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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 ten 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 (10xULN) 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 <10xULN at least 4 biopsies from the distal duodenum and at least one 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


Spurious HbA1c results in patients with diabetes treated with dapsone.

Aljenaee K1, Hakami O2, Davenport C3, Farrell G4, Tun TK2, Pazderska A1, Phelan N1, Healy ML1, Sreenan S2, McDermott JH2.
Abstract

Summary:

Measurement of glycated haemoglobin (HbA1c) has been utilised in assessing long-term control of blood glucose in patients with diabetes, as well as diagnosing diabetes and identifying patients at increased risk of developing diabetes in the future. HbA1c reflects the level of blood glucose to which the erythrocyte has been exposed during its lifespan, and there are a number of clinical situations affecting the erythrocyte life span in which HbA1c values may be spuriously high or low and therefore not reflective of the true level of glucose control. In the present case series, we describe the particulars of three patients with diabetes who had spuriously low HbA1c levels as a result of dapsone usage. Furthermore, we discuss the limitations of HbA1c testing and the mechanisms by which it may be affected by dapsone in particular.

Learning points:

Various conditions and medications can result in falsely low HbA1c. Dapsone can lead to falsely low HbA1c by inducing haemolysis and by forming methaemoglobin. Capillary glucose measurement, urine glucose measurements and fructosamine levels should be used as alternatives to HbA1c for monitoring glycaemic control if it was falsely low or high.

PMID: 31566188


EUS-B-FNA for Diagnosing Liver and Celiac Metastases in Lung Cancer Patients.

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Abstract

BACKGROUND:

In patients with suspected or proven lung cancer, assessment of regional nodal and distant metastases is key before treatment planning. By introducing the endobronchial ultrasound (EBUS)-guided scope into the esophagus and stomach (EUS-B), liver lesions and celiac nodes can be visualized. To date, the utility of EUS-B in diagnosing liver lesions and retroperitoneal lymph nodes is unknown.

OBJECTIVES:

To assess the feasibility, safety, and diagnostic yield of sampling of liver lesions and retroperitoneal nodes by EUS-B fine-needle aspiration (FNA) in a lung cancer staging setting.

METHOD:

Consecutive patients suspected of lung cancer in 2 Danish centers between 1 January 2015 and 31 December 2017 were included retrospectively when a lesion in the liver or a retroperitoneal lymph node was visualized and biopsied with EUS-B-FNA.

RESULTS:

23 left liver lobe lesions and 19 retroperitoneal lymph nodes were sampled by EUS-B-FNA. Sensitivity and diagnostic yield of sampled liver lesions were 86 and 83%, respectively. In 19/23 patients, there was a cytopathological diagnosis of malignancy. Sensitivity and diagnostic yield from retroperitoneal lymph node samples were 83 and 63%, respectively. In 10/19 patients, the diagnosis was malignancy. No complications were observed.

CONCLUSION:

EUS-B-FNA enables safe sampling of left liver lobe lesions and retroperitoneal lymph nodes. EUS-B should be considered as a minimally invasive technique to provide tissue proof of distant metastases lung cancer patients.

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PMID: 31563907

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Zonulin in serum as a biomarker fails to identify the IBS, functional dyspepsia and non-coeliac wheat sensitivity.


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PMID: 31563879

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Conflict of interest statement

Competing interests: NJT: Dr Talley reports personal fees from Allergans PLC (GI Development Programs), personal fees from Viscera Labs (IBS), personal fees from IM Health Sciences (FD), personal fees from Napo Pharmaceutical (IBS), personal fees from Outpost Medicine (IBS), from Progenity Inc San Diego (capsule SIBO), from Allakos (gastric eosinophilic disease), personal fees from Samsung Bioepis (IBD), personal fees from Synergy (IBS), personal fees from Takeda (gastroparesis), personal fees from Theravance (gastroparesis), grants and personal fees from Viscera USA (IBS), grants from Commonwealth Diagnostics (International) Inc (IBS), non-financial support from HVN National Science Challenge NZ (IBS), grants and personal fees from GI therapies (constipation), personal fees from Cadila Pharmaceuticals (CME), personal fees from Planet Innovation (Gas capsule), personal fees from Danone (Probiotic), personal fees from Pfizer (IBS), from Dr. Reddy's Laboratories (Webinar), personal fees from Arlyx (IBS), personal fees from Sanofi (Probiotic), outside the submitted work; In addition, Dr Talley has a patent Biomarkers of IBS licensed, a patent Licensing Questionnaires Talley Bowel Disease Questionnaires licensed to Mayo/Talley, a patent Nestec European Patent licensed, a patent Singapore Provisional Patent “Microbiota Modulation Of BDNF
Preparation of Gluten-Free Foods Alongside Gluten-Containing Food May Not Always Be as Risky for Celiac Patients as Diet Guides Suggest.

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PMID: 31560900

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

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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 titers were above 2 U/mL, for endomysial antibody. The blood samples had been collected at 2 time points (median interval of 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 timepoint, 15,398 were negative for tTGA and were 153 positive for tTGA (>4 U/mL). Based on medical records, 6 subjects received a diagnosis of celiac disease, for a cumulative incidence of celiac disease diagnosis of 0.06% (95% CI, 0.01%-0.11%). Forty-nine subjects with a negative result from the first serologic test for tTGA (0.32%) 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%) tested negative 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 was positive but second blood sample was negative for tTGA were older, had lower than average initial tTGA titers, and had a higher mean body mass index than adults whose blood samples were positive for tTGA at both time points or 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 in 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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PMID: 31560892


**Genetic and phenotypic characterization of indolent T-cell lymphoproliferative disorders of the gastrointestinal tract.**

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Abstract

Indolent T-cell lymphoproliferative disorders of the gastrointestinal tract are rare clonal T-cell diseases that more commonly occur in the intestines and have a protracted clinical course. Different immunophenotypic subsets have been described, but the molecular pathogenesis and cell of origin of these lymphocytic proliferations is poorly understood. Hence, we performed targeted next-generation sequencing and comprehensive immunophenotypic analysis of 10 indolent T-cell lymphoproliferative disorders of the gastrointestinal tract, which comprised CD4+ (n=4), CD8+ (n=4), CD4+/CD8+ (n=1) and CD4-/CD8- (n=1) cases. Genetic alterations, including recurrent mutations and novel rearrangements, were identified in 8/10 (80%) lymphoproliferative disorders. The CD4+, CD4+/CD8+, and CD4-/CD8- cases harbored frequent alterations of the JAK-STAT pathway genes (5/6, 82%); STAT3 mutations (n=3), SOCS1 deletion (n=1) and STAT3-JAK2 rearrangement (n=1), and 4/6 (67%) had concomitant mutations in epigenetic modifier genes (TET2, DNMT3A, KMT2D). Conversely, 2/4 (50%) of the CD8+ cases exhibited structural alterations involving the 3' untranslated region of the IL2 gene. Longitudinal genetic analysis revealed stable mutational profiles in 4/5 (80%) cases and acquisition of mutations in one case were a harbinger of disease transformation. The CD4+ and CD4+/CD8+ lymphoproliferative disorders displayed heterogeneous Th1 (T-bet+), Th2 (GATA3+) or hybrid Th1/Th2 (T-bet+/GATA3+) profiles, while the majority of CD8+ disorders and the CD4-/CD8-disease showed a type-2 polarized (GATA3+) effector T-cell (Tc2) phenotype. Additionally, CD103 expression was noted in 2/4 CD8+ cases. Our findings provide insights into the pathogenetic bases of indolent T-cell lymphoproliferative disorders of the gastrointestinal tract and confirm the heterogeneous nature of these diseases. Detection of shared and distinct genetic alterations of the JAK-STAT pathway in certain immunophenotypic subsets warrants further mechanistic studies to determine whether therapeutic targeting of this signaling cascade is efficacious for a proportion of patients with these recalcitrant diseases.

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PMID: 31558678


Association study identified biologically relevant receptor genes with synergistic functions in celiac disease.

Banerjee P1, Bhagavatula S1, Sood A2, Midha V3, Thelma BK4, Senapati S5.

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Abstract

Receptors are essential mediators of cellular physiology, which facilitate molecular and cellular cross-talk with the environment. Nearly 20% of the all known celiac disease (CD) genes are receptors by function. We hypothesized that novel biologically relevant susceptibility receptor genes act in synergy in CD pathogenesis. We attempted to identify novel receptor genes in CD by re-analyzing published Illumina Immunochip dense genotype data for a north Indian and a European (Dutch) cohort. North Indian dataset was screened for 269 known receptor genes. Association statistics for SNPs were considered with minor allele frequency >15% and association P ≤ 0.005 to attend desired study power. Identified markers were tested for cross-ethnic replication in a European CD dataset. Markers were analyzed in silico to explain their functional significance in CD. Six novel SNPs from MOG (rs29231, p = 1.21e-11), GABBR1 (rs3025643, p = 1.60e-7), OR2H2 (rs1233388, p = 0.0002), ABCF1 (rs9262119, p = 0.0005), ADRA1A (rs10102024, p = 0.003), and ACVR2A (rs7560426, p = 0.004) were identified in north Indians, of which three genes namely, GABBR1 (rs3025643, p = 5.38e-8), OR2H2 (rs1233388, p = 3.29e-5) and ABCF1 (rs9262119, p = 0.0002) were replicated in Dutch. Tissue specific functional annotation, potential epigenetic regulation, co-expression, protein-protein interaction and pathway enrichment analyses indicated differential expression and synergistic function of key genes that could alter cellular homeostasis, ubiquitination mediated phagosome pathway and cellular protein processing to contribute for CD. At present multiple therapeutic compounds/drugs are available targeting GABBR1 and ADRA1A, which could be tested for their effectiveness against CD in controlled drug trials.

The intestinal expansion of TCRγδ+ and disappearance of IL4+ T cells suggest their involvement in the evolution from potential to overt celiac disease.
Celiac disease (CD) is characterized by a spectrum of intestinal inflammatory lesions. Most patients have villous atrophy (overt-CD), whilst 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 analysed 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 IFNγ, 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. This article is protected by copyright. All rights reserved.
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


Set-Up of Bacterial Cellulose Production From the Genus Komagataeibacter and Its
Use in a Gluten-Free Bakery Product as a Case Study.

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Abstract

The use of bacterial cellulose (BC) in food systems is still limited due to production costs. Nine clones belonging to Komagataeibacter hansenii, Komagataeibacter nataicola, Komagataeibacter rhaeticus, Komagataeibacter swingsii, and Komagataeibacter xylinus species were screened for cellulose productivity in growth tests with five different carbon sources and three nitrogen sources. The water-holding and rehydration capacities of the purified cellulose were determined. The structure of the polymer was investigated through nuclear magnetic resonance (NMR) spectroscopy, attenuated total reflection Fourier transform infrared (ATR-FT-IR) spectroscopy and X-ray diffraction (XRD) analysis, and observed by scanning electron microscope (SEM). Natural mutants of K. rhaeticus LMG 22126ᵀ and K. swingsii LMG 22125ᵀ showed different productivity. The factors "bacterial isolate" and "nitrogen source" significantly affected the production of cellulose (p < 0.01) rather than the factor "carbon source" (p = 0.15). However, on average, the best conditions for increasing yield were found in medium containing glucose and peptone. Water-holding capacity (WHC) values ranged from 10.7 to 42.3 (g water/g cellulose) with significant differences among strains (p < 0.01), while the rehydration capacity varied from 4.2 to 9.3 (g water/g cellulose). A high crystallinity (64-80%) was detected in all samples with δα fractions corresponding to 67-93%. The ATR-FT-IR spectra and the XRD patterns confirmed the expected structure. BC made by GVP isolate of K. rhaeticus LMG 22126ᵀ, which was the strain with the highest yield, was added to a gluten-free bread formulation. Results obtained from measurements of technological parameters in dough leavening and baking trials were promising for implementation in potential novel foods.
The Connection between Celiac Disease and Hepatic Steatosis: High levels of Pigment Epithelium-Derived Factor.

Dikker O, Dağ H.
Free Article
PMID: 31550729

Transsplenic Arterial Radioembolization of Hepatic Metastases in a Patient with Celiac Artery Occlusion.

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PMID: 31547922

Evaluation of the behaviour of unripe banana flour with non-conventional flours in the production of gluten-free bread.

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Abstract

Gluten-free breads were developed by incorporating unripe banana flour in a blend of alternative flour/cassava starch, 45/50. A factorial design was applied to determine the simultaneous effect of percentage of unripe banana flour (2, 8, 15%) and the type of alternative flour (quinoa, oyster mushroom, yellow pea and lentil flour) on structural and colour properties of bread. Principal component analysis was used to evaluate the behaviour of the formulations from a comprehensive perspective. Three formulations, denoted as P8 (pea + 8% unripe banana flour), Q15 (quinoa + 15% unripe banana flour) and L15 (lentil + 15% unripe banana flour) exhibited the closest profiles to reference (wheat bread). Breads with oyster mushroom flour showed a profile significantly different from the rest of formulations. The interactions among the factors were significant for all studied properties and showed that the unripe banana flour fortification did not lead to proportional responses on the bread properties, but the behaviour of unripe banana flour in breadmaking relied on the percentage and the type of alternative flour used. The P8, Q15 and L15 exhibited high fibre content and carbohydrate content lower than the reference. In addition, P8 formulation can be classified as intermediate glycaemic index.

PMID: 31547687

Comparative Study on Gluten Protein Composition of Ancient (Einkorn, Emmer and Spelt) and Modern Wheat Species (Durum and Common Wheat).
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Abstract

The spectrophotometric Bradford assay was adapted for the analysis of gluten protein contents (gliadins and glutenins) of spelt, durum wheat, emmer and einkorn. The assay was applied to a set of 300 samples, including 15 cultivars each of common wheat, spelt, durum wheat, emmer and einkorn cultivated at four locations in Germany in the same year. The total protein content was equally influenced by location and wheat species, however, gliadin, glutenin and gluten contents were influenced more strongly by wheat species than location. Einkorn, emmer and spelt had higher protein and gluten contents than common wheat at all four locations. However, common wheat had higher glutenin contents than einkorn, emmer and spelt resulting in increasing ratios of gliadins to glutenins from common wheat (< 3.8) to spelt, emmer and einkorn (up to 12.1). With the knowledge that glutenin contents are suitable predictors for high baking volume, cultivars of einkorn, emmer and spelt with good predicted baking performance were identified. Finally, spelt, emmer and einkorn were found to have a higher nitrogen partial factor productivity than common and durum wheat making them promising crops for a more sustainable agriculture.

Comprehensive Detection of Isopeptides between Human Tissue Transglutaminase and Gluten Peptides.

Lexhaller B¹, Ludwig C², Scherf KA³,⁴.
Abstract

Celiac disease (CD) is a chronic inflammation of the small intestine triggered by the ingestion of gluten in genetically predisposed individuals. Tissue transglutaminase (TG2) is a key factor in CD pathogenesis, because it catalyzes both the deamidation of specific glutamine residues and the formation of covalent Nε-(γ-glutamyl)-lysine isopeptide crosslinks resulting in TG2-gluten peptide complexes. These complexes are thought to activate B cells causing the secretion of anti-TG2 autoantibodies that serve as diagnostic markers for CD, although their pathogenic role remains unclear. To gain more insight into the molecular structures of TG2-gluten peptide complexes, we used different proteomics software tools that enable the comprehensive identification of isopeptides. Thus, 34 different isopeptides involving 20 TG2 lysine residues were identified in a model system, only six of which were previously known. Additionally, 36 isopeptides of TG2-TG2 multimers were detected. Experiments with different TG2-gluten peptide molar ratios revealed the most preferred lysine residues involved in isopeptide crosslinking. Expanding the model system to three gluten peptides with more glutamine residues allowed the localization of the preferred glutamine crosslinking sites. These new insights into the structure of TG2-gluten peptide complexes may help clarify the role of extracellular TG2 in CD autoimmunity and in other inflammatory diseases.

Free Article
PMID: 31547042

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Lactic Acid Fermentation as a Pre-Treatment Process for Faba Bean Flour and Its Effect on Textural, Structural and Nutritional
Properties of Protein-Enriched Gluten-Free Faba Bean Breads.

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Abstract

Lactic acid fermentation could be used as a potential modification tool for faba bean flour to enable its incorporation in boosting the nutritional profile of gluten-free breads. Gluten-free breads made with fermented or unfermented faba bean flours were compared with commercial soy flour. The amounts of faba- and soy-bean flours were adjusted to obtain the same protein content in bread (16%). Both fermented and unfermented faba bean flour resulted in larger bread volume (2.1 mL/g and 2.4 mL/g, respectively) compared to bread made with soybean flour (1.5 mL/g). Breads made with unfermented and fermented faba flour had higher porosity (82% and 72%, respectively) than bread with soy flour (61%). The faba breads also were softer than the soy bread. Fermentation of faba flour prior to bread making significantly increased crumb hardness (584 vs. 817 g). Fermentation increased in vitro protein digestibility (72.3% vs. 64.8%). Essential Amino Acid and Biological Value indexes were significantly higher for breads containing fermented faba flour compared to breads made with unfermented faba and soy flour. The Protein Efficiency Ratio and Nutritional Index increased by fermentation from 33 to 36 and 1.6 to 2.7, respectively. Pre-fermentation of faba bean flour improved the nutritional properties of high-protein, gluten-free faba bread. A sensory panel indicated that fermentation did not affect the crumbliness, evenness of pore size and springiness of breadcrumb.

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A Cooking-Based Intervention Promotes Gluten-Free Diet Adherence and Quality of Life for Adults with Celiac Disease.

Wolf RL¹, Morawetz M², Lee AR³, Koch P², Contento IR², Zybert P², Green PH³, Lebwohl B⁴.

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PMID: 31546057

Linear growth of children with celiac disease after the first two years on gluten-free diet: a controlled study.


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Abstract

BACKGROUND:

Celiac disease (CD) is a lifelong disorder with gluten-induced manifestations in different organs especially growth. Gluten free diet (GFD) is required to achieve remission and prevent abnormal growth. Study reports on growth of children with celiac disease on long-term GFD are not consistent.

OBJECTIVE:

We evaluated the effect of GFD on growth of children with the classical form of CD (diagnosed by serology and small intestine mucosal biopsy) on long-term GFD (>2 years).

METHODS:

We studied growth parameters (weight gain/day, BMI and BMI-SDS, height growth velocity, Ht-SDS) and lab data in 30 prepubertal children, aged 7.4±2.6 years, with CD, who were on GFD since the age of 3.2±1.6 years of age (>2 years on GFD) for duration of 1 year. The anthropometric data of 30 randomly selected normal, age and sex matched, children were used as control. Lab investigations of CD children included complete blood count (CBC), renal and liver functions (aspartate transaminase - AST, alanine aminotransferase - ALT, and alkaline phosphatase- ALP, serum albumin, fasting blood glucose, vitamin D, and thyroid function and antibodies.

RESULTS:

The weight gain per day was on average or above, for age and sex, in 27 children and below average in 3. Two out of those 3 children had slow linear growth (decreased Ht-SDS by -0.56 and -0.1, over one year). BMI-SDS was normal in 26/30 patients (>1.5). BMI-SD changed from -0.36±1.1 to -0.33±1.1 during the year of treatment. BMI-SDS decreased in 9 children during the follow up period that was explained by their fast-linear growth (increased Ht-SDS) in seven of them. The Ht-SDS was <2 in four out of 30 children at the beginning of the study (2 years after being on GFD) and in 2 children after a year of follow-up (catch-up growth). Ht-SDS remained normal or increased in 28/30 children during the year of treatment (-0.38±1.2 to -0.22±1.1), with a positive trend: 0.15±0.4 SDS. Only one patient crossed down 1 Ht-SDS during the year of follow up, with low weight gain/day and decreased BMI-SDS that can be explained by poor compliance with GFD. Ht-SDS and BMI-SDS increased significantly in the CD group versus controls during the year of follow-up. All patients had normal serum albumin, liver enzyme and hemoglobin levels. 33.3% of patients had low serum ferritin level and 33.3% had a vitamin D deficiency.

