Peptide-MHC class I and class II tetramers: From flow to mass cytometry.

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Abstract

To develop better vaccines and more targeted treatments for cancer and autoimmune disorders, the disease-specific T cells and their cognate antigens need to be better characterized. For more than two decades, peptide-major histocompatibility complex (pMHC) tetramers and flow cytometry have been the gold standard for detection of CD8+ and CD4+ T cells specific to antigens in the context of MHC class I and class II, respectively. Nonetheless, more recent studies combining such reagents with mass cytometry, i.e. cytometry by time of flight (CyTOF), have offered far more comprehensive profiling of antigen-specific T-cell responses. In addition, mass cytometry has enabled ex vivo screening of CD8+ T-cell reactivities against hundreds of MHC class I restricted candidate epitopes. MHC-class II molecules, on the other hand, have been challenging to combine with mass cytometry as they are more complex and bind with lower affinities to cognate T-cell receptors than MHC-class I molecules. In this review, I discuss how techniques originally developed to improve the staining capacity of pMHC tetramers in flow cytometry led to the successful combination of such reagents with mass cytometry. Especially, I will highlight very recent advances facilitating the combination with pMHC-class II tetramers. Together, these mass cytometry-based studies can help develop more targeted treatments for cancer and autoimmune disorders. This article is protected by copyright. All rights reserved.

PMID: 31891448
Potassium bicarbonate improves dough and cookie characteristics through influencing physicochemical and conformation properties of wheat gluten.

Chen G¹, Hu R¹, Li Y¹

Abstract

Baking soda (NaHCO₃) has critical technological functions in cookie products. Health concern on excessive sodium consumption is increasing; therefore, it is necessary to explore NaHCO₃ alternatives, such as KHCO₃, for bakery products. This study investigated the impact of KHCO₃ on the technological behaviors of cookie dough and end-uses in comparison with control samples prepared with NaHCO₃ and explore the changes of physicochemical and conformation properties of soft wheat gluten during the process. Dough rheological measurements demonstrated that addition of KHCO₃ reduced dough stickiness, and adding KHCO₃ achieved similar dough and baking performances as using NaHCO₃, which were partially attributed to the decrease of gliadin to glutenin ratio, changes of secondary structure, and intensive aggregation of gluten by introducing KHCO₃. Cookie sensory attributes were also not adversely affected by using KHCO₃. Therefore, partially replacing NaHCO₃ with KHCO₃ in cookie products can be an effective approach for sodium reduction.

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Conflict of interest statement
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.


**Pregnancy and coeliac disease.**

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**Abstract**

Coeliac disease (CD) is a small bowel disorder known for its intestinal manifestations like diarrhoea and weight loss. Less known are the extraintestinal manifestations of CD like haematological abnormalities but also altered female reproduction and pregnancy outcomes. Especially, undiagnosed CD may lead to adverse reproductive outcomes such as intrauterine growth restriction, stillbirth and preterm birth. In diagnosed and treated CD, adverse pregnancy outcomes might be prevented.

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PMID: 31888907

**Conflict of interest statement**

Competing interests: None declared.


**Celiac Disease: A Common Unrecognized Health Problem with a Very Delayed Diagnosis.**

Rodrigo L¹.
Abstract

Celiac disease (CD) is a clinical entity of autoimmune nature, related to the presence of a permanent gluten intolerance that affects genetically predisposed individuals, producing a chronic inflammation process that usually occurs in the small bowel [...].

PMID: 31888055

Setup of Quantitative PCR for Oral Neisseria spp. Evaluation in Celiac Disease Diagnosis.


Abstract

Coeliac disease (CD) is a multifactorial autoimmune disorder and gut dysbiosis contributes to its pathogenesis. We previously profiled by 16S rRNA sequencing duodenal and oropharyngeal microbiomes in active CD (a-CD), gluten-free diet (GFD) patients, and controls (CO) and found significantly higher levels of *Neisseria* spp., with pro-inflammatory activities, in a-CD patients than in the other two groups. In this study, we developed a fast and simple qPCR-based method to evaluate the abundance of the oral *Neisseria* spp. and the diagnostic performances of the test in CD diagnosis. The *Neisseria* spp. abundances detected by quantitative PCR (qPCR) were: CO = 0.14, GFD = 0.15, a-CD = 2.08, showing a similar trend to those previously measured by next generation sequencing (NGS). In particular, *Neisseria* spp. values obtained by both methods were significantly higher (p <
0.001) in a-CD than in the other two groups GFD and CO-the latter almost overlapping. We calculated by ROC curve analysis the threshold of 1.12 ng/μL of Neisseria spp. to discriminate between CO+GFD and a-CD patients with 100% and 96.7% of diagnostic sensitivity and specificity, respectively. In conclusion, our data, if confirmed in other cohorts, suggest the q-PCR evaluation of oral Neisseria spp. could be a fast and simple method to assess CD-associated dysbiosis for diagnostic purposes. PMID: 31888008


Prevalance of Celiac Disease in Patients with Inflammatory Bowel Disease in Turkish Population.

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Abstract

Background:
Celiac disease (CD) and inflammatory bowel disease (IBD) involve inflammation of the gastrointestinal lumen, which environmental, genetic, and immunological factors have a role in their pathogenesis. The prevalence of celiac disease in IBD ranges from 0% to 14%. In this study, our aim was to determine the prevalence of CD in IBD patients followed by us who are attending the hospital or outpatient clinic over a period of time of seven years.

Methods:
Seven hundred and fifty nine patients (425 M, 334 F, mean age: 46.75, 396 ulcerative colitis (UC), 363 Crohn's disease (CrD)) diagnosed and followed up for IBD between January 2009 and July 2016 were evaluated retrospectively, and clinical, demographic, laboratory, and endoscopic data were collected.

Results:
CD was investigated in 79 (10.4%) inflammatory bowel disease patients according to symptoms, and in 5.06% (n = 4) of them, we diagnosed CD. The most common indication for investigating for CD was iron deficiency anemia unresponsive to iron supplementation.

**Conclusions:**

We did not find an increased prevalence of celiac disease in Turkish IBD patients in this study. In the presence of refractory iron deficiency anemia without any other cause in IBD patients, investigations for celiac disease should be considered.

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**Conflict of interest statement**

The authors declare that they have no conflicts of interest.


**Marked coagulopathy without liver disease or anticoagulation therapy.**

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3. WWAMI Medical Education Program and Department of Biological Sciences, University of Idaho, 875 Perimeter Drive, Moscow, ID, 83844-3051, USA. Electronic address: dpfeiffer@uidaho.edu.

**Abstract**

Symptomatic coagulopathies in celiac disease (CD) are rare. Here, we report a profound case of coagulopathy in a celiac. A 66-year old female without liver disease or anti-coagulation therapy presented with multiple ecchymoses, guaiac positive melanic stool, and a recent 4.5kg weight loss. Laboratory values included hemoglobin, 3.8g/dL; MCV, 66 fl; serum iron, 17μg/dL; platelet count,
580K/μL; white count, 14.2K/μL, and vitamin D, <5.0ng/mL. Additional values included partial thromboplastin time (PTT), >200s; prothrombin time (PT), >150s; INR, 20.5, putting her at extreme risk of bleeding. Vitamin K deficiency was assumed. The patient was given two units of fresh frozen plasma, packed red cells, and vitamin K intravenously. Endoscopy and biopsies demonstrated duodenal mucosal atrophy with cobblestoning, erosive gastritis, flattened duodenal villi and numerous intraepithelial lymphocytes. Transglutaminase serology demonstrated IgA TTG>100 U/mL (normal<3U/mL), confirming a diagnosis of CD. The patient's coagulopathy resolved within two days following admission. This case underscores the importance of CD testing in all patients with coagulopathies of unknown origin. Although coagulopathy is an uncommon presentation of CD, in extreme cases such as this, it has the potential to be life-threatening.

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**Inactivation of Salmonella spp. in wheat flour by 395 nm pulsed light emitting diode (LED) treatment and the related functional and structural changes of gluten.**

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Abstract

Salmonella spp. is one of the top foodborne pathogens associated with low-moisture foods and they exhibit significant resistance to conventional thermal treatments. UV light pulses emitted from light emitting diode (LED) has shown antimicrobial potential in high-moisture foods and water. However, limited information is available about the antimicrobial potential of UV light with different wavelengths, including 395 nm in low-moisture foods. The objectives of this study were to investigate the antimicrobial potential of 395 nm pulsed LED light in wheat flour and the resulting quality changes. This study demonstrated a maximum 2.91 log reduction of Salmonella cocktail in wheat flour treated with 395 nm pulsed LED for 60 min in a semi-closed system. Oxidation occurred in
wheat flour after 30 and 60 min exposure to the 395 nm LED, which subsequently led to bleaching, and polymerization of gluten components through disulphide linkage. The water holding capacity of gluten was reduced by oxidation, and the contents of secondary structures were altered significantly after pulsed LED treatment, but the rheological properties were not deteriorated. The disulfide bond formation naturally happens during dough formation and the oxidation triggered by pulsed LED treatment may play a role on accelerating this process. The 395 nm pulsed LED treatment could be a promising decontamination technology for wheat flour with an additional benefit of bleaching of the flour without chemicals. INDUSTRIAL RELEVANCE: A number of foodborne outbreaks and recalls have been related to low-moisture foods in these decades and recently several outbreaks were reported due to the occurrence of Salmonella in wheat flour. However, it is difficult to solve this problem through conventional thermal approaches because of the increased thermal resistance of Salmonella at low water activity environment. The emerging LED light source can produce light with monochromatic wavelengths without the use of mercury vapor lamps. It also has high durability, low heat generation, and is relatively easy to be adapted in an existing production line. Therefore, there is a great potential of using certain UV wavelengths emitted from LED to disinfect the low-moisture foods in food industries. To the best of our knowledge, no research was conducted on decontamination of wheat flour by using LEDs and only limited studies are available on the influence of pulsed LED treatment on food quality. The aim of this study was to explore the possibility of using 395 nm pulsed LED treatment as a novel tool for decontamination of Salmonella in a low-moisture food product (wheat flour) with industrial feasibility, and investigate the influence of the pulsed LED treatment on quality changes in the product.

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A survey of primary-care pediatricians regarding the management of Helicobacter pylori infection and celiac disease.

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Abstract

BACKGROUND:

Adherence of primary-care pediatricians to guidelines in pediatric gastroenterology is essential to achieve optimal clinical outcomes. The study aim was to examine adherence of primary-care pediatricians to the European and North American Societies for Pediatric Gastroenterology, Hepatology and Nutrition guidelines on the management of Helicobacter pylori (H. pylori) infection and celiac disease.

METHODS:

We conducted a cross-sectional study during March-July 2017 using the survey platform of Maccabi Healthcare Services, the second largest state-mandated health organization in Israel. We sent the study questionnaire to a random sample of 300 pediatricians via electronic mails and to increase the response rate, we performed a telephone interview. Overall, 108 (36%) pediatricians provided completed questionnaires.

RESULTS:

Using professional guidelines for the management of H. pylori infection and celiac disease was reported by 34 and 37% of pediatricians, respectively. Referral to H. pylori testing was reported by 78 and 52% of pediatricians in children with suspected duodenal ulcer and unexplained iron deficiency anemia, respectively, with the stool antigen enzyme immunoassay being mostly (51%) used as the first choice diagnostic test. Most pediatricians reported prescription of triple therapy; proton pump inhibitors/clarithromycin/amoxicillin (59%) or metronidazole (21%). For celiac disease, overall adherence to all guidelines was high both for initial evaluation and for confirmation of diagnosis.

CONCLUSIONS:

Adherence to the guidelines on management of H. pylori infection was low, while adherence to the guidelines on celiac disease management was high among primary-care pediatricians. Educational interventions are needed to improve H. pylori infection management among primary-care pediatricians.

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Gluten Deprivation: What Nutritional Changes Are Found During the First Year in Newly Diagnosed Coeliac Children?

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Abstract

AIM:

A gluten-free diet (GFD) can expose children to excessive calories and fat intake. The study is intended to verify whether and how food intake, laboratory parameters, and growth are modified by a year of GFD.

METHODS:

In 79 CD (coeliac disease) children (mean age 7.9 ± 3.8 years, 52 females, 27 males) diagnosed over 24 months, 24-h food diaries, food-frequency patterns, anthropometric and laboratory parameters (mainly blood sugar, insulin, lipid profile, and homocysteine) were prospectively collected before and during the first year of GFD. Nutrient intakes were compared over time and with recommendations. They were also used as regressors to explain the levels and changes of metabolic and growth variables. p-values < 0.05 were considered statistically significant.

RESULTS:

Average macronutrient intake did not change during the year. Caloric intake remained below 90% (p ≤ 0.0001) and protein intake above 200% (p ≤ 0.0001) of recommendations. Lipid intake was stable at 34% of overall energy intake. Unsaturated fats increased (less omega-6 and more omega-3 with a ratio improvement from 13.3 ± 5.5 to 8.8 ± 3.1) and so did fibers, while folate decreased. The children who experienced a containment in their caloric intake during the year, presented a slower catch-up growth. Some differences were found across gender and age groups. In particular, adolescents consumed less calories, and females more omega-3. Fiber and simple sugar intakes
emerged as implicated in lipid profile shift: fibers negatively with triglycerides (TG) ($p = 0.033$), simple sugars negatively with high-density lipoprotein (HDL) ($p = 0.056$) and positively with TG ($p = 0.004$). Waist-to-height ratio was positively associated with homocysteine ($p = 0.018$) and Homeostasis Model Assessment ($p = 0.001$), negatively with fibers ($p = 0.004$).

**CONCLUSION:**

In the short run, GFD is nutritionally very similar to any diet with gluten, with some improvements in unsaturated fats and fiber intake. Along with simple sugars containment, this may offer CD patients the opportunity for a fresh start. Caloric intakes may shift and should be monitored, especially in adolescents.

**Free Article**
**PMID:** 31881668

**Mental Health Disorders and Psychosocial Distress in Pediatric Celiac Disease.**

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**Abstract**

**OBJECTIVES:**

Celiac disease (CeD) has been associated with increased mental health disorders (MHD) and psychosocial distress in children, which may complicate treatment with the gluten-free diet (GFD). This single-center cross-sectional study examined psychological comorbidities in children with CeD to assess psychological needs in CeD care.

**METHODS:**

Participants were 73 parents (95% mothers) of children (ages 3-18) attending a multidisciplinary celiac disease clinic. Parents completed electronic surveys about their child's MHD history,
psychological symptoms, and GFD experiences. Rates of MHD were calculated and compared to NIMH population-level data. Differences in psychosocial symptoms and GFD experiences were examined based on child age, time since CeD diagnosis, and MHD.

RESULTS:

Thirty-four percent of children had at least one MHD; anxiety disorders (16%, p<0.001) and attention-deficit/hyperactivity disorder (ADHD; 16%, p = 0.01) were more common than general population rates(1). More than one quarter of parents reported current child psychosocial distress (28-39%), and approximately half reported parent stress (51%) and financial burden (46%) associated with the GFD. Parents of children with new CeD diagnoses reported lower confidence in the GFD (p<0.01) but MHD, stress, and financial burden did not differ by time since CeD diagnosis. Children with MHD had more anxiety, anger, overall distress, and parent distress than those without MHD (ps < .05).

CONCLUSIONS:

Comorbid CeD and MHD was common and was associated with increased child and parent psychosocial distress. Our findings emphasize the importance of psychological screening and services to assess for and treat comorbid MHD and to mitigate psychosocial distress associated with the GFD.

PMID: 31880669

Similar articles

The value of a biopsy in celiac disease follow up: assessment of the small bowel after 6 and 24 months treatment with a gluten free diet.


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Abstract

INTRODUCTION:

A routine small bowel biopsy (SBB) during the follow up of celiac disease (CD) is controversial. Little information is available regarding the histological changes during gluten free diet (GFD) in the long term.

OBJECTIVES:

The aim of the study was to evaluate a novel criterion to compare duodenal histology in CD patients after six months and two years of gluten withdrawal.

METHODS:

This was a cross-sectional study of 200 patients with confirmed Marsh I-III who were under the six months (group A, n = 100) and 24 months (group B, n = 100) of a GFD. Nineteen patients were excluded due to an inadequate adherence to the GFD and another 23 patients were excluded as they were unwilling to undergo a re-endoscopy and did not comply with the necessary criteria. Endoscopy with a duodenal biopsy, serological assays and clinical evaluation were performed and compared with baseline data in the remaining 58 patients (20 patients in group A and 38 patients in group B).

RESULTS:

A significant complete histological recovery was found in 47.4% of patients in group B compared to 30% in group A (p = 0.026). A partial histological recovery was reported in seven (35%) and eleven (28.9%) patients in groups A and B, respectively. Any changes in mucosal histology after GFD was observed in 35% of patients in group A and 23.7% in group B. Serological assessment and endoscopic appearance normalized in 78.9% vs 75.0% in group B and 68.4% vs 65.0% in group A, respectively. However, this improvement did not reach statistical significance (p > 0.05).

CONCLUSIONS:

The results of this study show that histological recovery in patients with Marsh ≥ III is slow and does not correlate with symptomatic improvement. We suggest that the long-term effects of a GFD can play an important role in achieving histological improvement, especially in older patients.

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PMID: 31880159
Similar articles
The spectrum of clinical and subclinical endocrinopathies in treatment-naïve patients with celiac disease.

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Abstract

INTRODUCTION:

Strong association exists between celiac disease and autoimmune endocrinopathies such as type I diabetes and hypothyroidism; there is a lack of data on the involvement of other endocrine organs such as pituitary-gonadal axis. Furthermore, there is lack of data on the spectrum of involvement of endocrine organs varying from organ autoimmunity to subclinical and clinical disease. We evaluated consecutive treatment-naïve patients with celiac disease (CeD) for clinical and subclinical endocrinopathies.

METHODS:

Of 154 screened, 74 treatment-naïve patients with CeD were recruited. They underwent hormonal and/or functional assessment of beta cell of pancreas, thyroid gland, pituitary-gonadal axis, and parathyroid glands.

RESULTS:

Of the 74 patients with CeD, 31 (41.9%) had at least one clinical or subclinical endocrinopathy and 9 (12.2%) had multiple endocrinopathies. Most common of them were clinical or subclinical type I diabetes and autoimmune thyroid disease. Interestingly, 8 (10.8%) patients also were found to have functional hypopituitarism and 7/54 (12.9%) having isolated hypogonadotrophic hypogonadism.
CONCLUSIONS:

Patients with CeD have high percentages of not only clinical endocrinopathy including pituitary-gonadal axis dysfunction but also subclinical endocrinopathy. Whether commencement of gluten-free diet will lead to reversal of subclinical endocrinopathies requires further follow up studies.

PMID: 31879833

Safeness of Diets Based on Gluten-Free Buckwheat Bread Enriched with Seeds and Nuts-Effect on Oxidative and Biochemical Parameters in Rat Serum.

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Abstract

Buckwheat breads enriched with seeds (e.g., poppy, carum, amaranth, sunflower, and pumpkin) and nuts can be excellent sources of selected macro- and microelements and bioactive components, such as phenolics, essential oils, unsaturated fatty acids, fiber, and vitamins; however, no studies described their impacts on body biochemical parameters and antioxidant status. The aim of this study was to determine the safety (the analyses of blood morphological and biochemical parameters) of short-term diets based on buckwheat breads supplemented with the commonly used functional ingredients. Additionally, we confirmed the usefulness of these fortified breads in a reduction of blood cholesterol and triacylglycerols, as well as an improvement of in vivo antioxidant status of Wistar rats. Enriched breads presented an increased phenolic content; however, it has not been translated into an elevation of antioxidant capacities. During short-term in vivo experiments, the studied breads increased the body mass of the rats, except the control buckwheat bread. Compared to the control, the poppy-milk bread markedly lowered (-23%) and egg yolk-carum bread significantly increased (+17%) the total cholesterol concentration in serum. All the fortified breads
decreased triacylglycerols' levels by about 50%. Bread enriched with the poppy-milk, milk-seed, egg yolk-carum, and a mix of additives decreased superoxide dismutase activity by 68%, 66%, 73%, and 71%, respectively. Catalase activity was significantly decreased in the rats fed with carum bread (-62%) and markedly increased in the groups fed with egg yolk-carum bread (+89%), hazel nuts-amaranth bread (+72%), and milk-seeds bread (+65%). The results confirmed the usefulness and safety of functional additives in buckwheat breads.

Free Article
PMID: 31877881

Similar articles


High Fibre Gluten-Free Fresh Pasta with Tiger Nut, Chickpea and Fenugreek: Technofunctional, Sensory and Nutritional Properties.

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Abstract

Gluten-free pasta production with a low glycaemic index and improved nutritional profile is still a challenge for the food industry. In this study, pasta was produced from fenugreek (FF), chickpea (CPF) and tiger nut (TNF) flours. CPF and FF are interesting for a balanced contribution of soluble and insoluble fibre by combining the health benefits of each type of fibre that promotes health. TNF, also rich in insoluble fibre, can provide additional healthy properties. The partial substitution of TNF for FF (0, 2.5, 5, 7.5 and 10% w/w solids) was assessed, and the relation linking chemical composition, structure, cooking and rheological properties and predictive in-vitro starch digestion (eGI, expected glycaemic index) was analysed. The results revealed that FF, rich in galactomannans, not only improves the nutritional profile and lowers the eGI but also helps to naturally enhance the structure of the pasta product and, thus, cooking behaviour (higher swelling index and fewer cooking losses).

Free Article
PMID: 31877757
Withdrawning gluten-free food from prescriptions in England: a mixed-methods study to examine the impact of policy changes on quality of life.

Peters M¹, Crocker H¹, Jenkinson C¹, Violato M¹.

Abstract

BACKGROUND:

Some local areas in England stopped have gluten-free prescriptions for coeliac disease. An explanatory mixed-methods study has investigated the impact of these changes.

METHODS:

A cross-sectional survey with 1697 participants was followed by 24 qualitative interviews. The survey included questions on the use of prescriptions and healthcare services, as well as the Coeliac Disease Assessment Questionnaire (CDAQ) to assess quality of life. The survey data were analysed by descriptive statistics, analysis of variance and regression analysis, and the interviews were analysed by thematic analysis. Findings from the interviews guided the survey analysis.

RESULTS:

Dietary burden was significantly different between prescribing and nonprescribing areas, with little impact on other aspects of quality of life. Survey participants in nonprescribing areas who felt more impacted by the prescription changes reported a lower quality of life. Satisfaction with and use of services was lower in nonprescribing areas. Interviews indicated that, after initial frustrations, most people adapted to the changed prescription policy. However, there was a clear preference for gluten-free prescriptions to be available, in particular for staple foods.

CONCLUSIONS:
The main quality of life impact was on Dietary burden. It is encouraging that most participants in the present study maintained a good quality of life. However, issues of worse experiences of care, lower follow-up opportunities and inequity arose, and these should be taken into consideration in decisions on gluten-free food prescriptions. The new guidelines for the National Health Service in England have retained prescriptions for bread and flour mixes, which is more limited than the range of staple foods preferred in the present study.

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**Adult-onset autoimmune-type enteropathy: potential relationship to an adverse drug reaction.**

Chetty R¹, Cino M¹, Okrainec A¹.

Author information:

**Abstract**

**Objective:**

To describe an example of adult-onset autoimmune enteropathy (AIE) that coincided with drug-induced reaction.

**Design:**

A 54-year-old patient was presented with Stevens-Johnson syndrome after a course of quinolones. This was followed shortly thereafter by epigastric pain, diarrhoea and weight loss. She also developed an autoimmune neutropenia.

**Results:**

Several biopsies were performed from the upper and lower gastrointestinal tract (GIT). The duodenal biopsies showed intraepithelial lymphocytosis; therefore, coeliac disease was considered.
However, confirmatory serology was negative and the patient did not respond to a gluten-free/gliadin-free diet. Both upper and lower GIT biopsies consistently showed an absence of goblet cells resembling the changes of an AIE.

**Conclusion:**

This is an unusual case of autoimmune-pattern enteropathy in an adult that was potentially drug-induced.

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**Conflict of interest statement**

Competing interests: None declared.


