ICDS
2017 India

September 8th - 10th, 2017
Le Meridien, New Delhi

presented by

ISSCD International Society for the Study of Celiac Disease

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ABSTRACTS
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17TH INTERNATIONAL
CELIAC DISEASE SYMPOSIUM

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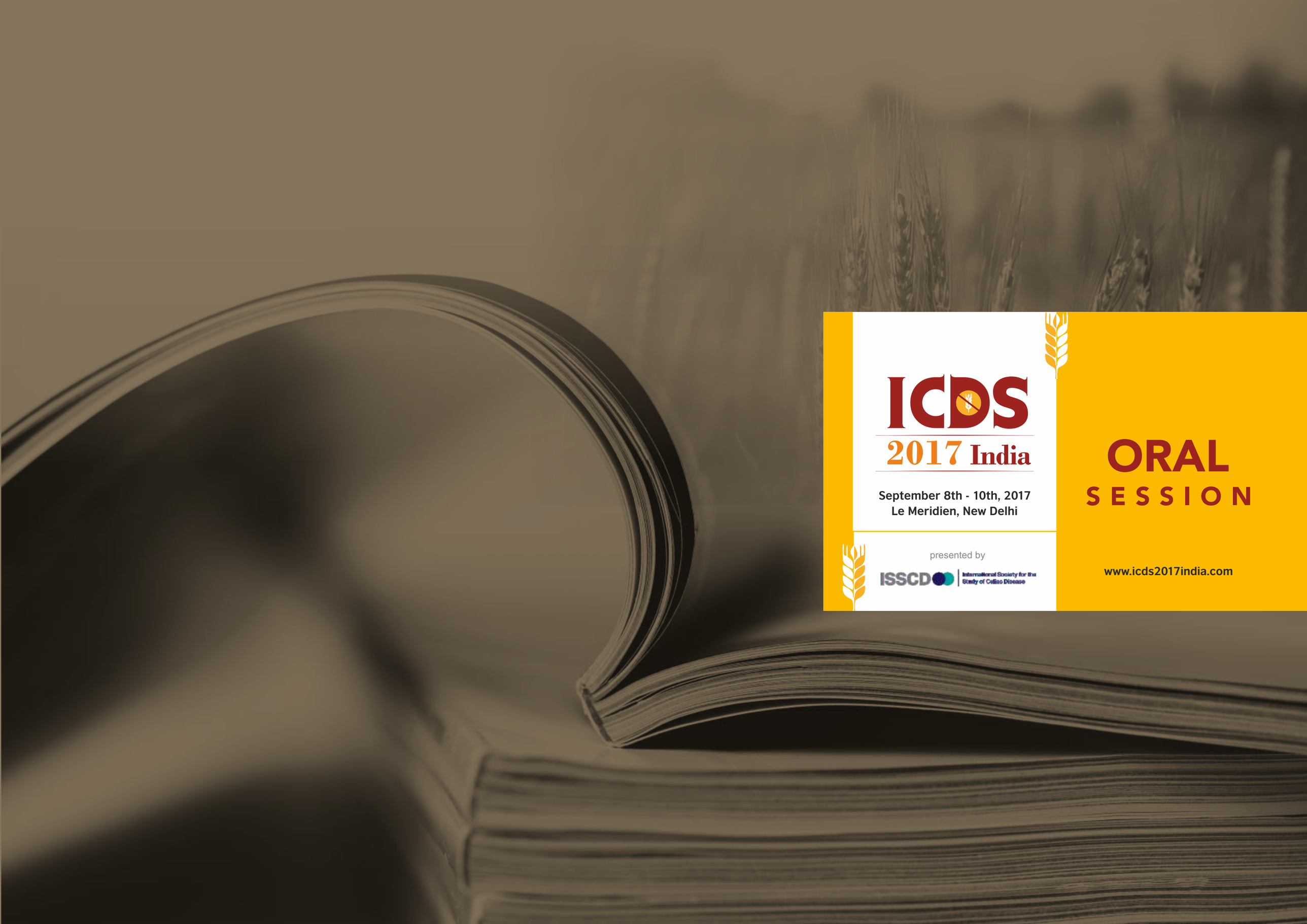

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ORAL

SESSION

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17TH INTERNATIONAL CELIAC DISEASE SYMPOSIUM

SESSION 1: DIAGNOSIS & CLINICAL PRESENTATION

O001

Latiglutenase symptom response for seropositive vs. Seronegative celiac disease patients

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Background
Recent work has focused on post hoc analysis of the Alvine CeliAction ALV003-1221 trial that revealed strong symptom benefit data for seropositive patients. Here we provide additional analysis of the seronegative patient population to try to understand the reasons for the very different efficacy of latiglutenase on these two patient subpopulations practicing a gluten-free diet (GFD).

Methods
The CeliAction study was double-blind, placebo-controlled, dose-ranging conducted in moderately to severely symptomatic CD patients. Symptoms were recorded daily using the Celiac Disease Symptom Diary (CDSDÓ). Symptom benefit was expressed as a reduction in symptoms (RIS) from baseline relative to placebo. Responder analysis was determined as the percentage of patients who improved (RIS) by 30% or 50%; again results were expressed relative to placebo. Quality of life analysis is also reported.

Results
398 patients completed the 12-week study of which 43% were seropositive. Despite the notable trial (Hawthorne) effect observed in all study cohorts, a statistically significant and dose-dependent reduction was detected in the severity and frequency of abdominal pain, bloating, tiredness, and constipation in seropositive, but not in seronegative, CD patients. In subjects receiving 900 mg latiglutenase, the RIS for abdominal pain and bloating severity were 57% (p=0.038) and 44% (p=0.023), respectively, for seropositive patients and -39% (p=0.075) and 3% (p=0.929), respectively, for seronegative patients. Similarly, strong seropositive and weak seronegative results were observed for responder analyses as well as for correlations to baseline severity

Conclusion
Although the ALV003-1221 study was not originally powered to unequivocally establish the symptomatic benefit of latiglutenase in seropositive CD patients, our data demonstrates that despite adherence to a GFD such patients experience sufficient inadvertent gluten exposure to produce gluten-related symptom flares. The mechanism for latiglutenase activity appears to be very different for seropositive vs. seronegative patients and requires further investigation.

O002

Non-invasive biomarkers for assessment of villous abnormalities in patients with celiac disease and other enteropathies: An alternative to mucosal biopsies

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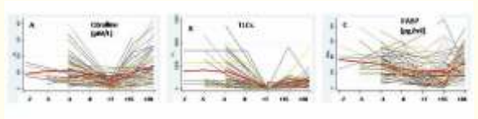
Background
While villous atrophy is hallmark of celiac disease (CeD), demonstration of which however requires endoscopy. There is a need of non-invasive biomarker both for diagnosis and monitoring of villous atrophy.

Methods
Levels of citrulline (synthetic marker of enterocytes) and I-FABP (marker for enterocytic injury) in plasma and regenerating gene-1α (Reg1α) (marker of enterocyte regeneration) in serum were estimated in treatment-naïve patients with CeD (n=110), other enteropathies (n=46), healthy controls (n=209) and disease controls (n=103). Expression of I-FABP and Reg1α were also done in duodenal biopsies using immuno-histochemistry and quantitative PCR. In order to validate citrulline synthesis in intestinal mucosa, expression of pyrolline-5-carboxylate synthase (P5CS), a rate limiting enzyme in citrulline synthesis, was performed. To further confirm validity of above markers, a human model was selected having cycles of enterocyte injury and recovery such as patients with haematological malignancies receiving high-dose chemotherapy for HSCTs (n=70) and their samples were obtained at various time points both before and after HSCT.

Results
Citrulline levels in plasma and expression of P5CS in tissue were significantly lower in CeD as compared to controls (p<0.001), levels increased significantly after GFD. While plasma I-FABP level was significantly higher, tissue expression of I-FABP was lower in CeD as compared to controls(p<0.001). Plasma I-FABP level decreased and tissue expression of I-FABP increased after GFD. Reg1α in serum and in tissue were higher in CeD which decreased after 6-months of GFD (p<0.003). In human model of enteropathy, sequential decrease and then increase in citrulline levels occurred, following a pattern of enterocyte injury and recovery, which corresponded to total leucocytes count in peripheral blood (Fig).

Conclusion
Consistent changes in plasma citrulline in all above experimental groups along with changes in expression pattern of P5CS suggest that plasma citrulline is a reliable marker of enteropathy both for diagnosis and monitoring of villous atrophy.

Figure:) In 70 Individuals with HSCTs, Plasma citrulline (A) and total leukocyte counts (B) show that almost all patients follow the same pattern whereas I-FABP (C) show alteration in their pattern unlike citrulline and TLCs. The level of plasma citrulline (Fig. A) follows the pattern of fall and rise of TLCs (Fig. B), the level of i FABP fluctuates (Fig. C)



O003

The diagnosis and management of gluten ataxia

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Background
The term gluten ataxia (GA), introduced in 1998, describes patients with positive antigliadin antibodies (AGA) and progressive cerebellar ataxia in the absence of alternative causes. Strict gluten-free diet (GFD) results in stabilization and/or improvement of the ataxia. The diagnosis of GA remains problematic due to the limited availability of the correct serological markers and variable AGA assays and some confusion related to the presence of enteropathy (coeliac disease) which is not a prerequisite for its diagnosis.

Methods
We present our 20-year experience of diagnosing and managing GA. All patients were seen, treated and followed up at regular intervals at the Sheffield Ataxia Centre.

Results
The prevalence of GA was 20% amongst all ataxias and 51% amongst idiopathic sporadic ataxias. Of 474 patients assessed, 262 (55%) were female. Mean age at presentation was 52 (range 16-95) and mean duration of ataxia was 13. Mild ataxia (walk unaided) affected 74%, moderate ataxia (walking aid) 18% and severe ataxia (wheelchair bound) 8%. Enteropathy was seen in 47% and peripheral neuropathy in 8%. MR spectroscopy of the cerebellum showed vermian involvement. Endomysium and Transglutaminase type 2 antibodies were not sufficient to diagnose GA as 53% of patients without enteropathy were negative. AGA remains the most reliable test in the diagnosis of GA. The type of assay used and the serological cut-off for AGA positivity requires adjustment for GA patients. GA patients without enteropathy have a primarily CNS based immunological response resulting in low levels of AGA in the serum. Patients with GA who strictly adhere to a GFD (with elimination of AGA) show improvement of the ataxia on clinical and MR spectroscopy assessments.

Conclusion
GA is the commonest cause of sporadic ataxia and one of the few treatable ataxias. Early diagnosis and treatment with strict GFD is imperative to prevent irreversible neurological damage.

SESSION 2: GENETICS & FUNCTIONAL GENOMICS

O004

Small intestinal and faecal microbiota of adult celiac patients and first-degree relatives

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Background
Celiac disease (CeD) is an autoimmune disease characterized by the hypersensitive reaction to gluten in the small intestine of genetically susceptible individuals. Approximately 1% of the world population is affected by CeD. Recently, the potential role of intestinal microbiota as a contributing factor to development of CeD has been hypothesized. While most of the research is focused on paediatric subjects, understating of changes in adult intestinal microbiota before and during active CeD disease has not received considerable attention.

Methods
We collected small intestinal biopsies and faecal samples from 62 individuals. These individuals were grouped based on diagnosis into treatment naïve CeD (TnCeD; n=23), first-degree relatives (FDR; n=15) and controls (DC; n= 24). Bacterial composition of samples was investigated for both biopsy and faecal samples using 16S rRNA gene targeted amplicon sequencing using Illumina MiSeq. Bacterial community data was analysed using QIIME (Version 1.8) and R packages viz. Phyloseq (v1.16.2) and taxon-taxon network inference was done using the SpiecEasi method.

Results
Community level comparisons showed major differences in the alpha and beta diversity between the small intestinal and faecal microbiota irrespective of the diagnosis groups. Differences in the bacterial community structure based on diagnosis groups were more visible in biopsies than in the faecal samples

using constrained ordination. Known opportunistic pathogens such as, *Acinetobacter* and *Brevundimonas* were enriched in the biopsies of TnCeD group. In biopsy samples, the inferred taxon-taxon interaction network suggested negative interactions between *Akkermansia* and *Acinetobacter* in the TnCeD samples.

Conclusion
The differences in the bacterial community between the biopsy and faecal samples highlight the importance of investigating microbiota changes at the site of disease manifestation. The results of the alpha and beta diversity analysis indicate subtle changes at community level between the TnCeD and FDRs indicating the effect of genotype and disease status.

O005

Impact of family risk on developing celiac disease autoimmunity and celiac disease in genetically at risk children followed in the prospective TEDDY study

Lindfors K[3], Laitinen A[11], Lee H[5], Kurppa K[11], Lernmark A[4], Rewers M[8], Hagopian W[1], She J[2], Toppari J[12], Ziegler A[7], Akolkar B[6], Krischer J[10], Liu E[9], Agardh D[4]

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Background
Having a first-degree relative (FDR) with celiac disease (CD) increases the risk of developing CD. The aim was to investigate whether disease risk in HLA-DQ2/DQ8 positive children undergoing CD screening is attributed to an affected sibling, mother, father or multiple family members in HLA-genotyped prospective birth cohort selected from the general population.

Methods
Included were 6293 unrelated genetically at-risk children followed from birth in The Environmental Determinants of Diabetes in the Young (TEDDY) study for median 8.5 years (range 1.7-12.5). Children were screened annually for tissue-transglutaminase autoantibodies (tTgA) from age two using radio-ligand binding assays. At time of analysis, 1122 (17.8%) children had persistent celiac disease autoimmunity (CDA) (i.e. tTgA positivity in two consecutive samples) and 418 (6.6%) CD. FDRs´ CD status were collected from self-reported questionnaires. The Fisher's exact test was used for proportion comparisons and hazard ratio (HR) was estimated using Cox proportional hazard model adjusted for gender, HLA and country of residence.

Results
Amongst included children, 34 (0.5%) reported a father, 78 (1.2%) a mother, 79 (1.3%) a sibling, and 29 (0.5%) multiple family members with CD. The number of CDA and CD case with FDR were 105 and 64, respectively. HR for CDA was 2.4 (95% CI 1.9-2.9) when having any FDR with CD and 3.5 (95% CI 2.7-4.6) for CD. More than 60% of children reporting a father or multiple FDRs were HLA-DQ2 homozygous compared with <50% if a mother or single sibling had CD (p<0.0001), but the risk for CD and CDA didn't differ between the FDR groups.

Conclusion
Having a FDR with CD was associated with at least a 2-fold risk of CDA or CD in the TEDDY cohort. The risk remained unchanged irrespective whether the FDR were a sibling, mother, father or multiple family members were affected by CD.

O006

Epigenetic features in small intestnal mucosa of celiac disease

Greco L[2], Galatola M[2], Cielo D[2], Severino M[2], Gallo D[2], Not T[1], Bilbao J[3], Troncone R[2], Auricchio R[2]

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Background
Multiple GWAS in Celiac Disease did not identified causative polymorphisms. Indeed the derived gene expression focused on whole intestinal mucosa, which is composed by at least two different compartments: epithelium and *lamina propria*. Gene expression as well as gene methylation is strictly confined to specific cell compartments. Our aim was to perform an analysis of gene expression and DNA methylation for 16 candidate genes in two cell types isolated from intestinal biopsies: epithelial and of lamina propria cells.

Methods
Epithelium was separated from *lamina propria* in active CD patient biopsies and in CTR using magnetic beads. Gene-expression was done by Real-Time-PCR. Methylation analysis required bisulfite conversion and NGS.

Results
Reverse modulation of gene-expression and methylation in the same cellular compartment was observed in IL21 and SH2B3 gene, compared to controls. C1ORF106, cREL, and TNFAIP3 showed significantly different methylation in CD-patients without changes in gene expression. Finally an altered gene expression (in at least 1 compartment) was observed in 11 candidate genes.

Conclusion
In this study we defined the selected CD associated as prevalently "Epithelial" or "Lamina Propria" genes. We showed that the genes directly or indirectly linked to inflammatory processes are, as expected, up-regulated whereas the genes involved in Cell Adhesion/Integrity of Intestinal Barrier are preferentially down-regulated in CD. We could suggest a direct correlation between gene-expression level and the methylation profile for IL21 and SH2B3 genes in the same cellular compartment. The characterization of the regulatory mechanism which controls the preferential gene expression, can help to further clarify the pathogenic role of these candidate genes.

SESSION 3: PATHOGENESIS (Part I)

O007

Biased T cell selection in celiac disease is driven by structural elements with similar function

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Background
T cells that recognize a number of protease resistant peptides from wheat, rye and barley are considered the main drivers of inflammation and pathogenesis in celiac disease (CD). The susceptibility to CD is strongly associated with specific antigen presenting molecules, namely the MHC alleles HLA-*DQ2.5* and *HLA-DQ8/8.5*. T cell populations that recognize the immunodominant gliadin epitopes HLA-DQ2-glia-a2 or HLA-DQ8-glia-a1 typically have T cell receptors (TCRs) that are characteristically biased in their *TRAV/TRBV* gene usage. Moreover, these TCRs frequently carry an arginine containing sequence motif in their hypervariable CDR3 regions. T cells that recognize DQ8/8.5-glia-g1 have a comparable bias in their *TRAV/TRBV* usage, however no specific motif in the CDR3 regions is apparent.

Methods
We investigated the structural and functional basis for *TRAV/TRBV* biased TCR–peptide–HLA-DQ interactions in CD using T cell stimulation assays, surface plasmon resonance (SPR) and X-ray crystallography.

Results
Our data revealed the structural and functional conservation of particular functional elements in the T cell recognition of the immunodominant CD epitopes HLA-DQ2-glia-a2, HLA-DQ8-glia-a1 and DQ8/8.5-glia-g1. Despite the distinct epitope specificities and origins of the TCRs, each TCR–peptide–HLA-DQ interface featured a TCR arginine residue bound to a specific position of each antigen. Affinity measurements showed that this arginine was essential for antigen binding in all cases.

Conclusion
We provide evidence that biased TCR gene usage in CD is driven by the selection of structural elements with convergent binding properties. The conservation of specific TCR elements across CD associated T cell populations with distinct peptide specificity, HLA restriction and TRAV/TRBV bias suggests the presence of an overarching mechanism that drives the shaping of the pathogenic T cell repertoire in CD.

