein secretion crucial to coeliac disease, which could provide a novel therapeutic target.



IDENTIFICATION OF OPTIMAL IMMUNOHISTOCHEMICAL PARAMETERS TO SEPARATE GOELIAC DISEASE FROM NORMAL DUODENAL BIOPSIES, WITH IMPLICATIONS FOR DIGITAL IMAGE ANALYSIS DEVELOPMENT

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Abstract

Introduction

Coeliac disease (CD) has ≈1% prevalence and is due to an immune response to gluten that damages the small intestine. Manifestations range from no symptoms, through anaemia to severe intestinal symptoms, with complications (bone thinning, infertility, lymphoma and duodenal cancer). Other gluten sensitive conditions (GSC), including non coeliac gluten sensitivity and irritable bowel syndrome, fail to fulfil CD criteria, but together are considerably more common than CD. The exact relationship between these conditions remains unclear. Treatment of CD is a lifelong gluten free diet (GFD), but importance of a GFD is unclear in other GSC. We hypothesise that more objective and accurate CD diagnosis might be achieved by digital image analysis, either alone, or as part of multiparameter clinical and laboratory analysis.

Methods

We set out to determine which two routine immunohistochemical (IHC) stains best separate CD (n = 10, Modified Marsh Score grade at least 3a) and normal duodenal biopsies (n = 10). Sections were immunostained and parameters evaluated manually in CD and normal as follows: The total number of lymphocytes was determined by counting immunopositive lymphocytes (CD3+, CD4+ and CD8+) per 100 enterocytes from the entire length of three representative villi (intraepithelial lymphocytes) and three high power fields from the basal layer of the small bowel. The proliferation index of crypts was assessed by counting numbers of cells positive for the proliferation marker, mib-1, out of the lowest 50 epithelial cells on each side of three representative crypts.



Results

Results of immunostaining were compared using the Student's T-test.

Immunostain/ location	Intraepithelial lymphocyte <i>p</i> values	Basal (lamina propria) <i>p</i> values
CD3+ lymphocytes	2.097 x 10 ⁻⁶ ▲	0.15400 ▲
CD4+ lymphocytes	0.264 ▼	0.01250 ▲
CD8+ lymphocytes	1.383 x 10 ⁻⁷ ▲	0.00126 ▼
Mib1+ epithelial cells in lowest 50 epithelial cells each side of crypts	Not applicable	0.00167 ▲

Discussion

We conclude that, when developing a deep learning analytical algorithm for digital image analysis, provided that our algorithm is able adequately to segment villous epithelium, lamina propria and crypt bases, the optimal IHC stains to accompany hematoxylin and eosin (H&E) staining are CD8 and mib1. In light of these results, we have now produced the relevant stained slides (H&E, CD8, Mib1) on 500 cases (250 CD, 200 normal, 50 equivocal with follow up), as the substrate upon which to begin building an analytical algorithm.





COMPARATIVE GENE SET ENRICHMENT ANALYSIS OF COELIAC DISEASE ONLINE DATA

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Abstract

Introduction

The aim of this work is mainly related to finding a robust set of biomarkers for diagnosis, in order to avoid invasive practices, speed up the process and improve the response, ie to approach the challenge from a bioinformatics point of view. The work is based on a careful search for gene expression data from online repository, with a re-analysis that integrates gene expression data and Gene Ontology terms. Finally, the new evidence will give a direction to improve the knowledge on coeliac disease.

Methods

Two of the most important online repositories are: the Gene Expression Omnibus (GEO), from the National Center for Biotechnology Information (NCBI), and ArrayExpress, from

the European Molecular Biology Laboratory (EMBL) - European Bioinformatics Institute (EBI). Few datasets are strictly related to coeliac disease, with a significant number of samples, and not redundant. The Gene Ontology (GO) project is explained by the Gene Ontology Consortium (2015): biological process (BP) is chosen as ontology domain. Gene Set Enrichment Analysis (GSEA) is a set of statistical methods to classify genes in groups, which are related to common biological function, chromosomal location or regulation. A preliminary comparison with other inflammatory pathologies is under evaluation. The work is developed in R environment. The packages, downloaded by the online open source repository Bioconductor, are: GEOquery, limma, genefilter, and topGO.



Results

The studies are not standardised, therefore the candidate genes subset is chosen with a trade off among all the scores (logFC, p -value, adjusted p -value, hypothesis tests) and it is possible to provide GO graphs. From them, a little framework on the biological process involved in each study on coeliac disease is suggested from the relationships with the groups of differential expressed genes: 1) peptidyl-tyrosine phosphorylation, phosphatidylinositol 3-kinase signalling, and response to endoplasmic reticulum stress; 2) mitosis regulation, microtubule cytoskeleton organisation, and protein destabilisation; 3) signalling pathway and cellular response about interferon-gamma; 4) immune response and

immune system development; 5) protein phosphorylation, apoptotic process, and regulation of cell adhesion; 6) cytokine mediated signalling pathways.

Discussion

The integration of data, from different studies and technologies, represent the most promising approach for investigating in details the complexity of coeliac disease. Our work defines the possible workflow to apply this approach, and the availability in the future of more data sets, also from other omics approaches, will offer the opportunity to apply it for a more complete view of molecular mechanisms of this multifactorial condition.



GET INVOLVED IN OUR 50TH ANNIVERSARY YEAR

'50 years of helping people live gluten free' is our theme for Awareness Week and to help us celebrate the occasion, we'd like you to have a party as part of your Awareness Week activities.

Awareness Week takes place from 14-20 May, but you can have your celebration at any point in the month! If you can commit to raising £50 for our 50th year that would be fantastic as the monies raised will support our research efforts. To register your party and to receive a helpful party pack please email katie.stokes@coeliac.org.uk





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Coeliac UK is the charity for people who need to live without gluten. For nearly 50 years we've been helping people with coeliac disease and other gluten related conditions live happier, healthier lives. We do this by striving for better gluten free food in more places, providing independent, trustworthy advice and support and funding crucial research to manage the impacts of gluten and find answers to coeliac disease. And we do it all so that one day, no one's life will be limited by gluten.

Visit www.coeliac.org.uk/research for more information on Coeliac UK's:

- Research Strategy
- funding opportunities
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