CONCLUSIONS:

Most of our children with CD grew normally both in height and weight during GFD. Significant catch-up growth occurred in some of them after 2 years of being on GFD. Those with low BMI-SDS and/or Ht-SDS needed further management, including reinforcement on the importance of GFD and investigations on factors affecting growth pattern. Measuring weight gain /day appears to be a
sensitive indicator for monitoring growth in these children. Vitamin D and iron status should be monitored, and deficiencies corrected.

PMID: 31544803


**Translation, Cultural Adaptation, and Evaluation of a Brazilian Portuguese Questionnaire to Estimate the Self-Reported Prevalence of Gluten-Related Disorders and Adherence to Gluten-Free Diet.**

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Abstract

BACKGROUND:

A Spanish version of a questionnaire intended to estimate, at the population level, the prevalence rates of self-reported gluten-related disorders and adherence to gluten-free diets has been applied in four Latin American countries. However, idiom issues have hampered the questionnaire application in the Brazilian population. Thus, the aim of the present study was to carry out a translation, cultural adaptation, and evaluation of a Brazilian Portuguese questionnaire to estimate the self-reported prevalence of gluten-related disorders and adherence to gluten-free diets in a Brazilian population.

MATERIALS AND METHODS:

Two bilingual Portuguese-Spanish health professionals carried out the translation of the original Spanish version of the questionnaire to Brazilian-Portuguese. Matching between the two translations was evaluated using the WCopyFind.4.1.5 software. Words in conflict were conciliated, and the conciliated version of the Brazilian Portuguese instrument was evaluated to determine its clarity, comprehension, and consistency. A pilot study was carried out using an online platform.

RESULTS:

The two questionnaires translated into Brazilian Portuguese were highly matched (81.8%-84.1%). The questions of the conciliated questionnaire were clear and comprehensible with a high agreement among the evaluators (n = 64) (average Kendall's W score was 0.875). The participants did not suggest re-wording of questions. The answers to the questions were consistent after two applications of the questionnaire (Cohen's k = 0.869). The pilot online survey yielded low response rates (9.0%) highlighting the need for face-to-face interviews.

CONCLUSIONS:

The translation and evaluation of a Brazilian Portuguese questionnaire to estimate the self-reported prevalence rates of gluten-related disorders and adherence to gluten-free diets was carried out. The instrument is clear, comprehensible, and generates reproducible results in the target population. Further survey studies involving face-to-face interviews are warranted.
Impact of FODMAP Content Restrictions on the Quality of Diet for Patients with Celiac Disease on a Gluten-Free Diet.

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Abstract
Restrictive diets as gluten-free (GFD) or reduced in Fermentable, Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) are used to improve gastrointestinal (GI) symptoms in sensitive individuals. Aiming at comparing the nutritional quality and effects of a regular GFD regimen (R-GFD) and a low-FODMAP GFD (LF-GFD), in 46 celiac patients with persistent GI symptoms we conducted a randomized, double-blind intervention-controlled study. Patients received a personalized diet, either a strict GFD (n = 21) or a LF-GFD (n = 25) for 21 days. A validated food-frequency questionnaire before intervention and a 7-day weighed-food record after the intervention assessed the diets. Patients were 41.1 ± 10.1 years (mean ± SD), 94% women, with mean BMI 21.8 ± 2.9 kg/m². On day 21, patients on R-GFD still showed poor nutritional adequacy compared to dietary recommendations, with decreased energy intake, even though an improvement in carbohydrates and folates was observed (all p < 0.025). In both groups, intake of iron, calcium, vitamin D, sodium and folates did not meet daily recommendations. As expected, consumption of legumes and grains was lower and that of fruits was higher in the LF-GFD group than in the R-GFD one (all p < 0.05). The nutritional quality of both diets was not different. When restrictive diets are useful to improve the persistent GI symptoms, careful nutritional surveillance and counseling is mandatory.

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Open repair of proximal abdominal aneurysms analyzed according to the anatomy, clamping site and theoretical fenestrated endovascular design.

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Abstract

AIM:
To report our experience with hostile-necked, juxta-, para- and supra-renal aortic aneurysms (p-AAA) open repair (OR) and stratify the results according to the equivalent endovascular repair.

METHODS:

Data from all patients treated between 2010 and 2015 were prospectively collected and retrospectively reviewed. Pre-operative CT scans were analyzed in order to plan a hypothetical equivalent endovascular approach (2, 3 and 4 fenestrations). Post-operative results were recorded based on the cross-clamping level: supra-celiac (SC), supra-renal (SR), infra-renal (IR). Major adverse event (MAE) were defined as the presence of one of the following: all-cause mortality, bowel ischemia, myocardial infarction, paraplegia, respiratory failure, stroke and renal insufficiency.

RESULTS:

One hundred fifty-seven patients were treated; 93 met the CT scan criteria (slice thickness <1.5mm) and were included in the study. Thirty-day mortality was 2.2% (SC 7.4%; SR 0%; IR 0%) and MAE was 31.2% (SC 51.9%; SR 27.3%; IR 13.6%) in the entire cohort. After endovascular planning, 11 (11.8%) patients would have been treated with a 2-fen device, 20 3-fen (21.5%) and 62 4-fen (66.7%). Only 35.5% of the 4-fen patients received a SC aortic cross-clamping, while 43% SR and 21% IR. Renal/visceral perfusion was performed in 45 (72.5%) 4-fen patients, and in 20 (64%) 2/3-fen patients (p<.001); renal/visceral revascularization was needed in 23 (37.1%) 4-fen and in 5 (19.2%) 2/3 fen patients (p=.054).

CONCLUSIONS:

Implementing a FEVAR endovascular program could reduce those MAE, but it must be clear that FEVAR for juxtarenal disease may overcomplicate treatment and include manipulation of visceral vessels that would not need to be affected if infrarenal clamping is possible in OR, when it gives excellent results.

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PMID: 31536799

Lymphocytic gastritis in a patient with dyspepsia.

Collins K1, Rezuke WN1.
Lymphocytic gastritis (LG) is uncommon and presents histologically with a nonspecific inflammatory pattern. It is most often associated with celiac disease and Helicobacter pylori gastritis and is rarely associated with other conditions including lymphoma. LG is of clinical importance since its recognition should prompt further clinical evaluation for other disorders.

PMCID: PMC6745353 Free PMC Article
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Duval L\textsuperscript{1}, Habes S\textsuperscript{1,2}, Chatellier T\textsuperscript{3}, Guerzider P\textsuperscript{4}, Bossard C\textsuperscript{5}, Masliah C\textsuperscript{3}, Archambeaud I\textsuperscript{1}, Toucheff Y\textsuperscript{1,6}, Matysiak-Budnik T\textsuperscript{1,2,6}.

Abstract

Nivolumab may induce severe celiac-like enteropathy, that may appear very rapidly, after only two injections of nivolumab, and may be successfully treated with corticosteroids. This observation underlines the importance of histological analysis of duodenal biopsies and the necessity to rule out a real celiac disease in patients with nivolumab-induced diarrhea.
Simulated sandwich enzyme-linked immunosorbent assay for a cost-effective investigation of natural and engineered cellular signaling pathways.

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Abstract

The ability to separate, identify, and quantify proteins from complex mixtures are key foundational methods across biochemistry teaching and research. In particular, enzyme-linked immunosorbent assay (ELISA) is an important technique that is used to measure antigen concentrations in both industry and academia. There are four categories of ELISA, direct, indirect, competitive, and sandwich, each with their own applications. Sandwich ELISAs are used to determine antigen concentrations from complex mixtures of protein, such as a cell lysates, and are regularly used as medical diagnostics to diagnose illness and diseases ranging from hepatitis to celiac disease. One major problem with teaching the sandwich ELISA technique to students is the prohibitive cost due to the need to coat a 96-well plate with a capture antibody. One solution to this problem would be to significantly reduce the role of each student in the lab, but this does not adequately prepare students to perform the procedure in a research or industry lab. Instead, this laboratory exercise teaches students the procedural knowledge needed to perform a direct sandwich ELISA, but uses a simulated experience performed within a wet-lab environment. The presented scenario is the analysis of phosphorylated proteins within a synthetic signaling pathway, but because the lab uses simulated samples, it can be tailored to different topics and educational aims. The procedure is 10- to 26-fold less expensive per student to deploy than an authentic sandwich ELISA. Students in the
course report that the ELISA lab significantly strengthened the connection between theory and practice.


PMID: 31532903


Red patches on the tongue with white borders • history of geographic tongue • incompletely treated celiac disease • Dx?

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PMID: 31532821


Obesity is associated with significantly increased risk for diarrhoea after controlling for demographic, dietary and medical factors: a cross-sectional analysis of the 2009-2010 National Health and Nutrition Examination Survey.
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Abstract

BACKGROUND:

Obesity is associated with increased risk for various gastrointestinal and liver diseases. However, the relationship between obesity and abnormal bowel habits is poorly understood.

AIM:

To investigate the relationship between body mass index (BMI) and bowel habit, controlling for clinical, demographic and dietary factors, in a representative sample of the United States adult population.

METHODS: Data were extracted from the 2009-2010 National Health and Nutrition Examination Survey. Survey responses were included in this study if respondents completed the bowel health questionnaire (BHQ), were ≥20 years of age, and did not report history of IBD, celiac disease or colon cancer. BMI was divided into the following categories: underweight, normal weight, overweight, obese and severely obese. Stepwise logistic regression provided risk ratios of constipation and diarrhoea controlling for confounding factors (dietary, life-style, psychological and medical).

RESULTS:

A total of 5126 respondents completed the BHQ, had BMI data available, and met eligibility criteria. Of these, 70 (1.40%) were underweight, 1350 (26.34%) were normal weight, 1731 (33.77%) were overweight, 1097 (21.40%) were obese and 878 (17.13%) were severely obese. Up to 8.5% of obese and 11.5% of severely obese individuals had chronic diarrhoea, compared to 4.5% of normal weight individuals. Stepwise regression revealed that severe obesity was independently associated with increased risk of diarrhoea.

CONCLUSION:

Obesity is positively associated with chronic diarrhoea in a nationally representative US adult population after adjusting for several known confounding factors.

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PMID: 31532005

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Coeliac disease and HLA-conferred susceptibility to autoimmunity are associated with IgE sensitization in young children.

Mustonen N\textsuperscript{1,2}, Siljander H\textsuperscript{1,2}, Peet A\textsuperscript{3}, Tillmann V\textsuperscript{3}, Härkönen T\textsuperscript{1,2}, Niemelä O\textsuperscript{4}, Uibo R\textsuperscript{5}, Ilonen J\textsuperscript{6,7}, Knip M\textsuperscript{1,2,8,9}, DIABIMMUNE Study Group.

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PMID: 31531864

Similar articles


Gastrointestinal findings in 26 adults with common variable immunodeficiency: The fickle nature of the disease manifests in gastrointestinal biopsies.

Pehlivanoğlu B\textsuperscript{1}, Ardeniz Ö\textsuperscript{2}, Hassoy H\textsuperscript{3}, Sezak M\textsuperscript{4}, Özdemir H\textsuperscript{4}, Ünal NG\textsuperscript{4}, Onay H\textsuperscript{5}, Doğanavşargil B\textsuperscript{1}.
Abstract

BACKGROUND/AIMS:

The aim of the present study was to demonstrate the histopathological findings in gastrointestinal (GI) biopsies in adults with common variable immunodeficiency (CVID).

MATERIALS AND METHODS:

A total of 172 GI biopsies of 26 patients with CVID obtained over a 16-year period were reevaluated. Findings were analyzed using descriptive analyzes and χ² test.

RESULTS:

Female-to-male ratio was 1.36. The median age at diagnosis was 36±13.94 (16-72) years. Chronic esophagitis was noted in 3 patients. The absence of plasma cells in the stomach, duodenum, and colon was observed in 16, 14, and 9 patients, respectively. Divergent results for the presence of plasma cells in concurrent stomach and duodenum samples were found in 11 (44%) patients. Nodular lymphoid hyperplasia (NLH) was notable in the duodenum (56%). The mean number of eosinophils in one high-power field was significantly higher in duodenal biopsies with NLH (27.21 vs. 14.37, p=0.002). Active inflammation was more prominent in the colon (91%) than in the stomach (65%) and duodenum (60%). Helicobacter pylori infection was found in 57.6%, including a case with persistent infection by the coccoid form. Celiac-like villous blunting and increased intraepithelial lymphocytes were seen in 40% and 24%, respectively. In addition, 23% had giardiasis associated with acute duodenitis and duodenal NLH (p<0.05).

CONCLUSION:

CVID gastroenteropathy is a challenging entity, and due to the heterogeneity in the presence and distribution of plasma cells throughout the GI tract and diverse disease course, multiple concurrent biopsies may be needed for tissue diagnosis. Duodenal CVID may present with villous alterations and giardiasis, and NLH appears to be an important clue in the duodenum. The association between duodenal NLH and eosinophil infiltration deserves further investigation.

PMCID: PMC6750817 Free PMC Article
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Does celiac disease cause autoimmune sensorineural hearing loss?

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Abstract

BACKGROUND/AIMS:

The primary aim of this study is to identify whether an autoimmune sensorineural hearing loss is an extraintestinal neurological manifestation in adult CD patients. The secondary aim is to identify whether the duration of a gluten-free diet has an effect on the hearing levels of CD patients.

MATERIALS AND METHODS:

This prospective study consisting of 103 adult CD patients and 79 healthy controls between May 2012 and August 2018 at the University of Gaziantep Gastroenterology and Otorhinolaryngology Departments. CD patients were divided into two groups as remission or active, according to their gluten-free diet duration and serum levels of anti-t-TG. The control group was checked both for CD symptoms and anti-t-TG serum levels. Both participants performed a pure tone audiometry after detailed ear nose and throat examination.

RESULTS:

Only 4 of 103 CD patients showed sensorineural hearing loss. There was no statistically significant difference between hearing levels of the CD patients and the control group in both measurements of air and bone conductions. The hearing levels comparing the remission and active CD patients did not show any difference in air and bone conduction frequencies.

CONCLUSION:

In this study with a higher number of CD patients when compared with the previous studies, it has been shown that CD does not appear to cause autoimmune sensorineural hearing loss. In addition,
the status of the patients regarding the activeness or the remission of CD did not display a differ
between the CD patients in terms of hearing levels.

PMCID: PMC6750822  Free PMC Article
PMID: 31530521

The Role of Gastrointestinal-Related Fatty Acid-Binding Proteins as Biomarkers in Gastrointestinal Diseases.

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Abstract

The fatty acid-binding proteins play a major role in intracellular transportation of long-chain fatty acids. Nine fatty acid-binding proteins have been identified, with each having individual tissue-specific functions in addition to regulation of fatty acids. This review focuses on the three fatty acid-binding proteins found in the gastrointestinal tract and discusses their role as diagnostic or disease monitoring markers in neonatal necrotizing enterocolitis, acute mesenteric ischemia, celiac disease, and inflammatory bowel disease. Of these three fatty acid-binding proteins, intestinal fatty acid-binding protein is of the most interest due to its exclusive expression in the gastrointestinal tract. The elevation of intestinal fatty acid-binding protein in blood and urine reflects enterocyte damage, regardless of the underlying cause. The short half-life of intestinal fatty acid-binding protein also means it is a relatively sensitive marker. In contrast, there is currently less evidence to support liver fatty acid-binding protein and ileal bile acid-binding protein as sensitive biomarkers in these conditions. More extensive studies with specific endpoints are required to validate the roles of these fatty acid-binding proteins in gastrointestinal diseases.

PMID: 31529416

Similar articles
Development of an Index Score for Intestinal Inflammation-Associated Dysbiosis Using Real-World Stool Test Results.

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Abstract

BACKGROUND:

Gut microbiota play an important role in human health. However, the application of gut microbiome in regular clinical practice is limited by interindividual variations and complexity of test results.

HYPOTHESIS:

It is possible to address interindividual variation by using large data-based exploratory-pattern analysis.

METHODS:

The current study was conducted using a large data set (n = 173,221) of nonselective incoming patients' test results from a stool test. The data set included assays for the detection of 24 selected commensal microorganisms and multiple biomarkers in feces. Patients were grouped based on their levels of inflammation biomarkers such as calprotectin, eosinophil protein X, and IgA. Group mean values of biomarkers and commensal microbes were used in an exploratory-pattern analysis for association from which an index score for intestinal inflammation-associated dysbiosis (IAD) was developed. The IAD score was evaluated in one questionnaire-based study (n = 7263) and one
prospective case series study (n = 122) with patients of inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and celiac disease.

**RESULTS:**

We identified a microbial profile strongly associated with fecal inflammation biomarkers. Developed on the pattern of the microbial profile, the IAD score demonstrated a strong association with fecal inflammation biomarkers and was significantly different between patients with IBD and those with IBS or celiac disease.

**CONCLUSION:**

Using real-world data, we have developed a method to predict gut dysbiosis associated with different GI disease conditions. It may help clinicians simplify the process of interpreting gut microbial status and provide gut health assessment and treatment evaluation.

PMID: 31529411


**Investigation of Autoimmune Disease in Children with Chronic Spontaneous Urticaria.**

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**Abstract**

**INTRODUCTION:**

Chronic spontaneous urticaria (CSU) in childhood affects the quality of life of the patient and may be associated with other autoimmune diseases. The aim of this study was to investigate the association of autoimmune diseases with CSU in children.

**METHODS:**
In a 3-year period, from 2015 to 2018, forty-nine children were diagnosed with CSU and monitored in the Outpatient Pediatric Allergy Clinic of the University Hospital of Ioannina in Northwestern Greece. The comorbidity with other autoimmune diseases was investigated in this population by autoantibody evaluation.

RESULTS:

Of the 49 children with CSU, 1 had autoantibodies for celiac disease (CD), which was confirmed by duodenal biopsy via gastroscopy. Four children had high serum levels of anti-thyroid peroxidase antibodies but normal thyroid function. No other specific autoantibodies were detected.

CONCLUSION:

The prevalence of autoimmune diseases among our children with CSU was low. Nevertheless, we think it is important to test children with CSU for other autoimmune diseases. CD can be diagnosed in children with CSU even in the absence of other indicative signs.

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PMID: 31522183

Technical Considerations and Clinical Outcomes in the Endovascular Management of Celiac Arterial Aneurysms.

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Abstract

This retrospective case series details a single-center experience of 8 patients (mean age, 54.4 years) with celiac artery aneurysms (CAAs) who underwent 1 parent vessel-sparing, 5 partial parent vessel-sparing, and 2 non-parent vessel-sparing procedures. Technical success was achieved in 6 of 8 (75%)
patients. Both technical failures arose from type II endoleaks, which spontaneously resolved, resulting in clinical success of all cases. In-stent restenosis requiring reintervention complicated 3 of 5 (60%) partial parent vessel-sparing techniques, with 2 of 3 developing complete thrombosis. Two Society of Interventional Radiology grade C complications were recorded, none of which resulted in permanent sequelae. The endovascular management of CAAs is safe and amenable to various techniques.

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PMID: 31521454


Minerals and their bioavailability in relation to dietary fiber, phytates and tannins from gluten and gluten-free flakes.

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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
Celiac Disease: Extraintestinal Manifestations and Associated Conditions.

Therrien A, Kelly CP, Silvester JA.

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.

PMID: 31513026

E40, a novel microbial protease efficiently detoxifying gluten proteins, for the dietary management of gluten intolerance.

Abstract

Gluten proteins are the causative agent of Celiac Disease (CD), a life-long food intolerance characterized by an autoimmune enteropathy. Inadvertent gluten exposure is frequent even in celiac patients complying with a gluten-free diet, and the supplementation of exogenous gluten-digestive enzymes (glutenases) is indeed a promising approach to reduce the risk of dietary gluten boost. Here we describe Endopeptidase 40, a novel glutenase discovered as secreted protein from the soil actinomycete Actinoallomurus A8, and its recombinant active form produced by Streptomyces lividans TK24. E40 is resistant to pepsin and trypsin, and active in the acidic pH range 3 to 6. E40 efficiently degrades the most immunogenic 33-mer as well as the whole gliadin proteins, as demonstrated by SDS-PAGE, HPLC, LC-MS/MS, and ELISA. T lymphocytes from duodenal biopsies of celiac patients showed a strongly reduced or absent release of IFN-γ when exposed to gluten digested with E40. Data in gastrointestinal simulated conditions suggest that no toxic peptides are freed during gluten digestion by E40 into the stomach to enter the small intestine, thus counteracting the intestinal inflammatory cascade to occur in CD patients. E40 is proposed as a novel candidate in Oral Enzymatic Therapy for the dietary management of gluten toxicity.
Abstract

INTRODUCTION:

Median arcuate ligament syndrome has been known anatomically for approximately 100 years and results from a compression of the coeliac axis by fibrous attachment of the diaphragmatic crura. Owing to the rarity of the disease and limited available data, many aspects of treatment are controversial. Currently, laparoscopic decompression is considered by several authors as standard surgical procedure. We present an analysis of the clinical routine of MALS therapy.