O008

From human to mouse and back: advances in the development of a mouse model for celiac disease

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Abstract
The development of new therapies for celiac disease (CD) has proven challenging because of our incomplete understanding of the mechanisms underlying the pathogenesis of the disease and the lack of a suitable mouse model. CD patients have increased expression of the pro-inflammatory cytokine IL-15 in the intestinal mucosa and IL-15 over-expression in the lamina propria is involved in the loss of oral tolerance to gluten and the development of a gluten-specific TH1 inflammatory immune response, intraepithelial lymphocytosis, and anti-gliadin and anti-transglutaminase 2 (TG2) antibodies. Because the adaptive immunity to gluten and epithelial stress are both required for licensing intraepithelial lymphocytes (IE-CTLs) to kill epithelial cells and subsequently inducing villous atrophy, we engineered a humanized HLA-DQ8 mouse model that over-express IL-15 both in the lamina propria and the intestinal epithelium. Following gluten challenge, this mouse presents all the main features of CD including an expansion in IE-CTLs, antibodies against gluten and TG2 and villous atrophy. In accordance with the requirement of CD4+ T cells for the development of the disease, our new transgenic mice do not develop antibodies and intestinal tissue damage when CD4+ T cells are

depleted. A gluten free diet in CD patients normalizes the celiac-specific antibodies and histological alterations. Importantly, following a gluten free diet, tissue damage decline in our mouse model. In addition, we have observed that there is a strong overlap between pathways significantly enriched among genes that are upregulated in the lamina propria of celiac disease patients versus the lamina propria and epithelium of our gliadin-fed transgenic mice. Thus our mouse model represents the first physiological animal model of active CD where the administration of gluten alone triggers tissue alteration and an invaluable premedical model that enables us to assess the efficacy of new therapeutic options such as TG2 inhibitors as a treatment for CD.

O009

Alterations of innate lymphoid cells may contribute to the pathogenesis of celiac disease

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Background
The small bowel (SB) epithelium harbors innate lymphoid cells (ILCs) that lack lineage markers of mature lymphocytes and rearrangements of immune receptor genes. We characterized the phenotype of ILCs in the SB mucosa in order to (1) study alterations of ILC subsets in patients with newly diagnosed or active CD (ACD) and those with refractory CD type 1 (RCD1), (2) assess whether the alterations are linked to epithelial cell damage and (3) determine if adherence to a gluten-free diet (GFD) restores the normal ILC composition.

Methods
Intraepithelial lymphocytes were isolated from SB biopsies (12 controls, 13 ACD patients, 3 RCD1 patients and 13 CD patients on GFD) and analyzed for surface markers, transcription factors, intracellular cytokines, and cytotoxic granules using flow cytometry. Serum levels of fatty-acid-binding protein 2 (FABP2) were determined by ELISA. Group differences were analyzed by the Kruskal-Wallis one-way analysis of variance and correlations were assessed using Spearman's *r*, with $p<0.05$ considered significant.

Results
We identified two ILC subpopulations based on the expression of NKp44 and CD103, which were further resolved as CD127- ILC1s, exILC2s, exILC3s within the NKp44+CD103+ fraction and CD127+ ILC1, CD56+ NK-like ILCs and ILC3s within the NKp44-CD103+ fraction. Frequencies of NKp44+CD103+ ILCs were decreased ($p<0.0001$), while NKp44-CD103+ ILCs were increased ($p<0.0001$) in ACD compared to controls. ILC composition of RCD1 was similar to ACD. Adherence to GFD did not lead to normalization of ILC frequencies. Increased NKp44-CD103+ ILCs correlated with the degree of villous atrophy (Marsh score) and FABP2 levels ($p<0.01$). Upon mitogenic stimulation, NKp44-CD103+ T-bet+ ILCs expressed IFN-γ, with higher levels in ACD compared to controls ($p<0.05$) but did not respond to gliadin stimulation.

Conclusion
Our findings suggest a role of ILCs in modulating and promoting persistent inflammatory responses in CD by providing a source of IFN-γ in a gliadin-independent manner.

SESSION 4: PEDIATRIC CELIAC DISEASE

O010

Celiac before the disease

Auricchio R[3], Galatola M[3], Cielo D[3], Salamone D[3], Malamisura B[2], Limongelli M[1], Massitti M[3], Miele E[3], Troncone R[3], Greco L[3]

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Background
Celiac disease is associated to a peculiar genomic profile, which does not suggest gross metabolic defects, but does indicate a peculiar use of 'healthy' metabolic profiles wrongly targeted to gluten peptides. Genetic, with HLA variants and candidate genes, may explain just half of the heredity, the remaining missing heredity could be due to epigenetic mechanisms. The epidemics of CD can be also explained by a series of environmental factors which influence the phenotype of CD and the development of intolerance to a common staple food.

Methods
300 new-borns from at risk families were recruited and followed-up for 6 years. From 10 children who developed CD and 12 who did not PBMC were obtained every 6 months since birth. We examined HLA and candidate gene haplotypes, and gene expression at 6 months, at the time of small bowel biopsy and 6-12 months after. Pregnancy and delivery data and clinical information (growth, diet, infection, therapy) were also collected.

Results
Although all infants were HLA DQ2/8+ and came from families with a proband, still the ***individual genetic component*** given by HLA and selected candidate genes haplotypes contributed to the development of CD. Among the ***environmental factors***, a higher rate of caesarean section (72% vs 55%) was observed in children who developed CD in the first 6 years of life compared to those who did not; inasmuch the incidence of respiratory infections before the time of diagnosis (up to 24 months) conferred a four-fold increased risk to develop CD and two-fold more than the incidence of gastroenteritis. Finally the ***expression*** of a small set of candidate genes allowed to predict celiac disease at least 9 months before the appearance of any clinical or serological signs of the disease.

Conclusion
In genetically predisposed infants, it is possible to predict, with unexpected accuracy, those who will develop CD one or more years before the actual appearance of the disease.

O011

Potential CD presenting at an early age have less chance to evolve to villous atrophy

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Background
Potential celiac disease (PCD) is still a controversial clinical condition: there is not yet agreement on prognosis and treatment. Aim of our study was to investigate the natural history of the disease and to identify risk factors associated with possible development of villous atrophy.

Methods
We prospectively enrolled 340 PCD children (twice positive anti-tTG IgA and anti-endomysium antibodies + duodenal mucosa Marsh 0 or 1): 67.1% females, most asymptomatic (86.7%), 50% first degree of CD patients and 15% with other autoimmune comorbidity (type 1 diabetes, thyroiditis). They were followed till 96 months (median 46.1) on a gluten containing diet, with serial clinical, serological and histological evaluations. 35 patients were prescribed a gluten-free diet because of persistence of symptoms; 88/340 (25.8%) became anti-tTG negative during the follow up (FU).

Results
During FU, 42 children developed villous atrophy (cumulative survival = 66% at 9 years), most of them in the first two years of FU, with no difference between sex. The best predictors of evolution to villous atrophy at the time of enrolment were: epithelial lymphocytes infiltration (χ 13.53, p .001), age >10 years (χ 13.22, p .001), HLA homozygosity (χ 7,725, p .021), intensity of anti-tTG intestinal deposit (χ 6,047, p .049). Familiarity for CD and other autoimmune disease did not affect the natural history of this condition.

Conclusion
PCD is confirmed to be a heterogeneous condition, but it seems possible to identify risk factors at the time of diagnosis and in first years of follow-up to discriminate children who will develop eventually villous atrophy.

O012

mTOR (mammalian target of rapamicin) as a potential therapeutic target in CD

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Background
The pathway of mTOR which is known to control metabolism, growth, and cell survival, has recently emerged as key regulator of innate immune cell homeostasis.

Damage to the intestinal mucosa of CD patients is mediated by innate and adaptive immune response. A-gliadin peptide P31-43, an undigested gliadin peptide is able to stimulate innate pathways, with IL15 as major mediator. Other undigested gliadin peptides can active adaptive immune response.

Alternative therapies to the gluten free diet in CD have been proposed. Either focused on the destruction of gliadin peptides present in the food, or by blocking the entry of peptides in the intestinal epithelium, preventing the activation of the immune response. Probiotics have characteristics that could be useful in both these areas.

This study describes a novel the effect of undigested gliadin peptide P31-43 on the mTOR pathway and NFK-β activation. Probiotics can prevent these effects.

Methods
Caco-2 cells, an intestinal cell line, were treated with P31-43 or crude gliadin peptic-tryptic peptides (PTG) alone and after pre-treatment with LP CBA L74 or Lactobacillus rhamnosus GG (1x10⁸) valuating the level of phosphorylation of mTOR, p70S6k/ p4EBP-1 and marker of inflammation pNFK-β by western blot. We analyzed marker of autophagy LC3 by immunofluorescence.

Results
Levels of phosphorylation of mTOR, p70S6k/ p4EBP-1 were increased after treatment of P31-43 and PTG. Moreover we observed an increase of phosphorylation of NFK-β. Pre-treatment with probiotic LP CBA L74 and Lactobacillus rhamnosus GG prevented both the mTOR pathway activation and the NFK-β phosphorylation. P31-43 reduced LC3 staining and probiotic treatment was able to prevent also this reduction.

Conclusion
Gliadin and gliadin p31-43 were able to induce inflammation markers including mTor pathways and NFK-β in intestinal epithelial cell line. Probiotics could prevent both these effects. These data indicated that mTOR could be a potential therapeutic target in CD.

17TH INTERNATIONAL CELIAC DISEASE SYMPOSIUM

SESSION 5: EPIDEMIOLOGY OF CELIAC DISEASE

O013

Re-exploring the iceberg of celiac disease in children: preliminary results of a multicenter Italian screening project based on a rapid HLA DQ typing test

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Background
We aimed to assess the prevalence of celiac disease (CD) autoimmunity and overt CD in Italian school age children by using HLA typing as the initial screening test, and to redefine the clinical spectrum of CD.

Methods
Children aged between 5-10 years, attending the primary school in Ancona and Verona, were invited to participate No exclusion criteria were formulated. Celiac Gen Screen (Biodiagene) based on a rapid single PCR reaction HLA on a single blood drop was used to identify HLA DQ2/DQ8 susceptible subjects. Serum anti-transglutaminase IgA antibodies (TTG) and total IgA were performed in HLA positive patients. Anti-endomysium antibodies (EMA) and anti-deamidated gliadin peptides IgG antibodies were searched in TTG positive and IgA deficient patients respectively. Biopsy was performed according to the ESPGHAN criteria.

Results
From May 2015 to November 2016, 4570 subjects have been HLA screened (80% of the eligible population).Out of the 1960 HLA positive subjects (42.9%, 95% CI 41.7-44.63), 1692 (86.3% of the screened population) underwent the serological evaluation. CD autoimmunity was found in 98 patients with 34 receiving a diagnosis of CD and 28 patients still under investigation. 36% of new diagnosed children were asymptomatic and 55% required biopsy for further confirmation. CD was already known in 21 children (0.37%, 95% CI 0.22-0.60) with a total prevalence of CD in the screened cohort ranging from 1.1 to 1.7%. The ratio of known/undiagnosed CD ranges from 1:1.6 to 1:2.9.

Conclusion
Preliminary results indicate a CD prevalence increased in age-school children, compared to previous Italian epidemiological data. Due to increased awareness of the disease, the ratio between known and unknown cases has profoundly changed but there are still 70% of cases remaining undiagnosed. Considering its high sensitivity and feasibility, the rapid HLA test would be an appropriate tool to perform screening of CD in the general population

O014

Prevalence, incidence and autoimmune comorbidities of celiac disease; A nationwide, population-based study in Denmark from 1977 to 2014

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Background
To describe and potentially identify trends with respect to prevalence, incidence, age, gender and autoimmune comorbidities of celiac disease (CD)

Methods
A Danish nationwide cohort study using data from *The National Patient Register*. Patients with a primary or secondary diagnosis code of CD during the period 1977 to 2014 were identified. Information on sex, date of birth, death or immigration was obtained from the *Danish Civil Registration System*. Autoimmune comorbidities were identified in *The National Patient Register* using diagnosis codes. The CD cohort was compared to the general population, using aggregated data obtained from *Statistics Denmark*.

Results
The CD cohort consisted of 9993 patients (64.4% women). The median age at diagnosis of CD varies from 30 years in 1980-1984, topping in 1995-1999 with 45 years and decreasing to 27 years in 2010-2014. The prevalence of CD in 2004 and 2014 was 66 and 154 per 100,000 persons, respectively, with a female/male ratio increasing from 1.57 to 1.95. Incidence rates (per 100,000 person-years) increased from 1.59 in 1980-1984 to 12.95 in 2010-2014. In 2006, the age and sex standardized prevalence of autoimmune comorbidities was 19.7% among the CD patients compared to 3.9% in the general population.

Conclusion
The prevalence of diagnosed CD has more than doubled in Denmark from 2004 to 2014, the female/male ratio has increased and the median age at diagnose has decreased. The prevalence of autoimmune comorbidity was 5 times higher among CD patients compared to the general Danish population in 2006.

Keywords:
Celiac Disease, Epidemiology, Autoimmune Comorbidity

O015

Dietary intake of fat-soluble vitamins and the risk of celiac disease autoimmunity and celiac disease in the TEDDY study

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Background
Nutrition may influence the functions of immune system. The aim was to examine if intake of fat-soluble vitamins (A, D, E, and K) were associated with the risk of developing celiac disease autoimmunity (CDA) and celiac disease (CD) in children.

Methods
Genetically at-risk children are followed from birth in The Environmental Determinants of Diabetes in The Young (TEDDY) Study. Participants screened positive for tissue transglutaminase autoantibodies (tTGA) on two consecutive visits were defined as having CDA. CD was diagnosed if Marsh score >1 or tTGA levels >100 U/mL without biopsy. Nutrient intakes from foods and supplements were estimated with 3-day food records completed quarterly during the first year and semi-annually thereafter. For each nutrient, every intake was log2-transformed. Average intake from 3, 6, and 9 months (time-constant) and intakes from subsequent ages (time-varying) were analyzed using Cox proportional hazard models adjusted for country, HLA, sex, CD family history, and energy. Hazard ratios (HRs) indicate the risk associated with a 2-fold increase in intake.

Results
Among 6740 screened children, CDA was confirmed in 1206 at a median age of 3.3 years (range 0.9-11.2 years) and CD was diagnosed in 450 at a median age of 4.3 years (range 1.2-11.1 years). The risk of CDA was inversely associated with average intake of vitamin E in year 1 (HR=0.91, 95% CI 0.86, 0.97, p=0.004) and from subsequent ages (HR=0.96, 95% CI 0.93, 0.99, p=0.015). Time-varying vitamin K intakes (intake estimation unavailable in Sweden) were inversely associated with lower risk of CDA (HR=0.94, 95% CI 0.91, 0.97, p <0.001) and CD (HR=0.93, 95% CI 0.88, 0.98, p=0.004). HRs for vitamin A and D intakes were nonsignificant.

Conclusion
The observed associations between fat-soluble vitamins and risk of CDA and CD need further investigation.

SESSION 6: REFRACTORY CELIAC DISEASE

O016

Villous atrophy in RCDII is caused by granzyme-B mediated apoptosis of enterocytes by aberrant IEL via CD103-E-cadherin interaction

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Background
Refractory celiac disease type II (RCDII) is an indolent intestinal tumor of aberrant intraepithelial T-lymphocytes (IEL). The severe enteropathy found in RCDII is caused by aberrant IEL that exert cytotoxicity against the enterocytes. In this study, we investigated if granzyme-B is involved in killing of enterocytes by aberrant IELs.

Methods
mRNA and protein expression were determined using RT-MLPA analysis and flowcytometry, respectively. Enterocyte-induced killing and degranulation by aberrant IEL were measured in the presence of a transwell or specific inhibitors, with flowcytometry. Secretion of granzyme-B was detected by ELISA.

Results
mRNA and protein expression of granzyme-B were significantly upregulated in aberrant IELs of patients with RCDII compared to levels of granzyme-B expression in patients with CD on a gluten free diet (GFD). RCDII cell lines also demonstrated increased levels of granzyme-B expression. Furthermore, in RCDII patients and cell lines degranulation of granzyme-B was observed in the presence of epithelial cells. Incubation of RCDII cell lines with epithelial cell line Caco2 showed that aberrant IEL induced apoptosis of Caco2. Treatment with a granzyme-B inhibitor demonstrated that killing of enterocytes was granzyme-B dependent and that degranulation by IELs was necessary. In addition, we found that the aberrant IEL induced cell death through triggering of the intrinsic apoptosis pathway via mitochondrial membrane depolarization and

caspase-3 and -9 activation. For degranulation of granzyme-B and killing of the enterocytes, binding of the epithelial cell to the aberrant IEL was necessary. Functional studies revealed that CD103-E-cadherin interaction was essential for release of granzyme-B and loss of enterocytes.

Conclusion
Killing of enterocytes is dependent on upregulated expression and degranulation of granzyme-B and on interaction with the aberrant IELs through CD103-E-cadherin binding. These data contribute to a better understanding of the pathogenesis of villous atrophy in RCDII and therefore might be important for identification of new treatment options.

O017

Nkp46 is a useful diagnostic biomarker in gastrointestinal T-cell lymphoproliferative diseases. A CELIAC network study.

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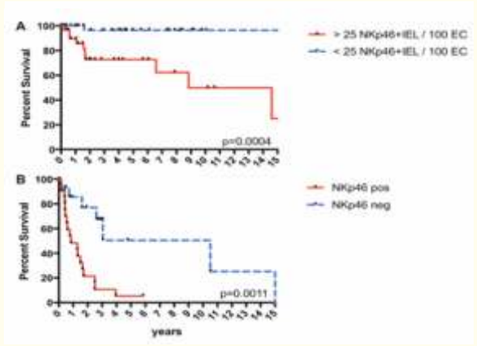
Background
Primary gastrointestinal (GI) T-cell lymphoproliferative diseases (T-LPD) are heterogeneous entities, which diagnoses and therapeutic options remain to be standardized. Beside aggressive lymphoma, such as enteropathy-associated T-cell lymphoma (EATL) and monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), the indolent T-cell lymphoproliferative disease (indolent T-LPD) has been recently described. A differential diagnosis to consider is type II refractory coeliac disease (RCDII) that may complicate CD. Intraepithelial lymphocytes (IEL) from RCDII are dependent for survival on IL-15, which reprograms T-lymphocytes towards a cytotoxic NK phenotype.

Methods
The expression of NK receptors was assessed on CD/RCD by flow-cytometry. The number of NKp46 positive IEL per 100 epithelial cells (NKp46+ IEL/100 EC) was studied by immunohistochemistry (IHC) on 195 biopsies from 84 CD/RCD and 44 GI T-cell lymphoma.