**Substrates, inhibitors, and probes of mammalian transglutaminase 2.**

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**Abstract**

Transglutaminase 2 (TG2) is a ubiquitous but enigmatic mammalian protein to which a number of biological functions have been ascribed but not definitively proven. As a member of the transglutaminase family, TG2 can catalyze deamidation or alternatively transamidation of selected Gln residues in proteins and peptides. It is also known to harbor other enzymatic properties, including protein disulfide isomerase, GTP-dependent signal transduction, and ATP dependent protein kinase activity. Given its multifunctional chemistry, it is unsurprising that a long list of proteins from the mammalian proteome have been identified as substrates and/or binding partners; however, the biological relevance of none of these protein-protein interactions has been clarified as
yet. Remarkably, the most definitive insights into the biology of TG2 stem from its pathophysiological role in gluten peptide deamidation in celiac disease. Meanwhile our understanding of TG2 chemistry has been leveraged to engineer a spectrum of inhibitors and other molecular probes of TG2 biology in vivo. This review summarizes our current knowledge of the enzymology and regulation of human TG2 with a focus on its physiological substrates as well as tool molecules whose engineering was inspired by their identities.

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PMID: 31874171


**T cell receptor cross-reactivity between gliadin and bacterial peptides in celiac disease.**

Petersen J1,2, Ciacchi L1,2, Tran MT1, Loh KL1, Kooy-Winkelaar Y3, Croft NP1, Hardy MY4,5, Chen Z6, McCluskey J6, Anderson RP7, Purcell AW1, Tye-Din JA4,5,8, Koning F3, Reid HH9,10, Rossjohn J11,12,13.

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Abstract

The human leukocyte antigen (HLA) locus is strongly associated with T cell-mediated autoimmune disorders. HLA-DQ2.5-mediated celiac disease (CeD) is triggered by the ingestion of gluten, although the relative roles of genetic and environmental risk factors in CeD is unclear. Here we identify microbially derived mimics of gliadin epitopes and a parental bacterial protein that is naturally processed by antigen-presenting cells and activated gliadin reactive HLA-DQ2.5-restricted T cells derived from CeD patients. Crystal structures of T cell receptors in complex with HLA-DQ2.5 bound to two distinct bacterial peptides demonstrate that molecular mimicry underpins cross-reactivity toward the gliadin epitopes. Accordingly, gliadin reactive T cells involved in CeD pathogenesis cross-react with ubiquitous bacterial peptides, thereby suggesting microbial exposure as a potential environmental factor in CeD.

PMID: 31873306

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The enemy within the gut: bacterial pathogens in celiac autoimmunity.

Verdu EF¹, Schuppan D²,³.

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PMID: 31873302

Similar articles

Elaboration of a spontaneous gluten-free sourdough with a mixture of amaranth, buckwheat, and quinoa flours analyzing microbial load, acidity, and pH.

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2. Department of Mathematics, Universitat Politècnica de Catalunya, Barcelona, Spain.

Abstract

Pseudocereals are gluten-free, nutrient-dense raw materials that are being considered for the production of gluten-free products, especially bread. This study proposes a gluten-free sourdough formula based on equal amounts of amaranth, buckwheat, and quinoa with a dough yield of 250, and an elaboration method to obtain ripe sourdough. Sourdough was characterized in terms of microbiology, pH, and total titratable acidity. The established protocol made it possible to obtain a spontaneous ripe sourdough with lactic acid bacteria populations of 9.60 ± 0.02 log CFU/g and total yeasts and non-Saccharomyces yeast populations (lysine positive) of 7.91 ± 0.15 and 7.52 ± 0.10 log CFU/g, respectively. Great pH stability and total titratable acidity were maintained in the ripe sourdough phase, with values of 4.04 ± 0.02 and 18.39 ± 0.56 ml NaOH 0.1 M/10 g, respectively, at the time of the next refreshment. The use of this sourdough could be an interesting alternative for the production of not only gluten-free bread but also other gluten-free products.

PMID: 31870194

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Investigating patterns of millennials' interest in gluten-free beer in Poland: A question of beer price and alcohol content.

Donadini G¹, Bertuzzi T¹, Kordialik-Bogacka E², Cywińska D², Rossi E¹, Spigno G³, Porretta S⁴.
Abstract

The quality perception of gluten-free beer was explored using conjoint analysis with a panel of Polish millennials (n = 200; aged 20 to 35), who were given 64 gluten-free beer concepts to evaluate and score on a 9-point scale of interest (1 = not interested at all; 9 = extremely interested). The constituent factors of the beer concepts were alcohol content, color, type of malt, price, drinking location and occasion, bottle size, label claims, type of farming, type of brewer, and bottle closure. Consumers judged price (38.4%) and alcohol (28.8%) five times more important than the other factors. Bottle size (5.3%), claims (4.8%), type of brewer (4.8%), malt type (4.6%), bottle closure (4.0%), beer color (3.6%), drinking location (2.3%), drinking occasion (2.0%), and type of farming (1.3%) were considered of little importance. The interest of Polish Millennials in gluten-free beer resulted moderate and not linked to medical needs. Males were more interested in gluten-free beers and gave more importance to alcohol content and less importance to price, compared to females. However, for both genders, interest and price were inversely correlated, while interest and alcohol content were directly correlated. PRACTICAL APPLICATION: The identification of the product factors that are preferred by consumers is paramount to translate consumers' needs and expectations into a beer designed to produce the best possible product in a relatively short period. Including information directly obtained from consumers before final design decisions are taken on the final beer output, helps ensuring development directions are on target and constitutes a cost-competitive approach to product development.

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PMID: 31869860

Similar articles

Interference of mycotoxin binders with ELISA, HPLC and LC-MS/MS analysis of aflatoxins in maize and maize gluten.

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Abstract

The aim of this study was to investigate the impact of mycotoxin binders on the determination of aflatoxins in maize and maize gluten using various analytical methods, including ELISA, HPLC and LC-MS/MS. Three types of commercially available mycotoxin binders, yeast cell wall, mineral, and a mixture of mineral and bacterium, were investigated at inclusion levels of 0.1%, 0.2% and 0.4%. The binders were added to maize and maize gluten contaminated with aflatoxins at concentrations between 6.9 and 26.7 μg kg⁻¹. The samples were analysed and the values were compared with corresponding controls (samples without binders) using ANOVA. The yeast cell wall binder had no significant effect (p=0.05) on the concentration of aflatoxins measured in either maize or maize gluten at any of the three inclusion levels, regardless of which analytical method was used. The mineral binder and the mixed mineral and bacterium binder had no significant effect (p=0.05) on the measured aflatoxin concentrations in either maize or maize gluten at any of the three inclusion levels when analysis was conducted using LC-MS/MS. Inclusion of these binders resulted in significant lower (p<0.01) detection of aflatoxins in both maize and maize gluten when analysis was conducted using ELISA; the effect was dose-dependent. They also resulted in significant lower detection of aflatoxins in maize extracted by methanol/water (70/30 v/v) (p<0.0001) and in maize gluten extracted by acetonitrile/water (80/20 v/v) (p<0.05) when analysis was conducted using HPLC. However, neither the mineral binder nor the mixed mineral and bacterium binder had significant effects (p=0.05) on aflatoxin concentrations measured in maize using HPLC, when extracted by acetonitrile/water (80/20 v/v). The study demonstrated that mycotoxin binders could result in underestimation of the levels of aflatoxin contamination, depending on the nature of the binder, the extraction solvent used in the analytical method, and the composition of tested sample.

PMID: 31869282

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A Quantitative Assessment of Gluten Cross-Contact in the School Environment for Children with Celiac Disease.

Weisbrod VM¹, Silvester JA², Raber C¹, Suslovic W¹, Coburn SS¹, Raber B¹, McMahon J¹, Damast A³, Kramer Z¹, Kerzner B¹.

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Abstract

OBJECTIVES:

A gluten-free (GF) diet is the primary treatment for celiac disease (CD). Gluten is used in schools, particularly in early childhood, art, and home-economics classrooms. This study aimed to measure gluten transfer from school supplies to GF foods that a child with CD may eat. Also, to measure efficacy of washing techniques to remove gluten from hands and tables.

METHODS:

Five experiments measured potential gluten cross-contact in classrooms: Play-Doh (n = 30); baking project (n = 30); paper mâché (n = 10); dry pasta in sensory table (n = 10); cooked pasta in sensory table (n = 10). Thirty participants ages 2 to 18 were enrolled. Following activities, gluten levels were measured on separate slices of GF bread rubbed on participant's hands and table surfaces. Participants were assigned one of three handwashing methods (soap and water, water alone, or wet wipe). Repeat gluten transfer measurements were taken from hands and tables. Gluten measurements made using R-Biopharm R7001 R5-ELISA Sandwich assay.

RESULTS:

Paper mâché, cooked pasta in sensory tables, and baking project resulted in rates of gluten transfer far greater than the 20 ppm threshold set by Codex Alimentarius Commission. However, Play-Doh and dry pasta resulted in few gluten transfers to GF bread >20 ppm. Soap and water was consistently the most effective method for removing gluten, although other methods proved as effective in certain scenarios.

CONCLUSIONS:
The potential for gluten exposure at school is high for some materials and low for others. For high-risk materials, schools should provide GF supplies and have a robust strategy to prevent gluten cross-contact with food.

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Similar articles


To Be or Not to Be a Pathogen: Candida albicans and Celiac Disease.

Renga G¹, Bellet MM¹, Stincardini C¹, Pariano M¹, Oikonomou V¹, Villella VR², Brancorsini S¹, Clerici C³, Romani L¹, Costantini C¹.

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Abstract

Celiac disease (CD) is an immune-mediated disorder triggered by the ingestion of gluten and characterized by reversible small-bowel mucosal atrophy in genetically predisposed subjects. Although the prevalence of CD has increased, many aspects of this pathology are still unrecognized. Candida albicans, a commensal of the human gastrointestinal tract, has been linked to CD for a long time based, among others, upon the observation of similarity between the fungal wall component, hyphal wall protein 1, and CD-related gliadin T-cell epitopes. We have recently demonstrated that Candida may switch from commensal to pathogen contingent upon several players, including mast cells, key sentinels of the immune system at the interface between the environment and the host, and the pleiotropic cytokine IL-9. However, other factors are likely to play a role by altering the balance between inflammation and tolerance. In this regard, tryptophan and its metabolites are increasingly being recognized in promoting mucosal homeostasis by balancing the immune response to external cues. Based on these premises, we will discuss how the output of Candida colonization in the gut is highly contextual, being determined at the intersection of many immunological (IL-9/mast cells) and metabolic (tryptophan) pathways that ultimately dictate the Candida commensalism vs. pathogenicity in CD, thus paving the way for novel therapeutic opportunities in CD.

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Most Patients With Celiac Disease on Gluten-free Diets Consume Measurable Amounts of Gluten.

Silvester JA1, Comino I2, Kelly CP3, Sousa C2, Duerksen DR4; DOGGIE BAG Study Group.

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Thyro-entero-gastric autoimmunity: Pathophysiology and implications for patient management.

Lahner E1, Conti L1, Cicone F3, Capriello S3, Cazzato M1, Centanni M3, Annibale B1, Virili C3.
Abstract

The association between autoimmune atrophic gastritis and thyroid disorders has been observed since the early 1960s and the expression "thyrogastric syndrome" was coined to indicate the presence of thyroid autoantibodies or autoimmune thyroid disease in patients with pernicious anemia, a late clinical stage of autoimmune atrophic gastritis. More recently, it was confirmed that autoimmune thyroid disorders, in particular Hashimoto's thyroiditis, may be frequently associated with other organ-specific, immune-mediated disorders, such as autoimmune atrophic gastritis or celiac disease. The association of Hashimoto's thyroiditis with autoimmune atrophic gastritis or celiac disease in adult patients is currently considered part of the polyglandular autoimmune syndromes which include several autoimmune disorders associated with an autoaggressive impairment of endocrine glands. From a clinical point of view, the thyro-entero-gastric autoimmunity may lead to potentially serious consequences like anemia, micronutrients deficiencies, and drugs malabsorption, as well as to an increased risk for malignancies. These alterations may frequently present in an underhand manner, with consequent diagnostic and treatment delays. Many aspects of the association between thyroid, gastric and intestinal autoimmune diseases still await clarification. The present review focuses on the embryological, genetic and pathophysiological aspects of thyro-entero-gastric autoimmunity. In particular, the current diagnostic criteria of autoimmune thyroid disease, autoimmune atrophic gastritis, and celiac disease are reviewed, along with the evidences for their association in poly-autoimmunity syndromes. The benefits of proactive screening of autoimmune thyroid disorders in patients with autoimmune gastritis or enteropathy and vice versa are also discussed.

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The Possible Role of Pathogenic and non-Pathogenic Bacteria in Initiation and
Exacerbation of Celiac Disease; A Comprehensive Review

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Abstract

Celiac disease (CD) is an immune-mediated enteropathy, generally of the proximal intestine, that occurs in genetically susceptible individuals triggered by the ingestion of gluten. The incidence and frequency of CD are increasing, and it is predicted that CD affects approximately 1% of the people worldwide. The common clinical manifestations of CD are divided in two sections, including classic and non-classic symptoms that can be created in childhood and adulthood. The relationship between pathogenic and non-pathogenic bacteria with CD is complex and multidirectional. In previous published studies, results demonstrated the triggering impact of bacteria, viruses, and parasites on initiation and development of inflammatory bowel disease (IBD) and Irritable Bowel Syndrome (IBS) [1]. Different studies revealed the inducing effect of pathogenic and non-pathogenic bacteria on CD. However, increasing evidence proposes that some of these microorganisms can also play several positive roles in CD process. Although information of the pathogenesis of the CD is quickly expanding, the possible role of bacteria needs further examination. In conclusion, with respect to the possible correlation between different bacteria in CD, the current review-based study aims to discuss the possible relationship between CD and pathogenic and non-pathogenic bacteria and to show various and significant aspects of mechanisms involved in the CD process.

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**Type 2 refractory celiac disease on third-generation capsule endoscopy and enteroscopy: typical appearance of ulcerative jejunitis.**

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Conflict of interest statement

None


**Pharmacologic Management of Chronic Urticaria in Pediatric Patients: The Gap Between Guidelines and Practice.**

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Abstract

Chronic urticaria is an uncommon disorder in children but can present considerable morbidity, as well as frustration for the healthcare provider and parent. The prevalence is 0.1-0.3% but can vary considerably by country. Chronic spontaneous urticaria (no identifiable cause) is responsible for 70-80% of chronic urticaria, about half of this due to a subtype called chronic autoimmune urticaria identified by the presence of autoantibodies to IgE or the IgE receptor. Chronic urticaria that is triggered by external physical stimuli is called chronic inducible urticaria and is present in another 15-20%. Allergies, infection, and other underlying diseases such as thyroid disease, celiac disease, or Helicobacter pylori infection cause a minor proportion of cases. Chronic urticaria has considerable impact on quality of life and healthcare costs. An adverse impact on quality of life is more prevalent in older children and adolescents and can be comparable to other diseases of childhood such as diabetes and epilepsy. Healthcare costs can be 50% higher than the national estimates for healthy patients and include more hospitalizations, longer duration of hospitalizations, and more emergency department (ED) and outpatient visits. Allergic and autoimmune diseases can be comorbidities that add to healthcare utilization. Resolution can take years. Guidelines are available for diagnosis and treatment. A good history is the key to identifying the cause. Minimal laboratory tests are required and should be guided by the history. Patients with easily controlled urticaria may not need any laboratory tests. Suggested treatment emphasizes the use of non-sedating antihistamines, utilized in a step-wise fashion beginning with normal doses and advancing the dose based on the response up to four times the recommended dose for age. Other treatments are left to the urticaria specialist and are not discussed in this paper. These guidelines are not well utilized based on real-world studies; sedating antihistamines and oral steroids are overutilized. Medications should be taken daily, not as needed. Additional medications, if required, should be added to prior medications in a step-wise fashion. The gap between the guidelines for diagnosis and treatment and what is happening in the real world needs to be closed to reduce the cost and morbidity associated with this disorder.

PMID: 31858489


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Abstract

We report a case of a hybrid surgical treatment of a 71-year-old fragile female with severe chronic obstructive pulmonary disease with a 5-year history of progressive back pain and diagnosis of descending thoracic aorta aneurysm (DTAA), but refused operation at first. Since the patient presented with an acute expanding painful pulsatile mass due to a ruptured DTAA contained by the subcutaneous tissue and had a high-risk surgical profile, we agreed that the simplest urgent operation should be performed. Cardiopulmonary bypass with or without deep hypothermic circulatory arrest was ruled out as an option. The initial approach would be permanent bypasses to the supra-aortic trunks and endovascular repair of the ruptured DTAA, but we ran into a problem: the absence of suitable diameter in the ascending aorta to land the prosthesis-zone 0. To overcome this obstacle, we opted to perform a diameter reduction of the ascending aorta by wrapping it with a Dacron tube to create a neck where we could land the endovascular prosthesis. Following this step bypasses from the proximal ascending aorta to the brachiocephalic artery, left common carotid artery and left subclavian artery were created. Since we gained ground to act in zone 0, the first endoprosthesis was landed in the wrapped zone and the aortic arch-from zone 0 to zone 3. The second and third endoprostheses covered the ruptured DTAA above the celiac trunk-zones 4 and 5. Good positioning of the endoprostheses was achieved and we attained procedural success.

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PMID: 31856350

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Coeliac disease in Pakistan: A bibliographic review of current research status.

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Abstract

Coeliac disease is a common disorder worldwide but its impact in Pakistan is unknown. We reviewed the literature to investigate what is published on coeliac disease and gluten-free diet in Pakistan. Search engines including Medline, Embase, Google were used to retrieve information. Only articles published in a medical journal were included. A total of 34 articles were retrieved, 28 of which were clinical. Of these, 14 pertained to adults and 14 described paediatric patients. Most consisted of descriptions of small series of patients or individual case reports. Five articles addressed treatment issues including gluten-free diet. Most (65%) were from Pakistani journals. All publications were from Sindh or Punjab. For a common disorder, there is a paucity of high quality scientific literature on coeliac disease from Pakistan. Systematic, prospective research studies are needed to investigate the impact of coeliac disease in Pakistan including prevalence, clinical presentations and challenges of gluten-free diet.

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Prevalence of autoimmune disease in women with premature ovarian failure.

Grossmann B1, Saur S2,3, Rall K4, Pecher AC2,3, Hübner S4, Henes J2,3, Henes M4.

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Abstract

Objective: The aim of the study was to investigate the relationship between premature ovarian failure and autoimmune disease. Methods: This interdisciplinary prospective study included 52 consecutively recruited women with premature ovarian failure, aged 18-40 years. Diagnosis of premature ovarian failure was defined as amenorrhoea lasting more than 4 months and anti-Müllerian hormone levels below the age-appropriate range. Women with an abnormal karyotype or Fragile X syndrome were excluded from the study. All participants were screened by a
rheumatologist for the presence of underlying autoimmune disease. **Results:** The average age at first diagnosis of premature ovarian failure was 29.5 years; 92.3% of participants \(^{*}(n = 48)\) presented with a secondary amenorrhea, while only 7.7% \(^{*}(n = 4)\) had primary amenorrhea. Of all 52 participants, 40.4% \(^{*}(n = 21)\) had at least one confirmed autoimmune disease, including Hashimoto's disease, systemic lupus erythematosus, rheumatoid arthritis, psoriasis, Crohn's disease, polyglandular autoimmune syndrome and coeliac disease. Response rates for hormonal stimulation therapy were low and the presence of autoimmune disease was associated with poor infertility treatment outcome. **Conclusions:** We found a high prevalence of autoimmune disease in women with premature ovarian failure. Screening for autoimmune diseases should be offered to all women with premature ovarian failure.

PMID: 31852274


**Effects of circulating levels of Th17 cells on the outcomes of acute Stanford B aortic dissection patients after thoracic endovascular aortic repair: A 36-month follow-up study a cohort study.**


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**Abstract**

T helper 17 (Th17) cells are related to the progression of aortic dissection. This study aimed to determine whether circulating Th17 levels are associated with the prognosis of acute Stanford type B aortic dissection (STBAD) after thoracic endovascular aortic repair (TEVAR). A cohort study was performed and STBAD patients \(^{*}(n = 140)\) received TEVAR were enrolled, the circulating Th17 levels were measured and the patients were divided into low and high Th17 groups, and 36 months of follow-up was performed. The data for mortality, survival outcomes, heart structure and function
changes, aortic regurgitation prevalence, and aortic remodeling outcomes were recorded. Lower mortality and fewer complications were observed in the low Th17 group than in the high Th17 group in the third year of follow-up. In addition, the low Th17 group exhibited better cardiac remodeling and cardiac function when compared with that in the high Th17 group in the second to third year after TEVAR. Aortic reflux was improved in both groups but was more pronounced in the low Th17 group. During follow-up, the true lumen of the proximal thoracic aorta at the level of the celiac trunk in both the low and high Th17 groups continuously enlarged and was more pronounced in the low Th17 group. Circulating Th17 cells were related to cardiac and aortic remodeling and prognosis during STBAD after TEVAR. Anti-inflammatory therapy may be useful for STBAD patients who have undergone TEVAR.

Free Article
PMID: 31852089 [Indexed for MEDLINE]

Bone Mineral Density in Patients With Celiac Disease: A Further Association With Extent of Disease on Capsule Endoscopy.

Zammit SC1, Sanders DS, Sidhu R.

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Letter: the gluten-free diet as a bottom-up approach for irritable bowel syndrome.

Rej A1, Buckle RL1, Shaw CC1, Trott N1, Aziz I1,2, Surendran Sanders D1,2.

**Letter: the gluten-free diet as a bottom-up approach for irritable bowel syndrome.**

**Authors' reply.**

Tuck C¹, Vanner S¹, Camilleri M², Jing Wang X².

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**Commentary: recognising the boom in coeliac disease prevalence was more than just increased awareness.**

Gibson PR¹.
Counting Intraepithelial Lymphocytes: A Comparison Between Routine Staining and CD3 Immunohistochemistry.

Cooper R1, Papworth NJ2, Harris C3, Horne J2, Lai J4, Rajak R2, Valentine KM2, Gaya SO3, Carr NJ4.

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Abstract

Counting intraepithelial lymphocytes (IELs) is a key part of the assessment of duodenal biopsies. Immunohistochemistry (IHC) for CD3 can aid identification of lymphocytes in this context, but it is not evident that counts on hematoxylin and eosin (H&E) and CD3 are comparable. This study aimed to compare the IEL counts in duodenal biopsies using H&E stains and CD3 IHC, and to examine the interobserver variability. Thirty-five paired H&E and CD3 sections were reviewed by 6 pathologists who counted the number of IELs per 100 enterocytes. The counts were categorized into groups: normal (<25 lymphocytes), mildly raised (25-40 lymphocytes), and markedly raised (>40 lymphocytes). CD3 IHC was associated with significantly higher IEL counts than H&E. Four cases with normal H&E counts had raised counts with CD3. There was moderate agreement between observers for both H&E and CD3. Lack of concordance between CD3 and H&E IEL counts suggests that counts derived from the 2 methods may not be comparable to each other and should not be considered equivalent. There was no significant improvement in interobserver variability with CD3 IHC.
Gastrointestinal symptoms in pediatric patients with type 1 diabetes mellitus.

Selbuz S¹, Buluş AD¹.

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Abstract

Background Various gastrointestinal (GI) symptoms are associated with diabetes. Common GI complaints associated with the manifestation of the disease include abdominal pain, diarrhea, nausea, bloating and vomiting. There have been very few studies examining GI problems of pediatric patients with type 1 diabetes mellitus (T1DM). The aims of this study were to find out the prevalence of GI symptoms in pediatric patients with T1DM and to determine the correlation among such symptoms, duration of diabetes and glycemic control. Methods One hundred and thirty-seven (median age 13.2 years, female 45.3%) patients with T1DM were examined. Demographic features, GI symptoms, signs and physical examination findings of the patients were recorded by pediatric gastroenterology specialists for the differential diagnosis and exclusion of other etiologies. Complete blood count, blood glucose, lipid profile, electrolytes, amylase, lipase, celiac antibodies and glycated hemoglobin (HbA1c) levels were evaluated and stool examination was performed. Endoscopy was performed on the patients who had refractory GI complaints. Gastric emptying (GE) time was evaluated using GE scintigraphy. Results Overall, 74 (54%) patients had ≥1 GI complaints. Patients often reported gastroesophageal reflux (32.8%) and abdominal pain (18%). The most significant findings in terms of GI symptoms were determined when patients were classified according to the glycemic control status. Reflux and dyspeptic symptoms were significantly more common in poorly or very poorly controlled diabetic patients (p=0.003 and p=0.004, respectively). Conclusions Diabetes can affect the entire GI tract, and GI symptoms are common in pediatric patients. We recommend that T1DM patients be evaluated for GI symptoms.