METHODS:

We conducted a prospective observational trial in patients with MALS between March 2016 and August 2018, in which clinical symptoms, diagnostic evaluation, procedures with complication analysis and follow-up data were recorded.

RESULTS:

A total of 18 patients (12 female, 6 male) with MALS, aged between 15 and 65 years, were included in this study. All patients presented with long-standing abdominal pain. Preoperative Doppler ultrasonography showed a flow velocity of the coeliac artery averaging 289.9 cm/second in mid-position of the diaphragm, 285.9 cm/second in expiration and 199.0 cm/second in inspiration. All operated patients underwent laparoscopic decompression; two patients received an angiographic intervention. Postoperatively, a significant decrease of the flow velocity in mid-position of the diaphragm was detected ($P = 0.018$). At follow-up after 5.2 months, 50.0% of the patients were pain-free, 37.5% reported symptomatic relief and 12.5% showed evidence for a recurrence.

CONCLUSION:

MALS is challenging both diagnostically and therapeutically. Laparoscopy with release of the median arcuate ligament is an essential part of the therapy and can be confirmed by Doppler ultrasonography. Disease outcome is also influenced by several predictive factors.

PMID: 31508996

Similar articles
The Skin in Celiac Disease Patients: The Other Side of the Coin.

Abenavoli L¹, Dastoli S², Bennardo L³, Boccuto L⁴,⁵, Passante M⁶, Silvestri M⁷, Proietti I⁸, Potenza C⁹, Luzza F¹⁰, Nisticò SP¹¹.

Abstract

Celiac disease (CD) is an autoimmune enteropathy that primarily affects the small intestine and is characterized by atrophy of intestinal villi. The manifestations of the disease improve following a gluten-free diet (GFD). CD is associated with various extra-intestinal diseases. Several skin manifestations are described in CD patients. The present paper reviews all CD-associated skin diseases reported in the literature and tries to analyze the pathogenic mechanisms possibly involved in these associations. Different hypotheses have been proposed to explain the possible mechanisms involved in every association between CD and cutaneous manifestations. An abnormal small intestinal permeability seems to be implicated in various dermatological manifestations. However, most of the associations between CD and cutaneous diseases is based on case reports and case
series and a few controlled studies. To better assess the real involvement of the cutaneous district in CD patients, large multicentric controlled clinical trials are required.

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

Goel G¹, Daveson AJM², Ee HC³, Tye-Din JA⁴,⁵, Wang S¹, Szymczak E¹, Williams L¹, Dzuris JL¹, Neff KM¹, Truitt KE¹, Anderson RP¹.

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**Abstract**

**BACKGROUND:**

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 IL-2 after gluten support a central role for T-cell activation in the clinical reactions to gluten in coeliac disease.

**AIMS:**

Establish a quantitative hierarchy of serum cytokines and their relation to symptoms in patients with coeliac disease during gluten-mediated cytokine release reactions.

**METHODS:**

Sera were analyzed from coeliac disease patients on 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 hours after consuming ten grams vital wheat gluten flour.
cytokines were assessed. Confirmatory analyses were performed by high sensitivity electrochemiluminescence immunoassay. Cytokine elevations were correlated with symptoms.

RESULTS:

Cytokine release following gluten challenge in coeliac disease patients included significant elevations of IL-2, CCL20, IL-6, CXCL9, CXCL8, IFN-γ, IL-10, IL-22, IL-17A, TNF-α, CCL2, and amphiregulin. IL-2 and IL-17A were earliest to rise. Peak levels of cytokines were generally at four hours. 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 highest elevations.

CONCLUSIONS:

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 likely source. Cytokine release after gluten could aid in monitoring experimental treatments and support diagnosis.

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PMID: 31505020

Gluten-Degrading Proteases in Wheat Infected by Fusarium graminearum-Protease Identification and Effects on Gluten and Dough Properties.

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Abstract

Recently, we have observed a relationship between poor breadmaking quality and protease activities related to fungal infection. This study aims to identify potential gluten-degrading proteases

secreted by fungi and to analyze effects of these proteases on rheological properties of dough and gluten. *Fusarium graminearum*-infected grain was used as a model system. Zymography showed that serine-type proteases secreted by *F. graminearum* degrade gluten proteins. Zymography followed by liquid chromatography-mass spectrometry (MS)/MS analysis predicted one serine carboxypeptidase and seven serine endo-peptidases to be candidate fungal proteases involved in gluten degradation. Effects of fungal proteases on the time-dependent rheological properties of dough and gluten were analyzed by small amplitude oscillatory shear rheology and large deformation extensional rheology. Our results indicate that fungal proteases degrade gluten proteins not only in the grain itself, but also during dough preparation and resting. Our study gives new insights into fungal proteases and their potential role in weakening of gluten.

PMID: 31502841

**Microbiome as an Immunological Modifier.**

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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
Enriching LMW-GS alleles and strengthening gluten properties of common wheat through wide hybridization with wild emmer.

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Abstract

Two advanced lines (BAd7-209 and BAd7-213) with identical high-molecular-weight glutenin subunit composition were obtained via wide hybridization between low-gluten cultivar chuannong16 (CN16) and wild emmer D97 (D97). BAd7-209 was better than BAd7-213, and both of them were much better than CN16 in a dough quality test. We found that BAd7-209 had more abundant and higher expression levels of low-molecular-weight glutenin subunit (LMW-GS) proteins than those of BAd7-213. Twenty-nine novel LMW-GS genes at Glu-A3 locus were isolated from BAd7-209, BAd7-213 and their parents. We found that all 29 LMW-GS genes possessed the same primary structure shared by other known LMW-GSs. Twenty-seven genes encode LMW-m-type subunits, and two encode LMW-i-type subunits. BAd7-209 had a higher number of LMW-GS genes than BAd7-213, CN16, and D97. Two wild emmer genes MG574329 and MG574330 were present in the two advanced lines. Most of the LMW-m-type genes showed minor nucleotide variations between wide hybrids and their parents that could be induced through the wide hybridization process. Our results demonstrated that the wild emmer LMW-GS alleles could be feasibly transferred and integrated into common wheat background via wide hybridization and the potential value of the wild emmer LMW-GS alleles in breeding programs designed to improve wheat flour quality.
Conflict of interest statement

Conflict of interest
The authors declare that there are no conflicts of interest in the reported research.


Determinants of glycaemic outcome in the current practice of care for young people up to 21 years old with type 1 diabetes under real-life conditions.

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Abstract

AIM:
To determine factors influencing the success of treatment for type 1 diabetes, defined as HbA₁c < 58 mmol/mol (<7.5%), in a large paediatric cohort under real-life conditions.

METHODS:
This is a monocentric observational study analysing the determinants of glycaemic outcome (sex, age, comorbidities, sociodemographic factors, diabetes technology) in an entire cohort of people with diabetes aged up to 21 years. Glycaemic outcome was defined as an individual's median HbA₁c and the prevalence of acute complications over this period.

RESULTS:
Of 700 young people with type 1 diabetes [age 13.6 years (range: 1.4-20.9 years); diabetes duration 5.8 years (range: 0.1-18.3 years)], 63% were using an insulin pump and 32% any type of continuous glucose monitoring. Mean HbA₁c was 61 mmol/mol [95% confidence interval (CI) 60-62; 7.7%, 95% CI 7.5-7.8]. Some 63% of children aged < 12 years reached HbA₁c (58 mmol/mol (<7.5%) compared with 43% of older participants. The prevalence of severe hypoglycaemia was 2.41 events and that of diabetic ketoacidosis 1.4 events per 100 person-years. Neither type of insulin therapy nor use of continuous glucose monitoring, sex or comorbidity with coeliac disease or thyroiditis was...
significantly associated with glycaemic outcome. However, age, diabetes duration, having a father not born in Germany, psychiatric comorbidities and family structure were associated with HbA1c.

CONCLUSIONS:

Current technologies and a multidisciplinary team approach allow high numbers of children and adolescents to realize tight glycaemic control with a low prevalence of acute complications. However, age-related challenges, sociodemographic factors and psychological comorbidities are barriers to achieving best possible glycaemic outcome.

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PMID: 31498923


Swedish Inflammatory Bowel Disease Register (SWIBREG) - a nationwide quality register.

Ludvigsson JF1,2,3,4, Andersson M5, Bengtsson J6, Eberhardson M7, Fagerberg UE8,9,10, Grip O11, Halfvarson J12, Hjortswang H13, Jäghult S14, Karling P15, Nordenvall C16,17, Olsön O18,19,20, Olsson M21, Reijer M22,23, Strid H5, Myrelid P21,24.

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Abstract

**Background:** Inflammatory bowel disease (IBD) is a chronic, inflammatory relapsing disease with increasing incidence. IBD research and long-term follow-up of patients have, however, been hampered by lack of detailed data on disease phenotype, patient-reported outcome measures, Physician Global Assessment, disease activity, and hospital-administered drugs. **Aim:** To review the Swedish IBD quality register (SWIBREG). **Methods:** Review of SWIBREG including questionnaire data from users and patients. **Results:** SWIBREG was launched in 2005, and as of April 2019, contains 46,400 patients with IBD (Crohn’s disease: n = 15,705, ulcerative colitis: n = 21,540, IBD unclassified and other colitis (including e.g., microscopic colitis): n = 9155). Of these IBD patients, 7778 had been diagnosed in childhood (16.8%). Earlier research has shown that combining SWIBREG and the Swedish National Patient Register (NPR) yields a positive predictive value of 100% (95%CI = 95-100%) for having a diagnosis of IBD. Moreover, out of all patients in the NPR with a diagnosis of IBD plus either IBD-related surgery or immunomodulatory/biological treatment during the past 18 months, SWIBREG covers 59.0%. SWIBREG records not only information on conventional therapies but also on biological treatment, surgery, smoking, disease activity, patient-reported outcome measures (PROMs), and patient-experienced measures (PREMs). Data are presented through a graphical decision support system. **Conclusion:** SWIBREG benefits patients with IBD, and offers an ideal opportunity for healthcare personnel and researchers to examine disease phenotype and activity, PROMS/PREMs, and hospital-administered drugs in patients with IBD.

PMID: 31498717

**Similar articles**

Non-immunological biomarkers for assessment of villous abnormalities in patients with celiac disease.

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Abstract

BACKGROUND:

Demonstration of villous abnormalities is an essential component of diagnosis of celiac disease (CeD) which requires duodenal biopsies. There is a need for non-invasive biomarker(s) which can predict the presence of villous abnormalities.

METHODS:

Levels of plasma citrulline, plasma I-FABP, and serum Reg1α were estimated in treatment naïve patients with CeD and controls. The levels of these biomarkers and their cyclical pattern was validated in a predicted model of enteropathy. Optimum diagnostic cutoff values were derived and the results were further validated in a prospective validation cohort.

RESULTS:

While level of plasma citrulline was significantly lower, the levels of plasma I-FABP and serum Reg1α were significantly higher in patients with CeD (n=131) in comparison to healthy (n=216) and disease controls (n=133), and their levels reversed after a gluten-free diet. In the model of predicted enteropathy (n=70), a sequential decrease and then increase in the level of plasma citrulline was observed; such a sequential change was not observed with I-FABP and Reg1α. The diagnostic accuracy for prediction of presence of villous abnormality was 89% and 78% if citrulline level was <30μM/L and I-FABP levels was >1100pg/ml, respectively. The results were validated in a
prospective validation cohort (n=104) with a sensitivity and specificity of 79.5% and 83.1%, respectively for predicting villous abnormalities of modified Marsh grade >2 at calculated cut-offs values of citrulline and I-FABP.

**CONCLUSIONS:**

Plasma citrulline <30μM/L is the most consistent, highly reproducible non-invasive biomarker which can predict the presence of villous abnormality and has the potential for avoiding duodenal biopsies in 78% patients suspected to have CeD.

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PMID: 31498492

**Micropipette Tip-Based Immunoassay with Electrochemical Detection of Antitissue Transglutaminase to Diagnose Celiac Disease Using Staples and a Paper-Based Platform.**

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**Abstract**

In this work, 1-200 μL polypropylene micropipette tips were used as platforms for performing immunoassays after converting their inner surfaces on a capture zone for the analyte of interest. We have used a micropipette-tip immunoanalytical platform for the detection of antitissue transglutaminase (IgA), the main biomarker for celiac disease. Modification of the tip wall with poly-l-lysine allowed adsorption of tissue transglutaminase (tTG), which will capture later anti-tTG (IgA) antibodies developed in celiac-affected people. A sandwich-type format was followed, incubating simultaneously the analyte and the detection antibody, labeled with horseradish peroxidase. With this new application for an extremely common lab material, we can perform quantitative analysis by dispensing the liquid into a low-cost and miniaturized staple-based paper electrochemical platform. The analytical signal was the reduction of the enzymatically oxidized substrate, recorded chronoamperometrically (i-t curve). The intensity of the current obtained at a fixed time after the application of the cathodic potential followed a linear relationship with anti-tTG (IgA) concentration.
The relative standard deviation obtained for immunoassays performed in different tips indicates the adequate precision of this new methodology, which is very promising for decentralized analysis. Negative and positive controls produced results that were in accordance with those obtained with spectrophotometric enzyme linked-immunosorbent assays.

PMID: 31497948

Similar articles


**HLA-DQ Genotypes Relative Risks For Celiac Disease in Arabs: A Case-Control Study.**

Al-Hussaini A¹², Eltayeb-Elsheikh N³, Alharthi H³, Osman A³, Alshahrani M¹, Sandogji I¹, Alrashidi S³, Bashir MS⁴.

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Abstract

**OBJECTIVES:**

It is unknown what degree of risk is conferred by the celiac disease (CD)-predisposing HLA-DQ genotypes in the population of Saudi Arabia compared to Western countries. In this study, our objectives were to determine the CD-risk gradient associated with the HLA-DQ genotypes and compare HLA-DQ genotypes between symptomatic CD patients and screening-identified asymptomatic CD patients.

**METHODS:**

We enrolled three groups of subjects: group I, 46 CD children diagnosed consecutively over the past 10 years; group II, 192 healthy controls; group III, 54 CD children diagnosed during a mass screening of schoolchildren. All the participants were typed for the DQA1 and DQB1 genes by polymerase chain reaction sequence-specific oligonucleotide probes.

**RESULTS:**

Comparing the CD patients to controls, we identified 5 groups in the CD risk gradient: 1) very high risk associated with the DQ2.5/DQ8 genotype [odds ratio (OR) = 47]; 2) high risk (homozygous
DQ2.5, DQ2.5/DQ2.2; OR = 4-5); 3) intermediate risk (heterozygous DQ2.5, DQ8/DQ2.2; OR = 1.6); 4) low risk (DQ8, DQ2.2), and 5) very low risk (DQ2.x, DQX.5, DQX.x). Heterozygous DQ8 was more common in group III compared to group I (12.7% versus 2.2%); however, other genotypes were very similar between the two groups.

CONCLUSION:

The highest risk of developing CD in Saudi Arabia is associated with the DQ2.5/DQ8 genotype. This article is protected by copyright. All rights reserved.
Gut microbiome investigation in celiac disease: from methods to its pathogenetic role.

Sacchetti L\textsuperscript{1,2}, Nardelli C\textsuperscript{1,2,3}.

Abstract

Our body is inhabited by a variety of microbes (microbiota), mainly bacteria, that outnumber our own cells. Until recently, most of what we knew about the human microbiota was based on culture methods, whereas a large part of the microbiota is uncultivable, and consequently previous information was limited. The advent of culture-independent methods and, particularly, of next-generation sequencing (NGS) methodology, marked a turning point in studies of the microbiota in terms of its composition and of the genes encoded by these microbes (microbiome). The microbiome is influenced predominantly by environmental factors that cause a large inter-individual variability (~20%) being its heritability only 1.9%. The gut microbiome plays a relevant role in human physiology, and its alteration ("dysbiosis") has been linked to a variety of inflammatory gut diseases, including celiac disease (CD). CD is a chronic, immune-mediated disorder that is triggered by both genetic (mainly HLA-DQ2/DQ8 haplotypes) and environmental factors (gluten), but, in recent years,
a large body of experimental evidence suggested that the gut microbiome is an additional contributing factor to the pathogenesis of CD. In this review, we summarize the literature that has investigated the gut microbiome associated with CD, the methods and biological samples usually employed in CD microbiome investigations and the putative pathogenetic role of specific microbial alterations in CD. In conclusion, both gluten-microbe and host-microbe interactions drive the gluten-mediated immune response. However, it remains to be established whether the CD-associated dysbiosis is the consequence of the disease, a simple concomitant association or a concurring causative factor.

PMID: 31494628

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.

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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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PMID: 31494097

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](https://clinicaltrials.gov/ct2/show/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

**Similar articles**

**E L S E V I E R**

**FULL-TEXT ARTICLE**

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 (T₂) 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 T₂ 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 (T₁). The enrichments also altered the colour and cooking properties.

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PMID: 31493705


Sucrase-Isomaltase Deficiency as a Potential Masquerader in Irritable Bowel Syndrome.
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Abstract

BACKGROUND:

Patients with irritable bowel syndrome (IBS) frequently have meal-related symptoms and can recognize specific trigger foods. Lactose intolerance is a well-established carbohydrate malabsorption syndrome that causes symptoms similar to IBS such as bloating, abdominal pain, and diarrhea. However, the prevalence of sucrase-isomaltase deficiency (SID) in this population is poorly defined. SID is a condition in which sucrase-isomaltase, an enzyme produced by brush border of small intestine to metabolize sucrose, is deficient. Just like lactase deficiency, SID causes symptoms of maldigestion syndromes including abdominal pain, bloating, gas, and diarrhea. In this study, we aim to determine the prevalence of SID in patients with presumed IBS-D/M and characterize its clinical presentation.

METHODS:

Patients with a presumed diagnosis of IBS-D/M based on symptoms of abdominal pain, diarrhea, and/or bloating who underwent esophagogastroduodenoscopy with duodenal biopsies and testing for disaccharidase deficiency were included. Patients with a history of inflammatory bowel disease, gastrointestinal malignancy, or celiac disease were excluded. Odds ratio was calculated for abdominal pain, diarrhea, and bloating in patients with versus without SID.

RESULTS:

A total of 31 patients with clinical suspicion for IBS-D/M were included with a median age of 46 years (IQR 30.5-60) and with 61% females. SID was present in 35% of patients. Among patients with SID, 63.6% had diarrhea, 45.4% had abdominal pain, and 36.4% had bloating. Patients with SID were less likely than controls to have abdominal pain (OR 0.16, 95% CI 0.03-0.81, p = 0.04) although no difference in diarrhea or bloating was found. Only two patients with SID underwent sucrose breath testing of which only one had a positive result. However, this patient also had a positive glucose breath test and may have had small intestinal bacterial overgrowth as a confounder.
CONCLUSION:

SID was found in 35% of patients with presumed IBS-D/M and should be considered in the differential diagnosis of patients presenting with abdominal pain, diarrhea, or bloating. Further studies should better characterize the clinical features of SID and investigate the effects of dietary modification in this group of patients.

PMID: 31493040

Celiac Disease Autoimmunity and Emotional and Behavioral Problems in Childhood.

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Abstract

BACKGROUND AND OBJECTIVES:

Celiac disease (CeD) is associated with psychopathology in children. It is unknown whether this association is present in children with celiac disease autoimmunity (CDA) identified by screening. We examined the associations between subclinical CDA and emotional and behavioral problems in children without previous CeD diagnosis.