Results
Nkp46 was the only NK receptor that differs between RCDII and CD or RCDI. By doing ROC analysis, a number of NKp46+ IEL/100 EC above 25 clearly discriminated RCDII from CD and RCDI, with excellent positive and negative predictive values of 100 and 95% respectively. Among CD and RCD patients, the survival was shorter if this count is above 25 (OS-5years 72.8% vs. 96.4%, P=0.0004) (Fig. A). NKp46 was expressed in EATL (n=20/25) and MEITL (n=4/4) but was never expressed in indolent T-LPD (n=0/15). Positive NKp46 GI T-cell lymphoma had a shorter survival compared to negative NKp46 cases (OS-5years 5.4% vs. 50.5%, P=0.0011) (Fig. B).

Conclusion
Nkp46 provides a new biomarker for both diagnosis and prognosis in GI T-LPD. We propose a diagnostic algorithm for GI T-LPD based on the NKp46 expression, which is adapted to immediate, individual patient management.



O018

Histological response to budesonide in patients with refractory celiac disease type 1 and 2

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Background
Refractory celiac disease (RCD) is defined by persistent or recurrent symptoms and villous atrophy despite strict adherence to gluten-free diet for at least 6–12 months. RCD is classified as type 1 (normal intraepithelial lymphocyte phenotype) and type 2 (clonal intraepithelial lymphocyte population with aberrant phenotype). Budesonide is an effective treatment to induce clinical remission in RCD. However, histological response is less frequent. The aim of this study is to evaluate the histological response to budesonide in patients with RCD type 1 and 2.

Methods
We conducted a monocentric retrospective study. Patients with a diagnostic of RCD type 1 and 2 who were treated with budesonide alone were included. Patients who didn't have follow-up biopsies while on treatment were excluded. Complete histological response was defined by normalisation of the architecture of the small intestinal mucosa (Marsh 0 or 1 score). Partial histological response was defined as an improvement of the Marsh classification of two or more steps.

Results
Over a period of 15 years, 10 patients with RCD 1 and 7 patients with RCD II were included. The mean duration of treatment with budesonide was 32.2 months [7-132]. Complete histological response was seen in 3 patients (17.6%) and partial histological response in 1 patient. Improvement in one step of the Marsh classification was seen in 6 patients. 7 patients (41.1%) had no change in the architecture of the small intestinal mucosa. Patients who had complete or partial histological response had been on budesonide for a mean period of time of 72 months, while patients with no response had a mean time of treatment of 19.9 months.

Conclusion
Budesonide is associated with histological improvement in less than 25% of patients with RCD type 1 and 2. This improvement seems to be associated with a longer duration of treatment.

SESSION 7: PATHOGENESIS (PART II)

O019

Reovirus infections promote inflammatory responses to dietary antigens and contribute to development of celiac disease

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Background
A break of immunological tolerance to dietary gluten is a key event in the development of Celiac Disease (CD). Interleukin-15 is known to be one driver, however not all celiac subjects overexpress this cytokine. Several evidences suggest a role for viral infections and the anti-viral cytokines type-1 interferons (IFN) in triggering CD. Thus, in this study we tested the hypothesis that viral infections can contribute to impair tolerance to dietary antigens, and that this process could be relevant in CD pathogenesis.

Methods
To dissect the mechanisms underlying virus-induced loss of tolerance to dietary antigens, we developed a murine model of viral infection using two strains of human reovirus, dsRNA virus causing asymptomatic infections in humans, able to infect mice intestine, but differing in their immunopathological outcomes.

Results
We demonstrated that Reovirus, despite being avirulent in humans and able to elicit protective immunity, can disrupt intestinal immune homeostasis at inductive and effector sites of oral tolerance, by suppressing peripheral regulatory T cell conversion, via type-I IFN, and promoting T helper-1 immunity to dietary antigen, a process mediated by interferon regulatory factor 1 (IRF1). Of note, these two responses might be dissociated. Moreover, higher titers of anti-reovirus antibodies were found in CD patients vs controls, and were associated with higher levels of IRF1, key transcription factor involved in TH-1 immunity to dietary antigen, supporting a role for reovirus in triggering CD.

Conclusion
This study demonstrates for the first time a role for reovirus infection in CD pathogenesis. In particular, we provide evidence for the mechanism behind viral induced impairment of oral tolerance. Furthermore we identify different groups of patients based on their immune-signature. These data could support future development of preventive strategies based on vaccination of at risk subjects, and individualized therapeutic options based on their immune phenotype.

O020

T cell receptor recognition of an immunodominant gluten epitope of coeliac disease in the context of HLA-DQ2.2

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Background
Coeliac Disease (CD) is a common, autoimmune-like disease caused by the ingestion of wheat gluten, or related proteins from rye and barley. By damaging the small intestine, CD poses a significant health concern, affecting ~1% of the population. CD is strongly associated with HLA allotypes where ~90% of patients express HLA-DQ2.5 (DQA1*05-DQB1*02) whilst the remaining patients express either HLA-DQ2.2 (DQA1*02:01-DQB1*02:01) or HLA-DQ8 (DQA1*03–DQB1*03:02). The repertoires of gluten

epitopes presented by these alleles have been studied extensively. The structural basis for the presentation of these epitopes by HLA-DQ2.5 and HLA-DQ8 as well as the recognition of these complexes by T cell receptors (TCR) have also been determined. To gain a complete picture of the molecular basis for disease pathogenesis in CD, we determined the crystal structure of HLA-DQ2.2/DQ2.2-glut-L1 in complex with a cognate TCR from a DQ2.2-glut-L1 reactive T cell clone isolated from a CD patient.

Methods
To determine the structural basis for the TCR/HLA/peptide interactions in CD we used a combination of T cell assays, surface plasmon resonance (SPR) and X-ray crystallography.

Results
We determined the structure of 555TCR/HLA-DQ2.2/DQ2.2-glut-L1 complex to 2.8Å. HLA/peptide interactions: The polymorphic DQalpha22 residue has a crucial role in the selection of serine or threonine at position 3 (p3) of the antigen binding cleft, observed in the HLA-DQ2.2 peptide binding motif. TCR/HLA/peptide interactions: 555TCR docked in a very similar fashion to the S2TCR/HLA-DQ2.5/DQ2.5-glia-alpha1 complex we previously described. Only weak interaction was evident between the 555TCR CDR3β and the DQ2.2-glut-L1 peptide, primarily with Q-p5 and Q-p7. The central region of the peptide was devoid of 555TCR contacts. Hence, the interface is dominated by TCR-HLA interactions.

Conclusion
Together with TCRs/HLA-DQ2.5-gluten and TCRs/DQ8-gluten structures previously determined, the 555TCR/HLA-DQ2.2/DQ2.2-glut-L1 complex presented here represent a basic set of structures that reveal the molecular interactions underpinning CD pathogenesis.

SESSION 8: TREATMENT OF CELIAC DISEASE

O021

Synergistic effects of IL-15 and IL-21 in celiac disease pathogenesis: experimental activity of a novel, dual IL-15 / IL-21 inhibitor

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Background
Both IL-15 and IL-21 are hypothesized to play central pathogenic roles in Celiac Disease (CD). Here, we characterized the combinatorial effects of both cytokines on the signalling pathways and transcriptional program in intraepithelial lymphocytes (IELs) from CD patients. We also investigated the effects of BNZ-2, a novel, oral, peptide antagonist of IL-15 and IL-21 in development for the treatment of active CD, on the cytokine-induced effects in IELs.

Methods
Healthy donors were enrolled in an IRB-approved study at the University of Chicago for collection and isolation of intestinal IELs by biopsy. IL-15, IL-21 or IL-15+IL-21 stimulated IELs were analyzed by Western blot for signalling studies. qPCR was used to analyze transcripts for IFN-gamma and Granzyme B (GrB). RNA-Seq was used for the gene expression profiling.

Results
IL-15 and IL-21 activate complementary signalling pathways in IELs: IL-15 increased pSTAT5, pAkt and pERK in a concentration-dependent manner (0.4-10 ng/mL), while IL-21 preferentially induced pSTAT1 and pSTAT3 (max effect ≥0.3 ng/ml) and augmented the IL-15 effects. Furthermore, RNA-seq performed 2h after stimulation with these cytokines, showed that IL-21 altered significantly the expression of 417 genes in IELs. Among these genes 152 were IL-21 specific (FDR<0.1). IL-15 had a profound impact on the transcriptional program of IEL, with 5162 genes being affected (FDR<0.1). Among these genes, 384 were further modulated by IL-21 (log2FC>0.5). For instance, IL-15 or IL-21 alone doubled gene expression of IFN-gamma and GrB above control, while IL-15+IL-21 synergistically-increased expression by 6-7-fold.

BNZ-2 blocked the IL15+IL-21 effects on all signalling pathways (pSTAT/pAkt/pERK), GrB/IFN-gamma gene expression, and other activated genes detected by RNA-seq in a concentration-dependent manner.

Conclusion
The combination of IL-15+IL-21 induces complementary signalling pathways that resulted in profound alterations of the transcriptional program in IELs. BNZ-2, by simultaneously blocking IL-15 and IL-21, constitutes a unique, potential therapeutic approach for CD.

O022

Simvastatin as a biomarker for intestinal villous health for recovering celiac disease patients

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Background
The only currently accepted means for monitoring the villous health of the small intestine is by an intrusive and expensive biopsy. We report new trial results using a minimally-invasive diagnostic tool for celiac disease (CD) management. Simvastatin (SV), a commonly used medication, is highly metabolized by CYP3A4 expressed on the villi of the small intestine. We therefore use the metabolic rate of SV as a biomarker for villous health.

Methods
A cross-sectional trial was conducted for 20 newly diagnosed and 10 long-term treated CD patients as well as 10 healthy non-CD control patients. SV was administered orally to the patients and blood (2 mL) was drawn at five timepoints (0 to 180 min). Quantification of SV and its primary metabolite simvastatin acid (SVA) in serum were measured using an Agilent 1290 LC system coupled to a 6530 qTOF, operated in electrospray positive ion mode. The Cmax values for SV and SVA were compared to approximations using various model fits to just two timepoints (60 and 120 min) to assess the accuracy for a practical diagnostic.

Results
A distinct differentiation in SV Cmax values was observed in the expected trend of high values for newly diagnosed CD, low values for healthy non-CD controls, and intermediate values for long-term treated CD. A Gaussian two-point fit for Cmax gave ROC plots (sensitivity vs. specificity) that nearly matched that for the full time period Cmax determination. An unexpected result was that SV levels for long-term gluten-free diet treated patients increased for patients with increasing weight suggesting that gluten-free diets may not be sufficiently under control for removing gluten.

Conclusion
This work substantiates the previous successful feasibility study indicating that the SV diagnostic of CD patients on a treatment program affords a minimally-invasive and economical means to monitor intestinal recovery without resorting to biopsy.

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SESSION 1: DIAGNOSIS AND CLINICAL PRESENTATION

P001

An acute cytokine signature elicited by a bolus gluten challenge identifies patients following a gluten-free diet (GFD) with celiac disease (CeD) from those without

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Background
A shortcoming of diagnostics for celiac disease (CeD) is their reliance on sustained gluten exposure for accuracy. Elevated IL-2 and IL-8 is observed 4h after a single injection of Nexvax2, a therapy targeting gluten-specific T cells in CeD. We assessed if an oral bolus gluten challenge induced similar responses and if this could be exploited to distinguish patients with CeD from those without.

Methods
A randomized double-blind placebo-controlled food challenge (DBPCFC) was undertaken in CeD participants using a drink containing wheat gluten flour (3g gluten) or matched gluten-free flour. Blood was collected at multiple time-points to 8h. A panel of 19 chemokines / cytokines were measured (multiplex ELISA) and the CeD patient reported outcome (CeD-PRO) recorded. An open-label challenge of bread (6g gluten) was then undertaken to compare these readouts in participants with CeD and "gluten sensitive" individuals following a GFD medically confirmed not to have CeD.

Results
The DBPCFC was completed in 21 CeD participants (12 gluten, 9 placebo) and the open-label in 19 CeD and 7 non-CeD. IL-2 and IL-8 increased 2-4h after gluten in those with CeD. In the DBPCFC, gluten significantly increased serum IL-2 (gluten: median fold change from baseline 12.6 vs placebo: 1.0, p=0.0001 2-tail Mann Whitney) and IL-8 (gluten: 2.4 fold vs placebo: 1.14, p=0.012) vs placebo. CeD-PRO score worsened more commonly after gluten than placebo at 3h. In the open-label study, IL-2 and IL-8 did not increase in anyone without CeD. Sensitivity and specificity for CeD based on elevated IL-2 was 89% and 100%, and for IL-8 74% and 100%.

Conclusion
A specific, acute cytokine response occurs after gluten ingestion in CeD similar to that after Nexvax2 and correlates with the onset of gastrointestinal symptoms. Measurement of IL-2 and IL-8 following gluten challenge allows "gluten sensitive" patients without CeD on GFD to be identified.

P002

Different clinical presentations of celiac disease in a group of egyptian children

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Background
Celiac disease (CD) is not uncommon in Egypt. With the availability of serological markers, CD in different At-Risk groups was reported. In this retrospective study, we tried to find the different clinical presentations of our patients, classic or not; and if they were diagnosed late compared to their peers worldwide.

Methods
One hundred files of celiac patients were revised. They fulfilled the diagnostic criteria for CD according to ESPGHAN 2005.

Results
They were < 15 years, 47 boys, 53 girls (M:F=1:1.12). Mean age at onset of symptoms was 3.2 years (9m-14y), mean age at time of diagnosis was 4.7years (1-14years), with a difference between both 1.5 years. The youngest patient diagnosed was 9 months. Chronic diarrhea was present in 63% of patients, FTT in 46%, short stature in 4%, anemia in 62%, constipation in 9%, delayed puberty in 4 %. Other autoimmune diseases were present, 7% had IDDM, 1 patient has ulcerative colitis& IDDM, 1 has autoimmune thyroiditis & IDDM, 1 patient has autoimmune thyroiditis only. Dermatitis herpitiformis present in 2%. Family history +ve in 4%.Total IgA was normal in 71/100 patients. TTG-IgA and EMA-IgA were done separately or together. TTG-IgA +ve in 56/56 patients did the test, EMA-IgA +ve in 31/75 patients. TTG-IgG +ve in 6/7 patients. Marsh III present in 82% of patients & Marsh II present in 15%.

Conclusion
High prevalence of infectious diarrhea & parasitism may lead to under-estimation of other causes of chronic diarrhea. Decreased awareness among pediatricians may be a cause of lack period between beginning of symptoms& definite diagnosis. Availability of serological markers in central laboratories only may add to difficulties in diagnosing the disease. Screening of apparently normal individuals is required to detect the real incidence of the disease.

P003

Transition to adulthood and long-term follow-up of celiac disease in patients diagnosed in childhood

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Background
It has been previously shown in pediatric CD that bulb specimens are frequently of poor quality and that morphological injury is common in the duodenal bulb in non-celiac patients, which can lead to false-positive diagnoses. Our aim was to address the same issue in adult CD.

Methods
We prospectively recruited cases of clinically recommended upper GI endoscopy; all patients also had signs and symptoms of CD and were checked for CD serology and biopsy sampled according with current recommendations. Biopsies were analyzed using our validated morphometric methods.

Results
Altogether 41 patients, mean age 45 years, 61% female, were recruited. Among these, 21 were finally diagnosed as adult CD (mean tTG 156 U / l, median EMA 1:500, and crypt hyperplastic mucosal lesion in distal duodenum) and the rest 20 were non-CD controls (serum negative and normal on distal duodenal biopsy). Quality of bulb biopsy samples was unsatisfactory and unreadable in 67% of CD cases and 50% of controls, even after reorientations and recuttings. All CD patients had, when measurable, VH:CrD<2 in the anatomical bulb (average 0.31, range 0.02-0.61). On the other hand also non-CD controls had a crypt hyperplastic diseased bulb mucosa in 80% of patients (average VH:CrD 1.65, range 0.7-4.1), but the injury was not that severe as in CD (p=0.0006). Inflammation was significantly higher in CD compared to controls (CD3 81.87 vs. 34.05, p<0.01; γδ IELSs 29.12 vs. 6.44, p<0.01). Bulb IgA deposits were positive in all CD patients and was able to discriminate CD cases from disease controls.

Conclusion
As reported in children, bulb biopsy samples in adults are frequently of poor quality and not reliable for accurate histological measurements. Interpretation of results from bulb samples should be done with caution, as non-CD patients may have mild injury in the bulb lining and could be misinterpreted as CD.

P004

Assessment of bulb biopsy samples in celiac disease diagnosis in adults

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P005

Study of bone density in celiac disease

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Background
Low bone mineral density (BMD) is common in celiac disease (CD).

Aim
The goals of the study were to identify the predictive factors of low BMD and of bone density variations.

Methods
The medical files of 607 patients with CD at Europeen Geoges Pompidou Hospital were reviewed [2000-2015]. Four hundred and four had an osteodensitometry and 133 had one before or until six months after beginning a gluten free diet (GFD). An univariate and multivariate analysis were performed for the different factors. The speed of variation of T and Z-score was calculated by the ratio between T and Z-score variation and the duration between these two measures.

Results
46% of patients had osteopenia and 17.5% had osteoporosis. The predictive factors of low BMD in celiac patients were, in lumbar spine and forearm tests, male gender (p<0.001), in lumbar spine and femoral neck test, low body mass index (BMI) (p<0.001) and in the three sites, old age at the diagnosis (p<0.001). In the femoral neck, secondary hyperparathyroidism was a predictive factor of low BMD at celiac disease diagnosis (p=0.016). The factors with an impact on gain of bone density were, in the forearm, female gender (p=0.034) and in the femoral neck, the HLA-DQ2/DQ2 status (p=0.008).

Conclusion
64% of celiac patients had low BMD. The predictive factors were male gender, old age at diagnosis, low BMI and secondary hyperparathyroidism. The gain of bone density was better in woman and in HLA-DQ2/DQ2 patients whereas gluten free diet had no impact.

P006

Prospective evaluation of transglutaminase antibody serum concentrations and epitope specificity to predict screen-detected celiac disease

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Background
Current ESPGHAN guidelines allow the non-invasive diagnosis of celiac disease (CD) in children with relevant symptoms, serum transglutaminase 2 antibody levels (TGA) above 10 times of the upper limit (ULN), endomysial antibody positivity (EMA) and HLA-DQ2 or DQ8 background. In this study we evaluated whether high serum antibody concentrations also predict CD in prospectively followed, regularly screened family members.