PMID: 31846427

Similar articles

Celiac Antigenicity of Ancient Wheat Species.
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Abstract

Ancient grains have gained renewed interest in the last few years due to their perceived nutritional benefits. The goal of this study was to examine the presence of celiac epitopes in different ancient grains and determine differences in the gliadin protein profile of such grains. To investigate celiac epitopes, an untargeted mass spectrometric method was used, and the gliadin protein profile was studied using reverse phase-HPLC. Our findings show that celiac epitopes can be detected in wheat-related ancient grains, such as einkorn, emmer, and Kamut, indicating that these ancient grains have the potential to elicit the immune response associated with celiac disease. Additionally, the results showed that the gliadin protein composition is significantly different between ancient grain species, which could result in varying functional properties in end-use applications.

Conflict of interest statement

The authors declare no conflict of interest.

Transcriptional profiling of human intestinal plasma cells reveals effector functions beyond antibody production.

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2. KG Jebsen Coeliac Disease Research Centre, University of Oslo, Oslo, Norway.
Abstract

Background:

Plasma cells (PCs) are terminally differentiated B-lymphocytes producing antibodies. In coeliac disease (CeD) there is increased density of PCs in the small-intestinal lesion. Many of these PCs produce disease-specific autoantibodies targeting transglutaminase 2 (TG2).

Objective:

The plasmacytosis of CeD motivated us to study the transcriptional programme of PCs from coeliac gut lesions.

Methods:

RNA-seq was performed on the PCs of CeD patients and disease controls, being specific or non-specific for TG2.

Results:

Being antibody-producing cells, 67% of the PCs' transcript was aligned to immunoglobulin genes. Strikingly, genes encoding ligands and receptors of chemokines and cytokines were abundant. Higher transcript levels of genes associated with cell activation and immune responses were observed in PCs of CeD patients compared to controls. TG2-specific compared to non-TG2 specific PCs expressed increased levels of CXCR3, CXCL10 and interleukin-15; factors that have been implicated in the pathogenesis of CeD yet with production attributed to other cells than PCs. The presence of transcripts of HLA class II and T-cell co-stimulatory molecules suggests that PCs may serve as antigen-presenting cells for CD4 + helper T cells.

Conclusions:

Our findings shed new light on the biology of intestinal PCs, implicating functions that go beyond the production of immunoglobulins.

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PMC Full text
Increased fasting small-bowel water content in untreated coeliac disease and scleroderma as assessed by magnetic resonance imaging.


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Abstract

Background and aims:

The regular overnight migrating motor complex (MMC) ensures that the normal fasting small-bowel water content (SBWC) is minimised. We have applied our recently validated non-invasive magnetic resonance technique to assess SBWC in newly diagnosed coeliac disease (CD), scleroderma (SCD) and irritable bowel syndrome (IBS), conditions possibly associated with small intestinal bacterial overgrowth (SIBO).

Methods:

A total of 20 CD and 15 SCD patients with gastrointestinal symptoms were compared to 20 healthy volunteers (HV) and 26 IBS with diarrhoea (IBS-D) patients, as previously reported. All underwent a fasting magnetic resonance imaging (MRI) scan on a 1.5 T Philips Achieva MRI scanner to assess fasting SBWC and colonic volumes. Stool and symptom diaries were completed for one week.

Results:

Compared to HV, all patients had significantly increased stool frequency and Bristol stool form score. SBWC was significantly increased in CD (median 109 mL; interquartile range (IQR) 53-224 mL) compared to HV (median 53 mL; IQR 31-98 mL; p < 0.01) and IBS-D (median 42 mL; IQR 28-67 mL; p < 0.01). A variable increase in SBWC was also found in SCD (median 77 mL; IQR 39-158 mL), but
this was not significant ($p = 0.2$). Colonic volumes were similar for all groups, being a median of 547 mL (IQR 442-786 mL) for CD, 511 mL (453-789 mL) for SCD, 612 mL (445-746 mL) for HV and 521 mL (428-757 mL) for IBS-D. When CD patients were subdivided according to the Marsh classification, the higher grades had larger colonic volumes.

**Conclusion:**

Fasting SBWC as assessed by MRI is significantly increased in newly diagnosed CD and SCD but decreased in IBS-D. Future studies should test whether increased resting fluid predisposes to SIBO.

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PMID: 31839961


**CD38 expression on gluten-specific T cells is a robust marker of gluten re-exposure in coeliac disease.**


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Abstract

Background:

Increasing efforts are being put into new treatment options for coeliac disease (CeD), a chronic disorder of the small intestine induced by gluten. Interleukin-2 (IL-2) and gluten-specific CD4 + T cells increase in the blood after four hours and six days, respectively, following a gluten challenge in CeD patients. These responses are unique to CeD and are not seen in controls. We aimed to evaluate different markers reflecting a recall response to gluten exposure that may be used to monitor therapy.
Methods:

CeD patients on a gluten-free diet underwent a one- \((n = 6)\) or three-day \((n = 7)\) oral gluten challenges. We collected blood samples at several time points between baseline and day 8, and monitored gluten-specific CD4 + T cells for their frequency and CD38 expression using HLA-DQ:gluten tetramers. We assessed the IL-2 concentration in plasma four hours after the first gluten intake.

Results:

The frequency of gut-homing, tetramer-binding, CD4 + effector memory T \((\text{tetramer} + \beta7 + \text{T}_{EM})\) cells and the IL-2 concentration measured shortly after the first dose of gluten increased significantly after the one- and three-day gluten challenges, but large interindividual differences were exhibited. The frequency of \(\text{tetramer} + \beta7 + \text{T}_{EM}\) plateaued between days 6 and 8 and was lower after the one-day challenge. We observed a consistent increase in CD38 expression on \(\text{tetramer} + \beta7 + \text{T}_{EM}\) cells and did not find a significant difference between the one- and three-day challenges.

Conclusions:

The optimal time points for monitoring therapy response in CeD after a three-day oral gluten challenge is four hours for plasma IL-2 or six to eight days for the frequency of \(\text{tetramer} + \beta7 + \text{T}_{EM}\) cells, but both these parameters involved large interindividual differences. In contrast, CD38 expression on \(\text{tetramer} + \beta7 + \text{T}_{EM}\) cells increased uniformly and irrespectively of the length of gluten challenge, suggesting that this parameter is more suited for monitoring drug efficacy in clinical trials for CeD.

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Establishment the Diagnosis of Celiac Disease.

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PMID: 31839106
Infertility in women with systemic autoimmune diseases.

Khizroeva J¹, Nalli C², Bitsadze V¹, Lojacono A³, Zatti S³, Andreoli L², Tincani A⁴, Shoenfeld Y⁵, Makatsariya A¹.

Abstract

Infertility consists by definition in failure to achieve a clinical pregnancy after 12 months or more of regular unprotected intercourse" while the term subfertility means a delay to achieve pregnancy. Several factors can contribute to infertility or subfertility in patients with systemic autoimmune diseases. The association of systemic autoimmune conditions with endometriosis, celiac disease and thyroid autoimmunity that are well known causes of infertility and/or subfertility need to be taken in consideration when difficulties in the onset of pregnancy is reported. The majority of the used antirheumatic drugs do not interfere with fertility. However, the use of cyclophosphamide, limited to severe disease, can provoke premature ovarian failure; to preserve fertility a preventive treatment is available. Nonsteroidal anti-inflammatory drugs can cause temporary infertility and corticosteroids are associated to a prolonged time to pregnancy in some rheumatic diseases. Data on the association of antiphospholipid antibodies (aPL) with infertility are still debated but in general an increased rate of aPL is described patients undergoing medically assisted reproductive techniques. In systemic lupus erythematosus aPL and other autoantibodies (i.e. anti-oocytes) can contribute to the infertility of some patients. Subfertility, rather than infertility, is observed in patients with rheumatoid arthritis; the particular physical conditions of these women can also
account for this. Physicians should not forget the patients' age, that is mandatory in order to preserve their chance to have children.

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**Effect of the frying process on the properties of gluten protein of you-tiao.**

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**Abstract**

Wheat is one of the most important grains in cereal products. Gluten protein is an important component of wheat and plays an important role in the human diet. The variations of gluten protein in you-tiao were investigated in this study during frying, with a view toward a theoretical basis for the improvement of processing methods and quality in you-tiao. During the processing of you-tiao, gluten protein altered significantly. Analysis of secondary structure and surface hydrophobicity indicated that gluten protein molecules were unfolded and decomposed after frying, providing the opportunity for protein reaggregation. The extractability and sodium dodecyl sulphate-polyacrylamide gel electrophoresis profiles demonstrated the decomposition and reaggregation of gluten protein. Analysis of the chemical interactions proved that gluten protein molecules aggregated mainly by disulfide bonds and hydrophobic interactions. Frying induced a loose and uneven gluten network.

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PMID: 31837526

**Similar articles**
Efficacy Study of Anti-Endomysium Antibodies for Celiac Disease Diagnosis: A Retrospective Study in a Spanish Pediatric Population.

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Abstract

The aim of this study was to assess the efficacy of anti-endomysium antibodies (EMA) as a serological marker for celiac disease (CD) diagnosis in a pediatric population. A retrospective study of pediatric patients who underwent a CD serological markers study: EMA and anti-tissue transglutaminase antibodies (anti-TG2). Clinical symptomatology, degree of histological lesion, human leukocyte antigen (HLA) haplotype compatible with CD (HLA DQ2 and/or DQ8), and final diagnosis were taken into account. We included 445 patients who were classified in two groups according to the final diagnosis. Group 1: 232 children with CD, 91.4% of whom exhibited small intestinal villous atrophy, 228 being EMA-positive and four EMA-negative. Group 2: 213 children with a non-CD diagnosis, 212 EMA negative and one EMA positive. Both antibodies, EMA and anti-TG2, reached similar sensitivities, 98% and 99% respectively, while EMA had a higher specificity (99%) than anti-TG2 (93%). By using both markers combined, compared to using anti-TG2 alone, 5.7% of patients are better diagnosed. However, when we compare the efficacy of EMA and anti-TG2 in asymptomatic and symptomatic patients, the sensitivity of EMA is 98% irrespective of symptoms, thus higher than for anti-TG2 ≥10 × upper limit of normal (ULN) (respectively 77% and 84%). Our results support the use of EMA to increase CD diagnostic accuracy in a non-biopsy approach, especially in asymptomatic children.
An explorative study identifies miRNA signatures for the diagnosis of non-celiac wheat sensitivity.

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Abstract

Non-celiac wheat sensitivity (NCWS), also referred to as non-celiac gluten sensitivity, is a recently described disorder triggered by wheat/gluten ingestion. NCWS elicits a wide range of symptoms including diarrhoea, intestinal discomfort, and fatigue in analogy with other wheat/gluten-related disorders and celiac disease in particular. From the pathological standpoint, NCWS patients only have a slight increase of intraepithelial lymphocytes, while antibodies to tissue transglutaminase (tTG) and villous atrophy, otherwise diagnostic features of celiac disease, are absent. To date, the diagnosis of NCWS relies on symptoms and exclusion of confounding diseases, since biomarkers are not yet available. Here, the expression levels of selected miRNAs were examined in duodenal biopsies and peripheral blood leukocytes collected from newly diagnosed patients with NCWS and, as controls, from patients with celiac disease and gluten-independent gastrointestinal problems. We identified a few miRNAs whose expression is higher in the intestinal mucosa of patients affected by NCWS in comparison to control patients affected by gluten-independent dyspeptic symptoms (Helicobacter pylori-negative) and celiac disease. The present study provided the first evidence that NCWS patients have a characteristic miRNA expression patterns, such peculiarity could be exploited as a biomarker to the diagnosis of this disease.

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Conflict of interest statement

The authors have declared that no competing interests exist.


High rates of serology testing for coeliac disease, and low rates of endoscopy in serologically positive children and adults in Israel: lessons from a large real-world database.

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Abstract

BACKGROUND:

Although coeliac disease is common worldwide, little is known regarding screening patterns in unselected populations, and on real-life adherence to professional guidelines for coeliac disease diagnosis and management.

OBJECTIVE:

To explore current practices in the diagnosis and management of coeliac disease, using data from a large Health Maintenance Organization in Israel that covers 54% of the population.

METHODS:
A population-based electronic database of about 4.5 million individuals was reviewed during the period of 1 January 2008 to 31 December 2015. Rates and results of coeliac disease serology testing and endoscopy procedures were examined. Subgroup analysis was performed by age, sex, ethnicity and socioeconomic status.

RESULTS:

Coeliac disease serology cumulative testing rate was 17.1% and 8.9% in the paediatric and adult population, respectively. The cumulative incidence of positive coeliac disease serology was 0.45% in children and 0.17% in adults, and was associated with age, sex, ethnicity and socioeconomic status sub-groups (P-value < 0.01). Gastrointestinal endoscopies were not subsequently performed in 44.1% of children and 47.1% of adults with positive coeliac disease serology. Within the study period, 36% of children and 56% of adults never achieved coeliac disease serology normalization.

CONCLUSION:

In a large real-life database, screening for coeliac disease was common. However, confirmatory intestinal biopsies were under-utilized, and coeliac disease serology often remained positive over a long period time in both children and adults.

PMID: 31834051

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**Therapeutic options for coeliac disease: What else beyond gluten-free diet?**


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Abstract

Coeliac disease is a chronic and systemic autoimmune condition triggered by gluten ingestion in genetically predisposed subjects. Currently, the only effective treatment available is a strict, lifelong...
gluten-free diet. However, patients perceive gluten withdrawal as an unsustainable burden in their life and some of them can exhibit persistent symptoms despite a strict diet. Thus, gluten-free diet represents a challenge, leading scientists to look for alternative or complementary treatments. This review will focus on non-dietary therapies for coeliac disease highlighting six therapeutic strategies: (1) decreasing gluten immunogenic content before it reaches the intestine; (2) sequestering gluten in the gut lumen before absorption; (3) blocking the passage of gluten through a leaky intestinal barrier; (4) preventing the enhancement of immune response against gliadin; (5) dampening the downstream immune activation; (6) inducing immune tolerance to gluten. Most developing therapies are only in the pre-clinical phase with only a few being tested in phase 2b or 3 trials. Although new approaches raise the hope for coeliacs giving them a chance to come back to gluten, for the time being a cautionary appraisal of new therapies suggests that they may have a complementary role to gluten withdrawal, mainly to prevent inadvertent gluten contamination.

Is celiac disease really associated with inflammatory bowel disease?

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Abstract

Celiac disease (CeD) and inflammatory bowel disease (IBD) are chronic gastrointestinal disorders of inflammatory origin that develop in response to environmental triggers in genetically predisposed individuals. CeD localizes in the duodenal mucosa, where intolerance develops to dietary gluten from wheat, barley, rye, and some varieties of oats. IBD, in turn, is subdivided primarily into Crohn's disease (CD) and colitis, with ulcerative colitis (UC) being the most thoroughly investigated form.
Safety of the AS04-adjuvanted human papillomavirus (HPV)-16/18 vaccine in adolescents aged 12-15 years: end-of-study results from a community-randomized study up to 6.5 years.

Bi D1, Apter D2, Eriksson T3, Hokkanen M3, Zima J4, Damaso S1, Soila M5, Dubin G6, Lehtinen M3, Struyf F1.

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Abstract

This manuscript discloses end-of-study safety data of a community-randomized controlled trial in Finland (NCT00534638), assessing the effectiveness of two vaccination strategies (gender-neutral versus females only) using the AS04-adjuvanted human papillomavirus (HPV)-16/18 (AS04-HPV-16/18) vaccine. The total vaccination cohort included 32,175 adolescents aged 12-15 y at vaccination of whom 14,837 received the AS04-HPV-16/18 vaccine and 17,338 received the hepatitis-B virus vaccine (control). Spontaneous reporting of serious adverse events (SAEs) combined with surveillance using nation-wide health registries showed an acceptable safety profile of the AS04-HPV-16/18 vaccine. During the study period (up to 6.5 y), the incidences (per 100,000 person-years) of reported SAEs considered as possibly related to vaccination were 39.1 (95% confidence interval [CI]: 25.3-57.7) and 39.8 (95%CI: 26.8-56.8) in the HPV and control groups, respectively. The most frequently reported new-onset autoimmune diseases (NOADs) were ulcerative colitis (incidence rates of 28.2 and 33.1 per 100,000 person-years in the HPV and control groups, respectively), insulin-dependent diabetes mellitus (21.9 and 37.1), Crohn’s disease (15.6 and 22.5), celiac disease (15.6 and 21.2), and juvenile idiopathic arthritis (14.1 and 15.9). Of 1,344 pregnancies reported (777 and 567 in the HPV and control groups, respectively), most resulted in elective termination (58.4% and 58.6%), birth of a live infant (32.7% and 32.3%), or in spontaneous abortion (8.0% and 7.9%). No major, registered congenital anomalies were identified. The incidence
rates of NOADs and pregnancy outcomes were generally balanced between groups. No specific safety signals were identified in the population-based health registry surveillance. Plain Language Summary

What is the context?
● Since first licensure in 2007 of the AS04-adjuvanted human papillomavirus (HPV)-16/18 vaccine (Cervarix, GSK), large quantity of safety data has been collected and confirmed its safety profile. This study provides further unique, population-based safety data from vaccinated Finnish adolescents monitored via health registries up to 6.5 y of follow-up.

What is new?
● The vaccine has shown an acceptable safety profile in girls and boys. The risk of new-onset autoimmune diseases (NOADs) was similar between the HPV vaccine group and the control group and in line with the expectations for the studied population.
● The study supports that safety surveillance via national health registries is in general more sensitive than the conventional safety reporting, notably for monitoring specific chronic diseases, e.g. autoimmune disorders.

What is the impact?
● This study highlights the importance of health registries in long-term vaccination safety surveillance. The population-based safety data reported in this study further support the routine administration of the HPV vaccine to girls and boys.

PMID: 31829767

Similar articles


**Double Threat: Interplay of Celiac Disease with Inflammatory Bowel Disease.**

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PMID: 31828460

Similar articles

Gluten-free breadmaking affected by the particle size and chemical composition of quinoa and buckwheat flour fractions.

Sciarini LS, Steffolani ME, Fernández A, Paesani C, Pérez GT.

Abstract

This study aimed at assessing the effect of physicochemical properties and the particle size of different fractions of buckwheat and quinoa on the behaviour of gluten-free dough and bread quality. Quinoa and buckwheat grains were milled with a hammer mill and then separated in three fractions. These fractions where then re-milled with a cyclonic mill to obtain samples of similar sizes. Results showed that the chemical composition of these fractions was very different and played a major role on bread quality. Proteins, lipids and fibre negatively affected bread quality, whereas starch-rich fractions were more adequate for breadmaking. Re-milling quinoa and buckwheat fractions increased bread volume, although chemical composition still influenced bread properties. For hammer-milled fractions, both the finest fractions resulted in breads with higher technological quality, as well as a final product with more fibre, minerals and proteins.

Gluten contamination in manufactured gluten-free foods in Turkey.

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Abstract

Gluten contamination in manufactured gluten-free foods (mGFFs) is a major health, well-being and economic issue worldwide for both mandatory and voluntary GFF-consumers. Although scarce, a number of surveys have shown that up to 21.5 % of mGFFs in circulation in the market are contaminated with gluten. However, at the present time there is no published work reporting gluten contamination in mGFFs produced in Turkey. In this paper miscellaneous mGFFs produced in Turkey were analysed for gluten concentration (G) to fill this knowledge gap, and to compare the situation in Turkey with worldwide efforts on this issue. A total of 200 mGFFs from 8 product categories (snack, pasta, bread, cookie, cracker, farina, traditional and others), and manufactured using 7 main ingredients (cereal mixture, buckwheat, corn, rice, locust bean, potato, and others) were analysed. A significant portion of mGFFs (17.5 %) were contaminated with gluten and therefore unacceptable as being GFF. The results point to buckwheat as the main cause of this contamination. If buckwheat is excluded, the ratio of unacceptable mGFFs dramatically decreases to 6.3 % and probably to 1.8 %, which are comparable figures to those reported for other countries. Almost all countries are subjected to the same regulations on GFFs, and the problem of gluten contamination could readily be solved to a great extent if pre-market measures are mandated. Enforcing mGFF-producers to screen their raw materials and final products to detect the presence of gluten, and preventing the release of contaminated mGFFs into the market would be a practical measure in favour of all stakeholders involved in GFF-consumption.

PMID: 31825749

The Postoperative outcomes of thoracoscopic-laparoscopic Ivor-Lewis surgery plus D2 celiac lymphadenectomy for patients with adenocarcinoma of the esophagogastric junction.

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Abstract

OBJECTIVES:

Adenocarcinoma of the esophagogastric junction (AEG) is one of the most aggressive and poor prognosis cancers. To date, no standard procedures have been established for the surgical treatment of Siewert type II. In this study, we proposed the approach of thorascopicscopic-laparoscopic Ivor-Lewis surgery plus D2 celiac lymphadenectomy (TLILD2) and aimed to investigate the patterns of lymph node metastasis and long-term survival.

METHODS:

From June 2015 to June 2018, 72 patients accepted TLILD2 and enrolled in this study. Relevant patient characteristics and postoperative variables were collected and evaluated. The disease-free survival (DFS) and disease-specific survival (DSS) were determined by the Kaplan-Meier method and compared by log-rank tests.

RESULTS:

There was no case of postoperative death in this study, and the most common complication was anastomotic mediastinal fistula (5/72, 6.9%). A total of 2811 lymph nodes were retrieved, and the positivity rate was 11.9% (334/2811). The positivity rate of celiac and mediastinal lymph nodes was 14.4% (314/2186) and 3.2% (20/625), respectively. The percentage of patients who had positive celiac and mediastinal lymph nodes reached up to 58.3% (42/72) and 8.3% (6/72), respectively. The DFS and DSS of these 72 patients were 94% and 93.4% at 1 year after surgery and 59.8% and 62% at 3 years after surgery, respectively. The pTNM stage showed a significant difference between DFS and DSS.

CONCLUSIONS:

TLILD2 could be a potential way to promote long-term survival of AEG patients. On the basis of the patterns of lymph nodes metastasis, we suggest that lower mediastinal and D2 celiac lymphadenectomy is necessary to improve the oncological outcome.

PMID: 31823049

Similar articles

Interleukin-15 (dys)regulation of lymphoid homeostasis: Implications for therapy of autoimmunity and cancer.

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Abstract

IL-15, a pleiotropic cytokine, stimulates generation of NK, NK-T, γδ, ILC1, and memory CD8 T cells. IL-15 disorders play pathogenetic roles in organ-specific autoimmune diseases including celiac disease. Diverse approaches are developed to block IL-15 action. IL-15 administered to patients with malignancy yielded dramatic increases in NK numbers and modest increases in CD8 T cells. Due to immunological checkpoints, to achieve major cancer therapeutic efficacy, IL-15 will be used in combination therapy, and combination trials with checkpoint inhibitors, with anti-CD40 to yield tumor-specific CD8 T cells, and with anticancer monoclonal antibodies to increase ADCC and antitumor efficacy, have been initiated.

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PMID: 31821442

Frequency and Predictors of Successful Transition of Care for Young Adults with Childhood Celiac Disease.

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Abstract

OBJECTIVES:

Transition from pediatric to adult care for individuals with chronic conditions is important to prevent gaps in care, though this has not been well-studied in celiac disease (CD). The aim of this study was to discern rates and predictors of successful transition of care for young adults with childhood-diagnosed CD.

METHODS:

An anonymous 21-question online survey was sent to individuals on our center’s email contact list seeking responses from those aged 18-25 years diagnosed with CD before age 18 years. Information collected included method of diagnosis, demographics, CD-related care, reasons for not seeking care, and symptoms.

RESULTS:

Respondents (n=98), 70% female, had a median age of 21 years (IQR 19-23 y). The majority were full or part-time students (67%; 95%CI=59-77%). Only 31% of respondents had successfully transitioned to an adult CD provider. Some 37% (95%CI=29-48%) were not receiving any CD medical care. An older age at diagnosis was associated with successful transition to adult gastroenterology (p=0.002) as well as with greater symptom scores (p=0.002). Receiving a referral for ongoing adult CD care predicted successful transition to an adult provider (OR 3.92, 95% CI 1.58-9.72).

CONCLUSIONS:

Transition of care for young adults with CD is inconsistent, particularly among asymptomatic patients. Receipt of a referral for an adult provider significantly improves follow-up rates.

PMID: 31821231

Similar articles
Gluten-sensitive enteropathy of the Irish Setter and similarities with human celiac disease.