METHODS:

In a population-based cohort study of 3715 children (median age: 6 years), blood titers of tissue transglutaminase autoantibodies were analyzed. CDA was defined as a measurement of tissue transglutaminase autoantibodies ≥7 U/mL (n = 51). Children with previous CeD diagnosis or children on a gluten-free diet, were excluded. The Child Behavior Checklist (CBCL) was filled in by parents...
and was used to assess behavioral and emotional problems of children at a median age of 5.9 years. Multiple linear regression models were applied to evaluate the cross-sectional associations between CDA and CBCL scores. Sensitivity analyses were done in a subgroup of children who were seropositive carrying the HLA antigen risk alleles for CeD.

RESULTS:

In basic models, CDA was not associated with emotional and behavioral problems on the CBCL scales. After adjustment for confounders, CDA was significantly associated with anxiety problems ($\beta = .29; 95\%$ confidence interval 0.02 to 0.55; $P = .02$). After exclusion of children who did not carry the HLA-DQ2 and/or HLA-DQ8 risk alleles ($n = 4$), CDA was additionally associated with oppositional defiant problems ($\beta = .35; 95\%$ confidence interval 0.02 to 0.69). Associations were not explained by gastrointestinal complaints.

CONCLUSIONS:

Our results reveal that CDA, especially combined with the HLA-DQ2 and HLA-DQ8 risk alleles, is associated with anxiety problems and oppositional defiant problems. Further research should be used to establish whether behavioral problems are a reflection of subclinical CeD.

Conflict of interest statement

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Further Support for Psychological Symptoms in Pediatric Celiac Disease.

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Quantitative Analyses of Key Odorants and Their Precursors Reveal Differences in the Aroma of Gluten-Free Rice Bread and Wheat Bread.

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Abstract

Rice flour is one of the most important raw materials in gluten-free products. However, the aroma of gluten-free rice bread is less accepted by consumers than that of commercial wheat bread. Therefore, 18 selected aroma compounds were determined in rice and wheat breads by stable isotope dilution assays (SIDA) to elucidate differences in the sensory characteristics, concentrations, and odor activity values (OAVs). The OAVs of most aroma compounds varied greatly between a rice and a wheat bread. In particular, 2-aminoacetophenone with a grape-like, medicinal aroma was characteristic for rice bread crumb and crust, while maltol was only relevant in wheat bread crust. Ehrlich pathway products varied in their concentration between the bread crumbs and were correlated with the contents of their corresponding free amino acid precursors in the flours and doughs. The analysis of rice flour revealed that only a few aroma compounds were retained in the bread. Consequently, the bread making process has a high relevance in aroma compound formation. In a comparison of breads prepared from fresh and stored rice flour, hexanal was identified as an important indicator for aging in rice bread and flour.
Score Based Diagnostic Approach to Coeliac Disease and Bone Mineral Density.

Coşkun ME, Hizli Ş, Yavuz S, Temel MT.

Abstract

OBJECTIVES:

We aimed to test the performance of score based diagnostic approach (SBDA) proposed in European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) 2012 guideline and to search the usefulness of bone mineral density (BMD) measurement in SBDA as an objective finding in the diagnosis of coeliac disease (CD).

METHODS:

The SBDDA scores of 153 biopsy proven coeliac diagnosed children (derived from symptomatology, serology, HLA analysis, histologic) were calculated. Additionally, BMD Z scores of children obtained at diagnosis were also investigated. The diagnostic sensitivity of SBDA was tested in different scenarios in which low BMD was scored as a diagnostic finding.

RESULTS:

The mean age of children was 9.48±3.59 years and 54.2% of them were female. All patients got 4 or more which is the minimum score to diagnose CD in SBDA. The mean BMD Z scores of 142 out of 153 patients was -2.70±1.16 and 73.9% of them were below -2. Moreover, different diagnostic scenarios without histology were tested. In one of them, BMD and HLA were not included and the sensitivity was 85.2%. In another one, low BMD was scored as an equivalent of malabsorption, HLA was not included and sensitivity was found 97.2%. The sensitivities of these scenarios were statistically different (p=0,001) CONCLUSION: In the absence of both HLA and histology, accepting low BMD as an equivalent of malabsorption has drastically increased the diagnostic sensitivity while the offered SBDA has showed a limited success. Therefore, BMD might be useful where HLA and biopsy are not available. This article is protected by copyright. All rights reserved.
Anesthesia Assistance in Screening Colonoscopy and Adenoma Detection Rate Among Trainees.


Abstract

BACKGROUND AND AIMS:

The use of anesthesia assistance (AA) for screening colonoscopy has been increasing substantially over the past decade, raising concerns about procedure safety and cost without demonstrating a proven improvement in overall quality indicators such as adenoma detection rate (ADR). The effect of AA on ADR has not been extensively studied among trainees learning colonoscopy. We aimed to determine whether type of sedation used during screening colonoscopy affects trainee ADR.

METHODS:

Using the electronic endoscopy databases of two hospitals in our medical center, we identified colonoscopies performed by 15 trainees from 2014 through 2018, including all screening examinations in which the cecum was reached. Multivariable logistic regression was used to determine factors associated with adenoma detection.
RESULTS:

We identified 1420 unique patients who underwent screening colonoscopy by a trainee meeting the inclusion criteria. Of these, 459 (32.3%) were performed with AA. Overall trainee ADR was 39.6%, with ADR increasing from 35.0% in year one of training to 42.8% in year three (p = 0.047). ADR for cases with AA was 37.9%, while ADR for conscious sedation cases was 32.0% (p = 0.374). Despite this 5.9% absolute difference, the use of AA was not associated with finding an adenoma on multivariable analysis when controlling for patient age, sex, smoking status, body mass index, trainee year of training, mean withdrawal time, supervising attending ADR, and bowel preparation quality (OR 0.85; 95% CI 0.67-1.09).

CONCLUSIONS:

Despite providing the ability to more consistently sedate patients, the use of AA did not affect trainee ADR. These results on trainee ADR and sedation type suggest that the overall lack of association between AA use and ADR is applicable to the trainee setting.

PMID: 31485995

Autoimmune Thyroid Diseases in Children and Adolescents with Maturity Onset Diabetes of the Young Type 2.

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Abstract

BACKGROUND/AIM:

The relationship between type 1 diabetes mellitus (T1DM) and autoimmune thyropathies is well known and has been described in the literature. Based on present knowledge, the relationship between thyropathies and other forms of diabetes, such as monogenic diabetes, has not been investigated. The aim of our study was to assess the prevalence of autoimmune thyroid diseases (ATD) in children and adolescents with maturity onset diabetes of the young type 2 (MODY2) in comparison with patients with T1DM and a control group.

PATIENTS AND METHODS:

We examined 23 children and adolescents with MODY2 (11 F/12 M; 13.5 ± 5.3 years) and 166 patients with T1DM (80 F/86 M; 14.0 ± 4.7 years). The control group consisted of 62 age-matched healthy subjects (34 F/28 M). ATD diagnosis was based on the finding of one or more positive thyroid autoantibodies and characteristic thyroid ultrasound lacking homogeneity, with a hypogenic or mixed echo pattern.

RESULTS:

ATD was diagnosed in 15 (10.5%; 9 F/6 M) patients with T1DM, in 4 with MODY2 (17.4%; 4 F), and in 1 (1.6%) control. A significantly higher ATD prevalence was detected in T1DM and MODY2 compared to the control subjects (p = 0.02), without differences between T1DM and MODY2 (p = 0.26). There were no gender differences noted in T1DM (p = 0.42); on the contrary, in MODY2 a higher prevalence was noted in females (p = 0.04). Celiac disease and a positive family history of ATD were not detected in subjects with MODY2.

CONCLUSION:

Our study showed an increased prevalence of ATD in patients with MODY2. Therefore, a careful follow-up of all children with MODY2 is recommended in order to assess the presence of thyroid disorders.

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PMID: 31484194

Similar articles

Screening of monogenic autoimmune diabetes among children with type 1 diabetes and multiple autoimmune diseases: is it worth doing?

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Abstract

Background Paediatric type 1 diabetes (T1D) and rare syndromes of monogenic multi-organ autoimmunity share basic features such as full insulin dependency and the presence of circulating beta-cell autoantibodies. However, the aetiopathogenesis, natural course and treatment of these conditions differ; therefore, monogenic multi-organ autoimmunity requires early recognition. We aimed to search for these monogenic conditions among a large cohort of children with T1D.

Methods Of 519 children with T1D followed-up in a single centre, 18 had multiple additional autoimmune conditions - either autoimmune thyroid disease (AITD) and coeliac disease (CD) or at least one additional organ-specific autoimmune condition in addition to AITD or CD. These 18 children were tested by direct Sanger sequencing (four patients with a suggestive phenotype of immune dysregulation, polyendocrinopathy, enteropathy, X-linked [IPEX] or signal transducer and activator of transcription 3 [STAT3]- and cytotoxic T-lymphocyte protein 4 [CTLA4]-associated syndromes) or by whole-exome sequencing (WES) focused on autoimmune regulator (AIRE), forkhead box protein 3 (FOXP3), CTLA4, STAT3, signal transducer and activator of transcription 1 (STAT1), lipopolysaccharide-responsive and beige-like anchor protein (LRBA) and interleukin-2 receptor subunit α (IL2RA) genes. In addition, we assessed their T1D genetic risk score (T1D-GRS).

Results We identified novel variants in FOXP3, STAT3 and CTLA4 in four cases. All patients had a severe phenotype suggestive of a single gene defect. No variants were identified in the remaining 14 patients. T1D-GRS varied among the entire cohort; four patients had scores below the 25th centile including two genetically confirmed cases. Conclusions A monogenic cause of autoimmune diabetes was confirmed only in four patients. Genetic screening for monogenic autoimmunity in children with a milder phenotype and a combination of AITD and CD is unlikely to identify a monogenic cause. In addition, the T1D-GRS varied among individual T1D patients.

PMID: 31483759

Similar articles
**Elevated serum interleukin-2 after gluten correlates with symptoms and is a potential diagnostic biomarker for coeliac disease.**

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Abstract

**BACKGROUND:**

Coeliac disease patients on a gluten-free diet experience reactions to gluten, but these are not well characterised or understood. Systemic cytokine release was recently linked to reactivation of gluten immunity in coeliac disease.

**AIM:**

To define the nature and time-course of symptoms and interleukin-2 changes specific for coeliac disease patients.

**METHODS:**

25 coeliac disease patients on a gluten-free diet and 25 healthy volunteers consumed a standardised 6 gram gluten challenge. Coeliac Disease Patient-Reported Outcome survey and global digestive symptom assessment were completed hourly up to 6 hours after gluten. Adverse events over 48 hours were recorded. Serum interleukin-2 was measured at baseline, and 2, 4 and 6 hours.
RESULTS:

Serum interleukin-2 was always undetectable in healthy controls, whereas it was undetectable at baseline and elevated >0.5 pg/ml at 4 hours in 92% of coeliac disease patients. All patient-reported outcome severity scores increased significantly after gluten in coeliac disease patients (P < .001 Wilcoxon signed rank test), but not in controls. Symptoms began after 1 hour, and peaked in the third. Nausea and vomiting characterised severe reactions, but mild reactions were limited to headache and tiredness. Peak interleukin-2 correlated with symptom severity, particularly for nausea and vomiting.

CONCLUSIONS:

Serum interleukin-2 elevations correlate with timing and severity of symptoms after gluten in coeliac disease. Standardised bolus gluten food challenge and interleukin-2 assessment could provide a valuable clinical test to monitor and diagnose coeliac disease in patients established on a gluten-free diet.

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PMID: 31483515

Lactobacillus-fermented sourdoughs improve the quality of gluten-free bread made from pearl millet flour.

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Abstract

The study investigated the effect of sourdough made from combinations of four Lactobacillus spp. on the physicochemical properties, consumer acceptability, and shelf life of bread made from pearl
millet flour. Fermentation based on both single and multiple species reduced the pH of the dough and increased its titratable acidity and \( \text{H}_2\text{O}_2 \) content. The addition of sourdough increased the elasticity and reduced the stiffness of the pearl millet dough. Sourdough fermented with \( L. \text{brevis} \) had the greatest effect on loaf height, specific volume, porosity, and moisture content. During storage, the moisture content of the bread crumb decreased, but that of their crust increased. Sourdough-based loaves retained their moisture better than conventional loaves and the sourdough suppressed the development of mold for a longer period. An organoleptic assessment showed that the sourdough-based bread was more palatable than either conventional or chemically acidified ones. The tissue softness, chewiness, and flavor of the pearl millet bread decreased during storage. The use of sourdough based on either \( L. \text{brevis}, L. \text{paralimentarius}, \) or \( L. \text{brevis} + L. \text{paralimentarius} \) is recommended to produce high-quality pearl millet-based bread.

PMCID: PMC6706481 [Available on 2020-09-01]
PMID: 31477977

Conflict of interest statement

Conflict of interest The authors declare that they have no conflict of interest.

High prevalence of autoimmune diseases in women with endometriosis: a case-control study.

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Abstract

The immune system seems to be involved in the pathogenesis of endometriosis. Peritoneal chronic inflammation is present and natural killer cells and macrophages abnormalities have been reported in women with the disease. Moreover, a higher production of serum autoantibodies has been found, which could be related to various factors; some still need to be clarified. The correlation between endometriosis and autoimmune diseases is still unclear with few and conflicting available data. The aim of this study was to evaluate the prevalence of autoimmune diseases, as conditions with a possible common pathogenetic factor, in women affected by endometriosis, in order to address future research on its pathogenesis. This retrospective case-control study includes one hundred and forty-eight women with endometriosis and 150 controls. All women were aged between 18 and 45. Informed consent was obtained from all participants of the study. Considered

Conflict of interest The authors declare that they have no conflict of interest.

autoimmune diseases include systemic lupus erythematosus (SLE), celiac disease (CD), inflammatory bowel disease (IBD), and autoimmune thyroiditis. Statistical comparison of patients and control group was performed by means of chi-square test or Fisher's exact test as appropriate. Statistical comparison of parametric variable (age) among the groups was performed by t-test for unpaired data. Age was expressed as mean. A value of .05 or less was considered as significant. In the case group, five patients were affected by IBD, while the disease was not observed in the control group ($p = .07$). SLE was found in eight patients in the case group, while only one was found in the control group ($p = .01$). Fifteen women in the case group were affected by CD, while the disease was present only in one woman in the control group ($p < .0001$). A significant correlation was also found between endometriosis and autoimmune thyroiditis: 80 patients with endometriosis had thyroid diseases versus 14 patients in the control group ($p < .0001$). Our study reports an association between endometriosis and autoimmune disorders, showing a higher prevalence of autoimmune diseases in women affected by endometriosis. These results support a possible autoimmune pathogenesis of endometriosis.

PMID: 31476950

Similar articles


**Clinical utility of fecal calprotectin: potential applications beyond inflammatory bowel disease for the primary care physician.**

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Abstract

Fecal calprotectin (FC) is an inflammatory marker released mainly from gastrointestinal granulocytes measured in stool samples. FC is noninvasive, economical, simple, and acceptable for patients. Levels of FC have proven reliable for intestinal inflammation, with good clinical sensitivity, and are useful in screening and monitoring inflammatory bowel disease (IBD), as well as in the differential diagnosis between IBD and irritable bowel syndrome (IBS). Given its advantages, FC represents an attractive biomarker that could be utilized in various gastrointestinal (GI) diseases apart from IBD,
and is currently being studied extensively by many research groups with significant amounts of data emerging. In this current review we aim to provide an outline of the utility of FC in distinguishing between IBS and IBD, as well as an up-to-date summary of the available clinical experience concerning FC in various common conditions of the GI tract commonly encountered by gastroenterology practitioners, such as IBS, microscopic colitis, acute gastroenteritis, *Clostridium difficile* infection, colorectal cancer, diverticular disease, coeliac disease, and other GI conditions.

**Conflict of interest statement**

Conflict of Interest: None


**Iatrogenic celiac and hepatic artery dissections during intra-arterial regional tumor therapies: a 16-year retrospective review.**

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**Abstract**

**PURPOSE:**

To identify the incidence and outcomes of iatrogenic celiac and hepatic artery dissections during transarterial therapies, including bland embolization, chemoembolization, radioembolization (TARE), and pre-TARE scintigraphic mapping.
METHODS:

The institution's quality assessment database, electronic medical record, and picture archiving and communication system were reviewed to identify all patients who underwent transarterial locoregional therapy from 1/2001 to 7/2017 and to determine the incidence of iatrogenic dissection, to assess patency of the arteries after dissection, and to assess the ability to complete therapy.

RESULTS:

2253 patients underwent 3776 transarterial hepatic oncology procedures. Among 3776 procedures, 40 (1.1%) were associated with dissection of the visceral vasculature, affecting 39 patients (1.7%). The incidence of flow-limiting dissections was 0.3% (13/3776) and non-flow-limiting dissections was 0.7% (27/3776). After dissection, 68% (27/40) of treatments were completed the same day. Among the 13 aborted treatments, 8 (62%) were completed on a subsequent encounter. Follow-up imaging was obtained in 26 of 40 cases at median time of 63 days. Complete resolution of the dissection was seen in 15/26 cases (58%), near complete resolution (< 30% luminal narrowing) in 3/26 (12%), unchanged appearance of a non-flow-limiting dissection in 4/26 (15%), progressive luminal narrowing in 3/26 (12%), and complete occlusion in 1/26 (4%).

CONCLUSION:

Iatrogenic dissections of visceral arteries rarely occur during tumor embolization procedures. 35/39 (90%) of patients underwent successful treatment despite the dissection.

PMID: 31471705


**Intestinal Permeability and IgA Provoke Immune Vasculitis Linked to Cardiovascular Inflammation.**

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Abstract

Recent experimental data and clinical, genetic, and transcriptome evidence from patients converge to suggest a key role of interleukin-1β (IL-1β) in the pathogenesis of Kawasaki disease (KD). However, the molecular mechanisms involved in the development of cardiovascular lesions during KD vasculitis are still unknown. Here, we investigated intestinal barrier function in KD vasculitis and observed evidence of intestinal permeability and elevated circulating secretory immunoglobulin A (sIgA) in KD patients, as well as elevated sIgA and IgA deposition in vascular tissues in a mouse model of KD vasculitis. Targeting intestinal permeability corrected gut permeability, prevented IgA deposition and ameliorated cardiovascular pathology in the mouse model. Using genetic and pharmacologic inhibition of IL-1β signaling, we demonstrate that IL-1β lies upstream of disrupted intestinal barrier function, subsequent IgA vasculitis development, and cardiac inflammation. Targeting mucosal barrier dysfunction and the IL-1β pathway may also be applicable to other IgA-related diseases, including IgA vasculitis and IgA nephropathy.
**High-throughput multiplexed autoantibody detection to screen type 1 diabetes and multiple autoimmune diseases simultaneously.**

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Abstract

**BACKGROUND:**

Islet autoantibodies (IAbs) are the most reliable biomarkers to assess risk of progression to clinical type 1 diabetes (T1D). There are four major biochemically defined IAbs currently used in clinical trials that are equally important for disease prediction. The current screening methods use a radio-binding assay (RBA) for single IAb measurement, which are laborious and inefficient for large-scale screening. More importantly, up to 40% of patients with T1D have other autoimmune conditions that can be identified through relevant autoantibody testing. Thus, there is a need to screen for T1D and other autoimmune diseases simultaneously.

**METHODS:**

Based on our well-established electrochemiluminescence (ECL) assay platform, we developed a multiplexed ECL assay that combines 7 individual autoantibody assays together in one single well to simultaneously screen T1D, and three other autoimmune diseases including celiac disease, autoimmune thyroid disease and autoimmune poly-glandular syndrome-1 (APS-1). The 7-Plex ECL assay was extensively validated against single antibody measurements including a standard RBA and single ECL assay.
FINDINGS:

The 7-Plex ECL assay was well correlated to each single ECL autoantibody assay and each RBA.