Methods
Antibody data were analyzed from the the PREVENTCD multicenter European study which enrolled and followed 1043 DQ2 and/or DQ8 positive newborns with at least one diagnosed CD family member for a period of 3-8 years (median 6.2). Serum TGA levels were determined in years 2007-2014 by the Celikey Varelisa test, in years 2015-2016 by the Celikey ELIA method, which both utilize the same TG2 antigen but have 5 U/ml and 7 U/ml positivity cut-offs. A subset of CD children was also analyzed on MedAll chip with TG2 epitope mutants. EMA tests were performed locally as needed. A small bowel biopsy was offered to symptom-free children with at least two seropositive results or when symptoms appeared. CD was diagnosed based on centralized, blinded evaluation showing Marsh III lesions.

Results
During follow-up, biopsy was performed in 144 children and 124 children were diagnosed with CD of whom 43% were symptom-free. Positive predictive values with 95% confidence intervals () of 2x, 4x, 6x and 10x ULN were 96.0 (90.1-98.5), 99.1 (94.3-99.9), 100 (95.4-100) and 100 (94.8 -100). There was no statistical difference for disease prediction between symptomatic and asymptomatic children with TGA+ levels >4.0xULN. Antibodies of all CD children had typical epitope targeting pattern.

Conclusion
TGA+ results >6xULN measured by the utilized test kits safely predicted CD both in symptomatic and asymptomatic children.

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P007

Development of a strategy for serologic testing for celiac disease in clinical practice

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Background
The diagnosis of celiac disease (CeD) starts with demonstration of IgA antibodies to human tissue transglutaminase (anti-tTG). We compared 3 kits for their performance in diagnosis of the disease and evaluated CeD seroprevalence in a south Indian population.

Methods
Sera from 90 patients with documented CeD and 92 healthy controls were tested for anti-tTG using three different kits. One thousand four hundred and fifty seven healthy adults residing in urban Vellore were tested using a two-step process for prevalence of anti-tTG.

Results
The sensitivity, specificity, false positivity, and false negativity (in percentages) of the three assays were 95.5, 82.6, 17.3, and 4.4 for Aeskulisa; 85.5, 100, 0, 14.4 for Quanta Lite; and 71.1, 100, 28.8, 0 for Celiac Microlisa. The positive and negative predictive values were 84.3% and 95% (Aeskulisa), 100% and 87.6% (Quanta Lite); and 100% and 78% (Celiac Microlisa). The ROC curves showed good discrimination with an AUC of 0.947, 0.950 and 0.886 for the Aeskulisa, Quanta Lite and Celiac Microlisa respectively. Of 1457 (males 695) healthy adults, ninety seven (6.6%) were seropositive for IgA anti-htTG in the Aeskulisa test while 2 tested positive in the Quanta Lite assay and one in the Celiac Microlisa assay, leading to a celiac disease seroprevalence of 1.4 (95% CI 0.3-4.4) per thousand population.

Conclusion
Sequential testing for anti-tTG using first a highly sensitive kit followed by a very specific kit is a useful strategy for screening for CeD in clinical practice.

P008

Celiac disease presenting as cardiomyopathy-a rare extra intestinal manifestation

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Abstract
Cardiac manifestations of celiac disease has been poorly described in the literature, some studies have emphasized on correlation of ischemic heart disease, atrial fibrillation and dilated cardiomyopathy. We describe a patient with celiac disease associated with cardiomyopathy whose cardiac function improved substantially after treatment with a gluten-free diet. A 35 years lady admitted with complaints of chronic diarrhoea, vomiting, weight loss and iron deficiency anemia for which she required blood transfusions and iron therapy since last 3 months. History of full term normal delivery 2 months ago. Physical examination revealed tachycardia, tachypnoea and skin changes, pedal edema suggestive of malabsorption. She had hypotension refractory to fluid resuscitation requiring multiple high dose inotropes and ICU care. Investigations revealed iron deficiency anemia, deranged LFT's, high INR, low albumin (2.4g/dl) and elevated tTG antibody. Her TSH, serum cortisol levels were normal. Echocardiography showed global hypokinesia with LV ejection fraction of 20% and features of dilated cardiomyopathy. Coronary angiography revealed normal coronary arteries. Gastroscopy revealed scalloping of duodenal folds. Diagnosis of celiac disease made on clinical features, serology and biopsy finding of subtotal villous atrophy, increased intraepithelial lymphocytes. Other causes of dilated cardiomyopathy were ruled out. She was monitored in the ICU, kept on gluten free diet and on intravenous steroids for acute celiac crises, celiac related cardiomyopathy as patient had severe diarrhoea, weight loss, hypocalcemia, hypoproteinemia and persistent hypotension. Patient improved within 48 hours of steroid treatment with discontinuation of inotropes over next few days. She was discharged on gluten free diet at six month follow up follow up showed weight gain with near normalization of all biochemical abnormalities, cardiac ejection fraction of 55%. Cardiomyopathy associated with celiac disease is a serious and potentially lethal condition. However, with early diagnosis and treatment with a gluten free diet, cardiomyopathy may be completely reversible.

P009

Celiac disease presenting as celiac artery stenosis and venous thrombosis-an unheard entity

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Extra-intestinal manifestations of celiac disease (CD) are seen in about 20% of patients including venous thrombosis but arterial stenosis is not described in the literature. We report a rare case of 26 year old female who presented with severe persistent upper abdominal pain worse after eating, anorexia, vomiting since last one month and chronic diarrhoea, weight loss and growth retardation since childhood. Amenorrhoea and chronic anaemia was significant past history. Physical examination revealed growth retardation (BMI- 15.92 kg/m2), pallor, icterus and soft mildly tender abdomen. Investigations revealed iron deficiency anemia, increased bilirubin, SGOT, CRP, INR and LDH with low albumin. Autoimmune liver profile was negative Ultrasound revealed mild splenomegaly, mildly altered echo texture of liver, portal and SMV thrombosis and changes of portal biliopathy. Anti endomysial antibody was positive and gastroscopy revealed small esophageal varices, flat duodenal folds .Diagnosis of celiac disease was made based on clinical features, blood parameters, positive serology and D2 biopsy report of total villus atrophy. Thrombophilia work up showed mildly reduced Protein C, Protein S and antithrombin III. CECT abdomen showed 70% stenosis of celiac artery trunk, SMV and portal vein thrombosis and changes of portal biliopathy with mild ascites. No relief of abdominal

pain even after gluten free diet and anticoagulation with IV heparin. Abdominal aortography revealed ostial 80% stenosis of celiac artery with acute band, same treated with PTA, post stenting TIMI-3 flow noted. Abdominal pain subsided within days. She was kept on gluten free diet, antiplatelet and oral anticoagulation on discharge with regular follow up. On follow up excellent improvement seen in form of no abdominal pain, good weight gain and normalization of hemoglobin-13 g/dl. We report first case to our knowledge of celiac disease presenting as severe abdominal pain due to celiac artery stenosis, managed successfully with arterial stenting.

PO10

Improvised light microscopic and computer-assisted image analysis based classifications for assessment of intestinal mucosal biopsies in adults

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Background
The existing histological classifications used for interpretation of small intestinal biopsies are based on qualitative parameters, and prone to inter-observer disagreements.

Methods
The intra and inter-observer agreements using original Marsh, modified Marsh, Corazza / Villanacci, and Ensari classifications were assessed first. This was followed by light microscopic and computer assisted image analysis (CIA) based histological assessment of duodenal biopsies from 147 controls and 210 patients with celiac disease (CeD). Receiver operating curve analysis, followed by multivariate and logistic regression analyses were performed to identify parameters, which could differentiate biopsies of controls and patients with CeD.

Results
The intra-observer and inter-observer agreements with existing classifications varied between 39.7%-64.5% and 12.9%-48.7%, respectively. The normative features in our control cohort were: C:V- 1:2 and normal intra-epithelial lymphocyte (IEL) count 13.4±8.1/100 epithelial cells. On multivariable analysis, villous height <33.5 µm, IEL count ≥ 25/100 ECs and villous area ≥750µm2 were found relevant for differentiation between biopsies from a patient with CeD and controls. We proposed two histological classification systems, based on LM and CIA characteristics, respectively [Table]. A much higher intra-observer (41.9%-86.2%) and inter-observer (27.2%-54.9%) agreements were achieved with our proposed LM-based classification. While the intra-observer agreements with the CIA based classification system were between 22.2%-81.3%, the inter-observer agreement was variable (4.7%-35.3%).

Histological Classes	Criteria	Corresponding modified Marsh types
Type 0	IEL count <25/ 100 ECs+ C: V <1:2	Type 0
Type I	IEL count ≥25/ 100 ECs+ C: V <1:2	Type I
Type 2	IEL count ≥25/ 100 ECs + C: V ratio >1:2	Types 3a & 3b
Type 3	IEL count ≥25/ 100 ECs + C:V ratio >1:5:1	Type 3c
Image analysis Classes	**Criteria**	
Type 0	IEL count <25/ 100 ECs + Villous height case to control ratio > 0.7 µm + villous area case to control ratio <0.9	NA
Type I	IEL count ≥25/ 100 ECs + Villous height case to control ratio > 0.7 µm + villous area case to control ratio <0.9	NA
Type 2	IEL count ≥25/ 100 ECs + Villous height case to control ratio < 0.7 µm 'OR' villous area case to control ratio ≥ 0.9	NA

IEL-intra-epithelial lymphocytes; EC- epithelial cells; C: V- crypt to villous ratio; NA- not applicable

Conclusion
In comparison to existing histological classifications, the improvised light microscopic and newly proposed CIA-based classification systems are based on quantifiable histological parameters and simple to use.

PO11

NMR Based Metabonomics Strategy for Identification of Biomarkers of Villous Abnormalities in Celiac Disease

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Background
Despite various studies on the pathology and molecular basis of CeD, not much is known on biochemical mechanism of mucosal injury. Thus, present study investigated the metabolic profile of duodenal biopsies from CeD patients and controls using NMR spectroscopy to identify biomarker of villous abnormalities in CeD.

Methods
The duodenal biopsies were collected from CeD patients (n=50; mean age 25.9±10.6 yrs) and disease controls (n=30; mean 34.4±10.1 yrs) and water soluble metabolites were extracted using perchloric acid extraction. The lyophilized powder obtained was dissolved in D2O for NMR spectroscopy. One dimensional and two dimensional total correlation spectroscopy NMR experiments were performed at 700 MHz (Agilent, U.S.A.) for metabolic profiling of biopsies. The concentration of metabolites was determined and compared using Mann Whitney (SPSS 20.0) test and p-value <0.05 was considered significant.

Results
Metabolic profiling of duodenal biopsies using NMR identified 44 metabolites, of which levels of 23 metabolites were quantified. CeD patients showed significantly lower ($p < 0.05$) glycine, histidine and glycerophosphocholine while higher concentrations of allantoin as compared to controls.

Conclusion
Present study demonstrated a distinct metabolic fingerprint of duodenal mucosa in CeD patients. Patients with CeD showed significantly lower concentration of histidine and glycine in comparison to controls. Both of these amino acids have been shown to exhibit anti-inflammatory effects. Thus, reduced levels of these might reflect compromised cytoprotective mechanism that might have contributed to the perpetuation of inflammation. Further, higher level of allantoin in CeD patients indicated increased oxidative stress that would have resulted in the inflammation. GPC is an essential membrane metabolite for regulation of growth, differentiation and renewal of enterocytes. Its lower level indicated villous atrophy in CeD. The results may have implications in finding biomarker of villous abnormalities in CeD.

PO12

Prevalence of ultrashort segment celiac disease among north indian patients with celiac disease

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Background
Ultrashort celiac disease (USCD) is an emerging concept when first part of duodenum is the only site of villous atrophy in newly diagnosed celiac disease (CD). The aim of this study was to assess the importance of D1 biopsy in diagnosing CD in adults and to study prevalence in north Indian patients.

Methods
Patients with history suggestive of malabsorption (chronic diarrhea, weight loss, iron deficiency anemia) or serologic suspicion of CD (positive IgA tTG) attending PGIMER, Chandigarh from October 2016 to May 2017 were enrolled in the study. We performed hemogram, biochemical parameters and IgA tTG for all patients. Esophagogastroduodenoscopy was done in all patients where the first (D1) and second part (D2) of duodenum were initially evaluated with white light followed by narrow band imaging. Biopsies were obtained from D1 and D2 in separate containers. Clinical data from patients diagnosed with USCD was compared with patients with conventional celiac disease (CCD) (villous atrophy beyond D1). The number of intraepithelial lymphocytes (IELs) were compared between D1 vs D2 in patients with CD.

Results
Total 48 patients (28 females, 20 males) were included in this study. Of these 5 patients were found to have evidence of USCD, giving a prevalence of 10.4%. The average age of patients in USCD group was 24.40±8.44 years and in the CCD group was 28.80±11.53 years (p=0.405). Although the tTG titres were higher in the CCD group (93.02±9.35 IU/ml) than the USCD group (40.80±22.03 IU/ml), this did not reach significance (p=0.074). IELs in the USCD and CCD groups were 60.80±39.23 and 83.07±32.16 in D1 (p=0.158), and 44±10.10 and 81.51±30.89 in D2 (P=0.010)

Conclusion
Prevalence of USCD in North Indian patients with CD was found to be 10.4%. A bigger sample size will more clearly bring out the differences in profile of USCD and CCD.

PO13

Can narrow band imaging predict duodenal histology in celiac disease? A prospective double blind pilot study

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Background
Celiac disease (CD) is characterized by varying degrees of villous atrophy. Image enhancement with narrow band imaging (NBI) delineates villous patterns better than routine endoscopy. Hence, this study was conducted to compare the diagnostic accuracy of NBI with histopathology in predicting the duodenal villous morphology in CD.

Methods
Amongst the 220 subjects (mean age-28.04 ±12.57 years, 124-females) included in the study, 147 were suspected to have CD (serology positive), 47 were follow up patients on gluten free diet and 26 had dyspepsia with no evidence of CD on complete evaluation. CD was diagnosed on the basis of modified ESPGHAN criteria. They underwent esophagogastroduodenoscopy (EGD) with duodenal biopsies along with NBI using an Olympus GIF-180 gastroscope to evaluate the villous pattern of duodenal mucosa. Villous patterns on NBI were classified into Normal-villous pattern (NVP), Distorted & blunted-villous pattern (DVP) and Absent-villous pattern (AVP). Histopathology was graded according to modified Marsh criteria. NBI findings were

correlated with histopathology. Chi- square test was used for statistical analysis.

Results
The NBI pattern in controls was NVP in 25, DVP in 1 with none having AVP, while on histopathology, all 26 had no villous atrophy. In those with CD (CD suspected and follow up, n=194) 95 had AVP, 72 had DVP and 27 had NVP on NBI, while on histopathology 98 had total villous atrophy, 77 had partial villous atrophy and 19 had no villous atrophy. Scalloping and grooving was seen in in 74.7% of CD subjects. Significant correlation was observed between NBI and histopathological examination (correlation coefficient 0.797, p<0.001). The overall sensitivity and specificity of NBI for delineating villous pattern were 93.71% and 88.89%, and the positive and negative predictive values were 97.04 % & 78.43% respectively.

Conclusion
NBI can predict villous atrophy with high sensitivity, specificity and positive predictive value in CD.

PO14

Evaluation of IgA-tTG as a diagnostic biomarker for celiac disease and histological features in indian population

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Background
Celiac Disease (CD) is a chronic small intestinal autoimmune disease related to dietary gluten, and is associated with autoantibodies in the serum against tissue transglutaminase 2 (tTG), a ubiquitous enzyme. The current study aimed to evaluate IgA-tTG as diagnostic biomarker for CD and its association with different histological features in North Indian Population.

Methods
The present study is a prospective open label observational study consisting of 290 patients (198 adult; 92 children) with symptoms of chronic diarrhea, anemia and other GI disturbances, All patients underwent esophagogastroduodenoscopy (EGD) using an Olympus GIF-180 gastroscope to evaluate the villous pattern of duodenal mucosa along with biopsies from first (D1) and second (D2) part of duodenum. IgA-tTG level was measured for all patients and modified Marsh grading was used for assessing histological changes. Data was analysed by SPSS software.

Results
Using a cut off of 10 EliA U/ml, sensitivity for diagnosis of CD was 84.27%, positive likelihood ratio was 84%, and positive predictive value was found to be 100%. No significant difference in IgA-tTG level was seen among patients with different level of disease activity, patients in remission and patients not in remission (histological remission). IgA-tTG level alone could not differentiate different stages of disease activity and villous atrophy. However, IgA-tTG level could predict crypt hyperplasia (p=0.017). Using ROC curve, IgA-tTG value of 136.5EliA U/ml could predict crypt hyperplasia, and IgA-tTG>136.5 had sensitivity 66.67%, specificity 87.85%, PLR 5.49, NLR 0.38, PPV 13.33% and NPV of 98.95% for prediction of crypt hyperplasia.

Conclusion
The study concluded that in north Indian population, IgA-tTG of >10 EliA U/ml was found to be a good biomarker of CD. IgA-tTG level >136.5 EliA U/ml was found to be a good predictor of crypt hyperplasia.

PO15

Single centre prospective study of the role of duodenal bulb biopsies in the diagnosis of celiac disease

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Background
Celiac disease is a systemic immune mediated disorder triggered by dietary gluten in genetically susceptible persons. D1 had been avoided as a possible biopsy site because of concerns over presence of Brunner's glands, gastric metaplasia, peptic duodenitis, and presumed reduced villous height. Prospective data from small studies has suggested that D1 may be the only site of villous atrophy in newly diagnosed celiac disease (ultra-short celiac disease). We wanted to verify this concept that whether the addition of duodenal bulb biopsy increase the diagnostic yield of celiac disease and was there any difference in histological grading between the two sites.

Methods
It was a prospective study of 98 cases of celiac disease who were symptomatic clinically and positive for celiac serology. Endoscopically four mucosal biopsies each, were taken from the bulb and distal duodenum of each patient and morphology was graded as per Modified Marsh grade.

Results
In our study of 98 patients, out of 196 biopsies, 60 patients showed same Marsh grade in the bulb and descending duodenum and 38 patients showed different Marsh grade at both the sites. Patients those have different Marsh grade, descending duodenum showed higher grade than the bulb part in 24 patients while 14 patients showed higher mucosal atrophy in bulb than descending duodenum. 92% of bulb biopsies were diagnostic of Celiac disease. Although there was a difference in morphological grade at both the sites, in none of the cases, the bulb biopsy was positive with negative distal duodenal biopsy for celiac disease.