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Abstract

Gluten-sensitive enteropathy of the Irish Setter is an immune-mediated intolerance to gluten, the protein found in wheat, barley, rye, and oats, reminiscent of human celiac disease. Intestinal histological lesions include partial villous atrophy, infiltration of the lamina propria by lymphocytes and plasma cells, and an increased intraepithelial lymphocyte count. Gluten-sensitive enteropathy is transmitted via autosomal recessive inheritance and its pathogenesis appears to involve cell-mediated immunity but not humoral immunity. In comparison to healthy dogs, levels of anti-gliadin antibodies in diseased Irish Setters are lower, although the significance of this finding is unclear. Irish Setters affected by gluten-sensitive enteropathy present with chronic intermittent diarrhea and weight loss. The use of a gluten-free diet is indispensable both for diagnosis of the disease and for therapy. In this review we discuss the similarities between gluten-sensitive enteropathy of the Irish Setter and human celiac disease.

PMID: 31820885

Tristetraprolin/ZFP36 Regulates the Turnover of Autoimmune-Associated HLA-DQ mRNAs.

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Abstract

HLA class II genes encode highly polymorphic heterodimeric proteins functioning to present antigens to T cells and stimulate a specific immune response. Many HLA genes are strongly associated with autoimmune diseases as they stimulate self-antigen specific CD4⁺ T cells driving pathogenic responses against host tissues or organs. High expression of HLA class II risk genes is associated with autoimmune diseases, influencing the strength of the CD4⁺ T-mediated autoimmune response. The expression of HLA class II genes is regulated at both transcriptional and post-transcriptional levels. Protein components of the RNP complex binding the 3'UTR and affecting mRNA processing have previously been identified. Following on from this, the regulation of HLA-DQ2.5 risk genes, the main susceptibility genetic factor for celiac disease (CD), was investigated. The DQ2.5 molecule, encoded by HLA-DQA1*05 and HLA-DQB1*02 alleles, presents the antigenic gluten peptides to CD4⁺ T lymphocytes, activating the autoimmune response. The zinc-finger protein Tristetraprolin (TTP) or ZFP36 was identified to be a component of the RNP complex and has been described as a factor modulating mRNA stability. The 3'UTR of CD-associated HLA-DQA1*05 and HLA-DQB1*02 mRNAs do not contain canonical TTP binding consensus sequences, therefore an in silico approach focusing on mRNA secondary structure accessibility and stability was undertaken. Key structural differences specific to the CD-associated mRNAs were uncovered, allowing them to strongly interact with TTP through their 3'UTR, conferring a rapid turnover, in contrast to lower affinity binding to HLA non-CD associated mRNA.

Conflict of interest statement

The authors declare no conflict of interest


Stimulatory Response of Celiac Disease Peripheral Blood Mononuclear Cells Induced
by RNAi Wheat Lines Differing in Grain Protein Composition.

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Abstract

Wheat gluten proteins are responsible for the bread-making properties of the dough but also for triggering important gastrointestinal disorders. Celiac disease (CD) affects approximately 1% of the population in Western countries. The only treatment available is the strict avoidance of gluten in the diet. Interference RNA (RNAi) is an excellent approach for the down-regulation of genes coding for immunogenic proteins related to celiac disease, providing an alternative for the development of cereals suitable for CD patients. In the present work, we report a comparative study of the stimulatory capacity of seven low-gluten RNAi lines differing in grain gluten and non-gluten protein composition, relevant for CD and other gluten pathologies. Peripheral blood mononuclear cells (PBMCs) of 35 patients with active CD were included in this study to assess the stimulatory response induced by protein extracts from the RNAi lines. Analysis of the proliferative response and interferon-gamma (INF-γ) release of PBMCs demonstrated impaired stimulation in response to all RNAi lines. The lower response was provided by lines with a very low content of α- and γ-gliadins, and low or almost devoid of DQ2.5 and p31-43 α-gliadin epitopes. The non-gluten protein seems not to play a key role in PBMC stimulation.
velocity reserve of patients with celiac disease.


Abstract

BACKGROUND:
Celiac disease (CD) is an enteropathy characterized with immune reaction to gliadin protein.

AIM:
In this study, we aimed to assess effect of CD on coronary microvascular circulation and the association between coronary flow velocity reserve (CFVR) and hs-CRP/Albumin ratio.

MATERIAL AND METHODS:
Study was conducted between March 2017 and November 2018 with CD at Umraniye Training and Research Hospital Gastroenterology Clinic. CFVR was defined as the ratio of hyperemic to baseline diastolic peak velocities. CFVR ≥ 2.0 was considered normal. C-reactive protein/albumin ratio (CAR) was calculated as hs-CRP/albumin.

RESULTS:
Serum albumin (4.27 ± 0.56 vs 4.50 ± 0.34; P value: .04) level was significantly lower in celiac group but higher Hs-CRP (2.44 ± 1.24 vs 1.82 ± 1.29; P value < .01), hs-CRP/albumin ratio (0.57 ± 0.30 vs 0.41 ± 0.31; P value: .03) were recorded in celiac group. Both hyperemic flow and CFVR substantially lower in the celiac group compared to controls. In univariate analysis; age, hs-CRP, and hs-CRP/albumin ratio were associated with low CFVR and hs-CRP/albumin level was an accurate predictor of low CFVR at the ROC curve.

CONCLUSION:
In this study, we found that in patients with CD, coronary flow reserve is impaired.

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PMID: 31816123

Pernicious anemia and the presence of antibodies involved in the development of this disease and other autoimmune diseases.

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Abstract

INTRODUCTION:

Pernicious Anemia (PA) is an autoimmune hematopoietic disease.

OBJECTIVES:

The aim of the study was to determine the occurrence of autoantibodies in patients with PA participating in the pathogenesis of the disease as well as the development of other autoimmune disorders - Connective Tissue Diseases (CTD) and Celiac Disease (CD). We have also strived to document the potential usefulness of the specific diagnostic and screening tests in patients affected with PA.

PATIENTS AND METHODS:

The study group consisted of 124 women and men with newly diagnosed PA and a control group (C) of 41 healthy people. Antibodies against intrinsic factor (IFAb), parietal cells (APCA), endomysium (EmA), and nuclear components (ANA) were determined in blood samples.
RESULTS:

Within the study group, the presence of antibodies involved in the pathogenesis of PA can be classified as 61.3% for IFAb or APCA, 46.0% for APCA, 30.6% for IFAb, 15.3% for IFAb and APCA. Statistical analysis shows that there is no significant difference in the occurrence of ANA and EmA between the PA and C groups. However, ANA was found in 16.1% of PA patients and in 4.9% of the controls. The occurrence of EmA in both groups is similar (3.2 vs. 2.4%), although, it has been shown that patients with IFAb or APCA are more prone to be EmA positive.

CONCLUSIONS:

Simultaneous determination of IFAb and APCA significantly increases the possibility to confirm the diagnosis of PA. Also, screening assessment for CTD and CD may be considered in patients with PA.

Free Article
PMID: 31813927

Mid- to Long-Term Outcomes in Management of Spontaneous Isolated Coeliac Artery Dissection (SICAD).

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Abstract

OBJECTIVES:
Spontaneous Isolated Coeliac Artery Dissection (SICAD) is a rare disease with few reports of management strategies. This study reports the mid- to long-term outcomes of conservative management and endovascular intervention of SICAD treatment.

**METHODS:**

Sixteen patients presenting with symptomatic SICAD from September 2006 to October 2018 were reviewed retrospectively. The clinical manifestations, initial radiological findings, methods of treatment, and serial follow up studies were analysed.

**RESULTS:**

The mean age of the patients was 51.2 ± 7.9 years, with a median follow up of 33.3 (range 1.0-118.9) months. Four patients received early intervention because of aneurysmal dilatation or distal hypoperfusion. Four patients who received conservative management showed progression of disease and were recommended for delayed intervention. Although collaterals prevented further hepatic ischaemia, one of these four patients failed in delayed intervention because of extensive thrombi completely occluding the hepatic artery. In the remaining eight patients who were managed conservatively, three (37.5%) showed regression of disease, one (12.5%) showed partial regression, and five (62.5%) showed no change in intimal flap or thrombosis, but all had symptomatic improvement. The median follow up duration for the seven patients who underwent successful intervention was 77.3 (range 34.3-118.9) months, and all stenting remained patent during the follow up period.

**CONCLUSIONS:**

Early intervention in symptomatic SICAD patients may be necessary in over 50% of patients, and endovascular stenting has durable long term outcomes.
Autism Spectrum Disorder: A 12-Month Follow-Up Clinical Trial.

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Abstract

The use of alternative interventions, such as gluten-free and casein-free (GFCF) diets, is frequent due to limited therapies for Autism Spectrum Disorder (ASD). Our aims were to determine the influence of a GFCF diet on behavior disorders in children and adolescents diagnosed with ASD and the potential association with urinary beta-casomorphin concentrations. Thirty-seven patients were recruited for this crossover trial. Each patient consumed a normal diet (including gluten and casein) for 6 months and a GFCF diet for another 6 months. The order of the intervention (beginning with normal diet or with GFCF diet) was assigned randomly. Patients were evaluated at three time-points (at the beginning of the study, after normal diet and after GFCF diet). Questionnaires regarding behavior and autism and dietary adherence were completed and urinary beta-casomorphin concentrations were determined at each time-point. No significant behavioral changes and no association with urinary beta-casomorphin concentrations were found after GFCF diet. A 6-month GFCF diet do not induce significant changes in behavioral symptoms of autism and urinary beta-casomorphin concentrations. Further studies with a long follow-up period similar to ours and including placebo and blinding elements are needed to identify better those respondents to GFCF diets.

PMID: 31813108

Similar articles

Gluten Detection Methods and Their Critical Role in Assuring Safe Diets for Celiac Patients.

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Abstract

Celiac disease, wheat sensitivity, and allergy represent three different reactions, which may occur in genetically predisposed individuals on the ingestion of wheat and derived products with various manifestations. Improvements in the disease diagnostics and understanding of disease etiology unveiled that these disorders are widespread around the globe affecting about 7% of the population. The only known treatment so far is a life-long gluten-free diet, which is almost impossible to follow because of the contamination of allegedly "gluten-free" products. Accidental contamination of inherently gluten-free products could take place at any level from field to shelf because of the ubiquity of these proteins/grains. Gluten contamination of allegedly "gluten-free" products is a constant threat to celiac patients and a major health concern. Several detection procedures have been proposed to determine the level of contamination in products for celiac patients. The present article aims to review the advantages and disadvantages of different gluten detection methods, with emphasis on the recent technology that allows identification of the immunogenic-gluten peptides without the use of antibodies. The possibility to detect gluten contamination by different approaches with similar or better detection efficiency in different raw and processed foods will guarantee the safety of the foods for celiac patients.
Association between psoriasis and celiac disease: a systematic review and meta-analysis.

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Abstract

BACKGROUND:

Multiple studies have examined the association between psoriasis and celiac disease (CD). However, these studies have shown conflicting results.

OBJECTIVE:

This study aims to analyze the association between psoriasis and CD.

METHODS:

We conducted a systematic review of the case-control, cross-sectional and cohort studies examining the association between psoriasis and CD in PubMed, Scopus and Cochrane databases. The adjusted effect sizes or crude data were extracted for quantitative analysis.

RESULTS:

Of initially identified 754 citations, 18 studies were included. Random effects meta-analysis found significant odds ratios (ORs) of 2.16 [95% confidence interval (CI), 1.74 to 2.69, 9 studies] for CD in psoriasis patients and 1.8 [95% CI 1.36 to 2.38, 8 studies] for psoriasis in CD patients. We also found a significantly increased risk of new-onset psoriasis in CD [hazard ratio = 1.75, 95% CI 1.58 to 1.93]. Subgroup analyses according to disease severity and geographical region could not be performed due to limited data.

CONCLUSIONS:

This two-way meta-analyses found a significant association between psoriasis and CD. Clinicians should be aware of this association and the psoriasis patients with bowel complaints might benefit
from screening for celiac disease through questionnaires or interviews with subsequent
gastroenterology consultation.

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PMID: 31809817

Deciphering crucial genes in coeliac disease by bioinformatics analysis.

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Abstract

Coeliac disease (CD) is a chronic autoimmune disease that is characterized by malabsorption in sensitive individuals. CD is triggered by the ingestion of grains containing gluten. CD is concomitant with several other disorders, including dermatitis herpetiformis, selective IgA deficiency, thyroid disorders, diabetes mellitus, various connective tissue disorders, inflammatory bowel disease, and rheumatoid arthritis. The advent of high throughput technologies has provided a massive wealth of data which are processed in various omics scale fields. These approaches have revolutionized the medical research and monitoring of the biological systems. In this regard, omics scaled analyses of CD by Comparative Toxicogenomics Database (CTD), DISEASES, and GeneCards databases have retrieved 2656 CD associated genes. Amongst, 54 genes were assigned by Venn Diagram of the intersection to be shared by these 3 databases for CD. These common genes were subjected to further analysis and screening. The Enrich database, GeneMANIA, Cytoscape, and WebGestalt (WEB-based GEne Set AnaLysis Toolkit) were employed for functional analysis. These analyses indicated that the obtained genes are mainly involved in the immune system and signalling pathways related to autoimmune diseases. The STAT1, ALB, IL10, IL2, IL4, IL17A, TGFβ1, IL1B, IL6, TNF, IFNG hub genes were particularly indicated to have significant roles in CD. Functional analyses of these hub genes by GeneMANIA indicated that they are involved in immune systems regulation. Moreover, 25 out of 54
genes were identified to be seed genes by the WebGestalt database. Gene set analysis with GEO2R tool from Gene Expression Omnibus (GEO) showed that there were 15 significant genes in GSE76168, 29 significant genes in GSE87460, 12 significant genes in GSE87458, 9 significant genes in GSE87457, 3753 significant genes in GSE112102 and 1043 significant genes in GSE102991 with differential expression in coeliac patients compared to controls. The IRF1 and STAT1 genes were common between the significant genes from GEO and the 54 CD related genes from three public databases. In the light these results, nine key genes, including IRF1, STAT1, IL17A, TGFB1, ALB, IL10, IL2, IL4, and IL1B, were identified to be associated with CD. These findings could be used to find novel diagnostic biomarkers, understand the pathology of disease, and devise more efficient treatments.

PMID: 31809599

**Celiac Disease.**

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**Abstract**

Celiac disease (CD) affects approximately 1% of the general population, although most cases remain unrecognized. Because CD is a multisystem disorder with protean clinical manifestations, a high index of suspicion is needed to make an appropriate diagnosis. A diagnosis of CD is made in a patient who is genetically predisposed based on the presence of compatible clinical features, positive highly specific celiac serologic findings, duodenal biopsies that document enteropathy, and improvement with a gluten-free diet. The differential diagnoses for the clinical features and the histologic findings seen in patients with CD are numerous and need to be considered; because the management of celiac disease consists of a lifelong gluten-free diet, ensuring that the diagnosis is correctly established is of utmost importance. The aim of this review is to provide practicing clinicians with the most current information on the diagnosis and management of CD, including new developments and the approach to controversial issues.

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PMID: 31806106

**Similar articles**
Celiac disease in Saudi children with isolated short stature: is it rare or are we not screening rigorously enough?

Saadah OI, ALNosani NM.

Abstract

Background Celiac disease (CeD) is an immune-mediated enteropathy induced by gluten exposure in individuals with genetic susceptibility. Short stature (SS) can be the sole clinical manifestation of CeD, in the absence of gastrointestinal (GI) symptoms. This study aimed to determine the prevalence of CeD in Saudi Arabian children with SS. Patients and methods Medical records were reviewed in a total number of 275 retrospective cases (during the period 2002-2014) of children with isolated SS from King Abdulaziz University Hospital, Jeddah. Their serum samples were tested with tissue transglutaminase (tTG) antibodies. Patients with a positive serology were scheduled for an upper endoscopy and intestinal biopsy to confirm CeD diagnosis before starting a gluten-free diet (GFD). Clinical, anthropometric and laboratory data were recorded for all patients. Results A total of 275 children with SS were included. The mean age ± standard deviation (SD) was 9.4 ± 4.0 years (range, 2.6-16.9 years) and males constituted the predominant gender group (151/275; 54.9%) over females (124/275; 45.1%). The mean ± SD height for age z score (HAZ) was -2.9 ± 1.0. Thirty-eight (13.8%) had positive serology, and 16 (5.8%) had biopsy-proven CeD. Apart from the difference in duration of delayed bone age between CeD patients and CeD-negative serology subjects (mean ± SD, 39.6 ± 10.5 vs. 18.6 ± 16.8, p = 0.02), no other major difference in other clinical or laboratory parameters was evident. Conclusions The prevalence rate of CeD in Saudi Arabian SS children was 5.8%, which is comparable to published reports of a number of other countries. Regular screening of children with SS is therefore justifiable.

PMID: 31804962
Comorbidities in adolescents with inflammatory bowel disease: findings from a population-based cohort study.

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Abstract

BACKGROUND:

Inflammatory bowel diseases are associated with various immune- and non-immune-mediated conditions. We aimed to assess the association of inflammatory bowel diseases with comorbidities at late adolescence.

METHODS:

Jewish Israeli adolescents who underwent a general health evaluation prior to enlistment to the Israeli Defense Forces from 2002 to 2016 were included.

RESULTS:

Overall, 891 subjects (595 Crohn's disease, 296 ulcerative colitis, median age 17.1 years) and 1,141,841 controls were analyzed. Crohn's disease was associated with arthritis (odds ratio (OR) 4.7, 95% confidence interval (CI) 2.4-9.1), thyroid disease (OR 2.6, 95% CI 1.2-5.5), atopic dermatitis (OR 2, 95% CI 1.1-3.6), autoimmune hepatitis (OR 4.4, 95% CI 2.3-8.6), nephrolithiasis (OR 3.6, 95% CI 1.2-11.4), and pancreatitis (OR 41.8, 95% CI 17.2-101.9). Ulcerative colitis was associated with arthritis (OR 3.6, 95% CI 1.0-9.8), thyroid disease (OR 4.8, 95% CI 1.2-19.4), autoimmune hepatitis
(OR 8, 95% CI 4.1-16.2), and pancreatitis (OR 51, 95% CI 16.1-158.9). Primary sclerosing cholangitis was associated with both diseases. Asthma, celiac, type 1 diabetes, psoriasis, and bone fractures were not more common in both diseases. Male predominance was noted for most associations.

CONCLUSIONS:

At adolescence, both Crohn's disease and ulcerative colitis are associated with multiple comorbidities, not limited to autoimmune disorders.

PMID: 31801156
Similar articles


Management of celiac trunk and superior mesenteric artery synchronous aneurysms as an extremely rare manifestation of Wegener granulomatosis.

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Abstract

Large-vessel aneurysm is an extremely rare complication of Wegener granulomatosis. We report a case of Wegener granulomatosis in a 49-year-old woman with large synchronous aneurysms of the celiac trunk (54 mm) and superior mesenteric artery (42 mm) who presented with abdominal pain. Because of the large diameter of the aneurysms and their proximity to each other, a combination of endovascular and hybrid repair was used for management. After surgical debranching and endovascular repair, the patient was discharged in good general condition. We concluded that abdominal pain in Wegener granulomatosis can be a rare manifestation of a large visceral aneurysm.

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PMCID: PMC6883309 Free PMC Article
Complications of liver transplant.

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Abstract

Liver transplantation has become a definitive treatment for patients with end-stage liver disease and those meeting Milan criteria for hepatocellular carcinoma. The morbidity and mortality associated with liver transplantation continues to decrease thanks to refinements in surgical technique, immunosuppression, and imaging. In particular, imaging plays a vital role by facilitating early detection of post-operative complications and enabling prompt treatment. Post-operative complications that lead to graft failure and patient morbidity/mortality can be generally categorized as vascular, biliary, parenchymal, and malignant. Vascular complications include stenosis and thrombosis of the hepatic artery, portal vein, and inferior vena cava; hepatic artery pseudoaneurysm; arteriovenous fistula; and celiac stenosis. Biliary abnormalities include strictures, bile leak, obstruction, recurrent disease, and infection. While imaging is not primarily utilized to diagnose allograft rejection, it plays an important role in excluding mechanical causes of graft dysfunction that can mimic rejection. Ultrasound is routinely performed as the first-line imaging evaluation for the detection and follow-up of early and delayed complications. Cholangiography and magnetic resonance cholangiopancreatography are useful in detecting and characterizing biliary complications. Computed tomography is often used to further evaluate abnormal findings on ultrasound or for the characterization of post-operative fluid collections. The aim of this review is to discuss and illustrate the imaging findings of complications associated with liver transplantation and their role in facilitating treatment.

PMID: 31797026
Adverse events associated with colonoscopy; an examination of online concerns.

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Abstract

BACKGROUND:

Colonoscopy as a screening and diagnostic tool is generally safe and well-tolerated, and significant complications are rare. The rate of more mild adverse effects is difficult to estimate, particularly when such effects do not result in hospital admission. We aimed to identify the rate and timing of adverse effects as reported by users querying symptoms on an internet search engine.

METHODS:

We identified queries made to Bing originating from users in the United States containing the word "colonoscopy" during a 12-month period and identified those queries in which the timing of colonoscopy could be estimated. We then identified queries from those same users for medical symptoms during the time span from 5 days before through 30 days after the colonoscopy date.

RESULTS:

Of 641,223 users mentioning colonoscopy, 7013 (1.1%) had a query that enabled identification of their colonoscopy date. The majority of queries about colonoscopy preceded the procedure, and concerned diet. 28% of colonoscopy-related queries were made afterwards, and included queries about diarrhea and cramps, with 2.6% of users querying respiratory symptoms after the procedure, including cough (1.2%) and pneumonia (0.6%). Respiratory symptoms rose significantly at days 7-10 after the colonoscopy.

CONCLUSIONS:

Internet search queries for respiratory symptoms rose approximately one week after queries relating to colonoscopy, raising the possibility that such symptoms are an under-reported late adverse effect of the procedure. Given the widespread use of colonoscopy as a screening modality
and the rise of anesthesia-assisted colonoscopy in the United States in recent years, this signal is of potential public health concern.

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Measuring Quality.

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A Case of Polyautoimmunity: Celiac Hepatitis, Grave's Disease and Autoimmune Hemolytic Anemia.

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Abstract

Celiac disease (CD) is an autoimmune disorder with high incidence of multi organ involvement; especially, gastrointestinal manifestations and an increased risk of malignancies. Here we report a case of CD with celiac hepatitis, autoimmune hemolytic anemia (AIHA) and Grave's disease (GD) with their complications. Polyautoimmunity requires comprehensive analysis. While CD and GD were previously diagnosed, AIHA and cirrhosis were diagnosed during admission upon extensive
work-up. Similarly, other autoimmune etiologies, such as autoimmune hepatitis (AIH), and/or primary biliary cholangitis were ruled out. All three diseases were treated afresh with strict adherence to a gluten-free diet (GFD) and carbimazole along with addition of medications for cirrhosis complicated by ascites. This was a rare case where non-adherence to a GFD led to such severe adverse events. A case of celiac hepatitis presenting with such a wide array of signs and symptoms has rarely been reported in the literature and the management of this patient was unique and challenging.

PMID: 31779758


**Masked bolus gluten challenge low in FODMAPs implicates nausea and vomiting as key symptoms associated with immune activation in treated coeliac disease.**


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**Abstract**

**BACKGROUND:**

In patients with coeliac disease, FODMAPs in gluten-containing foods, and participant anticipation of a harmful ('nocebo') effect, may contribute to acute symptoms after gluten challenge.
AIM:

To establish acute gluten-specific symptoms linked to immune activation in coeliac disease

METHODS: We included 36 coeliac disease patients on a gluten-free diet receiving placebo in the RESET CeD trial. Double-blind, bolus vital wheat gluten (~6 g gluten protein) and sham challenges low in FODMAPs were consumed 2 weeks apart. Assessments included daily Coeliac Disease Patient Reported Outcome (CeD PRO) symptom scores (0-10), adverse events and serum interleukin-2 (baseline and 4 hours).

RESULTS:

Median CeD PRO score for nausea increased most (sham: 0 vs gluten: 5.5; P < .001). Apart from tiredness (1 vs 4, P = .005) and headache (0 vs 2, P = .002), changes in other symptoms were small or absent. Only nausea increased significantly in occurrence with gluten (11% vs 69%, P < .001). Without nausea, only tiredness and flatulence were common after gluten. Nausea (6% vs 61%, P < .001; median onset: 1:34 hours) and vomiting (0% vs 44%, P < .001; 1:51 hours) were the only adverse events more common with gluten than sham. Interleukin-2 was always below the level of quantitation (0.5 pg/mL) at baseline, and after sham. Interleukin-2 was elevated after gluten in 97% of patients (median fold-change: 20), and correlated with severity of nausea (r_ = .49, P = .0025) and occurrence of vomiting (P = .0005).