INTERPRETATION:

The multiplexed ECL assay provides high sensitivity and disease specificity, along with high throughput and a low cost for large-scale screenings of T1D and other relevant autoimmune diseases in the general population. FUND: JDRF grants 2-SRA-2015-51-Q-R, 2-SRA-2018-533-S-B, NIH grants DK32083 and DK32493. NSFC grants 81770777.

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High Prevalence of Celiac Disease Among Screened First-Degree Relatives.

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Abstract

OBJECTIVE:

To investigate the prevalence of first-degree relatives (FDRs) with celiac disease detected at screening and diagnostic significance of anti-tissue transglutaminase (anti-TTG).

PATIENTS AND METHODS:
We performed a retrospective cohort study of 104 patients with a diagnosis of celiac disease and their FDRs, collecting data from electronic records of Mayo Clinic and celiac disease registry from December 20, 1983, to May 22, 2017. We collected demographics, presenting symptoms, indication for testing, family history, number of other family members screened, biopsy reports, and results of serologic tests.

RESULTS:

Of 477 FDRs identified, 360 were screened (mean screening rate per family, 79%±25%) and 160 FDRs (44.4%) were diagnosed with celiac disease, at a mean age 31.9±21.6 years (62% female). All diagnosed FDRs had positive anti-TTG titers. Clinical features were documented in 148 diagnosed FDRs, of those 9 (6%) had classic, 97 (66%) had non-classic symptoms, and 42 (28%) had no reported symptoms. Histology reports were available from 155 FDRs: 12 (8%) had Marsh 1, 77 (50%) had Marsh 3a, and 66 (43%) had Marsh 3b. A level of anti-TTG greater than or equal to 2.75 of the upper limit of normal identified FDRs with villous atrophy with 87% sensitivity, 82% specificity, and a positive predictive value of 95%.

CONCLUSION:

In a retrospective cohort study of patients diagnosed with celiac disease, we found a high prevalence of celiac disease among screened FDRs. High anti-TTG titers associated with villous atrophy on small bowel biopsies, irrespective of symptoms.

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PMID: 31447136


**Relationship between motivation, adherence to diet, anxiety symptoms, depression symptoms and quality of life in individuals with celiac disease.**

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Abstract

OBJECTIVE:

Celiac disease is an immuno-mediated pathogenesis disease characterised by a malabsorption of nutrients that causes partial or total atrophy of intestinal villi and the alteration of the absorbing epithelium. Several studies have demonstrated the presence of anxiety and depression symptoms and poor quality of life in people with celiac disease and emphasised the importance of diet in modulating these effects. However, few studies have investigated the role of motivation and the relationship it has with these factors. The purpose of this study was to fill this gap and investigate the relationship between motivation, diet adherence, anxiety symptoms, depression symptoms and physical functioning in people with celiac disease.

METHODS:

Questionnaires were administered to 433 people with celiac disease aged between 18 and 79 years (M = 32.73, DS = 11.54) to measure anxiety symptoms (State-Trait Anxiety Inventory-Y2), depression symptoms (Beck Depression Inventory), physical functioning (Scale of Physical Functioning), adherence to diet (Celiac Dietary Adherence Test) and motivation (Treatment Self-Regulation Questionnaire).

RESULTS:

We used Structural Equation Modelling to examine the relationships of variables. Results revealed a direct relationship between motivation and diet adherence, anxiety symptoms, depression symptoms and physical functioning. They also illustrated the role played by diet adherence in mediating the relationship between motivation and anxiety symptoms, depression symptoms and physical functioning.

CONCLUSION:

The results highlight the vital role played by motivation in people; indeed, analysis showed that motivation correlated to adherence to diet. It is therefore necessary to take this factor into account in the treatment of individuals with celiac disease.
Online resources for celiac disease.


Vascular anomalies of the celiac trunk and implications in treatment of HCC with TACE. Description of a case and review of the literature.

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Abstract

Knowledge of the vascular anatomy of the upper abdomen is important in the daily practice of surgeons specialized in the hepatobiliary and pancreatic area, and for general surgeons and radiologists, mainly those involved in interventional radiology. Since anatomical variants of the celiac axis and hepatic arteries are common, an accurate description of vascularization is required before procedures to avoid iatrogenic vascular changes. We reported a case of a young male patient with HBV related cirrhosis, who came to our institution for the treatment of 2 HCC nodules. The preprocedural contrast-enhanced CT examination showed combined variations of celiac trunk, hepatic arteries, gastroduodenal artery, and right inferior phrenic artery. The careful pre- and intraprocedural evaluation of vascularization allowed us to perform transarterial chemoembolization of the 2 nodules without complications. The incidence and developmental and clinical significance of this variation is discussed with a detailed review of the literature. Knowledge
Randomised clinical trial: a placebo-controlled study of subcutaneous or intradermal NEXVAX2, an investigational immunomodulatory peptide therapy for coeliac disease.

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Abstract

BACKGROUND:

Nexvax2 contains three gluten-derived peptides, intended to tolerize coeliac disease patients to gluten. Sequences cover six epitopes that trigger immune activation in human leucocyte antigen-DQ2.5-positive patients, most notably after an initial dose. Patients experience gastrointestinal symptoms with increases in serum interleukin-2. Consistent with Nexvax2’s induction of non-responsiveness, reactivity disappears after repeated doses, or is avoided with gradual dose escalation. Early clinical trials used intradermal dosing, but pharmacokinetics and rapid onset of effect suggest that subcutaneous delivery may also be effective.

AIMS:
To document the relative bioavailability of Nevax2 peptides after subcutaneous and intradermal dosing, and the tolerability and ability of subcutaneous dosing to induce non-responsiveness to Nexvax2 peptides.

METHODS:

A randomised, double-blind, placebo-controlled study was conducted to assess plasma pharmacokinetics after subcutaneous and intradermal Nexvax2 dosing in HLA DQ2.5-positive patients, who had symptoms after an oral gluten challenge. Randomisation was to semi-weekly Nexvax2 (n = 12) or placebo (n = 2) injections, over a 5-week subcutaneous dose escalation and 2-week maintenance period, the latter with four doses of 900 µg, two subcutaneous and two intradermal. Post-dose circulating peptide and interleukin-2 levels were assessed. Investigators recorded adverse events experienced by patients.

RESULTS:

Subcutaneous dosing resulted in slightly greater exposure. Interleukin-2 responses were seen with the gluten challenge but not after subcutaneous or intradermal dosing of 900 µg. Adverse events were generally mild and self-limited.

CONCLUSIONS:

Subcutaneous and intradermal dosing of Nexvax2 yield similar bioavailability of constituent peptides; subcutaneous dose escalation avoids an immune response to dominant gluten epitopes.

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PMID: 31407810

Jejunoileal fold pattern reversal in celiac disease.

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PMID: 31399788

**Coeliac disease: a protracted course to diagnosis.**

**W N.**
PMID: 31387734


**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 T2 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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Clustering of immune-mediated diseases in sarcoidosis.

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Abstract

PURPOSE OF REVIEW:

Sarcoidosis is an immune-mediated disease of unknown cause. Immune-mediated diseases appear to cluster in patients and in families. We review what is known on this topic for sarcoidosis, and what factors may underlie disease clustering.

RECENT FINDINGS:

In populations of patients with sarcoidosis, relative risk estimates of Sjögren's syndrome, systemic lupus erythematosus, autoimmune hepatitis, ankylosing spondylitis, multiple sclerosis (MS), celiac disease, autoimmune thyroid disease, and ulcerative colitis, varied between 2.1 and 11.6. In relatives of patients with sarcoidosis, relative risk estimates varied between 1.3 and 5.8 for sarcoidosis, MS, celiac disease, type 1 diabetes, Graves' disease, rheumatoid arthritis, Crohn's
disease, and ulcerative colitis. Shared risk loci in key immunological pathways provide evidence for a contribution to development of multiple diseases. Identical changes in the immune status, epigenetic alterations, and environmental triggers have been detected in several diseases, and drug-induced disease is likely responsible for a small portion of co-occurring disease.

**SUMMARY:**

Clustering of sarcoidosis and other immune-mediated diseases in patients and in their relatives occurs for sarcoidosis, MS, celiac disease, Graves' disease, and ulcerative colitis. Further research is needed to substantiate causal links and risk estimates in patients and their relatives.

PMID: 31365389

**A Gluten-Free Diet: The Express Route to Fructan Reduction.**

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PMID: 31365349

**Imaging Obtained Up To 12 Months Preoperatively Is Adequate for Planning Fenestrated/Branched Endovascular Aortic Aneurysm Repair.**

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Abstract

OBJECTIVES:

Patients referred for fenestrated/branched endovascular aortic repair (F/BEVAR) often present with a previous computed tomography angiogram (CTA), but it is unknown how recent the CTA must be to ensure accurate F/BEVAR planning. We sought to determine whether anatomic planning parameters change significantly between a CTA used for F/BEVAR planning and a CTA obtained 6 to 12 months prior.

METHODS:

Two blinded observers reviewed preoperative CTAs from 21 patients who underwent F/BEVAR. Each patient had a "recent" scan obtained 0 to 6 months before F/BEVAR planning and a "prior" scan obtained 6 to 12 months before the "recent" CTA. Standard measurements included (1) target vessel separation distances, (2) target vessel origin clock position, and (3) proximal F/BEVAR device diameter. Clinically significant differences for target vessel separation distance, target vessel origin clock position, and proximal F/BEVAR device diameter were predefined as >5 mm, >30 minutes, and >4 mm, respectively. Differences between "recent"/"prior" CTA scans were examined by paired t test.

RESULTS:

Mean time interval between paired "recent"/"prior" CTAs was 8.0 months (standard deviation: ±1.7). Mean difference in paired "recent"/"prior" target vessel distance (relative to celiac artery [CA]) was 2.6 mm for the superior mesenteric artery (SMA), 2.5 mm for the right renal artery (RRA), and 3.3 mm for the left renal artery (LRA). Of the 21 paired "recent"/"prior" CTAs, clinically significant differences were observed in 2, 4, and 2 patients for SMA, RRA, and LRA target vessel distance, respectively. Target vessel clock position (SMA reference at 12:00) varied by 12 minutes for the CA, 13 minutes for the RRA, and 15 minutes for the LRA. One paired "recent"/"prior" CTA was found to have a clinically significant difference for the LRA. No clinically significant differences were observed for proximal device diameter.

CONCLUSIONS:

In patients who underwent successful F/BEVAR, measurement comparisons between CTAs obtained up to 1 year prior were minor and unlikely to yield clinically significant changes to F/BEVAR design.

PMID: 31362600

Similar articles

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Abstract

BACKGROUND & AIMS:

The evaluation of patients with chronic watery diarrhea represents a diagnostic challenge for clinicians because organic causes, including inflammatory bowel disease, microscopic colitis, and chronic infection, must be differentiated from functional diarrhea and diarrhea-predominant irritable bowel syndrome. The purpose of this review is to summarize the available evidence on the usefulness of diagnostic tests in such patients.

METHODS:

We searched MEDLINE and EMBASE via OVID, from 1978 until April 2017. We included diagnostic test accuracy studies reporting on the use of fecal and blood tests for the evaluation of adult patients with functional diarrhea, including irritable bowel syndrome. We assessed the risk of bias of included studies using a modified version of the Quality Assessment of Diagnostic Accuracy Studies II, and the certainty in the evidence using the GRADE (Grading of Recommendations Assessment, Development, and Evaluation) approach. We calculated pooled sensitivity and specificity, and the
proportion of patients with true and false positive and negative results. We evaluated the following tests: erythrocyte sedimentation rate, C-reactive protein, fecal lactoferrin, fecal calprotectin, serologic tests for celiac disease, tests for bile acid diarrhea, the commercially available version of anti-cytotoxic distending toxin B and anti-vinculin antibodies, and tests for Giardia infection. We did not evaluate breath tests for small intestinal bacterial overgrowth, as they are not part of a standard diarrhea workup.

RESULTS:

Thirty-eight studies proved eligible to evaluate 1 or more of these tests. Erythrocyte sedimentation rate and C-reactive protein were similar at discriminating organic from functional disease, with sensitivity and specificity, respectively, of 0.54-0.78 and 0.46-0.95 for erythrocyte sedimentation rate and 0.73 and 0.78 for C-reactive protein. Among fecal tests, fecal calprotectin in a range of 50-60 μg/g (pooled sensitivity 0.81; 95% confidence interval [CI], 0.75-0.86; pooled specificity 0.87; 95% CI, 0.78-0.92) and fecal lactoferrin in a range of 4.0-7.25 μg/g (pooled sensitivity 0.79; 95% CI, 0.73-0.84; pooled specificity 0.93; 95%CI 0.63-0.99) presented the lowest proportion of false-negative results (low certainty in the evidence). Among tests for celiac disease, IgA tissue transglutaminase presented the best diagnostic test accuracy (sensitivity range, 0.79-0.99; specificity range, 0.90-0.99) with moderate certainty in the evidence. Among tests for bile acid diarrhea, the 75selenium homotaurocholic acid test performed better than serum fibroblast growth factor 19 and 7α-hydroxy-4-cholesten-3-one, but is not available in the United States. There was insufficient evidence to recommend serologic tests for irritable bowel syndrome at this time. There are several good diagnostic tests for Giardia infection.

CONCLUSIONS:

Moderate to low certainty in the evidence indicates that available fecal and blood tests may play a role in the diagnostic workup of adult patients with functional diarrhea. At the moment, no tests are available to reliably rule in irritable bowel syndrome.

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PMID: 31351880 [Indexed for MEDLINE]


**Catcher of the Rye: Detection of Rye, a Gluten-Containing Grain, by LC-MS/MS.**

Pasquali D1, Blundell M2, Howitt CA2, Colgrave ML1.
Abstract

Rye, wheat, and barley contain gluten, proteins that trigger immune-mediated inflammation of the small intestine in people with celiac disease (CD). The only treatment for CD is a lifelong gluten-free diet. To be classified as gluten-free by the World Health Organization the gluten content must be below 20 mg/kg, but Australia has a more rigorous standard of no detectable gluten and not made from wheat, barley, rye, or oats. The purpose of this study was to devise an LC-MS/MS method to detect rye in food. An MS-based assay could overcome some of the limitations of immunoassays, wherein antibodies often show cross-reactivity and lack specificity due to the diversity of gluten proteins in commercial food and the homology between rye and wheat gluten isoforms. Comprehensive proteomic analysis of 20 rye cultivars originating from 12 countries enabled the identification of a panel of candidate rye-specific peptide markers. The peptide markers were assessed in 16 cereal and pseudocereal grains, and in 10 breakfast cereals and 7 snack foods. One of two spelt flours assessed was contaminated with rye at a level of 2%, and trace levels of rye were found in a breakfast cereal that should be gluten-free based on its labeled ingredients.

PMID: 31333027

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.

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**Quinoa protein: Composition, structure and functional properties.**

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Abstract

Quinoa (Chenopodium quinoa willd.) is an annual herbaceous flowering plant showing appropriate nutritional and functional properties due to its high quality protein with a wide amino acid
spectrum, particularly rich in lysine. The mature quinoa seed predominantly consists of 11S-type globulin called chenopodin, comprising about 37% of the total protein, and also 2S albumin accounting for 35% of the seed protein both stabilized through disulfide bridges. Moreover, quinoa seed contains low concentration of prolamins (0.5-7% of total protein) making it suitable for patients with celiac disease. Different enzymatic, chemical and physical modification methods also can influence the structural and finally nutritional and functional properties of protein isolate. Consequently, considering appropriate nutritional and functional properties of quinoa protein, it can be considered as a good candidate to supply human food products.

Challenges to drug discovery for celiac disease and approaches to overcome them.

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Abstract

Introduction: The only available effective treatment for celiac disease (CD) is strict and long-term compliance with a gluten-free diet. Dietary gluten restriction must be strict and long term, but is difficult to achieve in many cases and alternative dietary strategies have been investigated in the past few years. Areas covered: This review highlights the progress that has been made in the development of new therapeutics for CD. Detailed information is provided on the targets of drugs for CD as their related mechanisms of action. The therapies are classified in five mechanisms: modification of gluten, intraluminal therapies, immunomodulation, intestinal permeability and modulation of adaptive response. The actual development phase and future approach are also described and discussed. Expert opinion: There are several limitations in each of the treatment targets related either through complications or the lack of complete response to a normal gluten containing diet. It is clear that the most desired therapy for celiac patients would induce gluten tolerance and progress has been made as per the treatments described herein. Therefore, it is
shortly expected that curative or complimentary tools to a gluten free diet will be available that will improve the quality of life of CD sufferers.

PMID: 31311347


**Efficient production of gluten hydrolase Kuma030 in E. coli by hot acid treatment without chromatography.**

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Abstract

Kumamolisin from Alicyclobacillus sendaiensis strain NTAP-1 is a serine protease with collagenase activity. After molecular engineering, a kumamolisin mutant, named Kuma030, was obtained with high proteolytic activity against gluten, which might cause celiac disease. Kuma030 exhibited its potential application in industrial and medicine, while challenges remained of its large-scale purification and production. In the studies here, we successfully overexpressed the Kuma030 in E. coli BL21 (DE3) by anchoring a SUMO (Small Ubiquitin-like Modifier) fusion protein at its N-terminal end. In addition, a fast protein purification procedure was developed according to the acidophilic and thermophilic properties of Alicyclobacillus sendaiensis. After a simple acid treatment followed by a heat treatment, a total of 9.9 mg functional Kuma030 was quickly obtained form 1 L LB media
culture. This purified Kuma030 was confirmed to be functional to cleave the PQ sequences in a designed protein substrate, and the gluten in actual food samples, such as whole wheat bread and beer, in a fast manner. Our studies provided an efficient strategy for the overexpression and purification of functional Kuma030 in E. coli, which might expand its broad practical applications.

Quantification of Wheat, Rye, and Barley Gluten in Oat and Oat Products by ELISA RIDASCREEN® Total Gluten: Collaborative Study, First Action 2018.15.

Lacorn M1, Weiss T1, Wehling P2, Arlinghaus M2, Scherf K3.

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Abstract

Background: Since its introduction to the analytical community, the R5 method to quantify gluten led to a strong improvement of the situation for the food industry and celiac patients. During recent years, some questions arose on the use of the Codex Alimentarius factor of two to convert from prolamin to gluten, an overestimation of rye and barley, inadequate detection of glutelins, and the inhomogeneous distribution of gluten in oats. These limitations of the R5 method, especially when measuring oat samples, led to AOAC Standard Method Performance Requirement (SMPR®) 2017.021, which was approved by stakeholders in 2017. Objective: We present a collaborative study of a method for the quantitative analysis of wheat, rye, and barley gluten in oat and oat products using a sandwich ELISA that is based on four different monoclonal antibodies including the R5 monoclonal anitbody. Methods: The sandwich ELISA detects intact gliadins and related prolamins from rye and barley, high-molecular-weight (HMW) glutenin subunits (GS) from wheat, HMW secalins from rye, and low-molecular-weight (LMW) GS from wheat. It does not detect D-hordeins from barley. Samples are extracted by Cocktail solution, subsequently followed by 80% ethanol, and analyzed within 50 min. Results: The measurement range is between 5 and 80 mg/kg gluten using a
calibrator made out of a gluten extract from four different wheat cultivars. The results of the collaborative test with 19 participating laboratories showed recoveries ranging from 99 to 137% for all three grain sources. Relative reproducibility SDs for samples >10 mg/kg gluten ranged from 10 to 53%. Conclusions: The collaborative study results confirmed that the method is accurate and suitable to measure gluten from all three grain sources and has demonstrated performance on oat matrices, which meets the criteria as specified in SMPR 2017.021. Data from in-house validation experiments are available as Annex B to this publication.

PMID: 31284896

**Similar articles**


**A multi-spectroscopic study on the interaction of food polyphenols with a bioactive gluten peptide: From chemistry to biological implications.**

Dias R1, Brás NF2, Pérez-Gregorio M1, Fernandes I1, Mateus N1, Freitas V3.