Conclusion
Biopsy from both sites are mutually exclusive and different Marsh grade can be seen in the same patient. Difference in biopsy from bulb and descending duodenum demonstrates patchy distribution of celiac disease. Thus, taking biopsy from both sites maximize the diagnostic yield.

PO16

Validation of indigenous point - of - care test for celiac disease among children and adults in a tertiary hospital in north India.

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Background
Traditional serological assays for diagnosis of celiac disease (CD) such as tissue transglutaminase (tTG) IgA antibody and anti-endomysial antibody (AEA) are expensive, not readily available and require a well-equipped laboratory with a long turnaround time. An indigenous human recombinant tTG based Point of care Test (POCT) for CD in collaboration with AIIMS, ICGEB (International Centre for Genetic Engineering and Biotechnology) and J Mitra Pvt. Ltd has been developed. This test detects anti-tTG antibodies (both IgA and IgG based) present in the serum within 20 minutes. We validate this POCT among children and adults in a tertiary care hospital.

Methodology
Design- Cross sectional study.

Setting - Paediatric and adult outpatient gastroenterology clinic of Tertiary care hospital in north India.

Participants-Total of 98 cases and 49 controls were enrolled over a period of six months (Dec-May 2017). We considered the data from previous study using tTG antibody as the acceptable levels of sensitivity and specificity for calculating sample size. Sera of newly diagnosed celiac cases based on TTG/AEA Positivity and Duodenal biopsy: Modified Marsh Grade 2 or more villous atrophy were collected. Simultaneously sera were also taken from controls who underwent upper gastrointestinal endoscopy for reasons other than suspicion of celiac disease and had TTG/AEA negative and duodenal biopsy normal. Patients already on GFD were excluded. Sensitivity and specificity of index test was measured.

Results
POCT agreed with 70/98 positive and 49/49 negative diagnoses based on the reference tests. Sensitivity of the index test was 71.4% and specificity was 100%.The positive predictive value (PPV) and the negative predictive value (NPV) were 100% and 63.63% respectively.

Conclusion
We have validated the indigenous card test in our setting. The kit could be used in primary and secondary health care settings where other CD specific serological tests are not readily available.

PO17

Etiological evaluation of anemia among celiac disease patients and evaluation of blood parameters as biomarker for disease activity among Indian celiac disease patients.

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Background
Celiac disease is an autoimmune disorder caused by intolerance to dietary gluten. Anemia is a co-morbidity commonly associated with this disorder. The current study is done to evaluate the different etiologies of anemia associated with celiac disease and evaluation of different blood parameters as biomarkers of celiac disease activity.

Methods
This is an observational study, Patients suffering from celiac disease were included in the study after obtaining informed consent. A total of 283 celiac disease patients were included. Diagnosis of celiac disease was done on the basis of clinical history, upper G.I. endoscopy and biopsy. Patients were evaluated for presence of anemia, which was followed by etiological evaluation of anemia as per standard guideline. Another objective of our study was to evaluate different blood parameters as biomarker for celiac disease activity prediction. Correlation was evaluated between MARSH grading and different blood parameters and IgA-tTG and different blood parameters. Data was analyzed by proper statistical test using SPSS software.

Results
Anemia was present in 83% of celiac disease patients. 76% had iron deficiency, 6% suffered from Helminthiasis, 18.75% had vitamin B12 deficiency and 4.76% had folic acid deficiency. Regarding biomarker evaluation for prediction of disease activity, High level of correlation was seen between MARSH grading and Hb% and MCV, High level of correlation was also seen between IgA-tTG level and MCV.

Conclusion
Anemia is common among celiac disease patients. Iron deficiency anemia is most common cause of anemia, followed by vitamin B12 deficiency. MCV correlated well with both disease activity and IgA-tTG level. Hb% was also found to be good predictor of Disease activity.

P018

Spectrum clinical & subclinical endocrinopathies in patients with treatment naive Celiac disease

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Background
Celiac disease (CeD) is associated with many autoimmune diseases including autoimmune thyroid disease and type I diabetes. What happens to other endocrine organs in CeD is not well-described. We evaluated treatment naïve patents with CeD for endocrine organ function(s).

Methods
Seventy-four treatment naïve patients with CeD underwent clinical, biochemical evaluation and assessment for functions of endocrine organs including, thyroid, pancreas, parathyroid, pituitary and adrenal glands. Biochemical assessment of endocrine organ functions was done using relevant tests e.g Chemiluminescence assay. Clinical endocrinopathy was defined if patient had both relevant clinical symptoms / history of treatment of endocrinopathy and abnormal biochemical / hormonal assessment and Subclinical endocrinopathy if they had abnormal biochemical / hormonal assessment, but no symptoms.

Results
Following was spectrum of clinical and subclinical enteropathies (Table)

Endocrinopathy Patients with CeD Type 1 diabetes (n=74) Clinical: 7 (9.5%)1 0 (13.5%) Subclinical: 3 (4.1) Hypothyroidism (n=74)Clinical: 10 (13.5%) 14 (18.9%) Subclinical: 4 (5.4%) Hypogonadism

(Age>15 years to ≤40 years)

(n=54) Clinical: 6 (11.1%) 12Subclinical: 6 (11.1%) Primary growth hormone deficiency in age <18 years (male) and < 17 years (females) (n=9) Clinical: 8 (88.9%)

Subclinical: Not evaluated 8 / 9 Primary hypoparathyroidism (n=74) Clinical:1 (1.4%) 1 (1.4%) Primary hyperparathyroidism (n=74) Clinical: 1 (1.4%) 1(1.4%) Total no. of endocrinopathies in all patients Clinical: 33 (44.6%)46Subclinical: 13 (17.6%) Patients with at least 1 endocrinopathy (clinical / subclinical) 31 (41.9%) Patients with one endocrinopathy (clinical / subclinical) 18 (24.3%) Patients with two or more endocrinopathies (clinical / subclinical) 13 (17.6%).

Following was spectrum of clinical and subclinical enteropathies:

Endocrinopathy		Patients with CeD
Type I diabetes(n=74)	Clinical: 7 (9.5%) Subclinical: 3 (4.1)	10 (13.5%)
Hypothyroidism (n=74) Hypogonadism	Clinical: 10(13.5%) Subclinical: 4 (5.4%)	14 (18.9%)
(Age>15 years to ≤40 years) (n=54)	Clinical: 6 (11.1%) Subclinical: 6 (11.1%)	12
Primary growth hormone deficiency in age <18 years (male) and < 17 years(females) (n=9)	Clinical: 8 (88.9%) Subclinical: Not evaluated	08-Sep
Primary hypoparathyroidism (n=74)	Clinical:1 (1.4%)	1 (1.4%)
Primary hyperparathyroidism (n=74)	Clinical:1 (1.4%)	1(1.4%)
Total no. of endocrinopathies in all patients	Clinical: 33 (44.6%) Subclinical: 13 (17.6%)	46
Patients with at least 1 endocrinopathy (clinical / subclinical)		31(41.9%)
Patients with one endocrinopathy (clinical/subclinical)		18(24.3%)
Patients with two or more endocrinopathies (clinical/subclinical)		13(17.6%)

Conclusion
41.9% of patients with CeD had at least one endocrinopathy either clinical or subclinical. High prevalence warrants early screening of endocrinopathies in patients with CeD. Whether high prevalence of endocrinopathies are the manifestation of CeD or associated autoimmune endocrine organ diseases, needs exploration. Furthermore, the response to gluten-free diet in them is worth exploring.

P019

Clinical profile of adult onset celiac disease in Central India - A single center experience.

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Background
Indian data regarding celiac disease is mostly available from northern states and mainly from pediatric age group. There are increasing reports of celiac disease being diagnosed in adults for first time however there are not many reports about adult onset celiac disease from Central part of India.

Aim
The aim of present study is to study the clinical profile of adult onset celiac disease patients in a tertiary care center in central India.

Methods
All patients who were diagnosed with Celiac disease for first time above the age of 18 years between 01/06/2009 to 31/05/2017 were included in this study and their clinical profile were recorded

Results
Total 75 patients above the age >18 years were diagnosed with celiac disease in this period. The mean age of presentation was 36 years with female preponderance (M:F - 0.67:1). The most common presentation was loose stools (42.6%) followed by abdominal pain (40%). Family history of celiac disease was present in 5.3% of patients. 37.3 % of patients were tobacco chewers and 18.6% patients were chronic alcoholic. Clinical examination was unremarkable in majority of patients except presence of pallor in 36% patients. The mean Hemoglobin was 8.5g/dl and mean MCV was 64.08 fl. 28 % patients had hypoalbuminemia. 17.33 % of patients had negative or equivocal IgA anti TTG. On UGI endoscopy typical features of celiac disease like scalloping, fissuring, cobble stoning of mucosal folds and blunted villi were present in all patients. On histology 72 % of patients had grade II-III (marsh) villous atrophy. All patients showed improvement in symptoms and weight gain within 3 months of staring gluten free diet.

Conclusion
1. Nonspecific abdominal pain with iron deficiency anemia is common mode of presentation in adults other than chronic diarrhea. 2. Its more common in female.

P020

Autoimmune thyroid disease in the first-degree relatives of patients with celiac disease

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Background
Approximately 7.5% of first-degree relatives (FDRs) of celiac disease (CeD) patients develop CeD. Since CeD patients are at a higher risk of developing other autoimmune disorders; this poses a question that whether their FDRs also have increased susceptibility to these disorders. We, therefore, screened FDRs of patients with CeD for presence of thyroid autoimmunity and associated thyroid dysfunction.

Methods
In this prospective case-control study, we recruited 194 FDRs of CeD patients (males 101) and 140 healthy controls (males 107). They were screened for CeD using anti-tissue transglutaminase antibodies. They were screened for thyroid auto-immunity using anti-thyroid peroxidase antibody (anti-TPO) and thyroid dysfunction using a symptom questionnaire and estimation of serum TSH levels.

Results
The prevalence of thyroid autoimmunity in FDRs was significantly higher in comparison to that in healthy controls (17.1% vs. 5.0%; p=0.0008). Significantly higher number of FDRs also had high serum TSH values as compared to controls (11.9% vs 3.7%; p=0.009). Amongst FDR's who showed thyroid autoimmunity, 42.4% were siblings, 45.4% parents and only 12.1% were children of the index patient with CeD. Familial clustering was seen in 2 families. Only 4 anti-TPO Ab positive FDR showed any symptoms. Significantly higher number of FDRs had positive anti-tTG Ab compared to controls (15.1% vs 1.6%).However, only 4 FDRs with positive CeD serology were symptomatic. Amongst FDRs, 4 were positive for both anti tTG and anti-TPO, 3 of them being siblings.

Conclusion
FDRs of patients with CeD have almost 4-fold higher risk of developing autoimmune thyroiditis, and some of them also associated thyroid dysfunction. Furthermore, autoimmune thyroiditis and even coexistent CeD in FDRs is mostly silent / asymptomatic. This association between CeD and autoimmune thyroiditis can be attributed to common genetic background or environmental factors. There is a need to develop right strategies for screening of FDRs for CeD and other related autoimmune disorders.

P021

Gluten sensitivity in patients with cerebellar ataxia: A prospective cohort study

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Background
Cerebellar ataxia is a heterogeneous group of disorders, which can be familial or sporadic. Sensitivity to gluten has been implicated in the pathogenesis of sporadic cerebellar ataxia. Gluten-related disorders are emerging in Asia. There is no data on prevalence of gluten sensitivity from Asian countries, we therefore screened a well-defined cohort of patients with cerebellar ataxia for presence of gluten sensitivity.

Methods
A cohort of 192 well-characterized patients with progressive cerebellar ataxia, familial or sporadic, were screened for presence of gluten sensitivity using Ig A anti-gliadin Ab (AGA), IgG-AGA, anti-transglutaminase 2 Ab (TG2), and anti-transglutaminase 6 (TG6) antibodies using commercially available ELISA kits. The data on their genetic testing for spinocerebellar ataxia (SCA) 1, 2, 3, 12 and Friedreich's ataxia (FRDA), and brain imaging were reviewed.

Results
Of 192 patients, 99 and 77 had sporadic and familial cerebellar ataxia, respectively and in 16 the pattern of inheritance could not be confirmed. Of all patients, genetic mutation for SCA types 1, 2, 3, 12 and FRDA were confirmed in 76 (40%) patients. Forty-two (21.8%) patients had either one or more serological test positive for gluten sensitivity [20 (10.4%) for IgA-AGA, two of 87 (2.2%) for IgG-AGA, one of 141 (0.71%) patients for anti-TG2-ab and 23/186 (12.3%) for TG6 Ab]. Nineteen of 30 (63.3%) seropositive patients had cerebellar atrophy. Enteropathy or celiac disease was not observed in the 10 patients those underwent duodenal biopsy.

Conclusion
Forty-two (21.8%) patients had either one or more serological test positive for gluten sensitivity. Immune mediated gluten sensitivity is not as common in India as in other populations. In patients with cerebellar ataxia, dietary gluten may have a causal relationship or at least disease modifying effect.

PO22

Gut bacterial concentration in adult celiac patients analyzed using non-invasive lactulose hydrogen breath test

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Background
Celiac Disease (CD) is common cause of malabsorption. It is chronic immune-based enteropathy triggered by dietary Gluten in genetically predisposed individuals and resolves with exclusion of gluten from diet. Gastrointestinal symptoms include diarrhea, malodorous flatulence and abdominal pain. These problems may arise due to abnormal bacterial concentration in GI tract. Relationship of hydrogen concentration in breath (which is indirect representation of bacterial concentration) with GI problems in celiac patients has not yet been analyzed.

Aim
To analyze gut bacterial concentration on basis of breath hydrogen levels in celiac patients.

Methods
53 patients of celiac disease with age range 24-60 years & 54 age and sex matched apparently healthy controls were enrolled. Hydrogen concentration in end expiratory breath at different time intervals was measured by non-invasive lactulose hydrogen breath test. Area under the curve was calculated to analyze the gut bacterial concentration. Small intestinal bacterial overgrowth (SIBO) was analyzed by non-invasive glucose hydrogen breath test. Rise in hydrogen concentration ≥10ppm over fasting value within 2 hours of glucose ingestion was considered as SIBO. Concentration of hydrogen was measured by using SC Microlyser from Quintron, USA.

Results
Out of 53 patients, 28 were females with Mean±SD of age 38.7 ± 16.3years and 25 males with Mean±SD of age 34.1±11.8 years. Mean±SD of hydrogen concentration (1356.1± 455.9 ppm) was significantly higher (p?0.05) in celiac patients as compared to controls (1081.2±408.3 ppm). It was observed that %age 9/53 (17%) of SIBO was significantly higher in celiac patients as compared to controls 1/54 (1.8%). Furthermore, SIBO positive celiac patients showed significantly higher (p?0.05) hydrogen concentration (1597.6 ± 479.1 ppm) as compared to SIBO negative patients (1141.2 ± 522.7 ppm).

Conclusion
This study indicates that higher hydrogen concentration in celiac patients may be due to excess of gut bacteria leading various GI symptoms in these patients.

PO23

Serum intestinal fatty acid binding protein in celiac disease: a pooled analysis of diagnostic performance

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Background
Celiac disease was a disorder that could result in intestinal damage. Duodenal biopsy was still considered mandatory to prove mucosal damage in celiac disease. Serological marker that frequently used to diagnose celiac disease such as IgA anti-tissue transglutaminase, endomysial antibody, or anti-deaminated gliadin was not specific for mucosal damage. Non-invasive method for predicting mucosal damage in celiac disease is necessary. Serum intestinal fatty acid binding protein (I-FABP) is thought as a sensitive marker to study enterocyte damage.

Method
Search was conducted in the databases such as MEDLINE, PubMed, Google scholar, and the conference abstracts for following terms "serum", "intestinal fatty acid binding protein", "I-FABP", "IFABP", "celiac", "coeliac", and other similar terms. The criteria for included studies were I-FABP as the diagnostic marker for histologically-proven celiac disease with villous atrophy for the result of mucosal damage compared to the placebo (no villous atrophy in histologic result or negative serology result).

Results
Seventeen articles found and the authors review each abstract of those studies. Four studies were eligible for further analysis according to the inclusion criteria. The cut-off values of I-FABP were vary in each study, ranging from 224 pg/mL to 405.1 pg/mL which were considered positive for celiac disease with histologically-proven villous atrophy (Marsh IIIA-C). The pooled diagnostic value of I-FABP in diagnosing celiac disease has sensitivity 74.7% (95% confidence interval (CI) 68.1%-80.6%), specificity 89.2% (95% CI 84.2%-93%), positive predictive value 86.5% (95% CI 81.3%-90.5%), and negative predictive value 79.1% (95% CI 74.8%-82.8%).

Conclusion
I-FABP was a useful diagnostic method for diagnosing celiac disease, especially as the non-invasive method for the intestinal mucosal damage predictor.

PO24

Comparison of histological findings of duodenal biopsies from celiac patients after 6 months and 2 years of gluten free diet

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Background
Celiac disease is characterized by histopathological small bowel mucosal changes which usually normalizes after gluten free diet. Little information is available regarding the histological changes during GFD in long term. Our aim was to evaluate a novel criterion to compare duodenal histology in celiac disease patients after 6 months and 2 years of gluten withdrawal.

Methods
Known cases of celiac disease with Marsh II& III (confirmed by serology and biopsy) invited to the clinic into two groups: group A (n=20), after 6 months and group B (n=37) after 2 years gluten free diet. All patients underwent upper GI endoscopy and 4 biopsies specimens were collected from bulb and second part of duodenum and also anti-tTG (IgA) was assessed. The histological abnormalities of duodenal biopsies were compared after 6 months and 2 years of gluten free diet according to Marsh classification.

Results
Fifty -seven patients (24 males 33 females, median age 39 years, range; 15-67 years) underwent endoscopy in addition to serological assessment. In group A (n=20), histology were improved in 7 (35%) patients from Marsh II to Marsh I, 7 (35%) showed normal histology and in 6 (30%) patients Marsh III were persisted. In group B (n=37), 9 (24%) were turned to Marsh I from Marsh III, 1 (3%) March II, 7 (19%) March III and 20 (54%) showed normal histology. Of those in group A, 5 patients (25%) had positive anti TTG compared with 7 (19%) in group B.