CONCLUSIONS:

Nausea and vomiting are relatively specific indicators of acute gluten ingestion, and correlate with immune activation. IBS-like symptoms without nausea are unlikely to indicate recent gluten exposure.

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PMID: 31769533

Protecting adults with celiac disease from pulmonary infections.

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Natural history and management outcomes of segmental arterial mediolysis.

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Abstract

BACKGROUND:

Segmental arterial mediolysis (SAM) is a poorly understood, nonatherosclerotic, noninflammatory disease resulting from arterial medial degeneration. Patients may present with aneurysm, dissection, stenosis, or bleeding from visceral or renal arteries. Treatment algorithms are poorly characterized.

METHODS:

A retrospective review of all patients diagnosed with SAM was performed at our institution. Patients were identified by established criteria that include clinical presentation in combination with radiographic and serologic findings. Demographics, presenting symptoms, diagnostic evaluation, management, and outcomes were reviewed.

RESULTS:

There were 117 patients diagnosed with SAM between 2000 and 2016; 67.5% (n = 79) were male. Mean age was 52.7 years (range, 23.4-90 years); 69.2% (n = 81) presented with acute abdominal pain, 22.2% (n = 26) with flank pain, and 19.7% (n = 23) with back pain; 15.4% (n = 18) had abdominal pain longer than 30 days; 13.7% (n = 16) had acute hypertension, and 5.1% (n = 6) were hypotensive; 10.3% (n = 12) were asymptomatic. There were 93 (79.5%) dissections and 61 (52.1%) aneurysms. Hemorrhage was seen in 10 (8.5%). The celiac axis was affected in 54.7% (n = 64), renal arteries in 49.6% (n = 58), superior mesenteric artery in 43.6% (n = 51), and inferior mesenteric
artery in 2.6% (n = 3). After diagnosis of SAM, aspirin was prescribed in 60.7% (n = 71). Statins were prescribed in 29.9% (n = 35). Antihypertensive medications were prescribed in 65% (n = 76), including beta blockers in 42.7% (n = 50); 40.2% (n = 47) of patients were prescribed anticoagulation. Interventions were performed in 26 (22%) patients; 13 had endovascular intervention only, 9 open surgery only, and 4 open and endovascular interventions. Of the 17 patients undergoing endovascular intervention, 19 procedures were performed, most commonly embolization (78.9% [n = 15]), followed by stenting (10.5% [n = 2]). Of the 13 patients undergoing open surgery, 14 procedures were performed, including arterial bypass (50% [n = 7]) and splenectomy with aneurysm ligation (15.4% [n = 2]). Other surgery involved thrombectomy (21.4% [n = 3]) and angioplasty (14.3% [n = 2]). Only 11.5% (n = 3) experienced a perioperative complication, including one hematoma, one abscess, and one death secondary to ongoing hemorrhage. Follow-up imaging was performed in 96.6% (n = 112). Mean follow-up was 1258 days (range, 2-5017 days). Of these, 27.7% (n = 31) had regression, 43.8% (n = 49) stability, and 28.6% (n = 32) progression. Average time between initial diagnosis and progression was 666 days.

CONCLUSIONS:

SAM is an uncommon disease that may require intervention; it is therefore important that the vascular surgery community be aware of this disease. Follow-up imaging is required to monitor for disease progression.

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Similar articles

Role of the NO/cGMP pathway and renin-angiotensin system in the hypotensive and diuretic effects of aqueous soluble fraction from Crataegus songarica K. Koch.

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Abstract

ETHNO-PHARMACOLOGICAL RELEVANCE:

Fruits of Crataegus songarica K. Koch. (Rosaceae) are commonly used in folk medicine for their diuretic properties to treat hypertension and congestive heart failure. To date, no scientific data has been published to support the diuretic potential.

AIM OF THE STUDY:

The purpose of this study was to evaluate efficacy and mechanism underlying the hypotensive and diuretic action of C. songarica in normotensive rats and to determine the constituents from the extracts by LC-DAD-MS.

MATERIALS AND METHODS:

Firstly, phytochemical profiling and antioxidant potential of C. songarica extracts was determined. Then, to evaluate changes in blood pressure, different groups of anesthetized normotensive rats were intravenously treated with crude extract (CS-Cr, 10-80 mg/kg), aqueous soluble (AS-CS, 0.1-20 mg/kg), and n-butanol soluble fractions of C. songarica (BS-CS, 1-80 mg/kg). The diuretic effects of CS-Cr (100-500 mg/kg, p.o), AS-CS (100-300 mg/kg, p.o) and BS-CS (100-300 mg/kg, p.o) were evaluated in comparison with hydrochlorothiazide (HCTZ, 10 mg/kg, p.o). The urinary volume, sodium, potassium and pH were estimated in the sample collected for 6 h from saline-loaded rats. Using pharmacological antagonists or inhibitors, we determine the involvement of acetylcholine, prostaglandins, and nitric oxide in C. songarica induced hypotensive and diuresis action. In addition, the activities of angiotensin converting enzyme, erythrocytary carbonic anhydrase and renal Na+/K+/ATPase were evaluated in vitro.

RESULTS:

From the LC-DAD-MS analyses, thirty-nine compounds were detected, showing a complex chemical profile and an expressive antioxidant activity "in vitro". Acute treatment with CS-Cr, AS-CS, and BS-CS exhibited significant hypotensive and diuretic potential in normotensive rats. However, AS-CS produced most potent and significant dose-dependent hypotension in normotensive rats, and also produced highly significant diuretic and saluretic effects. Despite the changes in urinary excretion of electrolytes, the plasmatic levels of sodium and potassium were not changed. Previous treatment with atropine and L-NAME significantly reduced the hypotensive and diuretic action of AS-CS in
normotensive rats. Moreover, the 7-day treatment with AS-CS also resulted in significant ACE inhibitory activity.

CONCLUSION:

This research supports and extends the ethnomedicinal use of C. songarica as diuretic and hypotensive agent. The results showed that AS-CS from C. songarica could present compounds responsible for hypotensive and diuretic activities with no signs of toxicity, and these effects could involve nitric oxide pathway activated by muscarinic receptors or/and inhibition of angiotensin converting enzyme.

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The large majority of coeliacs have a high degree of perceived dietary competence.

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Abstract

Purpose: The treatment for coeliac disease (CD) is a gluten-free diet (GFD), which impacts the health-related quality of life (HRQoL). The aim of the study was to develop the Gluten-Free Diet Perceived Competence Scale (GFD-PCS): a short and precise CD-specific patient-reported outcome measure. Methods: The GFD-PCS was developed from the scales 'Perceived Competence (Maintaining a Healthy Diet)' and 'Perceived Competence for Diabetes'. The scale was then programmed into a web-based questionnaire and distributed together with generic quality of life (WHO-5) and CD-specific HRQoL (CDQL) questionnaires. Results: There were 931 respondents. The 831 who reported 'diagnosed CD' were retained. The average age was 37.6 years (SD = 16.5). There was no statistically significant difference between males (M = 5.9, SD = 1.6) and females (M = 6.2, SD = 1.4) in GFD-PCS score. Respondents younger than 18 years (n = 104) scored lower (M = 5.8, SD = 1.4) than adults (M = 6.2, SD = 1.4). The psychometric properties of the GFD-PCS showed excellent internal reliability (α = .96) and satisfied construct and criterion validity. Conclusion: The GFD-PCS measures patient-perceived dietary competence for maintaining a GFD. The scale is psychometrically robust and provides a useful tool in assessing patients' difficulties with a GFD.

PMID: 31738623
Can We Cross Off Common Kitchen Practices as Causes of Gluten Cross-Contact?

McDonald BD¹, Kupfer SS².

Author information:
PMID: 31730765

B cell tolerance and antibody production to the celiac disease autoantigen transglutaminase 2.

du Pré MF¹,², Blazevski J³, Dewan AE¹,², Stamnaes J¹,²,³, Kanduri C¹,4, Sandve GK¹,4, Johannesen MK¹,3, Lindstad CB¹,³, Hnida K³, Fugger L⁵, Melino G⁶, Qiao SW¹,³, Sollid LM¹,²,³.

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Abstract
Autoantibodies to transglutaminase 2 (TG2) are hallmarks of celiac disease. To address B cell tolerance and autoantibody formation to TG2, we generated immunoglobulin knock-in (Ig KI) mice that express a prototypical celiac patient-derived anti-TG2 B cell receptor equally reactive to human and mouse TG2. We studied B cell development in the presence/absence of autoantigen by crossing the Ig KI mice to Tgm2−/− mice. Autoreactive B cells in Tgm2+/+ mice were indistinguishable from their naive counterparts in Tgm2−/− mice with no signs of clonal deletion, receptor editing, or B cell anergy. The autoreactive B cells appeared ignorant to their antigen, and they produced autoantibodies when provided T cell help. The findings lend credence to a model of celiac disease where gluten-reactive T cells provide help to autoreactive TG2-specific B cells by involvement of gluten-TG2 complexes, and they outline a general mechanism of autoimmunity with autoantibodies being produced by ignorant B cells on provision of T cell help.

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T- and NK-cell lymphoproliferative disorders of the gastrointestinal tract: review and update.

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Abstract

T- and NK-cell lymphoproliferative disorders of the gastrointestinal (GI) tract are uncommon, but are important to recognise as there may be morphological and immunophenotypic overlap between lymphoid lesions with vastly different clinical outcomes. Recent data have led to the reclassification of some lymphomas and inclusion of new entities in the 2016 revision of World Health Organization (WHO) classification of lymphoid neoplasms. It has become clear that enteropathy associated T-cell lymphoma (EATL), formerly thought to be composed of two subtypes known as type I and type II, are distinct entities. Type I EATL is now simply classified as EATL; it is strongly associated with coeliac disease and occurs mainly in Western populations. Type II EATL has been renamed monomorphic
epitheliotropic intestinal T-cell lymphoma (MEITL); it shows no definite association with coeliac disease and occurs worldwide with a predominance in Asian populations. There is also a group of aggressive intestinal T-cell lymphomas which do not meet criteria for EATL, MEITL, extranodal NK/T-cell lymphoma of nasal type or anaplastic large cell lymphoma. These neoplasms are now designated intestinal T-cell lymphoma, not otherwise specified. Indolent T-cell lymphoproliferative disorder of the GI tract has been included as a provisional entity in the most recent WHO classification. It is a clonal T-cell lymphoproliferative disorder (CD4+ or CD8+) with an indolent clinical course. Finally, benign NK-cell proliferations of the GI tract, variably designated 'NK-cell enteropathy' and 'lymphomatoid gastropathy' have also been recognised in the last two decades but have not been included in the WHO classification as their neoplastic nature is not established.

This review covers the aforementioned lymphoid proliferations, emphasising their salient clinicopathological features and genetic abnormalities. It also provides practical insights into resolving difficult differential diagnoses in daily surgical pathology practice.

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**Celiac disease associated SNP rs17810546 is located in a gene silencing region.**

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**Abstract**

GWAS studies have identified variant rs 17810546 in a non-coding region on chromosome 3 as a risk factor for several auto-immune diseases, including Celiac Disease. In silico analysis reveals that this variant is located in a transcription regulatory site. By means of reporter constructs we show that this region can override the expression rate of a gene as determined by its native promoter and that this modulation is influenced by the genetic composition of the haplotype which rs17810546 forms.
with a nearby other variant, rs761008. Secondly, we present data that this genetically imprinted modulation could be involved in Celiac Disease through the IL12A gene which is located 40 Kb downstream of this regulatory region. Based on our findings it is most likely that the IL12A gene does so as part of the cytokine IL-35.

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Two-year evaluation of fenestrated and parallel branch endografts for the treatment of juxtarenal, suprarenal, and thoracoabdominal aneurysms at a single institution.

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Abstract

OBJECTIVE:

Despite numerous recent pivotal and small-scale trials, real-world endovascular management of juxtarenal aneurysms (JRA), suprarenal aneurysms (SRA), and thoracoabdominal aortic aneurysms (TAAA) remains challenging without consensus best practices. This study evaluated the mortality, graft patency, renal function, complication, and reintervention rates for fenestrated and parallel endografts in complex aortic aneurysms repairs.

METHODS:

This retrospective review of consecutive included patients with JRA, SRA, or TAAA who underwent complex endovascular repair from August 2014 to March 2017 at one high-volume institution. Treatment modality was a single surgeon decision based on patients anatomy and the urgency of
the repair. Patient demographics, hospital course, and follow-up visits inclusive of imaging were analyzed. Ruptured aneurysms were excluded. Survival rates and outcomes were determined using the Kaplan-Meier method with log-rank tests.

RESULTS:

Seventy complex endovascular aortic repairs were performed; 38 patients with TAAA were treated with snorkel/sandwich parallel endografts (21 celiac, 28 superior mesenteric arteries, 58 renal arteries) and 32 patients with JRA/SRA were treated by fenestrated endovascular aneurysm repair (FEVAR) with 94 total fenestrations (2 celiac, 30 SMA, 62 renal). The mean patient age was 74.8 ± 10.0 years. Sixty percent were male, and the mean aortic aneurysm diameter was 6.0 ± 1.4 cm. Perioperative mortality was 3.1% (1/32) for FEVAR compared with 2.6% (1/38) for parallel endografts (P = .9). All-cause reintervention rates were 15.6% in FEVAR (5/32) vs 23.6% with parallel endografts (9/38; P = .4). Branch reintervention rates per each branch endograft were 4.3% for FEVAR (4/94; 2 renal stent occlusions, 1 colonic ischemia without technical issue found on reintervention, 1 perinephric hematoma) vs 3.7% for parallel endografts (4/107; 2 renal and 1 celiac stent thromboses, and 1 renal stent kink; P = .41). The endograft branch thrombosis rate was 2.1% in FEVAR (2/94) vs 2.7% in parallel endografts (3/109; P = .77). Reinterventions owing to endoleaks were performed in five patients (2 type I, 2 type III, and 1 gutter endoleak; 13.1%) with parallel grafts vs no endoleak reinterventions in FEVAR. The overall survival and freedom from aneurysm-related mortality at 24 months was 78% and 96.9% in FEVAR vs 73% and 93.4% for parallel endografts (P = .8 and P = .6). The median follow-up was 12 months (range, 1-32 months).

CONCLUSIONS:

Parallel and fenestrated endografts have acceptable and comparable mortality and patency rates in endovascular treatment of JRA, SRA, and TAAA. This study reaffirms that parallel endografts are a safe and viable alternative to fenestrated devices for complex aortic aneurysmal disease despite often treating more urgent patients and more complicated anatomy unable to be treated with FEVAR.

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A Celiac Care Index Improves Care of Pediatric Patients Newly Diagnosed with Celiac Disease.

Sparks B¹, Salman S², Shull M³, Trout A², Kiel A³, Hill I³, Ediger T², Boyle B².
Abstract

OBJECTIVES:

To describe quality improvement efforts to reduce variability in the care of children diagnosed with celiac disease through use of an institutional patient registry and a chronic care index.

STUDY DESIGN:

An institutional patient registry tracked rates of follow-up visits and repeat serologic testing. A Celiac Care Index that included anthropometrics, biopsy expectations, dietician consultation, and baseline laboratory evaluation was developed to standardize evaluation at diagnosis. Provider education sessions communicated expectations for this standard of care and order sets within the electronic medical record simplified test collection. Data was recorded and reviewed weekly and structured communications with providers were provided biweekly.

RESULTS:

Adherence with follow-up expectations (77%-89% P = .03) and repeat serologic testing (50%-90% P < .0001) significantly increased during the study period. Adherence with completion of the Celiac Care Index resulted in significant improvement in obtaining complete blood count (80%-98% P < .0001), iron (25%-78% P < .0001), ferritin (34%-80% P < .0001), alanine aminotransferase/aspartate aminotransferase (74%-96% P < .0001), thyroid-stimulating hormone (64%-90% P < .0001), vitamin D (36%-83% P < .0001), and hepatitis B immune status (30%-80% P < .0001). Iron deficiency demonstrated by low ferritin levels was common (41%) and a high rate of nonimmunity to hepatitis B (70%) was detected.

CONCLUSIONS:

The Celiac Care Index improved adherence with published care recommendations and reduced variability in baseline evaluation at diagnosis. Laboratory test results indicate further studies are needed to evaluate these recommendations.

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PMID: 31706635

Similar articles

Elsevier Full-text Article
Turner syndrome and osteoporosis.

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Abstract

Turner syndrome is one of the most common sex chromosomal anomalies, characterized by the complete or partial loss of one X chromosome. Females with Turner syndrome are characterized by skeletal abnormalities, short stature and primary ovarian insufficiency. The aim of this narrative review was to identify the underlying mechanisms of osteoporosis in Turner syndrome, summarize its clinical manifestations and provide suggestions regarding the management of osteoporosis. Girls and women with Turner syndrome have lower bone mineral density and a higher fracture rate than healthy individuals. The most important risk factors for osteoporosis are inadequately treated primary ovarian insufficiency, followed by intrinsic bone abnormalities. Comorbidities that further increase the risk of osteoporosis include vitamin D deficiency, celiac disease and inflammatory bowel disease. In addition, hearing problems can predispose to falls. Early initiation of hormone replacement therapy (HRT) at the age of 11-13 years, prompt titration to the adult dose after 2 years and long-term follow-up to ensure compliance with HRT are the cornerstones of osteoporosis prevention in women with Turner syndrome.

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PMID: 31706435

The Gluten-Free Diet: Use in Digestive Disease Management.

Newberry C¹.
Abstract

PURPOSE OF REVIEW:

Gluten is a commonly ingested polymeric protein found in wheat, barley, and rye that has gained recent notoriety because of its relationship to disease and health. Avoidance of gluten is appropriate in patients with a diagnosed gluten-related disorder and may have treatment implications in other diseases of the digestive tract. This review highlights current knowledge of gluten related disorders and the use of a gluten-free diet in gastrointestinal disease management.

RECENT FINDINGS:

Gluten-free diets should be used in patients with a diagnosed gluten-related disorder including celiac disease, non-celiac gluten sensitivity, and wheat-sensitive eosinophilic esophagitis. Use of this diet in management of other digestive conditions including gastroesophageal reflux disease, irritable bowel syndrome, and inflammatory bowel disease is controversial and not currently supported by the literature. This review provides a framework for classifying gluten-related disorders in terms of pathogenesis, understanding the literature that supports dietary avoidance in modulation of gastrointestinal disease, and identifies limitations of dietary restriction in patients.

PMID: 31705373

Three papers indicate that amount of gluten play a role for celiac disease - But only a minor role.

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Epilepsy, cerebral calcifications, and gluten-related disorders: Are anti-transglutaminase 6 antibodies the missing link?

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Abstract
PURPOSE:

Gluten-related disorders (GRDs) are a group of immune-mediated diseases often associated to neurologic manifestations. Epilepsies with cerebral calcifications, with or without coeliac disease (CD), are rare neurological disorders characterized by childhood-onset focal seizures, often refractory to antiepileptic drugs. Transglutaminase 6 antibodies (anti-TG6) have been considered a biomarker for gluten-related ataxia and neuropathy, but their prevalence in epilepsies with cerebral calcifications is unknown. The aim of this study is to evaluate anti-TG6 prevalence in patients with epilepsies and cerebral calcifications.

METHOD:

This was a cross-sectional study conducted at five Italian epilepsy centres. The following groups were included. Group 1: nine patients with CD, posterior cerebral calcifications and epilepsy (CEC); group 2: nine patients with epilepsy and posterior cerebral calcifications, without CD; group 3: twenty patients with focal epilepsy of unknown etiology; group 4: twenty-two healthy controls (HC). All subjects were tested for serological evidence of anti-TG6 IgA and IgG. Differences among groups were analysed using $\chi^2$ test.

RESULTS:

Anti-TG6 were present in 1/9 subjects (11%) of group 1, 2/9 subjects (22%) of group 2, 0/20 subjects in group 3, 3/22 (13.6%) of HC. No significant difference was found among the 4 groups.

CONCLUSIONS:

Anti-TG6 do not seem to be associated to epilepsies with cerebral calcifications.

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PMID: 31698178


Coeliac disease in Finland: what can we learn?

Burki TK.

PMID: 31696829
In vitro selection of anti-gliadin single-domain antibodies from a naïve library for cDNA-display mediated immuno-PCR.

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Abstract

Gluten intolerance, or adverse intestinal reactions to gluten, is a fairly common problem among certain groups of people. Celiac disease is the most severe form of gluten intolerance, which can lead to permanent damage in the digestive system. Since lifelong avoidance of gluten is the only available treatment, development of reliable techniques to identify gluten contamination in food is important. Gliadin, a component of gluten, is known to play a major role in gluten toxicity. In this study, cDNA display method was used to select specific single-domain antibodies against toxic gliadin from an alpaca-derived naïve VHH library. The cDNA display method is a promising in vitro display technique, which uniquely converts an unstable mRNA-protein fusion molecule to a stable mRNA/cDNA-protein fusion molecule using a well-designed puromycin linker. Three candidate VHHs were selected and the affinities of the VHHs were observed by pulldown assay and indirect ELISA method. In addition, a novel cDNA display mediated immuno-PCR method (cD-IPCR) was successfully applied to detect gliadin in food. We believe this work demonstrates the potential application of the cDNA display method in selecting binders against toxic and heterogeneous targets such as gliadin with an immunization-free preparation manner.
Preparing the Patient for Home Parenteral Nutrition and for a Successful Course of Therapy.

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Abstract

Preparing the patient for home parenteral nutrition (HPN) is a collaborative effort among many different clinicians. Identifying patients who will transition home with parenteral nutrition (PN) as early as possible allows for a thoughtful and safe approach. Communication regarding the HPN goals is critical to the patient's success, whether the requirement for PN is temporary or permanent. Management of these complex patients is best served by a multidisciplinary team with expertise in the area of nutrition support. Adherence to available guidelines that define best practice is imperative in all aspects of care for the patient on HPN.

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PMID: 31668177

Consumers' Sensory Perception of Food Attributes: Identifying the Ideal Formulation
of Gluten- and Lactose-Free Brownie Using Sensory Methodologies.

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Abstract

Products for consumers with special needs (celiac) and those who prefer a differentiated diet are necessary due to growing demand and a niche market to be exploited. The incorporation of other substances in the formulation of cakes requires a detailed analysis of their characteristics and sensorial attributes. However, the use of these flours may change the sensory characteristics of a product that is normally made from wheat flour. This study aimed to identify the ideal formulation of gluten- and lactose-free brownies made with rice flour and beans/lentils in consumer perception, through the combination of sensory tests. Using these data, the aim was to define recommendations for the reformulation of a product of high consumer acceptance, using easily accessible ingredients. The sensory methods used were descriptive analysis with a group of 20 trained evaluators and a group of 100 consumers evaluated through the check-all-that-apply and just-about-right questionnaire; all groups performed the acceptance test by hedonic scale. Data were analyzed using multivariate techniques and correlation matrices. The results showed that the attributes selected by the trained evaluators and consumers were sufficient to indicate that color and texture were the most striking characteristics that should be improved in brownie formulations without gluten and lactose. PRACTICAL APPLICATION: The study assumes that from the combination of sensory methods it is possible to verify the attributes that are most attractive to consumers in gluten-free and lactose-free cake formulations, using easily accessible ingredients that have technological, nutritional, and sensory quality, such as those formulated with wheat.

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PMID: 31665555

Giant celiac artery aneurysm.
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Abstract

Celiac artery aneurysms (CAAs) are rare but potentially devastating lesions. Given the high rates of mortality on rupture at large sizes, they should be treated promptly with either surgical or endovascular interventions in appropriate-risk patients. Several options exist for treatment, including surgical repair and endovascular embolization with or without stent or stent graft placement. Because of their rarity, there are few reports of successfully treated CAA lesions. Herein, we describe successful endovascular treatment of one of the largest CAAs reported in the literature.

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PMCID: PMC6806657 Free PMC Article
PMID: 31660470

Progressive study of the effect of superfine green tea, soluble tea, and tea polyphenols on the physico-chemical and structural properties of wheat gluten in noodle system.