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**Abstract**

This study aims to exploit the molecular and cellular mechanisms concerning the functionality of dietary polyphenols (catechin, procyanidin B3, procyanidin C2, epigallocatechin and epigallocatechin gallate) in a nutritional context to prevent Celiac Disease (CD). In that sense, the interaction between the main CD bioactive peptide (32-mer peptide) and some polyphenols was fully characterized at the intestinal level under near physiological conditions by means of different spectroscopic techniques and dynamic simulations. Accordingly, it is proposed that the primarily polyphenol-binding sites on the 32-mer peptide correspond to leucine, tyrosine and phenylalanine containing domains being this interaction entropy-driven. Although procyanidin B3 and trimer C2 had a similar low-affinity constant at 310 K, both procyanidins were able to reduce the 32-mer peptide apical-to-basolateral translocation in in vitro simulated intestinal epithelial barrier thus
prospecting the occurrence of additional and still unexplored regulatory mechanisms by which dietary polyphenols might modulate the transepithelial transport of CD bioactive peptides.


**18F-Fluciclovine Uptake in Celiac Ganglia: A Pitfall in Prostate Cancer PET Imaging.**

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Abstract

We present 4 cases of patients who underwent F-fluciclovine PET for prostate cancer demonstrating physiologic uptake in the celiac ganglia, which could be mistaken for metastatic lymphadenopathy if the celiac ganglia have a nodular configuration and uptake higher than bone marrow. Uptake in celiac, cervical, and sacral ganglia has been reported previously as an important pitfall in Ga-PSMA-HBED-CC PET for prostate cancer. In our patients, only celiac ganglion uptake was visualized. Advances in PET scanner technology may cause physiologic uptake of F-fluciclovine in celiac ganglia to become more visually distinguishable from muscular uptake in adjacent diaphragmatic crura.

PMID: 31283598


**Clinical manifestations and gastrointestinal pathology in 40 patients with autoimmune enteropathy.**

Villanacci V¹, Lougaris V², Ravelli A³, Buscarini E⁴, Salviato T⁵, Lionetti P⁶, Salemme M¹, Martelossi S⁷, De Giacomo C⁸, Falchetti D⁹, Pelizzo G¹⁰, Bassotti G¹¹.
Abstract

Autoimmune enteropathy (AIE) is a rare condition that may affect pediatric and adult patients, frequently associated with primary immunodeficiencies. We performed a retrospective study on clinical and histological findings from 40 AIE patients. Histological presentation showed a prevalent celiac disease pattern (50%), followed by the mixed pattern (35%), independently of age, chronic active duodenitis (10%), and GVHD-like pattern (5%). Patients with primary immunodeficiencies (24/40) presented mainly with the celiac disease pattern (72.2% versus 22.2%; p < .0001), while patients without primary immunodeficiencies presented with a mixed histological pattern (61.1% versus 13.6%; p < .0001). Our study shows that the prevalent histological presentation is the celiac disease-like pattern, independently of age, and, for the first time, that the histological presentation of AIE differs significantly between patients with and without primary immunodeficiencies. These findings may be helpful for more precise and timely diagnosis and management of this rare disorder.
Abstract

An FDG PET with diagnostic CT was performed on a 52-year-old man for investigation of lymphocytosis and the clinical suspicion of lymphoma. The PET/CT demonstrated diffuse small bowel uptake, prominent mesenteric lymph nodes without significant FDG uptake, and other features suggestive of celiac disease. Subsequently, the patient was found to have markedly elevated celiac disease antibodies (deamidated gliadin IgG and tissue transglutaminase IgA) and to be HLA DQ2 and DQ8 allele positive on genotyping for celiac disease. Gastroscopy and duodenal biopsy also confirmed the diagnosis.

PMID: 31274556

Celiac Disease: Updates on Pathology and Differential Diagnosis.

Dai Y1, Zhang Q2, Olofson AM3, Jhala N4, Liu X3.

Abstract

Celiac disease is a gluten-triggered immune-mediated disorder, characterized by inflammation of the enteric mucosa following lymphocytic infiltration and eventually resulting in villous blunting. There have been many developments in refining diagnostic laboratory tests for celiac disease in the last decade. Biopsy-sparing diagnostic guidelines have been proposed and validated in a few recent prospective studies. However, despite these developments, histologic evaluation of duodenal mucosa remains one of the most essential diagnostic tools as it helps in the diagnosis of celiac disease in individuals who do not fulfill the biopsy-sparing diagnostic criteria and in those not responding to a gluten-free diet. Histologic evaluation also allows for the assessment of mucosal recovery after treatment and in the identification of concurrent intestinal diseases. Therefore,
pathologists should be familiar with the histologic spectrum of celiac disease and need to be aware of other disorders with similar symptoms and histopathology that may mimic celiac disease. This review aims to provide pathologists with updates on celiac laboratory testing, biopsy-sparing diagnostic criteria, histopathology, complications, and differential diagnoses of celiac disease. PMID: 31274508


**Transformation of polyphenols found in pigmented gluten-free flours during in vitro large intestinal fermentation.**

**Rocchetti G¹, Lucini L², Giuberti G³, Bhumireddy SR⁴, Mandal R⁴, Trevisan M³, Wishart DS⁵.**

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**Abstract**

In this work, 18 gluten-free flours (prepared from cereals, pseudocereals and legumes), differing in pigmentation, were screened for their phenolic profiles, cooked and, then, subjected to digestion and large intestinal fermentation in vitro. A combined targeted/untargeted metabolomic approach was used to elucidate the microbial biotransformation processes of polyphenols following digestion. This preliminary work demonstrated an increase in 3,5-dihydroxybenzoic acid (on average from 0.67 up to 1.30 μmol/g dry matter) throughout large intestinal fermentation of pseudocereals (esp. quinoa), due to their high alkylresorcinol contents. Isoflavones were converted into equol- or O-desmethylangolensin- derivatives, whereas anthocyanins were degraded into lower-molecular-weight phenolics (i.e., protocatechuic aldehyde and 4-hydroxybenzoic acid, with the latter exhibiting the highest increase over time). A decreasing trend was observed for antioxidant activities (i.e.,
Physicochemical, microstructural and digestibility analysis of gluten-free spaghetti of whole unripe plantain flour.

Patiño-Rodríguez O, Agama-Acevedo E, Pacheco-Vargas G, Alvarez-Ramirez J, Bello-Pérez LA.

Abstract

Plantain is a climacteric fruit having economic relevance in several tropical regions. Unripe plantain is an alternative source of indigestible carbohydrates (dietary fibre) and undigestible starch fraction. Unripe plantain flour was explored in this work as an alternative ingredient (whole and pulp) in spaghetti formulations. Chemical composition, cooking quality, texture analysis, and microstructure of spaghetti formulations were analyzed. The microstructure results showed that the presence of fiber in the food matrix helped the reduction of the starch granule swelling in the cooking process. Spaghetti made with whole plantain flour exhibited lower rapidly starch fraction, with increased resistant starch fractions. Overall, the whole unripe plantain flour exhibited good potential for gluten-free spaghetti having highest content of fiber and lower starch digestion rates.

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PMID: 31260951

Effect of dietary fiber-rich fractions on texture, thermal, water distribution, and gluten properties of frozen dough during storage.

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Abstract

The effect of dietary fiber-rich fractions on the texture, thermal, water distribution, and gluten properties of frozen dough during storage was investigated. These fractions could greatly improve retention of the texture properties, which was mainly related to water loss, and changes in freezable water proportion (FW) and gluten secondary structure. Kinetic studies showed that the fractions could change the nucleation type and ice crystal growth rate, with konjac flour significantly decreasing the ice growth rate from 0.0177 to 0.0048. These fractions could decrease FW by 15%-27% and restrict water mobility during storage. Moreover, gluten β-sheets shifted toward β-turns, while the β-sheet values of potato and okara flours showed no significant change during storage. SEM confirmed that okara flour could suppress the deterioration of gluten. Generally, the potato, okara, and konjac flours represent excellent fortification materials that could improve the texture, reduce water mobility, and suppress deterioration of frozen dough during storage.

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PMID: 31253335 [Indexed for MEDLINE]

Changes in peptidomes and Fischer ratios of corn-derived oligopeptides depending on enzyme hydrolysis approaches.

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Abstract

Enzyme hydrolysis of corn gluten meal (CGM) is a promising process to prepare oligopeptides with high Fischer ratios (HFOPs). However, the relationship between Fischer ratios and enzyme hydrolysis approaches remains poorly understood. In this study, peptidomes of varying corn protein hydrolysates (CPHs) before and after activated carbon adsorption were profiled and analyzed according to sequence composition and chain length. Fischer ratios of HFOPs depended on sequences in CPHs by differing enzyme hydrolysis approaches, especially branched-chain amino acid (BCAA)-aromatic amino acid (AAA)-containing oligopeptides. Activated carbon adsorption increased BCAA-containing oligopeptide contents and decreased oligopeptide contents including AAAs, preferring BCAA-AAA-containing oligopeptides with long chain length. Employing a three-enzyme hydrolysis approach, HFOPs were obtained with a yield of 49%, comprising 90% of dipeptides and tripeptides and possessing additional bioactivities. This work revealed the mechanism of HFOP production depending on the release and selective removal of oligopeptides and confirmed CGM was a promising alternative for value-added HFOP production.

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PMID: 31253328 [Indexed for MEDLINE]
Use of agricultural by-products in extruded gluten-free breakfast cereals.


Abstract

The objective of this study was to evaluate the effect of the extrusion moisture and temperature on the physical characteristics of breakfast cereals. The chemical composition, microbiological risk and acceptance of the selected breakfast cereal with the best physical quality were assessed to determine the technological viability of the use of these by-products by the food industry. The response surface method and a rotatable central composite design were used, and a desirability test was performed based on adjusted regression models. The breakfast cereal produced under these conditions had protein, lipid and dietary fiber contents of 7.55, 0.97 and 6.12 g 100 g−1, respectively. In regards to the sensory analysis, the evaluated breakfast cereal received average acceptance scores ranging from "neither like or dislike" to "like moderately". The use of rice, passion fruit and milk by-products was shown to be an alternative for the production of extruded breakfast cereal.
Rheological and microstructural characteristics of low molecular weight glutenin subunits of commercial wheats.

Dangi P\textsuperscript{1}, Chaudhary N\textsuperscript{1}, Khatkar BS\textsuperscript{2}.

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Abstract

A study was conducted on the effects occurred in rheological properties of base flour dough by the addition of gluten, glutenin and purified low molecular weight glutenin subunits (LMW-GS) using a 4 g sample Microdoughlab (MDL). Incorporation of these elements brought about a significant increase in the dough strength in the order of LMW-GS < gluten < glutenin. LMW-GS from variety C306 brought a decrease in the dough development time (DDT; 2.03 min), dough stability (DS; 3 min) and peak energy (EP; 2.90 Wh/kg) values. On the contrary, the effects of LMW-GS extracted from variety PBW 550 were more strong as indicated by an increase in DDT (2.75 min), DS (3.30 min) and EP (4.20 Wh/kg). The alterations in the microstructure of dough by the inclusion of gluten, glutenin and LMW-GS, which lacks resemblance among different samples, were contemplated subjecting it to Scanning Electron Microscopy (SEM).

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PMID: 31253302 [Indexed for MEDLINE]

Physicochemical properties of starch in relation to rheological properties of wheat dough (Triticum aestivum L.).

Cao X\textsuperscript{1}, Tong J\textsuperscript{2}, Ding M\textsuperscript{2}, Wang K\textsuperscript{1}, Wang L\textsuperscript{1}, Cheng D\textsuperscript{1}, Li H\textsuperscript{1}, Liu A\textsuperscript{1}, Liu J\textsuperscript{1}, Zhao Z\textsuperscript{1}, Wang Z\textsuperscript{2}, Gao X\textsuperscript{4}. 
Abstract

Wheat dough has been considered as a complex blend where gluten forms the continuous reticular skeleton and starch granules act as filling particles. The effect of starch on dough behaviors is not clear and the mechanism of starch affecting dough properties needs to be revealed. In this study, the micro-structure and physiochemical properties of starch from six wheat varieties (lines) with different dough properties were investigated, and the rheological properties of wheat dough were determined. Six varieties with significant different starch properties perform various dough behaviors, among which Xinmai 26 with preeminent dough quality has the highest amylose content, B-type starch granule content, short-range ordered degree and starch swelling power but lowest relative crystallinity and gelatinization enthalpy of starch. The findings indicate that starch physicochemical properties also influence the dough behaviors and provide helpful information for demonstrating the effects of starch on dough properties in the protein-starch matrix.

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PMID: 31253276 [Indexed for MEDLINE]

The effects of phosphorylation modification on the structure, interactions and rheological properties of rice glutelin during heat treatment.

Wang YR¹, Yang Q¹, Fan JL¹, Zhang B¹, Chen HQ².
Abstract

Rice glutelin (RG) and phosphorylated rice glutelin (PPRG) were treated with heating for different time (15, 30, and 45 min), the effects of phosphorylation modification on the structure, interactions and rheological properties of rice glutelin during heat treatment were investigated. The results showed that the turbidity of PPRG samples were higher than those of RG samples after heating. Particle size distribution showed that the protein aggregates with particle size of 1000-1500 nm were formed after heating for 45 min. Changes in protein structure indicated that the protein unfolded after heating for a short time, and aggregated when heating time extended to 45 min. In addition, the microstructure of PPRG sample became tight when heated for 45 min. Rheological analysis showed that phosphorylation modification and heat treatment improved RG viscoelasticity. These results suggest that phosphorylation modification improves thermal aggregation of RG, which will facilitate the application of RG in food industry.

Copyright © 2019 Elsevier Ltd. All rights reserved. PMID: 31253262 [Indexed for MEDLINE]
Abstract

The effect of cropping system (conventional vs. organic) and soil tillage (conventional vs. reduced tillage) on the health potential of durum wheat grain as well as on semolina and pasta quality traits was investigated in a long-term field experiment. Total antioxidant capacity, total arabinoxylans, alkylresorcinols, yellow pigments and total phenolics, which were assessed in kernels, revealed differences between the two cultivation systems only in 2011, whereas in the 2010 rainy season, cropping management did not influence these compounds. Proteins and W index were higher in the conventional system, except for the exceptionally rainy years. In contrast, the quality of cooked spaghetti was comparable in both management systems. Soil tillage differently affected bioactive compounds but had no impact on semolina and pasta quality. Overall, climatic conditions was the major factor affecting the quality of durum wheat. Our results indicate that an organic system does not represent a constraint to obtaining durum wheat grain with healthy potential relative to conventional wheat.

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PMID: 31253259 [Indexed for MEDLINE]

How microwave treatment of gluten affects its toxicity for celiac patients? A study on the effect of microwaves on the structure, conformation, functionality and immunogenicity of gluten.

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Abstract

The microwave heating of wheat kernels, flour, and gluten, has attracted attention lately because it has been claimed to abolish gluten toxicity for celiac patients. Nevertheless, contradictory results have been reported regarding the effect on gluten celiac-immunotoxicity. In order to better understand the effect of the microwave treatment on gluten structure, conformation, functionality and celiac-immunotoxicity, a central composite design with two factors, power level, and treatment time, was used to investigate a possible quadratic and interaction effects between both factors. Extractable gliadins content was affected by the power and time in a linear and quadratic fashion; extractable glutenins were not affected. Gluten secondary structure was affected by the microwave treatment and related to the polymer's disaggregation phenomenon observed. In fact, the microwave treatment increased the amount of potentially toxic epitopes released after peptic and tryptic digestion, showing inefficiency as a treatment to detoxify the gluten for celiac disease patients.

Dysregulation of the PD-1/PD-L1 pathway contributes to the pathogenesis of celiac disease.

Ponce de León C1, Angel López-Casado M2, Lorite P1, Palomeque T1, Isabel Torres M3.
Classification of starch-gluten networks into a viscoelastic liquid or solid, based on rheological aspects - A review.

Brandner S¹, Becker T¹, Jekle M².

Abstract

A material structure determines its processing and product characteristics. Therefore, knowledge on the exact network character is also important in the case of wheat dough to control the process and the product quality. However, the high complexity of wheat dough makes the exact description of the network structure difficult. Several network models, which propose to transfer the observations resulting from rheological or microscopic measurements into structural relationships, exist. This review summarizes the classification features suitable for the characterization of polymer systems, especially food systems, present their typical properties, and verify transferability to wheat dough systems. Thereby, the ambivalent character of dough to behave as solid and liquid becomes evident. As with every polymer network, filler particles have a significant impact on the mechanical properties. Even if the particle content in dough is much higher than the percolation threshold that normally limits the filler usage in reinforced rubbery systems, the general effects of filler particles on the mechanical behavior are also applicable for dough systems.

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PMID: 31238074
Will Science Sway Beliefs About Gluten?

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Comment on


PMID: 31233735 [Indexed for MEDLINE]

Dietary management of celiac disease: Revisiting the guidelines.

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Abstract

OBJECTIVE:

Medical nutrition therapy (MNT), by lifelong compliance with a gluten-free diet, is likely the only treatment for celiac disease (CD). Clinical practice guidelines (CPGs) regarding the management of CD emphasize the role of MNT over other treatment options. The aim of the present study was to review and critically appraise CD-specific MNT CPGs and identify areas in need of improvement for better adherence and outcomes.

METHODS:

A comprehensive search was performed using PubMed, Guidelines International Network (GIN), Google Scholar, gray literature, and websites of CD scientific organizations for CPGs, consensus and practice papers on the dietary management of CD, published in the English language.

RESULTS:

A total of 12 CPGs were retrieved and critically appraised by three independent reviewers using the Appraisal of Guidelines Research & Evaluation (AGREE) II instrument. All CPGs were of low quality based on AGREE II. Among the 12 CPGs, the National Institute for Health and Care Excellence guidelines achieved the highest score and were unanimously recommended without modifications by the three reviewers, whereas the American Gastroenterology Association, Alberta Health Services, British Society of Paediatric Gastroenterology, Hepatology and Nutrition, Clinical Resource Efficiency Support Team, and Federation of International Societies of Pediatric Gastroenterology, Hepatology and Nutrition guidelines received the lowest scores.

CONCLUSIONS:

The present study reveals the low quality of guidelines regarding the MNT of CD patients, indicating the need for updated and improved guidelines taking into consideration the proposed items of AGREE II.

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PMID: 31220686
The Risk of Autoimmune Disorders in Treated Celiac Disease Patients in Olmsted County, Minnesota.

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Abstract

BACKGROUND:

Patients with autoimmune disorders (ADs) are at increased risk for celiac disease (CD), but data are conflicting on the risk of ADs in treated patients with CD. We aimed to assess the incidence of ADs in treated patients with CD.

METHODS:

Using the Rochester Epidemiology Project, we retrospectively searched for the medical records at Mayo Clinic and Olmsted Medical Center from January 1997 to December 2015 for patients with CD who met accepted diagnostic criteria. For each patient with CD, we identified 2 age and sex-matched controls during the same study period. The incidence rate of AD diagnosis 5 years after index date was calculated using Kaplan-Meier analysis for the CD cases and controls and compared using the log-rank test.

RESULTS:

We identified 249 treated patients with CD during the study period and 498 matched controls, with mean (standard deviation) ages of 32 (22) years and 33 (22) years, respectively. One third of patients (n = 85) and controls (n = 170) were boys. Five years after the index date, 5.0% of patients with CD and 1.3% of controls had a de novo AD diagnosis (P = 0.006). In the presence of a prior AD, the cumulative risk of a de novo or additional AD was significantly higher in the CD group.
compared with controls (P<0.001). Children had a significantly higher risk of AD development compared with adults (P = 0.010).

CONCLUSIONS:

Treated patients with CD are at higher risk for the development of ADs. The risk of a new AD is higher in children, especially when >1 AD diagnosis exists.

PMID: 31219935

Should We Assess Vitamin D Status in Pediatric Patients With Celiac Disease?

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Abstract

OBJECTIVES:

Screening for vitamin D status in celiac disease (CD) has been recommended but the literature provides varying support. We sought to assess the vitamin D status in newly diagnosed children with CD and in a non-CD control population and relate them to vitamin D intake.

METHODS:

In a cross-sectional study, serum 25-hydroxyvitamin D (25-OHD) levels were drawn in children with newly diagnosed CD and compared with pediatric outpatients with functional abdominal complaints. Anthropometric data as well as vitamin D intake based on milk and multivitamin ingestion were collected.