Conclusion
The result of this study shows that histological recovery in adults with celiac disease may be delayed and around 20% are still sever mucosal abnormality. We therefore recommended that biopsies should be taken 2 years after starting a GFD in adults with celiac disease especially in those with GI and extra-GI symptoms.

Keywords
Celiac Disease, DFD, Marsh classification

PO25

How quickly iron deficiency anemia improves gluten free diet? How reliable is HLA typing in excluding coeliac disease?

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Background
Iron deficiency anemia (IDA) represent a feature of coeliac disease (CD) and in most cases improve with gluten free diet (GFD). How quickly the IDA improve with GFD has not been properly studied before. The aim of this study was to evaluate the effect of six weeks gluten free diet on iron deficiency anemia in patients with CD. We also assessed the specificity of a negative HLA in excluding CD.

Methods
Out of 250 Celiac disease patients detected by serologic testing and confirmed by duodenal biopsies, 29 new cases (18[62.1%] female; mean age 40.28 ±SD=15.574) with IDA were selected for this study. The level of Hg, ferritin, serum iron and TIBC were evaluated at the beginning and after 6 weeks gluten

free diet (GFD). HLA typing was performed according to the Real-time PCR based SYBER Green method.

Results
65.5% of CD patients were HLA DQ2 positive followed by DQ8 in 24.1%, DQ2/DQ8 and 3.4% were negative. Most prevalent symptoms in CD patients were bloating/osteoporosis (62.1%) and weight loss (51.7%) The mean level of Hg, ferritin, serum iron and TIBC in CD group before diet were 11.604 (normal range= 12-16), 43.7807 (normal range= 12-300), 57.252 (normal range=55-160) and 393.75 (normal range= 50-320) and after diet were 11.9010, 50.5279, 61.4386 and 394.8459 respectively. After 6 weeks GFD only the level of ferritin (P= 0.001) was significantly increased.

Conclusion
Improvement of IDA is slow and patients would require iron therapy if symptomatic. Negative CD HLA account for 3.4% of patients, suggesting a negative HLA should be interpreted with caution.

Key words
Celiac disease, iron deficiency anemia, Hg, ferritin, serum iron, TIBC

PO26

Diagnostic value of anti TTG titer in celiac disease

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Background
Duodenal biopsy is required for diagnosis of celiac disease in adults, although some studies have suggested adequate accuracy of serology alone.

Aim
We aimed to assess the correlation between anti-tissue transglutaminase (tTG) titer and pathological findings and to define the specific level of tTG for predicting celiac disease in adults without the need for biopsy sampling.

Methods
This descriptive study was done on 411 participants. The tTG titer and pathological findings of duodenal biopsy samples were used for this study. Analysis of Receiver operating characteristic (ROC) curve was used to find a cut-off point of anti-tTG antibody for mucosal atrophy.

Results
Median (interquartile range) tTg titers in patients Marsh 1, 2 and 3 were 86 (43-199), 250 (187.5-250) and 200 (144-250), respectively and it was significantly higher in patients graded as Marsh≥2 (P<0.001). There was a significant correlation between the Marsh grading and tTg titers (r=0.112, P=0.025). ROC curve analysis showed 81.38% sensitivity and 62.50 specificity for cut-off point≥100 IU/mL of anti-tTG For Marsh≥ II.

Conclusion
In patients with anti tTG more than 100 and clinical symptom we can omit endoscopy and pathology for definite diagnosis of celiac disease

PO27

Risk of autoimmune liver diseases in celiac patients: a systematic review

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Background
Several studies have reported on association between celiac disease and autoimmune liver diseases (ALD), hyper transaminasemia and even cirrhosis. Most studies are about prevalence of celiac in liver disease,and a few are about prevalence and incidence of CLD in celiac, and still there is controversies about the most common type of liver disease in these patients

Aim
Aim of this study was to conduct a systematically review the existing papers about all kind of autoimmune liver disease in celiac disease.

Methods
The systematic review was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines .We searched Medline/PubMed, Scopus, ISI and ProQuest until September 2016 based on the relevant medical subject headings (MeSH) of autoimmune liver diseases and celiac disease and all studies that investigated the relative risk or incidence of ALDs in patients with celiac disease were included. Two authors separately extracted the data .Annual incidence rates of ALD in celiac and non-celiac populations were calculated using the following formula: (Incidence/ (sample size*follow up time)) *100,000. Moreover, incidence rate and ratios were calculated if possible.

Results
Out of 395 articles found in the initial search, 9 were eligible for full text assess and 4 studies were identified to be included in this systematic review. Risk of developing primary biliary cirrhosis in celiac patients was between 25.4 to 27.6 times higer in celiac and risk of developing primary sclerosing cholangitis was 3.9 times higher. In these studies they report standardized incidence ratio of 27.6 after 9 years for PBC .Hazard rate of 8.52 to 10.98 for PBC and 2.38 to 5.18 in PSC with p<0.001.

Conclusion
Our review reveals that celiac patients are at a higher risk of developing all kind of autoimmune liver diseases especially PBC.

PO28

Not all flat mucosa mean celiac disease: differential diagnosis of seronegative villous atrophy

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Background
Although villous atrophy (VA) is the typical lesion of celiac disease (CD), the finding of a flat mucosa with negative celiac serology represents a clinical challenge in terms of differential diagnosis. We aimed to assess the prevalence of the various etiologies of seronegative villous atrophy (SNVA) and to identify differences between seronegative (SNCD) and seropositive CD (SPCD) forms.

Methods
Thirty-one consecutive SNVA patients (mean age 43 years, 67% women) were retrospectively identified between 1998-2014 in our CD Center. All cases were negative for tissue transglutaminase, anti-endomysial and deamidated gliadin antibodies. Tests for HLA-DQ2/8, anti-enterocyte autoantibodies, drug-related enteropathy, *Giardia* stool antigen, serum immunoglobulins, bacterial overgrowth and HIV were performed. Clinical, histological and laboratory findings of SNCD were compared with those detected in 796 SPCD patients.

Results
SNCD was the most frequent cause of SNVA, being found in 14/31 pts (45%), followed by giardiasis (20%), chronic variable immunodeficiency (16%), autoimmune enteropathy (10%), olmesartan enteropathy (3%), small intestinal bacterial overgrowth (3%) and eosinophilic enteritis (3%). SNCD differed from SPCD for a significantly higher mean age (49 vs. 36 years, *P*<0.005) and a significantly higher classical presentation (100% vs. 34%, *P*<0.001). Moreover, SNCD showed a trend for a more pronounced association with autoimmunity, a family history of CD and a more severe small intestinal damage.

Conclusion
SNCD is the most common cause of SNVA, but its diagnosis needs to be carefully confirmed by excluding other gluten-independent causes of SNVA in order to avoid an unnecessary, lifelong withdrawal of gluten.

PO29

Gluten ataxia: A case report

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Background
Gluten ataxia is the commonest neurological manifestation of gluten-related disorders, with a growing number of cases described in the last years. Here we present the case of a young woman with progressive idiopathic neurological impairment and a familial history of celiac disease.

Case Description
A 38-years woman was admitted because of progressive slurring of speech, clumsiness of hands and unsteadiness of gait since one year. She also complained head tremulousness, and a tendency to sway while walking, with occasional falls, and sometimes blurred and double vision, in the absence of intestinal symptoms. She has two children suffering from celiac disease, and she was under thyroid hormone therapy.
On physical examination, dysarthria, right deviation of the head and trunk, lightly widened base gear with lateropulsion to the left, and tandem difficulty, unmodified by eye closure were evident. Moreover, clear cerebellar signs, such as finger-nose incoordination, disdyadkokinesia and fragmentation of tracking movements were found, without strength or sensitivity deficit. Laboratory tests, including metabolic and endocrinologic analyses, were within normal range. Celiac serology, including anti-TTG6 dosage, was negative, as the ANA, ENA, GAD-Ab, ANNA1, ANNA2, Yo, amfifisina, Ma1-2, CV2. By contrast, a strong positivity of anti-Purkinje cell antibodies was evident (1:6400). Genetic tests for cerebellar ataxia syndromes were negative, whilst the presence of a HLA-DQ2 haplotype was found. Electromyography was normal, whereas a slowdown of BAERS, PEV and VEMPS was documented, and a stabilometric examination showed a marked postural instability. The MRI of the brain showed a moderate cerebellar atrophy of the warm and left hemisphere, with a hypometabolism at PET-scan. A mild increase of intraepithelial lymphocytes at immunohistochemistry of the duodenal specimens was found. Following the suspicion of gluten ataxia, a gluten-free diet was established, leading to clinical

benefit and stability of lesions at 12 and 24 months of follow-up.

PO30

Validation of a novel single-drop rapid HLA-DQ2/-DQ8 method to identify people susceptible to celiac disease

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Background
Major histocompatibility complex(HLA) HLA-DQ2 and/or DQ8 is considered an essential risk factor for celiac disease (CeD). About 90% -95% of patients with CeD have HLA DQ2/DQ8 haplotype and HLA DQ2/DQ8 typing is considered as an additional diagnostic test. Conventional PCR-based HLA typing method is expensive and complex, requires a well-trained person to perform the test and it takes hours to provide the result. We assessed the efficacy of a new-fangled sequence-specific, primer based rapid single PCR reaction HLA method for detection of HLA-DQ2/-DQ8. The rapid test takes about one and half hours to complete the test.

Methodology
For detecting the sensitivity of the rapid test in comparison to the gold standard test, we required subjects with a positive HLA-DQ2/DQ8 haplotype where HLA haplotype has been determined by the standard SSO-PCR testing (Gold standard) as well as DQ2/DQ8 negative samples. We performed rapid HLA test using a BioDiagene Celiac Gene Screen kit, that foresees a rapid DNA extraction (1 min), a DNA amplification and a detection using a fluorescence reader. In addition to 101 patients with known HLA for assessment of sensitivity, we also determined HLA-DQ2/DQ8 status in additional 219 samples (CeD n=209 and healthy controls n=10) using rapid HLA haplotype detection test.

Result
Of 101 known HLA results, 79 were positive HLA-DQ2/DQ8 and 22 were HLA-DQ2/DQ8 negative samples by the standard test, all 79 reported positive and 22 reported negative by rapid test. There was an excellent concordance rate between testing by the standard method and rapid method. Amongst unknown samples, 186 of 209 of CeD, and 2 of 10 healthy controls were either/or HLA-DQ2/DQ8 positive by the rapid test.

Conclusion
Rapid single PCR reaction HLA gene test
method showed an excellent concordance with the standard test. Rapid testing could be a cost reducing and an effective tool for CeD gene screening.

PO31

Autoimmune diseases associated with celiac disease: experience of a gastroenterology Moroccan unit

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Background
The coeliac disease (CD) is an autoimmune enteropathy. It is most of the time associated with other autoimmune disorders. It is therefore necessary to search for autoimmune diseases each time the CD diagnosed, and to think about CD; before every autoimmune disorder.

Methods
Retrospective descriptive study covering a period of 20 years (January 1995 -July 2016); including all the patients with a CD. The diagnosis of autoimmune diseases was based on clinical arguments and the result of specific examinations.

Results
Out of a total of 241 patients followed-up for CD & NBSP; in the department, 32 patients had at least one autoimmune disease associated with CD Which corresponds to 13.2 % .There were 26 women and 6 men with a sex ratio w/m of 4.3 .The average age was 37 years (14-70 years). The diagnosis of associated autoimmune diseases preceded the diagnosis of coeliac disease in 10 cases, succeeded to it in 10 cases and was concomitant to it; in 12 cases. For the serology 75% (24 cases) of the patients were seropositive, 21.8% (7cases) were seronegative and not realized in 2.7%;. It was autoimmune hepatitis in 6 cases (18.75%), all type 1, type 1 diabetes in 4 cases (12.5%), biermers disease in 3 cases (9.3%), 3 cases of colic crohn (9.3) and 2 cases (6.25%)for the following diseases: dermatitis herpetiformis, microscopic colitis, one case of collagenous colitis and one case of lymphocytic colitis and behcet disease, and 4%. The following diseases: seronegative primitive biliary cirrhosis, basedow disease, alopecia, addison disease, rheumatoid polyarthritis, Acute articular rheumatism, psoriasis, lymphocytic gastritis, sjogren gougerotsyndrom, IgA nephropathy and autoimmune thrombocytopenic purpura. There were 3 patients who had two autoimmune diseases associated with CD. The autoimmune diseases had no impact on the evolution of CD; under GFD; and were; stabilized under specific treatment in all our patients except for diabetics since the FDG is rich in bicarbonate.

Conclusion
Autoimmune diseases must be systematically searched in CD, which are dominated in our study by autoimmune hepatitis

PO32

Evolution of patients with coeliac disease under gluten-free diet (About 236 Moroccan cases) Moroccan University Experience

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Background
The aim is to evaluate the clinical and paraclinical evolution of patients under GFD;

Methods
Retrospective study over a period of 21 years (1995 to 2016), including 236 cases of CD; followed in Morocco. The evolution under GFD has been evaluated (18- 24 months.;

Results
The mean age was 32 year. Twenty-one patients had a first-degree family history of CD. At the time of diagnosis. Malabsorption diarrhea was found in 47% of cases. Extra-digestive malabsorption disorders were mainly represented by weight loss in 68.2%, reproductive disorders in 24.5% of cases especially menstrual cycle disorders and neurological signs in 6.7% of cases (n=16) mainly migraine and peripheral neuropathy. Anemic syndrome was noted in 61% of patients (n=144), while a liver function disorders were found in 38.5% (n=91).Bone densitometry was performed in 30.9% of patients (n=73) among whom 30.5% had osteoporosis and 37% had osteopenia. Histologic analysis of JB showed IEL greater than 30% in all patients, severe villous atrophy (VA) in 75.8% of cases (n=179), moderate VA in 15,6% (n=37) and no VA in 1.2% of the cases (n=3). After 18 months of GDF, 82.6% of patients (n=195) showed a good clinical evolution. No patient reported diarrhea or anemic syndrome. Mean weight gain was 6.7 kg+5 kg, a net improvement in liver function and reproductive disorders was observed in 90.1% (n=82) and 90% (n=52) of patients.Also,87.5% (n=14) of patients with neurological disorders.11% of osteoporotic patients became osteopenic, while all osteopenic patients their bone osteodensitometry was normalized. Histologically, JB was performed at 159 patients, all patients had IEL<30%;55.9% (n=89) had no VA, 28.9% (n=46) maintained moderate VA and 15% (n=24) maintained severe VA. During follow-up 9.3% of patients (n=22)were lost to follow-up, while 8% had complications.ofthese,18 died,6 due to small intestinal lymphoma,4 due to severe cachexia; 3 had gastricadenocarcinoma,2 hadsmallintestinaladenocarcinoma, 1 had HCC, 1 had cerebral thrombophlebitis; and 1 had refractory sprue type II. Only survivor had developed neuroendocrine tumor surgically treated.

Conclusion
Adherence to GFD showed digestive and extradigestive clinical improvement 82.7% of patients

PO33

Towards an individual screening strategy for first degree relatives of celiac patients: based on sex, age and HLA-genotype.

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Background & Aims
Celiac disease (CD) is known to be more prevalent in first-degree relatives (FDRs) of CD patients. In this study we aim to investigate the effect of sex, age at time of index diagnosis and HLA-genotype on CD diagnosis in FDRs.

Methods
A retrospective cohort study of 609 FDRs of 190 celiac index patients diagnosed between 1994 and 2015. Sex, age at time of CD diagnosis in the index patient as well as screening and diagnostic results (celiac specific antibodies, HLA-typing, duodenal histology) of the FDR were recorded.

Results
CD screening was done in 427 FRDs (70%), resulting in a prevalence of CD of 15%. In 335 FDRs HLA-typing was performed and found to be HLA-DQ2 and/or DQ8 positive in 87.5%. CD was diagnosed more often after screening in females and in HLA-DQ2 homozygosity ($p<0.05$). All FDRs who were adolescents (n=4, age 11-24 years) or parents (n=13) at the moment of index diagnosis were diagnosed during first screening. In FDRs younger than 10 years of age at time of index diagnosis, repeated testing was necessary in order to diagnose CD, with only 63% being diagnosed during first screening. The younger the child, the longer the time to its own CD diagnosis, with children of 0-1 years having the longest mean time to diagnosis (3.9+2.5 years, $p<0.001$).

Conclusion
Repeated CD serology in HLA-DQ2 and/or DQ8 positive siblings and offspring of CD patients, younger than 10 years of age at the moment of index CD diagnosis, can lead to an early diagnosis and should be continued until early adolescence (10-12 years), especially in HLA DQ2 homozygous sisters. In addition, one-time testing could be sufficient to diagnose CD in adolescents and parents. Our results may be useful in developing future recommendations for CD screening frequency and follow-up duration.

PO34

Flow-cytometric HLA-DQ:gluten tetramer blood test excludes celiac disease independently of

gluten consumption

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Background
Celiac disease is characterized by presence of gluten-specific HLA-DQ2 or HLA-DQ8-restricted CD4+ T-cells. Current diagnostic tests of celiac disease, disease-specific antibody levels and duodenal histology, normalize when a gluten-free diet is initiated. The increasing popularity of gluten-free diet without prior investigation for CD may therefore hamper CD-workup. We aimed to develop a diet-independent, blood-based test for CD, by detecting gluten-specific T cells.

Methods
We included 143 HLA-DQ2.5+ subjects. Two gluten-free groups; 62 treated CD (TCD)-subjects and 19 gluten sensitive (GS) controls with prior exclusion of CD, and two gluten-consuming groups; 10 untreated CD (UCD)-subjects and 52 healthy control (HC)-subjects, donated blood for HLA-DQ:gluten tetramer-staining and flow cytometry. Laboratory and statistical analyses were performed blinded, except for UCD-subjects. We performed test precision analysis in 10 subjects.

Results
An optimal model based on flow-cytometry variables gave ROC curve area of 0.957 (standard deviation 0.037) for TCD/GS, and 0.951 (0.026) for UCD/HC. Optimal cut-offs gave sensitivity 0.968 and specificity 0.947 for TCD/GS, and 1.00 and 0.904 for UCD/HC, respectively. Of six HC-subjects with UCD-equivalent frequency of HLA-DQ:gluten tetramer+ cells, two were diagnosed with CD and HLA-DQ:gluten tetramer-sorted blood cells from the other four HC-subjects displayed gluten-specific proliferation in vitro. CD38-expression on HLA-DQ:gluten tetramer+ cells had similar accuracy as gluten-specific antibodies in differentiating UCD from TCD.