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Abstract
In this study, the improving effects of green tea powder, soluble tea, and tea polyphenols on the mixing and tensile qualities of dough and texture of tea-enriched noodles, as well as the physico-chemical and structural properties of gluten proteins were progressively investigated. Dough strength and noodle texture were significantly increased by all the three tea products. Tea polyphenols in particular presented the most effective improvement with highest dough stability, resistance, and noodle chewiness. SEM indicated that tea products all induced a more developed gluten network, and polyphenol noodle showed the most continuous and ordered structure. FT-IR and fluorescence spectrum indicated that tea polyphenols promoted an enhancement in α-helix structure and the hydrophobic interactions. Tea polyphenols induced the SH/SS interchange during processing and cooking, and enhanced the water-solids interaction in noodles. AFM results showed that polyphenols induced the polymerization of gluten protein molecular chains, with increased chain height and width.

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PMD: 31655476 [Indexed for MEDLINE]

**Quality-of-life Evaluation of Healthy Siblings of Children with Chronic Illness**

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**Abstract**
**Background:**

Chronic disease of children can cause changes in the health-related quality of life (HrQoL) of the family members.

**Aims:**

To evaluate the HrQoL of healthy siblings of children with chronic disease.

**Study Design:**

Cross-sectional study.

**Methods:**

The study included healthy sibling of children with chronic disease (cerebral palsy, epilepsy, diabetes, celiac disease, hematologic/oncologic disease, or asthma) and healthy sibling of healthy children to evaluate the quality of life. We used the Pediatric Quality of Life Inventory questionnaire; the physical health and psychosocial health scores were calculated using the responses of the sibling and parent. The primary endpoint was the comparison of HrQoL scores of healthy siblings of children with chronic disease and that of healthy siblings of healthy children.

**Results:**

This study included a respective healthy sibling of 191 children with chronic disease and healthy sibling of 100 healthy children. The physical health, psychosocial health, and total health scores of healthy siblings of children with chronic disease were significantly lower than that of healthy siblings of healthy children (p<0.001). Among the healthy siblings of children with chronic disease, the lowest psychosocial health score was found in the siblings of children with cerebral palsy, hematologic/oncologic disease, and asthma (p<0.001). The global impact on the quality of life for healthy siblings of children with chronic disease was significantly higher in the self-report of the children than that of the parents (30.4% versus 15.1%, p<0.05).

**Conclusion:**

Most healthy siblings of children with chronic disease are physically and psychosocially affected and there is low parental awareness of this condition. This can increase the risk of emotional neglect and abuse of these children. Therefore, special support programs are needed for the families of children with chronic diseases.

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[Link]
Fibres of milling and fruit processing by-products in gluten-free bread making: A review of hydration properties, dough formation and quality-improving strategies.

Föste M¹, Verheyen C², Jekle M³, Becker T⁴.

Abstract

Gluten-free (GF) breads often lack proteins, minerals and fibres and have an imbalanced energy value, as they are primarily based on flour or starch. To nutritionally fortify GF bread, dietary fibres from milling and fruit processing by-products can be utilized. However, fibre addition changes sensorial, nutritional and also technological properties, such as dough or batter hydration. This review evaluates and compares different methods for quantifying the hydration properties of GF fibres and the resulting batters. Revelations are that the hydration properties of fibres vary greatly, depending on the utilized measuring technique, thus impeding the calculation of the appropriate water amount for GF batter processing. In addition, bran and fibres increase the loss factor tan δ and delay thermal transformation, compromising the specific loaf volume. Finally, operational strategies, such as enzymatic or extrusion treatments are discussed regarding their efficiency to increase water absorption in order to further improve GF bread quality.
Grange syndrome due to homozygous YY1AP1 missense rare variants.

Ciuffetelli Alamo IV, Kwartler CS, Regalado ER, Afifi RO, Parkash S, Rideout A, Guo DC, Milewicz DM.

Abstract

Grange syndrome (OMIM 602531) is an autosomal recessive condition characterized by severe early onset vascular occlusive disease and variable penetrance of brachydactyly, syndactyly, bone fragility, and learning disabilities. Grange syndrome is caused by homozygous or compound heterozygous loss-of-function variants in the YY1AP1 gene. We report on the case of a 53-year old female with novel homozygous missense variants in YY1AP1 (c.1079C>T, p.Pro360Leu), presenting with a history of brachysyndactyly, hypertension, and ischemic stroke. Imaging studies revealed stenosis of the bilateral internal carotid with extensive collateralization of cerebral vessels in a moyamoya-like pattern, along with stenosis in the splenic, common hepatic, celiac, left renal, and superior mesenteric arteries. Functional studies conducted with the patient's dermal fibroblasts suggest that the p.Pro360Leu variant decreases the stability of the YY1AP1 protein. This is the first report of a missense variant associated with Grange syndrome characterized by later onset of vascular disease and a lack of developmental delay and bone fragility.
Evaluation of N-terminal labeling mass spectrometry for characterization of partially hydrolyzed gluten proteins.

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Abstract

Gluten, a group of proteins found in wheat, barley, and rye, is the trigger of celiac disease, an immune disorder that affects about 1% of people worldwide. The toxicity of partially hydrolyzed gluten (PHG) in fermented products is less well understood due to the significant analytical challenges in PHG characterization. In this project, an N-terminal labeling mass spectrometry method, terminal amine isotopic labeling of substrates (TAILS), was optimized for the in-depth analysis of PHG and validated using a test protease (trypsin) with known cleavage specificity. Gluten N-termini in test and control groups were labeled with heavy and light formaldehyde, respectively. Trypsin-generated neo N-termini were identified by exhibiting an MS1 Log2 H:L peak area ratio with a significant difference (p < .01) from zero and native N-termini with no significant difference from zero (p > .01). Using this strategy, all abundant, theoretical, test protease-generated peptides in exemplar alpha/beta gliadins and gamma gliadins were identified.

SIGNIFICANCE: This study is the first study that modified and evaluated TAILS analysis for the analysis of partially hydrolyzed gluten proteins. The evaluation indicated that the TAILS analysis could be modified and expanded to the identification of multiple protease cleavage sites in gluten proteins and is worth further evaluation as a novel strategy for the analysis of natural hydrolysis of gluten in food processes. This strategy also may be further applied to characterize a broader range of partially hydrolyzed allergens in foods and provide reference for their safety assessment to both industry and regulatory authorities.

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PMID: 31629960

Similar articles

Celiac Disease: Against the Grain in Gastroenterology.

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Abstract

The incidence of celiac disease has risen quickly and has a worldwide distribution in Europe, North and South America, Asia, the Middle East and Africa. This is attributed in part to increased availability in screening but also to the fast-rising gluten consumption and perhaps unknown environmental factors. In daily practice, this means that more subclinical cases and very young and elderly patients are diagnosed. The pathogenesis of celiac disease is a T-cell driven process initiated by gluten, leading to increased intestinal permeability and villous atrophy. The process requires HLA genotypes DQ2, DQ8 or both. Additional non-HLA alleles have been identified in genome-wide association studies. Serological testing, followed by duodenal biopsies, are still required to confirm the diagnosis. Advances are in the making for novel biomarkers to monitor disease and for pharmacological support of celiac disease. Medical costs and patient-perceived disease burden remain high in celiac disease, which point to the need for ongoing research in drug development to improve quality of daily life. Drugs undergoing phase I and phase II clinical trials include intraluminal therapies and vaccines to restore immune tolerance. These therapies aim to reduce symptoms and mucosal injuries as adjunct therapies to a gluten-free diet.

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of Gluten on Metabolic Homeostasis in Mice Fed a High-Fat/High-Sucrose Diet.

Olivares M¹, Rodríguez J¹, Pötgens SA¹, Neyrinck AM¹, Cani PD¹,², Bindels LB¹, Delzenne NM¹.

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Abstract

SCOPE:

Cereals are important sources of carbohydrates, but also contain nutrients that could impact adiposity. The contribution of gluten to obesity and the effects of prebiotics-arabinoxyloligosaccharides (AXOS) and fructo-oligosaccharides (FOS)-that can be extracted from gluten-containing cereals are analyzed.

METHODS AND RESULTS:

Mice are fed a control diet, Western diet (WD, consisting of high fat/high sucrose), or WD with 5% gluten. Prebiotics are tested in the WD with gluten. Gluten does not increase body weight and has a minor effect on ileal inflammation. Gluten decreases the expression of browning markers in the fat and increases the triglycerides synthesis in the muscle. AXOS decreases body weight and adiposity in fat pads muscle and liver. AXOS promotes gluten cleavage by the induction of prolyl endopeptidase that is translated into a reduction of gluten immunogenic peptides. Gluten has minor effects on cecal microbiota composition, whereas prebiotics increased Bifidobacterium, Butyricicoccus, Prevotella, and Parasutterella, which are all negatively correlated to the cecal content of gluten peptides.

CONCLUSION:

While gluten may affect metabolic homeostasis, these effects are lessened when gluten is consumed along with cereal-derived fibers. If confirmed in humans, the authors bring new arguments to eat fiber-rich cereals to promote a healthy diet.

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PMID: 31608562

Similar articles
Trend of Antitissue Transglutaminase Antibody Normalization in Children With Celiac Disease Started on Gluten-free Diet: A Comparative Study Between Chemiluminescence and ELISA Serum Assays.

Sansotta N¹, Alessio MG², Norsa L¹, Previtali G², Ferrari A³, Guerra G², D'Antiga L¹.

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2. Clinical Chemistry Laboratory.
3. Research Foundation, Hospital Papa Giovanni XXIII, Bergamo, Italy.

Abstract

BACKGROUND:

The aim of this study is to compare the performance of antitissue transglutaminase (atTG) chemiluminescence immunoassay (CLIA) with the standard enzyme-linked immunosorbent assay (ELISA) methods in monitoring celiac children after the start of gluten-free diet (GFD).

METHODS:

Celiac children diagnosed between 2005 and 2016 at our centre were classified into 2 groups based on serum assay (ELISA vs CLIA) used for atTG monitoring, and were compared on percentage of decrease and time to normalization of atTG on GFD.

RESULTS:

Among 260 included children, the rate of normalization of atTG levels at 30 months' follow-up was 86% and 70% in ELISA and CLIA group, respectively (P<0.01). Median time to normalization was 11.7 and 14.7 months in ELISA and CLIA group respectively (P = 0.003). Marsh score at diagnosis was not associated with time to atTG normalization (P = 0.770), whereas older age at diagnosis and higher baseline atTG predicted longer time to atTG normalization (P = 0.01, P<0.01).
CONCLUSIONS:

The percentage and the time of the atTG normalization in celiac children on GFD should be interpreted according to the utilized assay: at 30 months’ follow-up children tested by CLIA are less likely to normalize atTG levels compared to those tested by ELISA. Younger age at diagnosis and lower baseline atTG are predictors of earlier atTG normalization, regardless of the adopted assay.

PMID: 31599818

Similar articles


[Prevalence of an association between coeliac disease and vitiligo].

[Article in German]

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Abstract

Coeliac disease and vitiligo are immune-mediated disorders that are often associated with other immune-mediated disorders. In a prospective study we included 174 patients with vitiligo between the ages of 3 and 79 years (mean 38.2 years) to investigate whether there is an increased risk for coeliac disease in patients with vitiligo. We determined immunoglobulin A and IgA- and IgG-antibodies against tissue transglutaminase, while also optionally measuring blood count, ferritin, and endomysial-IgA-antibodies. In 3 of 174 (1.7%) vitiligo patients, coeliac disease was diagnosed serologically and by duodenal biopsy. Assuming a coeliac disease prevalence of less than 0.0033%, the incidence is statistically significant. In two other patients with vitiligo, coeliac disease was already known and confirmed with biopsy. If these two patients are included in the calculation, 2.8% (5 von 176) of vitiligo patients have coeliac disease. This value is statistically significant even with a higher coeliac disease prevalence of 0.01. Thus, it is recommended that celiac-disease-specific antibodies also be determined during routine blood workup in vitiligo patients. In case of positive results, a gastroduodenoscopy with biopsy of the small intestine is recommended for diagnosis confirmation. If celiac disease is unlikely, a trial of gluten-free diet for a specific time should nevertheless be discussed with individuals affected by vitiligo because repigmentation appears possible.

PMID: 31584112 [Indexed for MEDLINE]

Similar articles

Husby S¹, Koletzko S², Korponay-Szabó I³, Kurppa K⁴, Mearin ML⁵, Ribes-Koninckx C⁶, Shamir R⁷, Troncone R⁸, Auricchio R³, Castillejo G⁹, Christensen R¹⁰, Dolinsek J¹¹, Gillett P¹², Hróbjartsson A¹³, Koltai T¹⁴, Maki M⁴, Nielsen SM¹⁰, Popp A¹⁵, Størdal K¹⁶, Werkstetter K², Wessels M¹⁷.

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Abstract

OBJECTIVES:

The ESPGHAN 2012 coeliac disease (CD) diagnostic guidelines aimed to guide physicians in accurately diagnosing CD and permit omission of duodenal biopsies in selected cases. Here, an updated and expanded evidence-based guideline is presented.

METHODS:

Literature databases and other sources of information were searched for studies that could inform on 10 formulated questions on symptoms, serology, HLA genetics, and histopathology. Eligible articles were assessed using QUADAS2. GRADE provided a basis for statements and recommendations.

RESULTS:

Various symptoms are suggested for case finding, with limited contribution to diagnostic accuracy. If CD is suspected, measurement of total serum IgA and IgA-antibodies against transglutaminase 2 (TGA-IgA) is superior to other combinations. We recommend against deamidated gliadin peptide antibodies (DGP-IgG/IgA) for initial testing. Only if total IgA is low/undetectable, an IgG-based test is indicated. Patients with positive results should be referred to a paediatric gastroenterologist/specialist. If TGA-IgA is ≥10 times the upper limit of normal (10× ULN) and the family agrees, the no-biopsy diagnosis may be applied, provided endomysial antibodies (EMA-IgA) will test positive in a second blood sample. HLA DQ2-/DQ8 determination and symptoms are not obligatory criteria. In children with positive TGA-IgA <10× ULN at least 4 biopsies from the distal duodenum and at least 1 from the bulb should be taken. Discordant results between TGA-IgA and histopathology may require re-evaluation of biopsies. Patients with no/mild histological changes (Marsh 0/I) but confirmed autoimmunity (TGA-IgA/EMA-IgA+) should be followed closely.

CONCLUSIONS:

CD diagnosis can be accurately established with or without duodenal biopsies if given recommendations are followed.
PMID: 31568151

Similar articles

Preparation of Gluten-Free Foods Alongside Gluten-Containing Food May Not Always Be as Risky for Celiac Patients as Diet Guides Suggest.

Weisbrod VM, Silvester JA, Raber C, McMahon J, Coburn SS, Kerzner B.

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PMCID: PMC6917866 [Available on 2021-01-01]
PMID: 31560900

Community-Based Study of Celiac Disease Autoimmunity Progression in Adults.


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6. Department of Dermatology and Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota.
Abstract

BACKGROUND & AIMS:

Celiac disease can develop at any age, but outcomes of adults with positive results from serologic tests for tissue transglutaminase antibodies (tTGA) without endoscopic determination of celiac disease (called celiac autoimmunity) have not been thoroughly evaluated. We investigated the proportion of adults with celiac autoimmunity at a community medical center and their progression to celiac disease.

METHODS:

We analyzed waste blood samples from a community clinic from 15,551 adults for tTGA and, if titer results were above 2 U/mL, for endomysial antibody. The blood samples had been collected at 2 time points (median interval, 8.8 years) from 2006 through 2017. We collected data from the clinic on diagnoses of celiac disease based on duodenal biopsy analysis.

RESULTS:

Of the serum samples collected at the first time point, 15,398 had negative results for tTGA, and 153 had positive results for tTGA (>4 U/mL). Based on medical records, 6 individuals received a diagnosis of celiac disease, for a cumulative incidence of celiac disease diagnosis of 0.06% (95% confidence interval, 0.01-0.11). Forty-nine (0.32%) individuals with a negative result from the first serologic test for tTGA had a positive result from the second test. Among the 153 adults who were tTGA positive at the first time point, 31 (20%) had a subsequent diagnosis of celiac disease, 81 (53%) remained positive for tTGA without a clinical diagnosis of celiac disease, and 41 (27%) had negative test results for tTGA at the second time point. Higher initial tTGA titers, female sex, and a history of hypothyroidism and autoimmune disease were associated with increased risks of subsequent diagnosis of celiac disease. Interestingly, adults whose first blood sample had a positive test result but second blood sample had a negative result for tTGA were older, had lower-than-average initial tTGA titer results, and had a higher mean body mass index than adults whose blood samples were positive for tTGA at both time points and adults later diagnosed with celiac disease.

CONCLUSIONS:

In an analysis of serum samples collected from a community clinic an average of 8.8 years apart, we found that fewer than 1% of adults with negative results from an initial test for tTGA have a positive result on a second test. Of adults with positive results from the test for tTGA, only 20% are later diagnosed with celiac disease; the remaining individuals maintain persistent increases in tTGA without diagnoses of celiac disease or have negative results from second tests.

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The intestinal expansion of TCRγδ+ and disappearance of IL4+ T cells suggest their involvement in the evolution from potential to overt celiac disease.

Vitale S1, Santarlasci V2, Camarca A3, Picascia S1, Pasquale AD1, Maglio M4, Maggi E5, Cosmi L2, Annunziato F2, Troncone R1, Auricchio R4, Gianfrani C1,4.

Abstract

Celiac disease (CD) is characterized by a spectrum of intestinal inflammatory lesions. Most patients have villous atrophy (overt-CD), while others have a morphologically normal mucosa, despite the presence of CD-specific autoantibodies (potential-CD). As the mechanism responsible for villous atrophy is not completely elucidated, we investigated biomarkers specific for the different celiac lesions. Phenotype and cytokine production of intestinal mucosa cells were analyzed by flow cytometry in gut biopsies of children with overt- or potential-CD and in healthy controls. Density of TCRγδ+ T cells was found markedly enhanced in intestinal mucosa of children with overt-CD compared to potential-CD or controls. By contrast, very few IL4+ T cells infiltrated the mucosa with villous atrophy compared to morphologically normal mucosa. IL4+ T cells were classical CD4+ T-helper cells (CD161−), producing or not IFN-γ, and negative for IL17A. Our study demonstrated that the transition to villous atrophy in CD patients is characterized by increased density of TCRγδ+ T cells, and concomitant disappearance of IL4+ cells. These findings suggest that immunomodulatory mechanisms are active in potential-CD to counteract the inflammatory cascade responsible of villous atrophy. Further studies are required to validate the use of IL4+ and TCRγδ+ T cells as biomarkers of the different CD forms.

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PMID: 31553811
A Single Institution's Experience of Primary Headache in Children With Celiac Disease.

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Abstract

BACKGROUND:

Few studies exist examining the frequency of primary headache in children with celiac disease and the impact of a gluten-free diet on primary headache symptomology. This study explores characteristics and frequency of headaches in children with celiac disease and response to gluten-free diet at a single institution.

METHODS:

Medical records were reviewed for children with celiac disease confirmed by the presence of elevated tissue transglutaminase IgA levels and histologic changes consistent with the diagnosis of celiac disease on small bowel biopsy. Eligible participants were contacted via letter for participation in a phone survey regarding headaches. Phone interviews were conducted 2 weeks after notification and lasted approximately 10 minutes. Headaches were classified according to ICHD-3 criteria.

RESULTS:

247 eligible patients or their families were contacted. A total of 132 (53.44%) agreed to participate. One participant was excluded due to insufficient information provided. Overall, 51 of 131 participants had recurrent headache defined as at least 1 episode per month (39\%, 95\% confidence interval [CI]: 31\%-47\%) and 33 had migraine with or without aura (25\%, 95\% CI: 18\%-33\%). Twenty-eight had frequent tension-type headache (22\%, 95\% CI: 15\%-29\%). Thirty-two participants noted
headaches before a confirmed diagnosis of celiac disease. Twenty-two of 32 participants (68.75%) noticed decreased headache frequency or intensity, or both, after starting the gluten-free diet.

**CONCLUSION:**

This study suggests that at least one-third of children and adolescents with celiac disease have recurrent headaches at the time of diagnosis. A gluten-free diet led to improved headache symptomology in a significant number of these patients.

PMID: 31552781


**Protein polymerization in dumpling wrappers influenced by folding patterns.**

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**Abstract**

The influences of folding patterns on the protein polymerization in dumpling wrappers were investigated. The dumpling dough sheet after the compounding rollers was folded with various patterns (control with no angle, 15°, 25°, 35° and 45° folding), before going through the sheeting and reduction rolls. Protein secondary structure, free sulfhydryl content, protein electrophoretic profiles, and texture of dumpling wrappers were determined. Results showed that folding could increase the proportion of α-helix conformation, and produce dumpling wrappers with enhanced toughness but reduce wrapper extensibility. The wrapper with 45° folding showed lower -SH content than the control and other folding angles. However, only a few variations in SDS band pattern and intensities were observed at the molecular weight position of around 35 kDa. Briefly, folding process could influence the gluten formation during the preparation of dumpling wrappers; the folding angle at 45° produced stronger gluten network and tougher wrappers.

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PMID: 31525593 [Indexed for MEDLINE]
Minerals and their bioavailability in relation to dietary fiber, phytates and tannins from gluten and gluten-free flakes.

Kiewlicz J¹, Rybicka I².

Abstract

Flakes are an assortment of grain products mainly consumed for breakfast. Most of them are important source of nutrients including minerals. Twenty commercial flakes from different raw materials were included in this study, both gluten (barley, rye, spelt, wheat) and gluten-free (amaranth, buckwheat, corn, quinoa, millet, oat, rice, teff). The content of minerals (Ca, Fe, K, Mg, Mn, Na and Zn), dietary fiber (total, soluble and insoluble), tannins and phytates was determined. Moreover, the phytates:mineral molar ratios and the percentage of the realization of mineral requirements were calculated. For the first time the mineral bioavailability from the gluten and gluten-free flakes was evaluated and compared. It allowed indicating amaranth and teff products as flakes with the highest impact on the realization of daily requirements for minerals, especially for magnesium and iron. This aspect is particularly important for people on a gluten-free diet who often represent mineral deficiencies.

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PMID: 31514050 [Indexed for MEDLINE]
Celiac Disease: Extraintestinal Manifestations and Associated Conditions.

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Abstract

Celiac disease is a common form of enteropathy with frequent extraintestinal manifestations (EIM). Misrecognition of these presentations may lead to significant delays in diagnosis. Any organ may be involved, either through an immune/inflammatory phenomenon, or nutritional deficiencies. Some EIM, such as gluten ataxia, may be irreversible if left untreated, but most will improve with a gluten-free diet. Knowledge of the various EIM, as well as the associated conditions which do not improve on a gluten-free diet, will avoid delays in the diagnosis and management of celiac disease and associated manifestations.

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PMID: 31513026

Serum cytokines elevated during gluten-mediated cytokine release in coeliac disease.

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Abstract

Cytokines have been extensively studied in coeliac disease, but cytokine release related to exposure to gluten and associated symptoms has only recently been described. Prominent, early elevations in serum interleukin (IL)-2 after gluten support a central role for T cell activation in the clinical reactions to gluten in coeliac disease. The aim of this study was to establish a quantitative hierarchy of serum cytokines and their relation to symptoms in patients with coeliac disease during gluten-mediated cytokine release reactions. Sera were analyzed from coeliac disease patients on a gluten free-diet (n = 25) and from a parallel cohort of healthy volunteers (n = 25) who underwent an unmasked gluten challenge. Sera were collected at baseline and 2, 4 and 6 h after consuming 10 g vital wheat gluten flour; 187 cytokines were assessed. Confirmatory analyses were performed by high-sensitivity electrochemiluminescence immunoassay. Cytokine elevations were correlated with symptoms. Cytokine release following gluten challenge in coeliac disease patients included significant elevations of IL-2, chemokine (C-C motif) ligand 20 (CCL20), IL-6, chemokine (C-X-C motif) ligand (CXCL)9, CXCL8, interferon (IFN)-γ, IL-10, IL-22, IL-17A, tumour necrosis factor (TNF)-α, CCL2 and amphiregulin. IL-2 and IL-17A were earliest to rise. Peak levels of cytokines were generally at 4 h. IL-2 increased most (median 57-fold), then CCL20 (median 10-fold). Cytokine changes were strongly correlated with one another, and the most severely symptomatic patients had the highest elevations. Early elevations of IL-2, IL-17A, IL-22 and IFN-γ after gluten in patients with coeliac disease implicates rapidly activated T cells as their probable source. Cytokine release after gluten could aid in monitoring experimental treatments and support diagnosis.