RESULTS:

Thirty-eight newly diagnosed CD patients (10.4±3.0 years old; 50% girls) and 82 controls (11.2±4.2 years old; 58.5% girls) were studied. Both groups were similar except for average daily D intake and BMI. There was no statistical difference in mean 25-OHD levels between CD (26.4±8.0 ng/mL) and
controls (23.5 ± 8.2 ng/mL) [P ≤ 0.07]. Both groups had high percentages of suboptimal D status (65.8% CD and 79.3% controls). 25-OHD levels significantly correlated with age (r = -0.262; P < 0.0038) and estimated vitamin D intake (r = 0.361; P < 0.0001).

CONCLUSIONS:

No significant difference in 25-OHD levels was noted between newly diagnosed CD and controls, but inadequate 25-OHD levels were common in both. 25-OHD levels were highly associated with vitamin D intake demonstrating similar vitamin D absorption between patients and controls. As CD is associated with bone disease and D status is frequently low, efforts at optimizing D, such as screening levels at diagnosis need to be conducted.

PMID: 31219934


Diagnostic Delays in Children With Coeliac Disease in the Central European Region.


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Abstract

OBJECTIVES:

Coeliac disease (CD) is a systemic autoimmune disorder affecting about 1% of the population. Many patients remain undiagnosed or are diagnosed with substantial delay. We assessed diagnostic delays in symptomatic CD children in Central Europe (CE).

METHODS:

Paediatric gastroenterologists in 5 CE countries retrospectively reported data of their patients diagnosed in 2016. Age at first CD-related symptom(s), first visit to paediatric gastroenterologist and confirmed diagnosis were used to determine diagnostic delays.

RESULTS:

Data from 393 children (65% girls, median age 7 years, range 7 months to 18.5 years) from Croatia, Hungary, Germany, Italy, and Slovenia were analysed. Median duration from first symptom(s) to visit to paediatric gastroenterologist was 5 months (range 0-10 years; preschool 4 months, school-aged 5 months), and further duration until final diagnosis was 1 month (range 0-5 years) with significant regional differences (P<0.001). Median diagnostic delay was 6 months (range 0-10 years; preschool 5 months, school-aged 7 months). Type of clinical presentation had little, however, significant effect on delays. Reduced body mass in delays longer than 3 years compared with delays shorter than 1 year was found (z score -0.93 vs -0.39, P<0.05).

CONCLUSIONS:

Time from first symptoms to CD diagnosis in children in 5 CE countries is slightly shorter compared with few other small paediatric studies, and significantly shorter than reported for adults. Nevertheless, delays of more than 3 years in 6.6% of children are worrisome. Raising awareness about the variable symptoms and implementation of reliable diagnostic tools will further reduce diagnostic delays.

PMID: 31219933

Similar articles


The use of high-in-β-glucan oat fibre powder as a structuring agent in gluten-free yeast-leavened cake.
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Abstract

The biggest challenge in the production of gluten-free baked products is creating a structure without gluten while maintaining physicochemical and sensory properties. The aim of this study was to evaluate the possibility of applying oat β-glucan as the thickening and structure-making agent instead of xanthan (control sample), due to its pro-health technological properties, in yeast-leavened gluten-free cake. Thus, high-in-β-glucan oat fibre powder was incorporated into cake formulations as 5, 10, 15 and 20% replacement of rice or corn flour. The complex analysis of physicochemical and sensory properties was conducted, where texture and rheological aspects were the most important. An analysis of the correlation between rheological and physical properties was also conducted. Corn and rice cakes differed, but the results showed the increase of β-glucan, total dietary fibre, springiness, cohesiveness, storage (G') and loss (G'”) modulus and the decrease of firmness and lightness. Improvement of porosity and volume was also noticed. Significant correlation was observed among G', G’”, specific volume and texture components. Accelerated texture changes were noticed after 24 h of storage. To sum up, it is justified to incorporate oat fibre into gluten-free baked products, both to increase nutritional value and improve cake structure.

PMID: 31216185


Age, HLA, and Sex Define a Marked Risk of Organ-Specific Autoimmunity in First-Degree Relatives of Patients With Type 1 Diabetes.

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Abstract

OBJECTIVE:

Autoimmune diseases can be diagnosed early through the detection of autoantibodies. The aim of this study was to determine the risk of organ-specific autoimmunity in individuals with a family history of type 1 diabetes.

RESEARCH DESIGN AND METHODS:

The study cohort included 2,441 first-degree relatives of patients with type 1 diabetes who were prospectively followed from birth to a maximum of 29.4 years (median 13.2 years). All were tested regularly for the development of autoantibodies associated with type 1 diabetes (islet), celiac disease (transglutaminase), or thyroid autoimmunity (thyroid peroxidase). The outcome was defined as an autoantibody-positive status on two consecutive samples.

RESULTS:

In total, 394 relatives developed one ($n = 353$) or more ($n = 41$) of the three disease-associated autoantibodies during follow-up. The risk by age 20 years was 8.0% (95% CI 6.8-9.2%) for islet autoantibodies, 6.3% (5.1-7.5%) for transglutaminase autoantibodies, 10.7% (8.9-12.5%) for thyroid peroxidase autoantibodies, and 21.5% (19.5-23.5%) for any of these autoantibodies. Each of the three disease-associated autoantibodies was defined by distinct HLA, sex, genetic, and age profiles. The risk of developing any of these autoantibodies was 56.5% (40.8-72.2%) in relatives with HLA DR3/DR3 and 44.4% (36.6-52.2%) in relatives with HLA DR3/DR4-DQ8.

CONCLUSIONS:

Relatives of patients with type 1 diabetes have a very high risk of organ-specific autoimmunity. Appropriate counseling and genetic and autoantibody testing for multiple autoimmune diseases may be warranted for relatives of patients with type 1 diabetes.

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PMID: 31213469

Autoantibodies common in patients with gastrointestinal diseases are not found in patients with endometriosis: A cross-sectional study.

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Abstract

OBJECTIVES:

Gastrointestinal symptoms are common in endometriosis, but the mechanisms behind these symptoms are yet poorly understood. Associations between endometriosis and irritable bowel syndrome (IBS), celiac disease, and various autoimmune diseases have been reported. These diseases express characteristic autoantibodies. The aim of the current study was to investigate autoantibodies against gonadotropin-releasing hormone 1 (GnRH1) and luteinizing hormone (LH) and their receptors, tenascin-C, matrix metalloproteinase-9, deamidated gliadin peptide, and tissue transglutaminase in a cohort of women with endometriosis, compared to controls and women with IBS or enteric dysmotility.

STUDY DESIGN:

One hundred seventy-two women with laparoscopy-verified endometriosis completed questionnaires regarding socio-demographics, lifestyle habits, medical history, and gastrointestinal symptoms, and sera were analyzed with ELISA for the abovementioned antibodies. Healthy female blood donors (N = 100) served as controls, and women with IBS or enteric dysmotility (N = 29) were used for comparison.

RESULTS:

A non-significantly higher prevalence of IgM antibodies directed at tenascin-C (7.6% vs. 2.0%; p = 0.06) was the only observed difference in autoantibody levels in endometriosis compared to controls. Antibody presence was not associated with any clinical parameters. Patients with IBS or
enteric dysmotility expressed higher levels of IgM antibodies against GnRH1 compared to both patients with endometriosis (p = 0.004) and healthy controls (p = 0.002), and higher levels of tenascin-C antibodies compared to healthy controls (17.2% vs. 2.0%; p = 0.006).

CONCLUSIONS:

Women with endometriosis do not express higher prevalence of autoantibodies found to be characteristic in other patient groups with gastrointestinal symptoms.

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PMID: 31213335
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**Hydrolyzed wheat gluten alleviates deoxynivalenol-induced intestinal injury by promoting intestinal stem cell proliferation and differentiation via upregulation of Wnt/β-catenin signaling in mice.**

**Zhou JY, Zhang SW, Lin HL, Gao CQ, Yan HC, Wang XQ.**

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**Abstract**

Disintegration of the intestine caused by deoxynivalenol (DON), which is a fungal metabolite found in cereal grain-based human and animal diets, triggers severe intestinal inflammatory disease. Hydrolyzed wheat gluten (HWG) can promote the development of intestine. Therefore, HWG was administered orally to male mice on 1-14 days, and DON was administered to them on 4-11 days. Feed, water intake and body weight were recorded all over the experimental period. Blood samples were collected then the mice were sacrificed to collect the jejunum for crypt isolation and
culture. The intestinal morphology was observed by electron microscopy, and Western blotting was used to investigate intestinal stem cell (ISC) proliferation and differentiation, as well as the primary regulatory mechanism of the Wnt/β-catenin signaling. The results showed that HWG increased the average daily gain and average daily water intake of mice under DON-induced injury conditions, and increased the jejunum weight, villous height in the jejunum, and promoted jejunal crypt cell expansion. The DON-induced decrease in Wnt/β-catenin activity, the expression of Ki67, PCNA and KRT20 were rescued by HWG in the jejunum, crypt and enteroid, as well as the number of goblet cells and Paneth cells. Furthermore, HWG increased jejunum diamine oxidase (DAO) activity. In conclusion, HWG alleviates DON-induced intestinal injury by enhancing ISC proliferation and differentiation in a Wnt/β-catenin-dependent manner.

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PMID: 31202940 [Indexed for MEDLINE]

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**HLA-DQB1*02 allele in children with celiac disease: Potential usefulness for screening strategies.**

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**Abstract**

Through a retrospective analysis of a real-life cohort of children with celiac disease (CD), who underwent HLA-DQ genotyping, we supported our previous findings indicating the presence of HLA-DQB1*02 allele in at least 90%-95% of pediatric patients. In the present study, reporting the HLA-DQ analysis from 184 children (age range: 1-16 years) diagnosed with CD in a single centre, we found that 97.29% of all these CD children \(n = 179\) out of 184 genotyped patients resulted to be carriers of at least one copy of HLA-DQB1*02 allele. If a widened screening for CD should result to be appropriate in the pediatric population after further clinical research, this observation might be potentially exploited to consider a two-step screening strategy, starting with the HLA-DQB1*02
targeted analysis followed by the specific serology for CD in these predisposed patients only. However, additional and larger studies are needed to support our findings.

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PMID: 31187602

Impact of aqualysin 1 peptidase from Thermus aquaticus on molecular scale changes in the wheat gluten network during bread baking.

Verbauwhede AE, Lambrecht MA, Fierens E, Shegay O, Brijs K, Delcour JA.

Abstract

The impact of Aqualysin 1 (Aq1), the thermo-active peptidase of Thermus aquaticus, on wheat albumin, globulin, gliadin and glutenin proteins during heat treatment of wheat dough and bread baking was examined. The level of protein extractable in sodium dodecyl sulfate containing
medium under non-reducing conditions (SDS-EP-NR) from wheat dough decreases upon heating to a lesser extent when Aq1 is used than in control experiments. The higher SDS-EP-NR level is caused by the release by Aq1 of peptides from the repetitive gluten protein domains during baking. These peptides are also extractable from bread crumb with salt solution. The resultant thermoset gluten network in bread crumb is mainly made up by protein from non-repetitive gluten domains.

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PMID: 31174801 [Indexed for MEDLINE]

Sugar beet and apple fibres coupled with hydroxypropylmethylcellulose as functional ingredients in gluten-free formulations: Rheological, technological and sensory aspects.

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3. Maize Research Institute, Department of Technology, Zemun Polje, Slobodana Bajića 1, 11080 Belgrade, Serbia.

Abstract

The presented study examined the influence of hydroxypropylmethylcellulose (HPMC), sugar beet fibre (SBF) and apple fibre (AF) incorporation coupled with adequate water levels on gluten-free (GF) batter rheology, bread quality and sensory characteristics. A Box-Behnken experimental design with independent variables: HPMC quantity (2-4 g/100 g), SBF and AF quantity (3-7 g/100 g) and water quantity (180-230 g/100 g depending on the fibre type) based on a maize flour/starch mixture was applied. GF breads with 4 g/100 g HPMC coupled with 3 g/100 g SBF and 7 g/100 g AF reached the highest specific volumes (2.44 cm³/g and 3.97 cm³/g) accompanied with the lowest crumb hardness (2.29 and 2.10 N, respectively). Appealing crust and crumb colour and good
sensory characteristics were achieved in GF breads with 4 g/100 g HPMC and 3, 5 and 7 g/100 g SBF or AF. The corresponding GF breads showed enhanced fibre content (4.56-6.07 g/100 g).


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Comment in


Mendelian randomization analysis of celiac GWAS reveals a blood expression signature
with diagnostic potential in absence of gluten consumption.

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Abstract

Celiac disease (CeD) is an immune-mediated enteropathy with a strong genetic component where the main environmental trigger is dietary gluten, and currently a correct diagnosis of the disease is impossible if gluten-free diet (GFD) has already been started. We hypothesized that merging different levels of genomic information through Mendelian randomization (MR) could help discover genetic biomarkers useful for CeD diagnosis. MR was performed using public databases of expression quantitative trait loci (QTL) and methylation QTL as exposures and the largest CeD genome-wide association study conducted to date as the outcome, in order to identify potential causal genes. As a result, we identified UBE2L3, an ubiquitin ligase located in a CeD-associated region. We interrogated the expression of UBE2L3 in an independent data set of peripheral blood mononuclear cells (PBMCs) and found that its expression is altered in CeD patients on GFD when compared to non-celiac controls. The relative expression of UBE2L3 isoforms predicts CeD with 100% specificity and sensitivity and could be used as a diagnostic marker, especially in the absence of gluten consumption. This approach could be applicable to other diseases where diagnosis of asymptomatic patients can be complicated.

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Effect of quinoa flour on baking performance, antioxidant properties and digestibility of wheat bread.

Xu X¹, Luo Z², Yang Q³, Xiao Z³, Lu X⁴.

Abstract

Quinoa flour (QF) was added in wheat flour to make nutritionally fortified wheat bread (WB). Effects of QF on baking performance, antioxidant activity and digestibility of WB were studied. The results indicated that with an addition of a small amount of QF (5%) would not affect the baking performance of WB, while higher amounts of QF (10% and 15%) resulted in smaller specific volume, increased hardness and coarse porosity, since QF changed gluten secondary structure and disrupted gluten network. However, sensory evaluation showed that the flavor of WB enhanced significantly with increasing QF addition. More importantly, WB containing QF exhibited improved antioxidant activity and reduced in vitro digestibility with lower estimated glycemic index (eGI) and higher content of slowly digestible starch (SDS) and resistant starch (RS). Our findings indicate that QF-fortified bread is promising to be developed as a functional food with relatively lower eGI and more effective antioxidant properties.
Common Problems Found in the Methodological Approach to Small Bowel Biopsies in the Diagnosis of Celiac Disease.

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3. Pathology Unit. Hospital Universitari i Politècnic La Fe. Valencia, Spain.

Abstract

Small bowel biopsy (SBB) is not always helpful to establish celiac disease diagnosis. Hence we have conducted a retrospective study to know the amount of SBB in our center that was not optimal for this purpose. Histological findings were not appropriate for diagnosis in 3.56% (34 out of 955). The main problem encountered was inadequate sample cutting, although this could be solved by a new recut in almost 30% of cases.

PMID: 31095092

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Dermatitis herpetiformis.

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Abstract

Dermatitis herpetiformis (DH) is a cutaneous manifestation of coeliac disease (CD), which causes an itching and blistering rash, typically on the elbows, knees and buttocks. DH and CD share a similar genetic background, small bowel mucosal alterations, and an autoimmune response against tissue transglutaminase in the serum and small bowel. DH is typically diagnosed during adulthood,
and it is slightly more common among males than females. The incidence of DH seems to be decreasing, in contrast to the detected four-fold increase in the incidence of CD. In addition to typical clinical picture, diagnosis of DH relies on the demonstration by direct immunofluorescence of pathognomonic granular IgA deposits in the papillary dermis. Circulating tissue transglutaminase antibodies support the diagnosis, but their absence does not exclude DH. Obtainment of small bowel mucosal biopsies is not necessary when DH is diagnosed, but if performed, the majority of patients are found to have villous atrophy, and even those with normal villous architecture evince CD-type inflammation. The treatment of choice in DH is a strict, life-long adherence to a gluten-free diet (GFD). In addition to alleviating the symptoms of DH and healing the small bowel mucosal damage, a GFD increases the quality of life for patients, and decreases the risk for lymphoma in DH. Further, the mortality rate of patients with DH treated with a GFD seems to be lower than that of the general population. However, as changing to a GFD has a rather slow effect on the DH rash, patients with severe skin symptoms should additionally be treated with dapsone medication. This review article is based on a presentation given at the British Society for Medical Dermatology blistering skin diseases meeting 2019.

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PMID: 31093998

Phenolic compounds and free sulfhydryl groups in whole grain wheat flour modified by xylanase.

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Abstract

BACKGROUND:
Knowledge of the structural behavior of dough elaborated using whole grain wheat flour (WGWF) and xylanase is fundamental for the elaboration of products with high nutritional content, especially when the particle size of the flour is altered. In the present study, we investigated the effect of varying concentrations of xylanase on the formation of dough with different particle sizes of WGWF.

RESULTS:

Phenolic compounds, fibers and proteins are the components that undergo the most change and interfere with dough formation. A small particle size favors the extraction of phenolic compounds and dietary fibers, resulting in a high-quality dough. There was a protective effect of the stable phenolic compounds on the gluten network. An increase in fiber degradation and a decrease in phenolic compounds was noted as the xylanase concentration increased. Although xylanase increased free sulfhydryl (-SH) groups in gluten, there was no change in dough formation and dough stability with an increasing xylanase concentration.

CONCLUSION:

The WGWF with a smaller particle size does not contribute to the loss of quality in dough elaboration. The addition of intermediate amounts of xylanase (20 mg kg\(^{-1}\)) in samples with a particle size of 158 μm can be used to improve dough characteristics. © 2019 Society of Chemical Industry.

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PMID: 31077384 [Indexed for MEDLINE]


Usefulness of Amplatzer Vascular Plug for Preoperative Embolization Before Distal Pancreatectomy with En Bloc Celiac Axis Resection.

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Abstract

PURPOSE:

We evaluated the usefulness of the Amplatzer vascular plug (AVP) for preoperative embolization before distal pancreatectomy with en bloc celiac axis resection (DP-CAR).

MATERIALS AND METHODS:

Between April 2010 and September 2017, 19 patients with locally advanced pancreatic body cancer underwent preoperative embolization of the common hepatic and the left gastric artery (CHA, LGA) with AVP or coils. We compared the embolization success rate, embolization-related complications, the time required for preoperative embolization before DP-CAR and the procedure costs in patients whose CHA was AVP- (n = 7) or coil (n = 12) embolized.

RESULTS:

The success rate for preoperative AVP and coil embolization was 100% and 83.3%, respectively. The median procedure time was shorter in patients whose CHA was embolized with AVP than coils; the difference was not significant (p = 0.045). The total cost was significantly lower for AVP than coil embolization (p = 0.01).

CONCLUSION:

The AVP is useful for the preoperative embolization of the CHA before DP-CAR.

PMID: 31076840

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Doppler ultrasonographic evaluation of celiac and mesenteric arteries in subjects with sickle cell disease.

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6. Department of Internal Medicine, Faculty of Clinical Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria.

Abstract

Vasculopathy, as occurring in sickle cell disease (SCD), can affect celiac and mesenteric arteries and result in stenosis, with elevated peak systolic velocity (PSV) on Doppler ultrasonography. In six subjects with confirmed SCD in steady state, routine Doppler ultrasonographic examination discovered features of celiac artery (CA) or superior mesenteric artery (SMA) stenosis with CA PSV >200 cm/s (median = 222.8 cm/s; range = 201.5-427.1 cm/s) and/or SMA PSV >275 cm/s (median 183.2 cm/s; range = 87.8-289.3 cm/s). Among the six subjects, five had elevated soluble P-selectin values (median 72.55 ng/mL), while all six (100%) had elevated cystatin C levels (median 4.15 mg/L). Peripheral oxygen saturation was suboptimal in five subjects. All subjects had low hemoglobin concentration levels (median 8.5 g/dL) while four had elevated white blood cell count. Although vaso-occlusive crises result from microvessel occlusion, these findings at the macrovascular level suggest that SCD patients may also be vulnerable to mesenteric ischemic injury, especially in the setting of anemic heart failure from hemolysis.