Conclusion
The HLA-DQ: gluten tetramer test is a sensitive and specific blood-based test for CD, and does not require a gluten challenge. The new test can therefore be used to rule out CD in test negative individuals and select positive subjects for a further work-up with gluten challenge and small intestinal biopsy. For subjects on a normal gluten containing diet, the new test may provide a non-invasive supplement in detection and diagnosis of CD. Registered at www.clinicaltrials.gov (NCT02442219).

PO35

A liberal biopsy practice is not efficient in finding more patients with celiac disease.

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Background
It is estimated that 1% of the general population in Europe is affected by celiac disease (CD), and many patients go undiagnosed. To identify patients with CD, several endoscopy centers have adapted a practice of performing duodenal biopsies in patients undergoing gastroscopy for non-CD indications. The effect of this practice is unknown.

Methods
We searched our hospital pathology database to identify cases were duodenal biopsies had been performed. In patients with an abnormal histological finding, we registered the indication for endoscopy and biopsy, anti-tissue transglutaminase (a-TG2) and endoscopic findings. We defined that there was an indication for biopsy if a patient had elevated a-TG2, s-IgA deficiency, endoscopic findings suggesting CD, or if a patient was deemed to have a high clinical risk of celiac disease (>20%).

Results
In 2013, the department of pathology evaluated duodenal biopsies of 2932 patients from both hospital and private endoscopists. 1546 of the patients were examined at our hospital, and represented 36% of upper endoscopies performed that year. 283 of these patients had an abnormal histological finding, 99 patients were subsequently diagnosed with CD. Of the patients diagnosed with CD, 91 patients had been referred to endoscopy based on clinical and serological suspicion of CD. Macroscopic findings suggestive of CD were found in another four patients. The last patients had undergone biopsies without indication; one patient had normal a-TG2 without villous atrophy, one patient was shown to have an elevated a-TG2 after biopsy, and two patients had villous atrophy with a normal a-TG2.

Conclusion
95 of the 99 patients diagnosed with CD would have been uncovered if we only had performed biopsies in patients with indication. To identify the remaining four patients we had to perform biopsies in an estimated 1000 patients. A liberal biopsy practice is not effective, and may also over diagnose CD.

PO36

Polycheck® Celiac IgA plus Total IgA - a novel test for serological screening of celiac disease simultaneously detecting specific anti-tTG2 antibodies and total IgA from the same sample of blood.

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Background
According to obligatory recommendations of European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), the diagnostic procedure for celiac disease (CD) should begin with the determination of autoantibodies against intestinal tissue transglutaminase (TG2) in IgA class. Due to the frequent co-occurrence of IgA deficiency in CD, determination of total IgA is necessary.

Aim
The aim of study was to create the new screening quantitative immunoassay panel for detection of specific CD antibodies with the simultaneous determination of IgA immunodeficiency.

Methods
Sera (n=104) of immunocompetent and IgA deficient children with and without CD were analysed with the Polycheck® screening enzyme immune assay consisted of TG2 and heavy chains of IgA as targets to detect anti-TG2 -IgA and total IgA. Quantification was determine using five known IgA concentrations as a standard curve.

Data were analyzed using Statistica 12.5 software (StatSoft, Poland).

Results
The sensitivity and specificity of the test when the cut off suggested by the manufacture was chosen (0.8 kU/L) as the cut off were 96,4% and 100% for anti-TG2-IgA, and 90% and 93% for total IgA, respectively. The calculated diagnostic accuracy (ACC) for total IgA was 0,913 and area under the ROC curve was 0.954. However, the analysis of the ROC curve and the results of the Youden's index showed that the best sensitivity (90%) and specificity (96%) for total IgA were for the cut off 0.69kU/L. ACC and area under the ROC curve for this cut of were 0,933 and 0,955, respectively.

Conclusion
Polycheck® Celiac IgA plus Total IgA test is a useful tool for serological CD screening consisting of both specific anti-tTG2 antibodies and total IgA, as it is recommended by ESPGHAN, allowing for detection of IgA deficiency from the same sample of blood in the same time.

PO37

Frequency and duration of symptoms prior to diagnosis of coeliac disease in Polish population

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Background
Celiac disease (CD) is one of the most common autoimmune diseases, even though in many cases remain undiagnosed. English study showed that the average time from first symptoms to diagnosis is over 13 years. The aim of the study was to assess the length of CD symptoms before and after diagnosis in the group of patients with diagnosed CD in the Polish population.

Methods
With the consent of the authors, "The Impact of Celiac Disease on Your Life, University of Oxford (Health Economics Research Center) & Celiac UK (September, 2015) questionnaire was translated and used. Out of 2 500 questionnaires distributed among members of the Polish Association of People with Celiac Disease and on Gluten-Free Diet (GFD) 961 (38.44%) of them were filled. One hundred seventy two patients (17.9%) introduced GFD without proper diagnosis of CD. The construction of the survey prevented them from completing further, so only patients with confirmed CD diagnosis were included to the study (n=789, 82.1%).

Results
The majority of respondents were adults (60%). The median of CD duration was 5.3 years. Abdominal pain, flatulence, diarrhea and weaker growth were most common in children (73%, 63%, 51%, 49% respectively). While in adults, there were bloating, chronic fatigue, abdominal pain and anemia (82%, 77%, 72%, 67%).
The symptoms that lasted the longest before CD diagnosis were anemia, headache, constipation and bloating (average duration was 9.2, 8.6, 8.5, 8.1 years, respectively). They persisted after the introduction of GFD for an average 3.1, 4.8, 2.7, 3.8 years, respectively).

Conclusion
In Polish population, CD symptoms occurred about 9 years prior to CD diagnosis. After diagnosis and introduction of GFD they persisted for about 3 years.

PO38

The level of serum intestinal fatty acid binding protein in first degree relatives of celiac patients

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Background
Serum intestinal fatty acid binding protein (I-FABP) is a

sensitive marker to study enterocyte damage. Recent study showed that serum I-FABP correlates with the severity of villous atrophy in celiac disease (CD), and upon a gluten free diet I-FABP amounts decreased significantly, however, not within the range observed in controls.

Aim
As we supposed that I-FABP could be a early marker of enterocyte damage the aim of this study was to analyzed I-FABP levels in the first degree relatives (FDRs) of CD patients depending on CD autoimmunization and CD risk haplotypes.

Methods
The study involved 167 FDRs. Antibodies against tissue tranglutaminase (tTG-IgA/IgG) using ELIA ImmunoCap system were determined in sera of all FDRs. HLA-DQ2/DQ8 genotyping was done using EUROArrayScan (Euroimmun).

Results
Out of 167 relatives 124 (74,4%) carried CD risk haplotypes. Positive tTG-IgA/IgG were found in 15 patients (8,9% of all relatives; 12,1 % of relatives with CD risk haplotype). Histopathological examination performed in 11 seropositive patients confirmed typical CD changes. The mean level of I-FABP in FDRs with CD autoimmunization was significantly higher (2055,2±1516 pg/ml) as compared with non-immunized relatives both HLA-DQ2/DQ8 - positive (1009,3±1122 pg/ml) and - negative (1194,1±1025,1pg/ml). There were no differences in I-FABP levels between FDRs with CD risk and no-risk haplotypes.

Conclusion
Serum I-FABP is a potential marker of gut damage in FDRs with CD autoimmunization, but not in those with genetic predisposition.

PO39

Significance of deamidated gliadin peptide antibodies in adult celiac disease patients.

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Background
Recently, a new serological test for antibodies to deamidated gliadin peptide has shown a high sensitivity and specificity for the patients with celiac disease (CD).

Aim
To compare the sensitivity and specificity for antibodies to deamidated gliadin peptide (Ab-DGP) and tissue transglutaminase antibodies (Ab-tTG) for diagnose of celiac disease in adult patients with gastroenterological symptoms.

Methods
A total of 124 patients aged 17 to 86 years (mean age 40,2 Â± 17, 1 years) with various diseases of the intestine. Patients were divided into 3 groups: Group 1 - 27 patients with newly diagnosed celiac disease, Group 2 - 40 patients complying with a gluten-free diet for a period of 6 months to 10 years and more, group 3 - 57 patients with other diseases of the intestine. Antibodies to deamidated gliadin peptide and tissue transglutaminase IgA and IgG were determined by ELISA using reagents «Orgentec Diagnostika GmbH, Germany». The diagnosis of celiac disease in all patients was confirmed morphologically using Marsh classification. Statistical analyzes were conducted using the computer program Statistica 6.0.

Results
In group 1 Ab-DGP IgA and Ab-tTG IgA were elevated in 92.5% of patients. The level of increased values of Ab-DGP IgA (at a rate of up to 10 U/ml) ranged from 11 to 210 U/ml (mean 81.1 ± 51,2 U/ml). The level of increased values of Ab-tTG IgA ranged from 17.7 to 280 U/ml (mean 105.6 ± 80,7 U/ml). Increasing Ab-DGP IgG was observed in 96.2% of patients of group 1. The level of increased values ranged from 12.2 to 200 U/ml and a mean of 73.9 ± 44.6 U/ml. Increasing Ab-tTG IgG was observed in 55.5% of patients of group 1, the level of increase reached 100U/ml (mean 76.5 ± 34.5 U / ml). 12 patients (30%) of the group 2 was positive IgA Ab-DGP, the higher values ranged from 12.7 to 59.7 (mean 25.9 ± 16.9 U / ml). Increasing Ab-DGP IgG was observed in 15% of patients, the level of increased values ranged from 12.9 to 43.9 (mean 23.2 ± 13.1 U / ml). Increasing Ab-tTG IgA and Ab-tTG IgG was observed only in 1 and 3 patients, respectively, over the normal limit in 2 times. In the group 3 the high level of IgA and IgG Ab-DGP was detected in only 4 patients (7%), and Ab-tTG IgA and IgG- in 2 patients (3.5%).

Conclusion
Ab-DGP and Ab-tTG IgA have a similar sensitivity and specificity and can be used for the diagnosis of celiac disease in adults. CD patients who keep the strict gluten-free diet is observed as a decrease of Ab-DGP, and Ab-tTG IgA and IgG.

PO40

Phase 1: A training program to increase awareness and treatment of the psychological needs of children with celiac disease

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Background
A variety of psychological problems have been identified in children with celiac disease (CD) but are often under-diagnosed and infrequently treated. To address this problem, our Celiac Program at Children's National partnered with the Celiac Disease Foundation, a national advocacy group, to develop an innovative approach to increase awareness, evaluation, and treatment. Phase 1 of our project included a manual aimed at providers to improve recognition of youth with CD at-risk for psychological difficulties; a live and web-based CME / CEU program; and a video highlighting the importance of the topic.

Methods
We developed the manual to offer a practical approach for identifying psychological issues including: direct cognitive and psychological effects of untreated CD; adjustment to the diagnosis of a chronic illness; and adherence to a gluten-free diet. A systematic approach is provided for issues including: recognition of commonly reported difficulties with attention and concentration, irritability, fatigue, change in sleep and appetite patterns, school absences, academic decline, social withdrawal, food-related phobias, anxiety, and depression. Indicators for the need for referral are also discussed. Each element was addressed by an expert at the CME/CEU program.

Results
To date, 249 participants earned continuing education credits, including 32 in-person, 62 via live stream, and 26 online through a partnership with INOVA. Physicians receive up to 4.5 AMA PRA Category 1 Credits through INOVA Health System; Psychologists receive up to 4.5 CEUs through the National Register of Health Service Psychologists. The video is streaming via the Children's National YouTube Channel.

Conclusion
The manual and CME/CEU program was the first step to improve the identification and treatment of youth with CD and psychological problems. We will continue to promote the materials at academic conferences. Phase two of our efforts will include a research project to establish prevalence rates of mental health issues in patients with CD.

PO41

Predictors for positive findings on EGD, colonoscopy, and biopsy in non-responsive celiac disease

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Background
Non-responsive celiac disease (NRCD), defined as failure to respond to a gluten-free diet (GFD) is not uncommon in celiac disease (CD) patients, with reported prevalence from 7-30%. EGD with small bowel biopsy or colonoscopy with biopsy are critical components of NRCD diagnostic algorithms.

Methods
We performed a retrospective review of all patients in our prospectively kept CD database between 2007 and June 2016 for NRCD. NRCD was defined as patients with biopsy-proven CD who had ongoing or recurrent symptoms despite a GFD for at least 6 months. We excluded those who had only one clinic visit for evaluation of NRCD. Biopsy via EGD were divided into normal (Marsh 0-1) and abnormal (Marsh 2-3).

Results
EGD with duodenal biopsy was performed as part of the diagnostic evaluation in 268 of 503 (53%) of NRCD patients. Longer duration of symptoms (OR 1.31, 95% CI 1.14-1.51, p<0.005), report of weight loss (OR 2.61 95% CI 1.44-4.72, p<0.005) and self reported strict GFD adherence (OR 0.62, 95% CI 0.46-0.83, p<0.005) predicted abnormal duodenal biopsy on univariate analysis. Age>35 years (OR 1.04, 95% CI 1.02-1.05, p<0.001) and weight loss (OR 3.89, 95% CI 2.21-6.84, p<0.0001) had positive associations with identifying etiologies on EGD. Diarrhea (OR 4.49, 95% CI 1.94-10.39, p<0.0001) and not having bloating (OR for bloating 0.29, 95% CI 0.12-0.67, p = 0.0013) predicted positive colonoscopic findings.

Conclusion
Independent positive predictors of an abnormal duodenal biopsy performed for NRCD evaluation were a longer duration of symptoms and report of weight loss. Self-reported strict GFD adherence was a negative predictor. Age>35 years and weight loss had positive associations with the identification of a specific etiology for NRCD at EGD, while diarrhea and not having bloating predicted diagnostic lower GI abnormalities. Clinicians should take these predictors into account when considering EGD and/or colonoscopy for NRCD evaluation.

PO42

Increase in plasma interleukin (IL)-2, IL-8, and IL-10 from 2 to 6 hours after oral gluten challenge differentiates between celiac disease (CeD) and non-celiac gluten sensitivity (NCGS) in patients on gluten-free diet (GFD)

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Background
Gluten challenge elevates circulating cytokines in CeD patients on GFD, and it is unclear if cytokine responses could differentiate between CeD and NCGS subjects

adhering to GFD.

Aim
To evaluate IL-2, IL-8 and IL-10 in plasma after gluten ingestion in CeD and NCGS subjects on GFD using highly sensitive assays.

Methods
Plasma had been collected before, and 2, 4 and 6 hours after participants with CeD (n=19) or NCGS (n=49) on GFD initially consumed gluten (5.7 grams) in one of two studies (Sarna et al, submitted; and Skodje et al, submitted). Plasma cytokines were measured by Mesoscale V-plex assays. Symptoms were measured by self-administered visual analog scale. CeD subjects were assessed for serology, duodenal histology, and frequency of gluten-specific T cells in blood using HLA-DQ: gluten tetramers.

Results
IL-2 fold changes from pre-challenge were significantly increased in CeD compared to NCGS after gluten challenge at 2 hours (CeD median: 1.2, 25th-75th percentiles 1.0-2.6; NCGS: 1.0, 0.94-1.0; Mann Whitney U test p=0.0012), 4 hours (CeD: 10.0, 2.0-25.6; NCGS: 1.0, 0.94-1.0; p<0.0001) and 6 hours (CeD: 3.6, 1.7-18.6; NCDS: 1.0, 0.96-1.1; p<0.001). Elevations in IL-8 and IL-10 were also significantly increased in CeD compared to NCGS at 4 hours and 6 hours (p<0.0001), but median elevations were between 1.2 to 1.8-fold. Sensitivity and specificity with optimized cutoffs for IL-2 were 74% and 98%, respectively, for IL-8 were 42% and 100%, and IL-10 were 32% and 100%. Average IL-2 fold change in CeD at 2 to 6 hours was correlated with baseline frequency of gluten-specific cells in HLA-DQ2.5+ subjects (n=16; p=0.0028, r=0.70), and overall discomfort at 6 hours (n=19; p=0.0446, r=0.49).

Conclusion
Increase in IL-2, IL-8 and IL-10 after oral gluten challenge is specific for CeD, but IL-2 is most sensitive. Measurement of circulating cytokines may assist in differentiating between CeD and NCGS.

PO43

Performance of QUANTA Flash® tissue transglutaminase (tTG) and deamidated gliadin peptide (DGP) Chemiluminescent Assays on Celiac Disease patients with and without intestinal abnormalities and response to gluten-free diet (GFD) in paired specimens

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Background
Despite the high sensitivity and specificity of most celiac disease (CD) specific assays, discrepancies between endoscopy results and serology are sometimes observed. Our aim was to assess the performance of new chemiluminescent assays (CIA) for tissue transglutaminase (tTG) and deamidated gliadin peptide (DGP) on a well-characterized clinical cohort of CD patients with endoscopy results.

Methods
Sera from 40 patients seen at the VU University Medical Center including 10 patients selected with low antibody titers (Celikey tTG, Fluorescence Enzyme Immuno Assay,FEIA; ThermoFisher or in-house assays) and no intestinal abnormalities (M0), 10 patients with intestinal abnormalities (M1-M3), and 10 patients with paired sera at diagnosis and following GFD were tested for anti-tTG and anti-DGP antibodies by QUANTA Flash CIA and QUANTA Lite recombinant (rh) and red-blood cell(RBC) ELISA assays (Anti-F-Actin IgA was assessed by QUANTA Lite ELISA (all methods Inova Diagnostics, USA).

Results
8 of 10 patients initially reported with low antibody titers but M0, were positive for endomysial antibody, rh and (RBC-based tTG ELISAs and CIA, and DGP IgG and/or IgA. One specimen was tTG negative by all assays, but DGP IgG and IgA positive. Of the 10 patients with M1-M3C, the initial anti-tTG testing by FEIA found 8/10 anti-tTG positive, while 10/10 were positive by CIA and RBC-tTG ELISA. 2/10 specimens were >10x upper limit of normal (ULN) by CIA, but 0/10 by FEIA. Analysis of the paired gluten-GFD specimens showed 100% were initially >10x ULN (range 13.2-197.2 x ULN) for CIA assay compared to 40% for FEIA. Following GFD, the CIA assay showed from a 3.5- 294 fold decrease in titer (P=0.0033). 3 F-Actin IgA positive specimens became negative after GFD.

Conclusion
The new CIAs showed excellent sensitivity, found 100% of the pre-GFD paired specimens to be >10 x ULN, and showed a dramatic decline of up to 294-fold following GFD.