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Abstract

Humans are living ecosystems composed of human cells and microbes. The microbiome is the collection of microbes (microbiota) and their genes. Recent breakthroughs in the high-throughput sequencing technologies have made it possible for us to understand the composition of the human microbiome. Launched by the National Institutes of Health in USA, the human microbiome project indicated that our bodies harbor a wide array of microbes, specific to each body site with interpersonal and intrapersonal variabilities. Numerous studies have indicated that several factors influence the development of the microbiome including genetics, diet, use of antibiotics, and lifestyle, among others. The microbiome and its mediators are in a continuous cross talk with the host immune system; hence, any imbalance on one side is reflected on the other. Dysbiosis (microbiota imbalance) was shown in many diseases and pathological conditions such as inflammatory bowel disease, celiac disease, multiple sclerosis, rheumatoid arthritis, asthma, diabetes, and cancer. The microbial composition mirrors inflammation variations in certain disease conditions, within various stages of the same disease; hence, it has the potential to be used as a biomarker.

PMID: 31502171

Safety and efficacy of AMG 714 in patients with type 2 refractory coeliac disease: a phase 2a, randomised, double-blind, placebo-controlled, parallel-group study.

Abstract

BACKGROUND:

Refractory coeliac disease type 2 is a rare subtype of coeliac disease with high mortality rates; interleukin 15 (IL-15) is strongly implicated in its pathophysiology. This trial aimed to investigate the effects of AMG 714, an anti-IL-15 monoclonal antibody, on the activity and symptoms of refractory coeliac disease type 2.

METHODS:

This was a randomised, double-blind, placebo-controlled, phase 2a study of adults with a confirmed diagnosis of refractory coeliac disease type 2. Patients were randomly assigned at a 2:1 ratio to receive seven intravenous doses over 10 weeks of AMG 714 (8 mg/kg) or matching placebo. Biopsy samples were obtained at baseline and week 12 for cellular analysis and histology. The change in the proportion of aberrant intraepithelial lymphocytes from baseline to week 12 with respect to all intraepithelial lymphocytes was the primary endpoint and was quantified using flow cytometry. Secondary endpoints were the change in aberrant intraepithelial lymphocytes with respect to intestinal epithelial cells; intestinal histological scores (villous height-to-crypt depth ratio; VHCD); intraepithelial lymphocyte counts; Marsh score; and patient-reported symptom measures, including the Bristol stool form scale (BSFS) and gastrointestinal symptom rating scale (GSRS). Main analyses were done in the per-protocol population of patients who received their assigned treatment, provided evaluable biopsy samples, and did not have major protocol deviations; only patients with non-atypical disease were included in the analyses of aberrant intraepithelial lymphocytes, including the primary analysis. Safety was assessed in all patients who
received at least one dose of study drug. This study is registered at ClinicalTrials.gov (NCT02633020) and EudraCT (2015-004063-36).

FINDINGS:

From April 13, 2016, to Jan 19, 2017, 28 patients were enrolled and randomly assigned to AMG 714 (n=19) and placebo (n=9). Six patients were not included in the primary analysis because of protocol deviation (one in the AMG 714 group), insufficient biopsy samples (one in the AMG 714 group), and atypical intraepithelial lymphocytes (three in the AMG 714 group and one in the placebo group). At 12 weeks, the least square mean difference between AMG 714 and placebo in the relative change from baseline in aberrant intraepithelial lymphocyte percentage was -4.85% (90% CI -30.26 to 20.56; p=0.75). The difference between the AMG 714 and placebo groups in aberrant intraepithelial lymphocytes with respect to epithelial cells at 12 weeks was -38.22% (90% CI -95.73 to 19.29; nominal p=0.18); the difference in change in Marsh score from baseline was 0.09% (95% CI -1.60-1.90; nominal p=0.92); the difference in VHCD ratio was 10.67% (95% CI -38.97 to 60.31; nominal p=0.66); and the difference in change in total intraepithelial lymphocyte count was -12.73% (95% CI -77.57-52.12; nominal p=0.69). Regarding symptoms, the proportion of patients with diarrhoea per the BSFS score decreased from ten (53%) of 19 at baseline to seven (37%) of 19 at week 12 in the AMG 714 group and increased from two (22%) of nine at baseline to four (44%) of nine at week 12 in the placebo group (nominal p=0.0008); and the difference between the groups in change in GSRS score was -0.14 (SE 0.19; nominal p=0.48). Eight (89%) patients in the placebo group and 17 (89%) in the AMG 714 group had treatment-emergent adverse events, including one (11%) patient in the placebo group and five (26%) in the AMG 714 group who had serious adverse events. The most common adverse event in the AMG 714 group was nasopharyngitis (eight [42%] patients vs one [11%] in the placebo group).

INTERPRETATION:

In patients with refractory coeliac disease type 2 who were treated with AMG 714 or placebo for 10 weeks, there was no difference between the groups in terms of the primary endpoint of aberrant intraepithelial lymphocyte reduction from baseline. Effects on symptoms and other endpoints suggest that further research of AMG 714 may be warranted in patients with refractory coeliac disease type 2.

FUNDING:

Celimmune and Amgen.

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Safety and efficacy of AMG 714 in adults with coeliac disease exposed to gluten challenge: a phase 2a, randomised, double-blind, placebo-controlled study.


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Abstract

BACKGROUND:

Interleukin 15 (IL-15) is implicated in the pathophysiology of coeliac disease. AMG 714 is the first anti-IL-15 monoclonal antibody to be investigated for the treatment of coeliac disease. We aimed
to investigate the effects of AMG 714 in patients with coeliac disease who underwent gluten challenge.

METHODS:

This randomised, double-blind, placebo-controlled, parallel-group, phase 2a trial was done at three clinical sites in Finland. Inclusion criteria included age 18-80 years, a confirmed diagnosis of coeliac disease, and adherence to a gluten-free diet for at least 12 months before screening. Patients were randomly assigned (1:1:1) to 150 mg AMG 714, 300 mg AMG 714, or placebo using permuted blocks and stratified by study site and sex. Patients and study staff were masked to treatment assignment. Treatments were administered by two subcutaneous injections every 2 weeks for 10 weeks (total six doses). Patients without severe villous atrophy at baseline received a gluten challenge (2-4 g daily) during weeks 2-12. Small bowel biopsy samples were obtained for histological assessments at baseline and week 12. The primary efficacy endpoint was the percentage change from baseline to week 12 in villous height-to-crypt depth (VHCD) ratio. Secondary endpoints were CD3-positive intraepithelial lymphocyte density; clinical symptoms measured by gastrointestinal symptom rating scale (GSRS), coeliac disease GSRS, and Bristol stool form scale (BSFS); and changes in anti-tTG and anti-DGP antibodies from baseline. The primary analysis was done in the per-protocol 1 population of patients who received at least one dose of study drug and who underwent the gluten challenge. Safety analyses were done in all patients who received at least one dose of study drug. This trial is registered at ClinicalTrials.gov, NCT02637141 and EudraCT, 2015-003647-19.

FINDINGS:

Between April 13, 2016, and Nov 22, 2016, 64 patients were enrolled and randomly assigned to either the 150 mg AMG 714 group (n=22), the 300 mg AMG 714 group (n=22), or the placebo group (n=20). Two patients did not start treatment and two did not provide post-treatment biopsy samples. 49 patients underwent the gluten challenge (per-protocol 1 population) and 11 patients did not because of baseline villous atrophy. AMG 714 did not prevent mucosal injury due to gluten challenge. The least square mean difference in the relative change from baseline in VHCD ratio was -2.49% (95% CI -16.82 to 11.83; p=0.73) between 150 mg AMG 714 and placebo and 6.39% (-7.07 to 19.85; p=0.34) between 300 mg AMG 714 and placebo. Neither comparison was statistically significant. The density of CD3-positive intraepithelial lymphocytes increased in all groups, with smaller increases in the 300 mg group (-41.24% [95% CI -79.28 to -3.20] vs placebo, nominal p=0.03) but not the 150 mg group (-14.32% [-54.39 to 25.74], nominal p=0.47). Clinical symptoms were ameliorated with AMG 714 treatment between baseline and week 12, particularly diarrhoea as measured by the BSFS (nominal p=0.01 for 150 mg vs placebo, and nominal p=0.0002 for 300 mg vs placebo). Serum antibody titres for anti-tTG and anti-DGP antibodies increased in all three treatment groups, with no significant difference between AMG 714 and placebo. Treatment-emergent adverse events occurred in 21 (95%) patients in the 150 mg AMG 714 group, 0 (95%) in the 300 mg AMG 714 group, and 19 (100%) in the placebo group. The most common treatment-emergent adverse events were gastrointestinal disorders (17 [77%] participants in the 150 mg AMG 714 group, 16 [76%] in the 300 mg AMG 714 group, and 13 [68%] in the placebo group). Injection site reactions were the most common individual adverse event, reported in eight (36%)
patients in the 150 mg AMG 714 group, 11 (52%) in the 300 mg group, and five (26%) in the placebo group. No serious adverse events occurred.

**INTERPRETATION:**

The primary endpoint, change in VHCD ratio from baseline after 12 weeks of treatment in patients with coeliac disease undergoing gluten challenge, was not significantly different between placebo and AMG 714 at either 150 mg or 300 mg. Effects on intraepithelial lymphocyte density and symptoms suggest that further research of AMG 714 may be warranted in patients with non-responsive coeliac disease.

**FUNDING:**

Celimmune and Amgen.

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PMID: 31494096


**Impact of enrichment with egg constituents on water status in gluten-free rice pasta - nuclear magnetic resonance and thermogravimetric approach.**

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Abstract

Effects of freeze-dried egg white, yolk and whole egg enrichment on water behaviour in fresh pasta dough, dried and cooked rice pasta with respect to control samples were studied by ¹H nuclear magnetic resonance (NMR) relaxometry and thermogravimetric analysis. Enrichments caused
lower mobility of water ($T_2$) localised within the starch-protein matrix in fresh dough as well as dried pasta. Water compartmentalization was also downgraded in cooked products. Water fractions with different $T_2$ values were linked to temperature peaks at the first derivative of the thermogravimetric (DTG) curve. From the DTG curve strong interaction of water molecules with proteins of egg white was revealed. Egg proteins also influenced viscoelastic properties of dough, and enhanced the firmness and chewiness of cooked pasta. Structural changes induced by various types of enrichment were reflected in the different molecular mobility at the water-matrix interface ($T_1$). The enrichments also altered the colour and cooking properties.

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**Antigen-specific tolerance to self-antigens in protein replacement therapy, gene therapy and autoimmunity.**

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Abstract

Trials of antigen-specific tolerance have been undertaken in the clinic for over fifty years and the results of these antigen-specific clinical trials are described in this review. Antigen-specific tolerization of the immune system in protein replacement therapy for hemophilia A is an accepted treatment. Clinical trials are ongoing for autoimmune conditions such as type 1 diabetes, multiple sclerosis, neuromyelitis optica, and rheumatoid arthritis with various antigen-specific strategies. Trials for tolerization in celiac disease aim for antigen specific tolerance to gluten, an environmental trigger, which may then halt the progression to autoimmunity targeting a self-antigen, tissue transglutaminase. Although many promising approaches have been demonstrated in pre-clinical models, this review will focus primarily on clinical trials of antigen-specific tolerance that have been taken to the clinic and with initial results reported in the peer reviewed literature. A separate article on approaches with CAR-T cells appears in this volume.

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PMID: 31476445
Small and large strain rheology of gluten and gluten-starch doughs containing wheat bran dietary fiber.

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Abstract

BACKGROUND:

The small and large strain rheology of gluten (G) and gluten-starch (G + S) doughs containing wheat bran dietary fiber (WBDF) were investigated.

RESULTS:

At the small strain stage, i.e. frequency and strain sweep tests, the doughs containing high WBDF concentration are more vulnerable and unstable, as indicated by the lower dough linear viscoelastic strain limit as well as the higher slope of elastic modulus. However, the elastic nature of doughs remarkably increased upon WBDF addition, indicating the reinforcement of the dough mechanical strength, which is also confirmed by the large strain test wherein the maximum strain significantly decreased from 4.37 to 1.82 for the G system and from 12.09 to 2.72 for the G + S system. The creep recovery test showed that WBDF induced the reduction in the strain of the doughs at a fixed stress, which may be related to the enhanced strain hardening capacity.

CONCLUSION:

The addition of WBDF resulted in more brittle and unstable doughs with undesirable higher mechanical strength. The presence of starch greatly weakened the dough strength and led to inferior resistance to both small and large deformations. These findings confirmed the impairment of dough viscoelasticity upon addition of WBDF. © 2019 Society of Chemical Industry.

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PMID: 31471913 [Indexed for MEDLINE]
Coeliac disease: older patients have the most extensive small bowel involvement on capsule endoscopy.

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Abstract

OBJECTIVE:

The relation between symptomatology, serology and findings on small bowel capsule endoscopy (SBCE) in patients with coeliac disease (CD) remains unclear. Clarifying such associations will help to determine whether symptoms and serology can predict severity and extent of disease on SBCE.

METHODS:

Patients with newly diagnosed CD were recruited. Information on SBCE was recorded. Signs and symptoms at presentation, serological markers and histological classification of the disease in the duodenum were noted.

RESULTS:

Sixty patients with newly diagnosed CD (mean age: 44.9 years, SD: ±17.4, 17-76) were included in this study. Older patients (P = 0.025) and patients presenting with iron deficiency anaemia had more extensive small bowel (SB) involvement (25.7% vs. 13.5%; P = 0.026). Those with weight loss were more likely to have SB involvement beyond the duodenum (37.5% vs. 5.8%; P = 0.027). Patients presenting with iron deficiency anaemia (53.5 vs. 42.4 years; P = 0.038) and weight loss (60.5 vs. 42.4 years; P = 0.009) were significantly older at diagnosis. Serum albumin was lower in those patients diagnosed later on in life (Pearson correlation -0.0361; P = 0.007). There was no significant association between anti-tissue transglutaminase antibody (P = 0.396) and extent of affected SB mucosa. Patients with more severe Marsh scores on histology from the duodenal bulb had more extensive SB involvement (P = 0.017).
CONCLUSIONS:

This is the largest study on the use of SBCE in newly diagnosed CD. Older patients are likely to have more extensive disease on SBCE at diagnosis. Symptoms and serology had no impact on the findings on SBCE apart from weight loss and iron deficiency anaemia.

PMID: 31464789

Factors Associated with Symptomology of Celiac Artery Compression and Outcomes following Median Arcuate Ligament Release.

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Abstract

BACKGROUND:

This study aims to identify potential risk factors for becoming symptomatic in patients with radiographic celiac artery compression (CAC) as well as prognostic factors for patients with median arcuate ligament syndrome (MALS) who underwent surgical ligament release.

METHODS:
This is a retrospective cohort study of patients with findings of CAC on computed tomography or magnetic resonance angiography (CT/MRA) who were asymptomatic and who were diagnosed with MALS at a single university hospital between January 2001 and 2018.

RESULTS:

Following a review of 1,330 CT/MRA reports, a total of 109 patients were identified as having radiographically apparent CAC. Among these, 48 (44.0%) patients were symptomatic. Univariate comparison between those with and without symptoms showed that symptomatic patients were more commonly younger than 30 years old [17/48 (35.4%) vs. 8/61 (13.1%), P = 0.006], had a history of prior abdominal surgery [25/48 (52.1%) vs. 18/61 (29.5%), P = 0.017], and had high-grade stenosis [32/43 (74.4%) vs. 25/61 (41.0%), P = 0.001]. Among 41 included patients who underwent surgical release of the median arcuate ligament including open, laparoscopic, and robotic approaches, 82.9% reported overall clinical improvement, 5/41 (12.2%) reported persistent pain, and 13/36 (36.0%) experienced pain recurrence. The only identified risk factor associated with symptom recurrence was American Society of Anesthesiologists class III [7/13 (53.8%) vs. 4/23 (17.4%), P = 0.029].

CONCLUSIONS:

The severity of stenosis and prior abdominal surgery both contributed to symptom development in patients with radiographically apparent CAC from the median arcuate ligament.

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PMID: 31449931

Deacetylation of 3-acetyl-deoxynivalenol in wheat flour is mediated by water-soluble proteins during the making of Chinese steamed bread.

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Abstract

To find the determining factors for 3-acetyl-deoxynivalenol (3-ADON) deacetylation during wheat-based food production, wheat flours with different heat treatments, different matrixes of the starch-gluten mixture, and different protein fractions (Osborne classification) were evaluated. The deacetylation behavior of 3-ADON was significantly suppressed for heat-treated wheat flours, indicating that heating induced change of the functional or chemical properties of wheat grain components, especially for proteins. Among the different matrixes, only 3% of the 3-ADON in starch was converted to DON, however, this value reached 60-75% for wheat flour. The results showed that proteins were responsible for the deacetylation of 3-ADON. After separation, only albumins mediated the deacetylation of 3-ADON into DON in four protein fractions. The proteins were identified by LC-MS/MS, and the results suggested that cytochrome P450, acetylesterase and histone deacetylase were the potential targeted enzymes that mediated the deacetylation of 3-ADON during dough preparation for wheat-based food production.

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PMID: 31442898 [Indexed for MEDLINE]
Health-related Quality of Life in Newly Diagnosed Pediatric Patients With Celiac Disease.

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Abstract

OBJECTIVES:

Celiac disease (CD) is a common chronic condition with potential adverse physical and psychosocial implications for affected children. The study purpose was to characterize health-related quality of life (HRQOL) in a large sample of pediatric patients with newly diagnosed CD using the PedsQL 4.0 Generic Core Scales, and compare it to that of healthy children and children with nonceliac gastrointestinal (GI) conditions using historic data.

METHODS:

The PedsQL was administered to 159 children with newly diagnosed CD and their parents at either the time of diagnostic esophagogastroduodenoscopy or before their initial dietitian appointment for gluten-free diet teaching. Mean parent-report and self-report PedsQL summary and subscale scores were calculated, then compared to published means from a sample of healthy children and a sample of children with nonceliac GI symptoms using 1-sample t tests.

RESULTS:

Compared to the healthy children, those with newly diagnosed CD had lower Total Scores, Physical Health, Psychosocial Health, Emotional Functioning, and School Functioning on parent report (P<0.008) with similar findings on self-report. Within the CD sample, clinically significant scores were found in 55.9% for School Functioning, 62.7% for Physical Health, 54.4% for Emotional Functioning, 43.7% for Social Functioning, and 49% for Total Score.

CONCLUSIONS:

Children and adolescents with newly diagnosed CD had lower HRQOL than healthy children and similar HRQOL to that of patients with nonceliac GI conditions. Patients with deficits in domains
such as school or emotional functioning may benefit from early interventions including a Section 504 plan or meeting with a psychologist or social worker.

PMID: 31436704

Baking performance of 25 edible dry bean powders: Correlation between cookie quality and rapid test indices.

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Abstract

This study was designed to evaluate the baking performances of 25 edible dry bean (Phaseolus vulgaris L.) varieties and to investigate correlations among cookie features and rapid test indices (i.e., water and lactic acid retention capacities, oil binding capacity and Rapid Visco Analyzer indices). Two bean powder particle sizes (≤0.5 mm, ≤1.0 mm) were investigated. Cookies were evaluated in terms of nutritional, geometrical and textural properties. Bean powders doubled the amount of cookie protein and increased cookie resistant starch content. Baking potential varied according to bean genotype and powder particle size: coarse powders resulted in larger (+26%) and thinner (-19%) cookies characterized by easier breaking texture (fracture strengths of 41-157 vs. 48-226 kPa for fine powders). Water retention and oil binding capacities and pasting properties significantly (p < 0.05) correlated with cookie features. In conclusion, these accumulated findings can be used in designing value-added traditional and gluten-free cookies.

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Lower HbA1c in patients with type 1 diabetes and celiac disease who reached celiac-specific antibody-negativity - A multicenter DPV analysis.

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Abstract

OBJECTIVES:

To study celiac-specific antibody status over 3 years in patients with type 1 diabetes and biopsy-proven celiac disease (T1D + CD). Furthermore, to determine clinical differences after diagnosis between patients reaching constant antibody-negativity (Ab-neg) and staying antibody-positive (Ab-pos).

METHODS:
A total of 608 pediatric T1D + CD patients from the multicenter DPV registry were studied longitudinally regarding their CD specific antibody-status. Differences between Ab-neg (n = 218) and Ab-pos (n = 158) patients 3 years after biopsy were assessed and compared with 26 833 T1D patients without CD by linear and logistic regression adjusted for age, gender, diabetes duration and migration background.

RESULTS:

Thirty-six percent of T1D + CD patients reached and sustained antibody-negativity 3 years after CD diagnosis. The median time until patients returned to Ab-neg was 0.86 (0.51;1.16) years. Three years after diagnosis, HbA1c was lowest in Ab-neg and highest in Ab-pos patients compared to T1D-only patients (adjusted mean (95%CI): 7.72 (7.51-7.92)% vs 8.44 (8.20-8.68)% vs 8.19 (8.17-8.21)%), adjusted P < 0.001, respectively. Total cholesterol, LDL-cholesterol and frequency of dyslipidemia were significantly lower in Ab-neg compared to T1D-only patients (167 (161-173) mg/dl vs 179 (178-179) mg/dl, P < .001; 90 (84-96) mg/dl vs 99 (98-99) mg/dl, P = .005; 15.7 (10.5-22.9) % vs 25.9 (25.2-26.6) %, P = .017). In longitudinal analyses over 6 years after diagnosis, a constantly higher HbA1c (P < .001) and a lower height-SDS (P = .044) was observed in Ab-pos compared to Ab-neg patients.

CONCLUSION:

Only one third of T1D + CD patients reached constant Ab-negativity after CD diagnosis. Achieving Ab-negativity after diagnosis seems to be associated with better metabolic control and growth, supposedly due to a higher adherence to therapy in general.

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**Efficacy of Celiac Branch Preservation in Billroth- I Reconstruction After Laparoscopy-Assisted Distal Gastrectomy.**

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Abstract

BACKGROUND:

The goal of the present retrospective study was to elucidate the efficacy of conserving the celiac branch (CB), which can reduce the adverse reactions of Billroth- I (B- I ) restoration after the laparoscopy-assisted distal gastrectomy (LADG).

METHODS:

Two hundred thirty-three patients with gastric cancer underwent B-I reconstruction after LADG with dissection 2 lymphadenectomy from July 2005 to July 2012 and were monitored for 5 y. The patients were separated into 2 groups: celiac branch preserved (P-CB) group (n = 98) and celiac branch resected (R-CB) group (n = 135). In addition to patient information, tumor features, and surgical details, short-term and long-term variables such as bowel condition, surgical complications, and endoscopy findings were evaluated.

RESULTS:

In short-term efficacy, the time of first flatus and liquid ingestion were slightly shorter in the P-CB group than in the R-CB group (3.84 ± 0.74 versus 4.38 ± 0.71, P = 0.0001; 5.04 ± 1.07 versus 5.67 ± 1.10, P = 0.0001). For long-term efficacy, the incidences of chronic diarrhea, gastroparesis, residual food, bile reflux, and reflux esophagitis were less in the P-CB group compared with the R-CB group (6.1% versus 22.2%, P = 0.001; 5.1% versus 17.8%, P = 0.004; 4.1% versus 17.8%, P = 0.004; 8.2% versus 17.8%, P = 0.036; 8.2% versus 17.8%, P = 0.036). Other parameters such as postoperative ileus and gallstones had a better efficacy trend in the P-CB group but did not suggestively vary among the groups.

CONCLUSIONS:

The CB has an imperative part in the gastrointestinal motility, and celiac preservation mainly exerts long-term efficacy in patients who underwent B-I surgery with LADG.

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Similar articles

Impact of secondary interventions on mortality after fenestrated branched endovascular aortic aneurysm repair.

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Abstract

BACKGROUND:

Fenestrated and branched endovascular aortic repair (F/BEVAR) is increasingly used to manage pararenal and thoracoabdominal aortic disease (TAAA). Device-related reintervention after F/BEVAR is common, but little is known about its impact on postoperative mortality. The purpose of this analysis was to describe secondary intervention (SI) after F/BEVAR and determine the impact of these procedures on patient survival.

METHODS:

A single-center review was done on all consecutive F/BEVARs performed from 2010 to 2016. Primary end points were incidence of secondary aortic, branch, and/or access vessel–related SI, and survival. SI was categorized as minor endovascular (branch restenting, access vessel treatment, or percutaneous coil embolization), major endovascular (new aortic graft placement), or open (bleeding, access vessel, and/or aortic). Kaplan-Meier methodology was used to estimate freedom from SI and survival. Multivariable analysis was used to identify predictors of SI.