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Healthy novel gluten-free formulations based on beans, carob fruit and rice: Extrusion effect on organic acids, tocopherols, phenolic compounds and bioactivity.

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Abstract

Rice and legumes have great potential in the development of novel gluten-free snacks that are healthier than traditional snacks. Novel gluten-free extruded foods (composed of rice: 50-80%, beans: 20-40% and carob: 5-10%) were analysed and the extrusion effects regarding organic acids, tocopherols, phenolic compounds and bioactive properties were evaluated. The total concentration of organic acids was not significantly affected by extrusion, while tocopherols showed a significant reduction. Extrusion did not produce an increase of the total phenolic content. For the bioactivity assays, commercial extruded rice, carob and most of the extruded samples showed anti-proliferative activity, which was higher than in the non-extruded samples, while for the anti-inflammatory activity, the extrusion process did not show a significant effect. Regarding the antimicrobial activity, low potential was observed with extruded and non-extruded samples showing high values of MIC and MBC as the microorganisms tested were multi-resistant isolated clinical strains.
Immunoisthiochemical analysis of the mouse celiac ganglion: An integrative relay station of the peripheral nervous system.

Kaestner CL, Smith EH, Peirce SG, Hoover DB.

Abstract

Celiac ganglia are important sites of signal integration and transduction. Their complex neurochemical anatomy has been studied extensively in guinea pigs but not in mice. The goal of this study was to provide detailed neurochemical characterization of mouse celiac ganglia and noradrenergic nerves in two target tissues, spleen and stomach. A vast majority of mouse celiac neurons express a noradrenergic phenotype, which includes tyrosine hydroxylase (TH), vesicular monoamine transporter 2, and the norepinephrine transporter. Over 80% of these neuron also express neuropeptide Y (NPY), and this coexpression is maintained by dissociated neurons in culture. Likewise, TH and NPY were colocalized in noradrenergic nerves throughout the spleen and in stomach blood vessels. Somatostatin was not detected in principal neurons but did occur in small, TH-negative cells presumed to be interneurons and in a few varicose nerve fibers. Cholinergic nerves provided the most abundant input to the ganglia, and small percentages of these also contained nitric oxide synthase or vasoactive intestinal polypeptide. A low-to-moderate density of nerves also stained separately for the latter markers. Additionally, nerve bundles and varicose nerve fibers containing the sensory neuropeptides, calcitonin gene-related polypeptide, and substance P, occurred at variable density throughout the ganglia. Collectively, these findings demonstrate that principal neurons of mouse celiac ganglia have less neurochemical diversity than reported for guinea pig and other species but receive input from nerves expressing an array of neurochemical markers. This profile suggests celiac neurons integrate input from many sources to influence target tissues by releasing primarily norepinephrine and NPY.

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PMCID: PMC6722036 [Available on 2020-11-01]
PMID: 31021409
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A novel angiotensin-I converting enzyme inhibitory peptide derived from the glutelin of vinegar soaked black soybean and its antihypertensive effect in spontaneously hypertensive rats.

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Abstract

Vinegar soaked black soybean is a traditional Chinese food widely used for the treatment of hypertension. While its pharmacodynamic substance was not fully unveiled. It contained abundant glutelin, thus the purpose of this study was to obtain potent antihypertensive peptides from vinegar soaked black soybean. Black soybean was soaked with vinegar and then glutelin was first catalyzed by alcalase. Ultrafiltration, ion exchange chromatography and reversed-phase high performance liquid chromatography were sequentially applied to separate and purify the angiotensin-I converting enzyme (ACE) inhibitory peptides from glutelin hydrolysates. As a result, the fraction L1-4 with the highest ACE inhibitory activity (83.41%) at the final concentration of 0.01 mg/ml was obtained and five peptides were then identified. These peptides were further optimized by virtual screening combining with in silico proteolysis. Finally, a novel tetrapeptide Phe-Gly-Ser-Phe (FGSF) was obtained. FGSF exhibited high in vitro ACE inhibitory activity (IC50 = 117.11 μM) and in vivo hypotensive effect which maximally reduced systolic blood pressure of 21.95 mmHg at 20 mg/kg body weight in spontaneously hypertensive rats. Our study demonstrated that FGSF derived from vinegar soaked black soybean might be used as a promising ingredient for pharmaceuticals against hypertension and its related diseases.
Gluten Challenge Induces Skin and Small Bowel Relapse in Long-Term Gluten-Free Diet-Treated Dermatitis Herpetiformis.

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Abstract
Dermatitis herpetiformis (DH) is an extraintestinal manifestation of celiac disease causing an itchy, blistering rash. Granular IgA deposits in the skin are pathognomonic for DH, and the treatment of choice is a lifelong gluten-free diet (GFD). Preliminary evidence suggests that there are patients with DH who redevelop gluten tolerance after adherence to a GFD treatment. To evaluate this, we performed a 12-month gluten challenge with skin and small-bowel mucosal biopsy samples in 19 patients with DH who had adhered to a GFD for a mean of 23 years. Prechallenge biopsy was negative for skin IgA and transglutaminase 3 deposits in 16 patients (84%) and indicated normal villous height-to-crypt depth ratios in the small bowel mucosa in all 19 patients. The gluten challenge caused a relapse of the rash in 15 patients (79%) in a mean of 5.6 months; of these 15 patients, 13 had skin IgA and transglutaminase 3 deposits, and 12 had small-bowel villous atrophy. In addition, three patients without rash or immune deposits in the skin developed villous atrophy, whereas one patient persisted without any signs of relapse. In conclusion, 95% of the patients with DH were unable to tolerate gluten even after long-term adherence to a GFD. Therefore, lifelong GFD treatment remains justified in all patients with DH.

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**Utilization of small broken riceberry flour in gluten-free bread.**

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**Abstract**

The aim of this study was to develop gluten-free bread formulations based on small broken riceberry flour, by using different ratios of rice flour and xanthan gum. Small broken riceberry and rice flour could be classified as low in amylose content (15.70 g and 20.50 g/100 g dry matter for small broken riceberry and rice flour, respectively). Additionally, small broken riceberry flour contained a total phenolic and total anthocyanin content approximately 500 times higher than that of rice flour. The addition of increased amounts of small broken riceberry flour and xanthan gum
resulted in darker coloured gluten-free bread. However, there was no significant difference regarding moisture and specific volume. The increase of small broken riceberry flour and xanthan gum also led to a significant increase in the firmness of bread crumbs. The sensory evaluation showed differences in flavour, texture and overall liking, since adding small broken riceberry flour tended to make gluten-free bread more favourable. Bread containing rice flour and small broken riceberry flour in the ratio of 30:70 and 1.0% xanthan gum was selected on the basis of the sensory quality. Moreover, such bread also contained high levels of total phenolic and anthocyanin content.

PMID: 30971119


**Synergistic antitumor effect of anti-PD-L1 combined with oxaliplatin on a mouse tumor model.**

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Abstract

Oxaliplatin (OXP) can change tumor microenvironment from immune-suppressive toward the immune-favorable condition. Almost all of the antitumor agents cannot totally cure cancer as monotherapy. So the current focus of cancer research became combining therapy using different treatment regimen, especially chemotherapy with checkpoint blockers. In this study, we assessed the activity of combining regimen using anti-PD-L1 with OXP in CT26 tumor-bearing BALB/c mice. We further analyzed the immune cell phenotypes in tumor site, lymph nodes, and spleen by flow cytometry analysis. Our study showed that combination therapy with OXP and anti-PD-L1 significantly increased survival in vivo and inhibited tumor growth of tumor-bearing mice. Inconsistent with better antitumor activity, our combination therapy led to an increase in tumor-infiltrating activated CD8+ T cells. In draining lymph nodes and spleen, regulatory T cells decreased significantly. Mice receiving either anti-PD-L1 or OXP alone had a larger tumor and lower survival rate in comparison with combination therapy receiving group. The time and order of administration of each component of the combination therapy affected antitumor response.

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Gluten Analysis in Processed Foodstuffs by a Multi-Allergens and Grain-Specific UHPLC-MS/MS Method: One Method to Detect Them All.

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Abstract

Background: Celiac disease, a complex, long-term autoimmune disorder and gluten intolerance, is estimated to affect from 1 to 5% of the world's population. Objective: As a consequence, to protect gluten-sensitive consumers, the development of reliable analytical methods allowing the detection of gluten in various food products is needed. Methods: Currently, ELISA is probably the most widespread used methodology. The method based on the R5 antibody has received type I status in Codex Alimentarius. However, the ELISA method suffers from some limitations, especially concerning quantification of nonwheat gluten. As a consequence, the development of another complementary methodology such as LC-tandem MS (MS/MS) is considered to be essential. Furthermore, this method could also be used for the simultaneous detection of gluten with other allergens, which will constitute a great additional benefit for producers of "free-from" food products and/or having a management policy integrated for several allergies and/or intolerances. Results: A multi-allergen and grain-specific ultra-HPLC coupled to MS/MS method allowing the identification and the discrimination of gluten from seven cereals, simultaneously with the detection and identification of 10 allergens in only one analysis, is thus described here. Conclusions: This method can be used for the analysis of a broad range of foodstuff matrices containing wheat and/or its derivatives, including cereals, flours, heat-treated and foodstuffs, but also more complex samples having undergone fermentation processes (such as beers).
Early-life exposure to common virus infections did not differ between coeliac disease patients and controls.

Simre K1,2, Uibo O2,3, Peet A2,3, Puustinen L4, Oikarainen S4,5, Tamminen K6, Blazevic V6, Tillmann V2,3, Hämaläinen AM7, Härkönen T8,9, Siljander H8,9, Virtanen SM10,11,12, Ilonen J13, Hyöty H4,5, Knip M8,9,12,14, Uibo R1; DIABIMMUNE Study Group.

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Abstract

AIM:

Our aim was to compare the presence of various common viruses (rhinovirus, enterovirus, adenovirus, Epstein-Barr virus, cytomegalovirus, norovirus, parechovirus) in stool and nasal swab samples as well as virus-specific antibodies in serum samples between children who developed coeliac disease and controls.

METHODS:

A case-control study was established based on the DIABIMMUNE Study cohorts. During the study, eight Estonian children and 21 Finnish children aged 1.5 years to five years developed coeliac
disease and each was matched with a disease-free control. Nasal swabs and stool samples were taken at the age of three to six months and the serum samples at the time of diagnosis.

RESULTS:

Rhinovirus ribonucleic acid was detected in the nasal swabs from five coeliac disease children, but none of the control children (p = 0.05). There were no statistically significant differences in the level of viral antibodies between cases and controls. Enterovirus immunoglobulin G class antibodies were found more frequently in the Estonian than in the Finnish children (63% versus 23%, p = 0.02).

CONCLUSION:

This study did not find any marked overall differences in laboratory-confirmed common viral infections between the children who developed coeliac disease and the controls. However, rhinovirus infections were detected slightly more often in those patients who developed coeliac disease.

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PMID: 30896051


Stenting of superior mesenteric and celiac arteries does not increase complication rates after fenestrated-branched endovascular aneurysm repair.

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Abstract
OBJECTIVE:

This study compared complications in patients undergoing fenestrated-branched endovascular aneurysm repair (F-BEVAR) without and with stenting of the superior mesenteric artery (SMA) or celiac artery (CA), with particular attention to the length of coverage above the CA.

METHODS:

A retrospective review was performed of a prospectively maintained database of patients treated with F-BEVAR for thoracoabdominal aortic aneurysms between July 2012 and May 2017. Data included demographics, risk factors, comorbidities, preoperative aneurysm characteristics, procedural data, and outcomes. Patients were grouped as follows: group 1, no SMA or CA stent; group 2, SMA or CA stent and <5 cm of coverage above the CA; and group 3, SMA or CA stent and ≥5 cm of coverage above the CA. Complications measured included death, myocardial infarction, respiratory failure, stroke or transient ischemic attack, paraplegia, acute kidney injury, mesenteric ischemia, and vascular complications. Individual and composite complications were compared between groups.

RESULTS:

There were 223 patients who had data analyzed (group 1, 53 [24%]; group 2, 101 [45%]; and group 3, 69 [31%]). Mean age was 72 years (76% male). There was no difference in patients' characteristics between groups, except for hypertension (less common in group 2) and history of previous aortic surgery (more common in group 3). Group 2 (15%) and group 3 (90%) had higher spinal drain use than group 1 (2%; P < .0001). Mean operative time was longer in groups 2 and 3 compared with group 1 (group 1, 224 minutes; group 2, 253 minutes; and group 3, 313 minutes; P < .0001). Group 1 had more intraoperative complications, without difference in the technical success and mortality rates. Failure to deliver a bridging stent occurred in only 3 of 695 vessels (0.4%) intended, without difference between groups (P = .79). The incidence of major complications (individually and composite analysis) was similar between groups. On 30-day computed tomography angiography, there was no difference in type I or type III endoleaks (2%, 3%, and 6%) and branch patency (98%, 99%, and 99%) for groups 1, 2, and 3, respectively. At 3 years of follow-up, there was no difference in survival, stent patency, and branch instability. Group 3 had a higher reintervention rate compared with groups 1 and 2 (P < .0001); however, there was no difference between groups 1 and 2 (P = .31).

CONCLUSIONS:

Patients who needed SMA or CA incorporation with stents during F-BEVAR for aortic repair had more complex procedures, as assessed by operative time, brachial access, number of vessels incorporated, and spinal drain use. However, the extension of the repair did not affect the outcomes, demonstrated by similar mortality and morbidity rates between groups.
Androgen deprivation therapy for prostate cancer and the risk of autoimmune diseases.

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Abstract

BACKGROUND:

Androgen deprivation therapy (ADT) has been a mainstay of treatment for advanced prostate cancer (PCa), but limited studies have been performed to investigate the association between ADT and autoimmune diseases.

METHODS:

We conducted a population-based nationwide cohort study of 17,168 patients newly diagnosed with PCa between 1996 and 2013 using the National Health Insurance Research Database (NHIRD) of Taiwan. Cox proportional hazards models with 1:1 propensity score-matched analysis were used to investigate the association between ADT use and the risk of autoimmune diseases. The autoimmune diseases included Graves' disease, Crohn's disease, psoriasis, systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, Guillain-Barre syndrome, Sjogren's syndrome, myasthenia gravis, pernicious anemia, hereditary hemolytic anemia, polyarteritis nodosa, Celiac disease, uveitis, polymyalgia rheumatica, dermatomyositis, Hashimoto's thyroiditis, hypersensitivity vasculitis, Behcet's disease, polymyositis, alopecia areata, Wegener's
granulomatosis, ulcerative colitis, autoimmune hemolytic anemia, pemphigus, multiple sclerosis, systemic sclerosis, Goodpasture syndrome, giant cell arteritis, thromboangitis obliterans, arteritis obliterans, and Kawasaki disease. The duration of ADT use as a time-dependent variable was also examined for its association with autoimmune diseases. We also performed six secondary analyses.

RESULTS:

Of the 17,168 selected PCa patients, 14,444 patients met all the inclusion and exclusion criteria. After propensity score matching, 5590 ADT users and 5590 non-ADT users were included in the study cohort. A propensity score-matched analysis (adjusted hazard ratio (aHR), 0.619, 95% confidence interval (CI), 0.51-0.75, P < 0.001) demonstrated a significantly decreased risk of autoimmune diseases in ADT users. A significant decrease in the risk of autoimmune diseases with increasing ADT duration was also demonstrated (P < 0.001).

CONCLUSIONS:

We observed that ADT use in patients with PCa was associated with a decreased risk of autoimmune diseases. These novel findings provide a potential role for androgen deprivation therapy in the modification of inflammation and autoimmunity in Asian patients with prostate cancer.

PMID: 30692587
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**Capsule endoscopy for small-intestinal disorders: Current status.**

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Abstract

Small-bowel capsule endoscopy (SBCE) is used widely because of its non-invasive and patient-friendly nature. SBCE can visualize entire small-intestinal mucosa and facilitate detection of small-intestinal abnormalities. In this review article, we focus on the current status of SBCE. Several
Platforms for SBCE are available worldwide. Third-generation SBCE (PillCam® SB3) has a high-resolution camera equipped with an adaptive frame rate system. Several software modes have been developed to reduce the reading time for capsule endoscopy and to minimize the possibility of missing lesions. The main complication of SBCE is capsule retention. Thus, the main contraindication for SBCE is known or suspected gastrointestinal obstruction unless intestinal patency is proven. Possible indications for SBCE are obscure gastrointestinal bleeding, Crohn's disease, small-intestinal polyps and tumors, and celiac disease. Colon capsule endoscopy (CCE) can observe inflamed colonic mucosa non-invasively, and allows for the continuous and non-invasive observation of the entire intestinal tract (pan-endoscopy). Recently, application of CCE as pan-enteric endoscopy for inflammatory bowel diseases (including Crohn's disease) has been reported. In the near future, reading for CE will be assisted by artificial intelligence, and reading CE videos for long periods will not be required.

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Characterization of gluten-free bread crumb baked at atmospheric and reduced pressures using TD-NMR.

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Abstract

This research aimed to study the effects of using a partial vacuum for bread baking on macromolecules and water distribution in gluten-free bread. Bread baking under partial vacuum results in greater oven rise and a larger gas fraction in the crumb. Because water's boiling point decreases under reduced pressure, it was expected that its distribution within the dough and its interactions with the others dough's constituents (mainly starch) would differ from those in bread baked under atmospheric pressure. Time-domain nuclear magnetic resonance was used, as it has the rare capacity to quantify both gelatinization and retrogradation of starch. Complementary rheological measurements made it possible to show that crumb Young's modulus was mostly influenced by the gas fraction whereas there was little change in starch gelatinization and retrogradation when dough was baked under partial vacuum. When insufficiently hydrated (48%), the volume of breads was practically the same whatever the baking process. Meanwhile, the
nuclear magnetic resonance results suggested that amylose short-term crystallization (on cooling) is dependent on water content. In addition, crumb Young’s modulus during storage at room temperature correlated with an increase in free induction decay signal intensity.

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PMID: 30623478
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Sex Difference in Celiac Disease in Undiagnosed Populations: A Systematic Review and Meta-analysis.

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Abstract

BACKGROUND & AIMS:
A higher proportion of female vs male patients receive a diagnosis of celiac disease. Little is known about sex-based differences in the prevalence of celiac disease in undiagnosed populations. We aimed to address this knowledge gap with a systematic review and meta-analysis.

METHODS:
We searched MEDLINE, Embase, Cochrane, and Scopus databases through 2017 for studies of screen-detected or undiagnosed celiac disease. Our final analysis included studies that included
screening and confirmatory tests (either second serologic analysis or a small intestine biopsy) and provided information on the sex of participants. Studies were excluded if they were performed with specific, high-risk, or referral populations. The primary outcome was the percentage of undetected celiac disease among female and male patients.

RESULTS:

We identified 4070 articles and analyzed data from 87. Our meta-analysis comprised data from 291,969 study participants. The pooled prevalence of undetected celiac disease in female participants was 0.589% (95% CI, 0.549%-0.629%) and in male participants was 0.415% (95% CI, 0.343%-0.487%). The risk of undetected celiac disease was higher among female than male participants (relative risk [RR], 1.42; 95% CI, 1.27-1.57; P < .00001). The I² was 5% (low heterogeneity among studies). In subgroup analyses, the RR of celiac disease for girls vs boys was 1.79 (95% CI, 1.44-2.22; P < .00001; I² = 18%), the RR for female vs male blood donors was 1.13 (95% CI, 0.76-1.69; P = .54; I² = 0), and the RR for women vs men with villous atrophy was 1.38 (95% CI, 1.07-1.79; P = .01; I² = 0).

CONCLUSIONS:

In a systematic review and meta-analysis, we found a higher risk for celiac disease in women than men in an undiagnosed populations (identified through general population screening). The increased risk for celiac disease among girls and women should be considered for screening, diagnosis, and management strategies.

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PMID: 30448593

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Celiac disease and neuromyelitis optica: A rare but possible association.

[Article in English, Spanish]

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