RESULTS:

A total of 308 F/BEVAR procedures were performed (75% physician-modified, 18% custom, 7% Zfen), with 1022 vessels revascularized (celiac, 228; superior mesenteric artery [SMA], 263; renal, 525). There were 117 (39%) extent I-III TAAA, 132 (44%) extent IV TAAA/4-vessel pararenal, and 54 (18%) <4-vessel pararenal repairs performed. Any type of SI occurred in 24% (74) of patients during the mean follow-up of 20 ± 21 months. The majority of reinterventions were endovascular (minor, 53% [n = 39]; major, 32% [n = 24]), whereas 12% (n = 9) were open and 3% (n = 2) hybrid. Primary indication for SI included: 22 (29%) with branch-related endoleaks (1C or III); 15 (22%) with
proximal or distal aortic degeneration; 8 (12%) with branch vessel thrombosis/stenosis; 10 (11%) with aortic device type III endoleak/loss of overlap; 4 (6%) with postoperative mesenteric or renal bleeding events; 5 (5%) with type II endoleak; 3 (5%) with access vessel complication; and 2 (3%) with graft infection. Most SIs were elective (65%; n = 48) with the remainder occurring emergently (24%; n = 18) or for symptoms/urgently (11%; n = 8). Compared with endovascular remediation, open SI was more likely to be emergent (89%, 8 of 9; P = .001). Freedom from SI was 80 ± 3% and 64 ± 4% at 1 and 3 years, respectively. One- and 5-year survival with or without SI was: 1 year, 88 ± 4% vs 81 ± 3%; 5 years, 76 ± 5% vs 59 ± 4% (log rank test, P = .06). There was no survival difference based on type of SI (log rank test, P = .3). Extent I-III TAAA (HR, 1.6; 95% CI, 0.98-3.3; P = .06) and history of cerebrovascular disease (HR, 1.8; 95% CI, 0.97-2.6; P = .07) were predictive of SI.

CONCLUSIONS:

SIs after F/BEVAR most frequently involve branch vessel or aortic device remediation procedures; however, they do not negatively impact out-of-hospital survival. These results further highlight the crucial role of imaging surveillance after F/BEVAR to maintain durability. Discussions with patients, periprocedural planning, and the next generation of device design must focus on issues surrounding the risk of device-related SI events.

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Quality Indicators and Heat Damage of Dried and Cooked Gluten Free Spaghetti.

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Abstract

The quality and safety indicators of commercial dried gluten free (GF) pasta were analyzed to investigate, for the first time, the real nutritional intake through the chemical composition and the heat damage during processing by quantification of furosine. Eight samples of GF spaghetti were compared with wheat spaghetti. Dried and cooked GF pasta had lower protein and ash content than wheat spaghetti. GF samples composed solely by corn flour had higher optimal cooking time.
Samples with emulsifier showed lower losses during cooking. Considering their composition, no trend could be established to explain textural behavior. Samples constituted merely by corn showed the highest resilience and elasticity. Spaghetti constituted only from corn and rice showed the highest firmness. The furosine content in dried samples ranged between 19 and 134 mg FUR/100 g proteins and in cooked samples ranged between 48 to 360 mg FUR/100 g proteins. Furosine content of GF pasta was in general lower than in wheat pasta, and those differences were even enlarged when comparing them after cooking. The results of PCA indicated it was possible to discriminate GF pasta regarding their technological and nutritional behavior.

**Fenestrated/Branched Endovascular Aortic Aneurysm Repair Using a Supraceliac Aortic Proximal Seal Zone Versus an Infraceliac Aortic Proximal Seal Zone.**

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**Abstract**

**BACKGROUND:**

Fenestrated/branched endovascular aneurysm repair (F/B-EVAR) achieves more extensive proximal seal than conventional infrarenal devices, thereby increasing aneurysm exclusion durability. Optimal seal zone length remains undefined. We assessed relative risks and benefits of extending the proximal seal above the celiac artery.

**METHODS:**

The prospective database of all complex endovascular aortic aneurysm repairs at a single institution (institutional review board-approved, physician-sponsored investigational device exemption trial, 10/2010-6/2017) was used to classify repairs according to the number of target
visceral-renal arteries incorporated: 4-vessel versus <4-vessel. Comparisons of aneurysm characteristics, perioperative details, and postoperative complications were performed, stratified by repair type. One-year survival, target artery patency, freedom from type 1 or 3 endoleak, and freedom from reintervention were estimated with Kaplan-Meier analysis.

RESULTS:

Among 175 F/B-EVARs, 38% (n = 67) were 4-vessel and 62% (n = 108) were <4-vessel. Intraoperatively, there was no difference in mean contrast use (76 mL vs. 74 mL, P = non significant [NS]) or dose area product (63,428 mGy cm² vs. 96,015 mGy cm²), but there was increased median procedure time (4.8 hr, interquartile range [IQR] = 4.1-5.8 versus 3.6 hr, IQR = 2.9-4.1, P < 0.0001) and mean operating room direct costs ($52,532, standard deviation [SD] = 18,640 versus $40,128, SD = 15,135, P < 0.0001) in 4-vessel repairs. There were no differences in mortality (1.9% vs. 4.5%), paraparesis (0% vs. 3.0%), or paralysis (0.9% vs. 0%), all P = NS. There were no differences in one-year survival, target artery patency, or freedom from reintervention. There was a lower 1-year freedom from type 1 or 3 endoleak with 4-vessel repairs (82% vs. 94%, log-rank P = 0.02), driven by an increased rate of type 3 endoleaks. Endoleak resolution after treatment was equivalent in both groups (4-vessel, 10 of 12, 83% resolved; <4-vessel, 7 of 7, 100% resolved, P = NS).

CONCLUSIONS:

With F/B-EVAR, utilization of a supraceliac seal zone, compared with an infraceliac seal zone, is associated with statistical differences in operative characteristics/resource utilization, but with negligible clinical significance. Further innovation to eliminate type 3 endoleaks at fenestrations/branches remains an unmet need. To achieve adequate F/B-EVAR proximal seal zone length, one should have a low threshold to incorporate the celiac artery.

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Do puroindolines affect the impact of enzymatic lipid hydrolysis on loaf volume in bread making?

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Abstract

This paper is the first to study whether and how interactions between puroindolines (PINs) and lipids affect bread loaf volume (LV). Flour from near-isogenic wheat lines differing in PIN haplotype and lipases were used in bread making. That lipase impact on LV strongly depended on the flour used supported the hypothesis that PINs modify the impact of enzymatic lipid hydrolysis on LV. In dough prepared from gluten-starch blends (GSB) differing in PIN levels, PINs did not affect enzymatic lipid hydrolysis itself. Gas cells in these GSB doughs were apparently not surrounded by surface-active compounds so that the impact of PIN-lipid interactions on LV could not be evaluated. This allowed concluding that lipase impact on LV is exclusively related to stabilization of gas cell interfaces in dough since lipase application did not change GSB LVs. Our results advance knowledge on PIN-lipid interactions and the impact of lipases in bread making.

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Characterizing the impact of starch and gluten-induced alterations on gelatinization behavior of physically modified model dough.

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Abstract

Gelatinization properties of physically modified starch-gluten matrices are often exclusively traced back to starch constitution without considering the state of gluten. Thus, gelatinization of model dough, combining reference (rS)/modified starch (mS) with reference (rG)/modified gluten (mG), was investigated using nuclear magnetic resonance and differential scanning calorimetry to relate structural alterations of biopolymers to their hydration properties. No differences were found in gelatinization onsets of model dough consisting of rS and mS combined with mG (starch: gluten = 50:50 (m/m)), although gelatinization enthalpy of mS mG (1.7 ± 0.4 J/g dm) was significantly lowered in comparison to rS mG (2.2 ± 0.2 J/g dm). Relaxation time $T_2$ was significantly reduced for mG in comparison to rG, demonstrating a tighter water binding of mG. This suggests that reduced gelatinization enthalpy of modified starch-gluten matrices is caused by a destruction of crystal parts of modified starch and by a tighter water binding of modified gluten.

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Abstract

The glutenin (Glu) and gliadin (Gli) were modified by protein-glutaminase (PG) to obtain soluble glutenin (PG-Glu) and gliadin (PG-Gli), and PG-Glu or PG-Gli was added to potato starch (PS) according to different amounts (0.5%, 1.0%, and 1.5%, based on dry starch weight, w/w) to explore the effect of modified proteins on the retrogradation behavior and digestibility of PS. The results showed that the long-term retrogradation of PS was accelerated by the addition of PG-Glu or PG-Gli. The addition of PG-Glu or PG-Gli led to an increase in hydrogen bonds within starch molecules and induced a significant increase in resistant starch content. The hydrolysis kinetic parameters, C∞ and k, both decreased with the increasing level of modified protein, indicating the deceleration of hydrolysis rate by the addition of PG-Glu or PG-Gli. In summary, the addition of PG-Glu or PG-Gli could promote the retrogradation of PS and mitigate the digestion of starch.

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Similar articles


Development of a novel model dough based on mechanically activated cassava starch and gluten protein: Application in bread.

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Abstract

This study focused on the development of a novel model dough for leavened food production, which was obtained by blending gluten protein with damaged cassava starch (DCS) induced by mechanical activation (MA). The characteristics of model dough and the interaction between DCS and gluten were investigated, and the quality of bread made from the model dough was also evaluated. The results showed that both the addition of gluten and the increased damage of DCS could improve the strength of model dough. The damage of cassava starch prevented the formation of gluten network. The enhanced DCS-gluten interaction had an impact on the performance of dough, attributing to the interaction of hydrogen bonds between both of them. Moderate interaction was required to obtain the bread with desired quality, and MA for moderating structural damage to starch was an effective approach in promoting the interaction between starch and gluten protein.

Juxtarenal endovascular therapy with fenestrated and branched stent grafts after previous infrarenal repair.

Sveinsson M, Kristmundsson T, Dias N, Sonesson B, Mani K, Wanhainen A, Resch T.

Abstract

BACKGROUND:

The treatment strategy for proximal aortic disease or type I endoleak after previous infrarenal repair has traditionally been open surgery. As endovascular treatment options with fenestrated
and branched stent grafts increasingly rival open surgery for juxtarenal and pararenal aortic aneurysms, secondary proximal repair may similarly be performed endovascularly. Fenestrated stent grafts are individually tailored to each patient, whereas a more readily available "off-the-shelf" branched stent graft is often suitable in more urgent settings.

METHODS:

All patients who had been reoperated on with a proximal fenestrated or branched cuff after previous infrarenal endovascular or open repair from two tertiary referral centers between 2002 and 2015 were included in the analysis. Patients were retrospectively enrolled in a digital database. Data were collected from chart review and digital imaging.

RESULTS:

There were 43 patients, 37 (86%) male and six (14%) female, who were treated. The indications for proximal endovascular repair were type I endoleak (58%), proximal aneurysm formation (30%), and stent graft migration (12%). Median follow-up time was 33 months (range, 3-120 months); 34 patients (79%) received a fenestrated cuff, and branched stent grafts were used in 8 (19%) cases. The majority of grafts had three (47%) or four (49%) fenestrations or branches. Technical success was accomplished in 93% of cases. In two cases, the celiac trunk occluded; in one case, the hepatic artery was overstented, and a renal artery could not be cannulated in one case. Median hospital stay was 5 days (range, 2-57 days). The 30-day mortality was 0%, and 1-year mortality was 5%. One patient died of an aneurysm-related cause during the study period.

CONCLUSIONS:

An endovascular approach with fenestrated or branched stent grafts for treatment of proximal endoleak, proximal aneurysm formation, or pseudoaneurysms after previous infrarenal repair seems to be a valid alternative to open surgery.

Correction to: Anatomical variations in the origins of the celiac axis and the superior mesenteric artery: MDCT angiographic
findings and their probable embryological mechanisms.

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Erratum for

- Anatomical variations in the origins of the celiac axis and the superior mesenteric artery: MDCT angiographic findings and their probable embryological mechanisms. [Eur Radiol. 2014]

Abstract

The original version of this article, published on 24 May 2014, unfortunately contained a referencing omission.

PMID: 31197443


The association between liver fat and systemic calcified atherosclerosis.

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2. Department of Family Medicine and Public Health, University of California San Diego, La Jolla, Calif.
Abstract

BACKGROUND:

The association of nonalcoholic fatty liver disease (NAFLD) with systemic calcified atherosclerosis, other than the coronary arteries, has not been clearly elucidated. We investigated the association between NAFLD and calcification in eight different vascular beds.

METHODS:

In a community-based cohort with computed tomography scans for carotid artery, coronary artery, thoracic aorta, abdominal aorta, iliac artery, renal artery, celiac trunk, and superior mesenteric artery, the association between NAFLD and arterial calcification was evaluated with adjustment for age, sex, hypertension, dyslipidemia, diabetes, obesity, current smoking status, and family history of heart disease in the first-degree relatives.

RESULTS:

In age- and sex-adjusted models, NAFLD was significantly associated with calcification in the coronary artery, carotid artery, thoracic aorta, celiac trunk, and superior mesenteric artery vascular beds (P < .05). However, adjustment for the traditional chronic venous disease risk factors attenuated the associations, except in the case of the thoracic aorta (odds ratio [OR], 1.38; 95% confidence interval [CI], 1.09-1.78) and celiac trunk (OR, 2.05; 95% CI, 1.16-3.65). In addition, NAFLD was independently associated with multiarterial calcification (four or more [OR, 1.33; 95% CI, 1.01-1.74], five or more [OR, 1.46; 95% CI, 1.09-1.97], and six or more [OR, 1.58; 95% CI, 1.09-2.30] of eight evaluated arterial segments).

CONCLUSIONS:

The association between NAFLD and arterial calcification is mainly mediated by conventional risk factors. The independent association between NAFLD and calcification in the thoracic aorta and celiac trunk as well as in a larger number of vascular beds needs confirmation in future prospective studies in diverse populations.

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Genome-Wide Association Study of Microscopic Colitis in the UK Biobank Confirms Immune-Related Pathogenesis.


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Abstract

BACKGROUND AND AIMS:
The causes of microscopic colitis are currently poorly understood. Previous reports have found clinical associations with coeliac disease and genetic associations at the human leukocyte antigen [HLA] locus on the ancestral 8.1 haplotype. We investigated pharmacological and genetic factors associated with microscopic colitis in the UK Biobank.

METHODS:
In total, 483 European UK Biobank participants were identified by ICD10 coding, and a genome-wide association study was performed using BOLT-LMM, with a sensitivity analysis performed excluding potential confounders. The HLA*IMP:02 algorithm was used to estimate allele frequency at 11 classical HLA genes, and downstream analysis was performed using FUMA. Genetic overlap with inflammatory bowel disease [Crohn's disease and ulcerative colitis] was investigated using genetic risk scores.

RESULTS:
We found significant phenotypic associations with smoking status, coeliac disease and the use of proton-pump inhibitors but not with other commonly reported pharmacological risk factors. Using the largest sample size to date, we confirmed a recently reported association with the MHC Ancestral 8.1 Haplotype. Downstream analysis suggests association with digestive tract morphogenesis. By calculating genetic risk scores, we also report suggestive evidence of shared genetic risk with Crohn's disease, but not with ulcerative colitis.

CONCLUSIONS:
This report confirms the role of genetic determinants in the HLA in the pathogenesis of microscopic colitis. The genetic overlap with Crohn's disease suggests a common underlying mechanism of disease.

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**Jejunal perforation and central retinal vein occlusion in a 55-year-old European man.**

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Conflict of interest statement

Competing interests: None declared.


**Measurement of Forearm Bone Density by Dual Energy X-Ray Absorptiometry Increases the Prevalence of Osteoporosis in Men With Celiac Disease.**

Walker MD¹, Williams J², Lewis SK³, Bai J², Lebwohl B³, Green PHR³.
Abstract

BACKGROUND & AIMS:

Guidelines advise measurement of bone mineral density (BMD) in patients with a diagnosis of celiac disease. The lumbar spine (LS) and hip sites are usually measured. Although skeletal sites rich in trabecular bone are believed to be vulnerable to osteoporosis in patients with celiac disease, most studies have not measured the cortical distal 1/3-radius.

METHODS:

We collected data from 721 patients (mean age, 43.6 years; 68.4% female) with celiac disease who underwent 3-site dual energy x-ray absorptiometry (DXA, at a median 1.22 years after diagnosis). We assessed skeletal site- and sex-specific osteoporosis prevalence and the incremental utility of 1/3-radius measurement by DXA.

RESULTS:

Mean T- and Z-scores were normal in patients, but 43.3% had osteopenia and 19.6% had osteoporosis. Osteoporosis was found in 12.1% of patients at the LS, 5.3% of patients at the total hip, 7.6% of patients at the femoral neck, and 11.5% of patients at the 1/3-radius. A greater degree of villous atrophy at diagnosis was associated with male sex and lower T-scores at the 1/3-radius (P = .03), but not other skeletal sites. Isolated forearm osteoporosis was detected in 4.9% of patients. A higher proportion of patients with isolated forearm osteoporosis were male and had a greater weight and body mass index (all P < .01, compared to patients with osteoporosis only at other sites). Z-scores were lower at the LS and 1/3-radius and osteoporosis was more common in men than women. In men, the 1/3-radius was the most frequent site for osteoporosis. Among patients 50 years or older, isolated forearm osteoporosis was present in 10.7%.

CONCLUSIONS:

Based on DXA analysis of patients with celiac disease, the prevalence of osteoporosis appears to be underestimated—particularly in men when BMD at the 1/3-radius is not measured. Degree of villous atrophy is associated with BMD at the 1/3-radius and nearly 5% of patients have osteoporosis limited to that site. Recommendations for osteoporosis screening in patients with celiac disease should include measurement of the distal 1/3-radius in addition to the hip and LS.
Effect of pH control during rice fermentation in preventing a gliadin P31-43 entrance in epithelial cells.

Gallo M1,2, Nigro F2, Passannanti F1, Nanayakkara M3,4, Lania G3,4, Parisi F1, Salameh D1, Budelli A5, Barone MV3,4, Nigro R1.

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Abstract

Coeliac disease is an increasingly recognised pathology, induced by the ingestion of gluten in genetically predisposed patients. Undigested gliadin peptide can induce adaptive and innate immune response that unleash the typical intestinal mucosal alterations. A growing attention is paid to alternative therapeutic approaches to the gluten-free diet: one of these approaches is the use of probiotics and/or postbiotics. We performed lactic fermentation of rice flour with and without pH control, using Lactobacillus paracasei CBA L74 as fermenting strain. We evaluated bacterial growth, lactic acid production during fermentation and gliadin peptide P31-43 entrance in CaCo-2 cells with and without pH control. When pH control was applied no differences were observed in terms of bacterial growth; on the contrary, lactic acid production was greater, as expected. Both samples could inhibit the P31-43 entrance in CaCo-2 cells but the effect was significantly greater for samples obtained when the pH control was applied.

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Efficacy of Enteric-Release Oral Budesonide in Treatment of Acute Reactions to Gluten in Patients With Celiac Disease.

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Abstract

Celiac disease (CeD) is a common gluten-responsive T cell-mediated enteropathy. The only current treatment is gluten avoidance; however, even when attempting to adhere to a gluten-free diet (GFD), symptomatic gluten exposures are frequent.¹.

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Neurologic Deficits in Patients With Newly Diagnosed Celiac Disease Are Frequent and
Linked With Autoimmunity to Transglutaminase 6.

Hadjivassiliou M1, Croall ID2, Zis P3, Sarrigiannis PG3, Sanders DS4, Aeschlimann P5, Grünewald RA3, Armitage PA2, Connolly D2, Aeschlimann D5, Hoggard N2.

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Abstract

BACKGROUND & AIMS:

Celiac disease is an autoimmune disorder induced by ingestion of gluten that affects 1% of the population and is characterized by gastrointestinal symptoms, weight loss, and anemia. We evaluated the presence of neurologic deficits and investigated whether the presence of antibodies to Transglutaminase 6 (TG6) increases the risk of neurologic defects in patients with a new diagnosis of celiac disease.

METHODS:

We performed a prospective cohort study at a secondary-care gastroenterology center of 100 consecutive patients who received a new diagnosis of celiac disease based on gastroscopy and duodenal biopsy. We collected data on neurologic history, and patients were evaluated in a clinical examination along with magnetic resonance imaging of the brain, magnetic resonance (MR) spectroscopy of the cerebellum, and measurements of antibodies against TG6 in serum samples. The first 52 patients recruited underwent repeat MR spectroscopy at 1 year after a gluten-free diet (GFD). The primary aim was to establish if detection of antibodies against TG6 can be used to identify patients with celiac disease and neurologic dysfunction.

RESULTS:

Gait instability was reported in 24% of the patients, persisting sensory symptoms in 12%, and frequent headaches in 42%. Gait ataxia was found in 29% of patients, nystagmus in 11%, and distal sensory loss in 10%. Sixty percent of patients had abnormal results from magnetic resonance
imaging, 47% had abnormal results from MR spectroscopy of the cerebellum, and 25% had brain white matter lesions beyond that expected for their age group. Antibodies against TG6 were detected in serum samples from 40% of patients; these patients had significant atrophy of subcortical brain regions compared with patients without TG6 autoantibodies. In patients with abnormal results from MR spectroscopy of the cerebellum, those on the GFD had improvements detected in the repeat MR spectroscopy 1 year later.

CONCLUSIONS:

In a prospective cohort study of patients with a new diagnosis of celiac disease at a gastroenterology clinic, neurologic deficits were common and 40% had circulating antibodies against TG6. We observed a significant reduction in volume of specific brain regions in patients with TG6 autoantibodies, providing evidence for a link between autoimmunity to TG6 and brain atrophy in patients with celiac disease. There is a need for early diagnosis, increased awareness of the neurologic manifestations among clinicians, and reinforcement of adherence to a strict GFD by patients to avoid permanent neurologic disability.

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[Cold urticaria and coeliac disease in a paediatric patient].

[Article in Spanish]

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Assessment of the potential allergenicity of genetically-engineered food crops.

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Abstract

An extensive safety assessment process exists for genetically-engineered (GE) crops. The assessment includes an evaluation of the introduced protein as well as the crop containing the protein with the goal of demonstrating the GE crop is "as-safe-as" non-GE crops in the food supply. One of the evaluations for GE crops is to assess the expressed protein for allergenic potential. Currently, no single factor is recognized as a predictor for protein allergenicity. Therefore, a weight-of-the-evidence approach, which accounts for a variety of factors and approaches for an overall assessment of allergenic potential, is conducted. This assessment includes an evaluation of the history of exposure and safety of the gene(s) source; protein structure (e.g. amino acid sequence identity to human allergens); stability of the protein to pepsin digestion in vitro; heat stability of the protein; glycosylation status; and when appropriate, specific IgE binding studies with sera from relevant clinically allergic subjects. Since GE crops were first commercialized over 20 years ago, there is no proof that the introduced novel protein(s) in any commercialized GE food crop has caused food allergy.

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Arthritis [Internet].

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Excerpt

Arthritis is derived from the Greek term “disease of the joints.” It is defined as an acute or chronic joint inflammation that often co-exists with pain and structural damage. [1] Arthritis affected both the Neanderthals and ancient Egyptians, but it was not until 1886 that Dr. John K. Spencer coined the term “osteoarthritis.” Arthritis describes a set of symptoms that includes pain, stiffness, and joint deformities subsequent to an inflammatory process. The destructive process can occur through multiple pathways. These include: Degenerative disease (osteoarthritis). Auto-immune or auto-inflammatory processes (rheumatoid arthritis and ankylosing spondylitis). Crystal deposition (gout and pseudogout). Infection (septic arthritis). Idiopathic (juvenile idiopathic arthritis). Many diseases can result in arthritis. Examples include systemic lupus erythematosus, psoriasis, Lyme disease, reactive arthritis, and celiac disease among numerous others. The goal of this activity is to provide a general overview of the most common arthritides and briefly touch on key aspects of the different major disease types.

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148. Celiac Disease [Internet].

Authors

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Excerpt

Celiac disease is an enteropathy of the small intestine. It is triggered by exposure to gluten in the diet of susceptible people. The susceptibility is genetically determined. The condition is chronic, and currently, the only treatment consists of permanent exclusion of gluten from the food intake.[1][2][3] Patients with celiac disease can present with diarrhea and failure to thrive; some may be asymptomatic.

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