PO44

Relationship between Gluten Consumption and Symptom Severity for celiac disease patients on a Gluten-Free Diet

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Background
It is common for celiac disease (CD) patients on a gluten-free diet (GFD) to accidently consume enough gluten to cause symptomatic distress. We present a model that correlates on average the amount of gluten intake and the severity of episodic symptoms for abdominal pain, bloating and tiredness.

Methods
This analysis uses data from the CeliAction study for latiglutenase (ALV003-1221; NCT01917630). In this trial the placebo arm improved their mucosal health due to a trial (Hawthorne) effect as measured by the ratio of villous height to crypt depth (Vh:Cd). Using a conversion factor for gluten ingestion vs. DVh:Cd from a previous gluten challenge trial (ALV003-1021; NCT01255696) we estimated the amount of gluten removed by these patients while in the ALV003-1221 trial. From daily symptom diary data we also estimated how much gluten remained in patient's diets to give an overall determination of their accidental gluten exposure while on a GFD prior to the trial. This data was combined with the data for frequency and severity of various symptoms to obtain a correlation of episodic gluten ingestion to symptom severity.

Results
CD patients on placebo treatment (n=122) were determined to consume approximately a mean of 570 mg/day and a median of 470 mg/day of gluten. The distribution of gluten ingestion events by weight is such that the most common abdominal pain severity is mild to moderate (3 on a scale of 0 to 10) and comprises 30% of all symptomatic events and corresponds to about 470 mg ingestion. Moderate to severe abdominal pain (score of 7) correspond to about 1 g ingestion, which comprises <5% of symptomatic events. Similar results are presented for bloating and tiredness.

Conclusion
Individuals following a GFD routinely consume gluten and the quantity of that ingested gluten is sufficient to trigger symptomatic responses and persistent histologic damage.

PO45

Celiac disease and Portal Hypertension : Co-existence or no existence

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Background
Various case series are available on celiac disease in patients with Cryptogenic cirrhosis and Idiopathic Portal Hypertension (IPH) / Non Cirrhotic Portal Fibrosis (NCPF).

This was a single centre case series reporting 7 patients with portal hypertension (cryptogenic cirrhosis / IPH) who were prospectively found to have celiac disease based on serology and duodenal biopsy.

Methods
We analysed seven patients with portal hypertension having cryptogenic cirrhosis (n=5) or IPH/ NPH (n=2) who were evaluated for coexisting celiac disease between March'16 to March'17. We studied IgA TTG Antibody and duodenal biopsy in these patients. Portal hypertension was proven on endoscopic/ USG findings. Known causes of chronic liver disease including viral serology, copper workup, autoimmune markers, alcohol were ruled out.

Results
All cases were women, mean age 22 years (18-41 yrs). Symptoms of portal hypertension before diagnosis of celiac disease ranged from 24-84 months (mean - 48 months). All patients with cirrhosis were admitted with decompensated disease. Two patients had IPH/ NCPF.

Conclusion
Similar to various published case series, we have described association of portal hypertension and celiac disease. The cause of this association is not clear. Though gliadin stimulated immunological process may be the link between two disease entities.

Dietary treatment with Gluten free diet (GFD) may prevent progression of portal hypertension. Therefore all patients with cryptogenic cirrhosis and IPH with portal hypertension should be screened for presence of celiac disease.

PO46

Are undefined sprue (US) and Non-coeliac refractory sprue (NCRS) two indipendent conditions? A clinical and epidemiological study

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Background
Flat Enteropathy is due to Coeliac Disease and other unrelated conditions. However, there are FEs in which CD cannot be confirmed/excluded and there are FEs in which, although CD is excluded, a definitive diagnosis cannot be made. We defined them US and NCRS. Although similar patients were described, it is unclear whether US and NCRS are two independent conditions or just umbrella terms covering FEs still awaiting to be identified.

Aim
To clarify the nature of US and NCRS.

Methods
The notes of patients seen between 1/1999 and 10/2016 were re-evaluated to select cases of US and NCRS.

Results
7 patients (2F, age at diagnosis of FE 46±26 years, all with severe malabsorption) were identified. 3 were DQ2+ and so were diagnosed as US: pt1 (F,32 years) died 8 years later of ulcerative jejunitis; pt2 (M,38) died 1 year later of pulmonary embolism complicating

systemic candidiasis and pt3 (M,71) died 4.5 years later of intestinal lymphoma. The remaining 4 were HLA DQ2/DQ8-, so a diagnosis of NCRS was made. 3 were DQ7.5+: pt4 (F,61) died 4.5 years later of EATL type 2; pt5 (M,25) is alive 10 years later and in good conditions; pt6 (M,69) is in good condition two years later and after stopping candesartan therapy. He refused follow-up. The last patient (M,29, DQ7.3+) is still alive 11 years later but diarrhea persists.

Conclusion
We described 7 patients with an unexplained FE. 57% of them died, mainly of lymphoproliferative disorders. However, 3 DQ2/DQ8- patients are still alive without evidence of malignancy. So, these 7 patients cannot have the same disease. DQ2+ patients dying of lymphoma could be affected by CD escaping diagnosis and becoming complicated. However, the 3 long surviving DQ2/8- patients could be affected by a still unidentified FE.

PO47

Prevalence of osteoporosis and osteopenia in men and premenopausal women with celiac disease: Systematic review and Meta analysis

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Background
Celiac disease as a cause of metabolic osteopathy has been recognized.

Bone densitometry has demonstrated, an important number of impaired bone mass and potential risk of fractures in Celiac disease. Different studies shown wide spectrum of low bone mineral density probably because of not considering a lot of confounding factors like age and menopause and drug use.

Aim
Aim of study was to systematically review prevalence of osteoporosis and osteopenia on men and premenopausal women with celiac disease.

Methods
The systematic review was conducted according to the preferred reporting items for systematic reviews (PRISMA) guidelines. We searched PubMed and Scopus databases based on the relevant medical subject headings (MeSH) of celiac disease and bone mineral density before 2017 were included.

Data extraction and analysis
Two authors separately extracted the data. We used Oxford center for evidence-based medicine checklist for quality assessment .19 eligible studies in the field of bone mineral density in celiac disease before gluten free diet(GFD) were included and evaluated.

Studies with accurate quantitative data were selected for meta-analysis using comprehensive meta-analysis version 2. Prevalence of osteopenia and osteoporosis were used as effect size for meta-analysis. Random effects model was used for pooling data across included studies. Cochrane Q ($p<0.05$ was considered statistically significant) and I2 index were presented to reveal the heterogeneity across the analyzed studies.

Results
A total of 563 premenopausal women and men, (410 female) from, UK, Brazil , India , Budapest , Poland were included in this systematic review.

Overall the pooled prevalence of osteoporosis were 14.4% [95%CI:9-20.5%] (Cochrane Q=7.889, p=0.96, I2=49.29%), and osteopenia were 39.6% [31.1-48.8%] (Cochrane Q=14.24, p=0.07, I2=71.92%) respectively.

Conclusion
Osteopenia and osteoporosis in pre menopausal women and men are prevalent from 41.9% to 46.9% and from 13.3 to 16.3% and significantly different from control groups.

PO48

Coeliac disease and reproductive disorders : Is there any correlation

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Background
The aim of our study is to evaluate the frequency of these disorders in the coeliac disease (CD) and their evolution under Gluten free diet.

Methods
It's retrospective descriptive study including 241 patients with CD from 1995 to 2016 in « Medecine C » in Ibn Sina University Hospital.

Results
About 241 patients suffering from coeliac disease, 58 patients presented reproductive disorders, either 28.9%. Recruiting 53 women and 5 men, with a sex ratio M/F of 10:6. The mean age was 32.25years ranging from 13 to 59 years old. The diagnosis of coeliac disease was based on: Histology, the anti endomysial antibodies and/or anti transglutaminase antibodies positive. The reproductive disorders were never isolated but always associated with digestive or extradigestives signs at the time of the diagnosis of CD. These disorders were manifested by : retarding puberty in 11 cases (19%),secondary amenorrhea in 13 cases (22.4%), Metrorrhagia in 12 cases (20.6%), absence of development of secondary sexual characters in 8 cases (12.5%), spontaneous abortion in 7 cases (10.9%), menometrorrhagia in 4cases (13.8%),primar sterility in 5 cases (8.6%), precocious menopause in 6 cases (10.3%),premature labour and/or IUGR in 3 cases (5%), primary amenorrhea in 2 cases (3.4%), and IUFD in one case 1.7%). Of the 29 patients stayed, the evolution of the reproductive disorders under Gluten Free Die was good in 26 cases (90%), with normalization of the cycles in 15 cases. The cycle was returned iN6cases, development of secondary sexual characters in 2 cases, fertility was returned in one case, one case developed her cycle after primary amenorrhea. The evolution was good in 3 cases as regard missed abortion four years after the gluten free diet in 1 patient, and amenorrhea continued in 2 cases.

Conclusion
In our study, these disorders well responded to the gluten free diet in 90% of cases, and these disorders were reversible under Gluten free diet.

SESSION 2: GENETICS AND FUNCTIONAL GENOMICS

PO49

HLA-DQ2 and DQ8 in the general population in southern India

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Abstract
Celiac disease occurs only in individuals who are able to express HLA DQ2 or DQ8. Celiac disease is very uncommon in south India. We evaluated the possibility that the genetic background leading to DQ2 and DQ8 expression is infrequent in the south Indian population. We have evaluated 200 healthy south Indian adults for their ability to express DQ2 or DQ8. Venous blood was taken, DNA extracted and PCR done using allele specific primers for following alleles DQA1*0301, 0302, 0501 and DQB1*02, 0201, 0302, respectively. The results are in the process of being analyzed and will be presented at the meeting. Knowing the frequency of HLA Dq2 / DQ8-determining haplotypes in southern Indian adult population will clarify whether the low prevalence of celiac disease in southern India is attributable to genetic factors.

PO50

Plant breeding to make wheat consumption safe for Celiac disease patients

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Abstract: The genes for gliadin proteins, said to be the primary culprits in elicitation of immune response in celiac disease, are coded by compound loci present on short arm (S) of chromosomes 1 and 6 of the three genomes of wheat (the *A, B* and *D* genomes). Majority of research work shows that gliadin synthesized from D genome have highest number of immunogenic epitopes followed by those in the A genome, while the B genome has been shown to have no or very few epitopes. Cultivated wheat in India is of two types: that which has all the three genomes (*AABBDD*; bread wheat) or that which lacks the *D* genome (*AABB*, durum and dicoccum wheats). Thus, durum wheat (primarily used for *dalia* and pasta preparation) already lacks all of the epitopes present in the *D* genome. If the A genome chromosomes/their segments carrying the gliadin genes can be modified or removed, the resulting wheat will have the least amount of epitopes or may lack them altogether. To test this hypothesis, cytogenetic stocks of bread wheat lacking the long arm of chromosome 1A (called as ditelosomic 1AL) and that for chromosome 6A (ditelosomic 6AL) were procured from Japan and used for hybridization with an Indian durum wheat variety. The second progeny of these crosses (called F2) was grown at ICAR-IARI farm and the plant DNAs were screened with EST based primers for the absence of 1AL and 6AL. Two F2 plants without the 1AL and 4 plants without the 6AL chromosomes were identified. These plants will be further hybridized with each other for pyramiding the 1AS and 6AS chromosomes to eventually develop a durum wheat genotype that is expected to lack most or all of the immunogenic CD epitopes.

PO51

The Small Intestinal Mucosa of First-Degree Relatives of Patients with Celiac Disease Exhibit a Protective Transcriptomic Phenotype

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Background
Celiac Disease (CeD) is characterized by gluten triggered damage of enterocytes in small intestine.

First-degree relatives (FDRs) of patients with CeD have 7.5% times higher risk of developing CeD, which is partly explained by their shared HLA DQ2 /DQ8 haplotype. However, a large percentage of FDRs do not develop enteropathy suggesting a possibility of presence of protective pathways in their intestinal mucosa. Our study examines these pathways through microarray analysis of intestinal mucosa of patients with CeD, FDRs, and controls. Identification of protective pathways unique to FDR intestinal mucosa may enable us to understand processes that regulate enterocyte damage in the intestinal mucosa.

Methods
Intestinal mucosal biopsies (4-5 pieces) from treatment naïve patients with CeD (n=12), FDRs (n=12) (anti-tissue transglutaminase negative) and controls (anti-tTG Ab negative) were obtained from each individual and subjected to microarray analysis using HT-12-v4 Human Expression BeadChips (Illumina). Resulting differentially expressed genes were analyzed by supervised and unsupervised PCA. Functional analysis was carried out using ToppFun, Reactome and MSigDB.

Results
In FDRs, 96 genes were upregulated and 1529 were found to be downregulated. Three transcriptional factors were upregulated in intestinal mucosa of FDR namely YY1 (yin yang 1), KLF5 (Kruppel Like Factor 5) and NF-kB. A group of 71 pseudogenes constituted a major proportion of upregulated genes in the FDRs intestinal mucosa. Cell replication, antigen processing and cross presentation pathways were down-regulated in the intestinal mucosa of FDRs.

Conclusion
Overall, our study provides a first glimpse into the processes active in FDR intestinal mucosa. While crypt-villous axis is severely affected in CeD patients, our gene expression analysis suggests that FDR mucosa focuses on maintenance of its crypt-villous architecture and immunomodulation. We also find a large subset of pseudogenes in the FDR intestinal mucosa suggesting novel regulatory mechanisms in intestinal mucosa.

PO52

Increased Expression of TLR4 and TLR9 but Not TLR2 and TLR7 mRNA by Peripheral Blood Monocytes in patients with Celiac Disease

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Background
In the development of celiac disease (CD) both adaptive and innate immunity are responsible. Compared to healthy population increased TLRs 2-4 expression has been detected in duodenal biopsies from CD patients. Activation of TLR2, TLR4 and TLR7 can leads to expression of pro-inflammatory cytokines. Therefore, the aim of this study was to investigate the TLRs 2,4,7,9 genes expression in the patients with celiac disease compare to healthy control.

Methods
120 blood samples from CD patients and 120 individuals as a control group who were referred to celiac department were collected during 2016. Among these patients, 20 duodenal biopsy specimens were selected randomly. Total RNA was isolated using a standard commercial kit. The mRNA expression of TLRs was quantified by relative qPCR with B2M as a reference gene.

Results
TLR4 and TLR9 mRNA were significantly higher expressed in blood samples from CD patients compared to the healthy controls ($P<0.05$); but not for TLR2 and TLR7 mRNA. Furthermore, TLR4 and TLR2 expression level was increased in CD biopsy specimens compared to controls, whereas expression of TLR9 mRNA was decreased in CD patients. There was no significant differences expression of TLR7 in biopsy specimens.

Conclusions
The alteration of TLR4 and TLR9 expression in the blood and biopsy samples of patients with CD supports the potential implication of innate immune system in the pathomechanism of this disease. Upregulation of TLR4 and TLR9 suggests the contribution of gut microbiota or dysregulation of the immune response to commensal flora in small bowel mucosa in celiac patients.
Key words: Celiac disease, Toll-like receptors (TLRs), Gene expression

PO53

HLA-DQ genetic study for type 1 diabetes and celiac disease in Iranian population

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Background
The HLA-DQ2 and DQ8 haplotypes have important role in Type 1 diabetes (T1D) and celiac disease (CD) pathogenesis. There is no information on their genetic risk or the distribution of the related alleles in the T1D population in Iran and therefore in this study we assessed the frequency of HLA DQ2 and DQ8 haplotypes in patients with T1D and CD compared to normal.

Methods
The study included 70 patients with T1D (mean age 26 years), 60 cases of CD (mean age 31 years), and 50 healthy individuals (mean age 29 years). Demographic and clinical information were collected using questionnaire. 10cc heparinized blood samples were collected, genomic DNA was extracted and alleles were genotyped by Real-time PCR using SYBR Green as a low-resolution method.

Results
The HLA-DQ risk heterodimer proportion in T1D patients was 51% for HLA-DQ2 and 23% for HLA-DQ8, 21% carried both alleles and 5% were negative for both predisposing alleles. In contrast CD patients have much higher DQ2 frequency (72%) and lower DQ8 frequency (11.6%), 14% carried both alleles and 3% were negative for both. The frequency of DQ2 and DQ8 alleles in Iranian healthy population are 19 and 5% respectively.

Conclusion
The result of this study showed that DQB1* 0302 has a higher correlation with incidence of T1D than in CD and DQB1*0201 and in both diseases has a much higher frequency than normal population which can be explained by similarities in pathogenesis in both diseases. Considering the higher incidence of CD in patient which are affected by T1D, the foundation of HLA-Typing for DQ2 and DQ8 alleles can be the basis of screening for CD in patients with type one diabetes.

Keywords
Type one diabetes mellitus, Celiac Disease, HLA-DQ, Frequency Study

PO54

Gene expression of IL-15 and histopathology of celiac disease

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Background
The chronic upregulation of IL-15 in both the lamina propria (LP) and in the intestinal epithelium is a hallmark of the disease but unclear if correlates with the degree of mucosal damages. The aim of this study was to assess the correlation between serum level and gene expression of IL-15 and abnormal histopathology degrees in patients with celiac disease.

Method
Formalin-fixed, paraffin-embedded tissue sections of duodenal biopsies from 85 patients (27 male, 58 female; mean range: 38.16 year) with active celiac disease (before treatment with GFD) were collected. The total RNA was extracted from whole biopsy samples using commercial kit. Specific primer pair was designed and the gene expression was investigated by Real-time PCR based on SYBER Green method. Also serum concentrations of IL-15 determined by enzyme-linked immunosorbent assay and compare with tissue expression.

Results
IL-15 gene expression level was increased in patients with Marsh II compared with Marsh I and Marsh III but this difference was statistically significant between Marsh II and Marsh I ($P=0.03$). On the other hand the serum concentration of IL-15 showed the greatest increase in March II compared to patients with Marsh I and Marsh III lesions but the differences were not statistically significant.

Conclusion
These data showed that IL-15 gene expression might be high only at early stage of histogenesis of CD. Alternatively Marsh III in its own might not reflect the severity of mucosal changes in CD similar to the lack of correlation between clinical presentation and histopathology.

Key words
Celiac disease, IL-15, histopathology

PO55

The evaluation of CXCR3, CXCL10 and CXCL11 genes expression as diagnostic marker in the early stage of celiac disease

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Background
Chemokine receptor CXCR3 and its ligands including CXCL9, CXCL10 and CXCL11 have been suggested to be one of the most relevant chemokine axes to promote the arrival of cells into inflamed tissues. These axes are known to be active in different inflammatory processes such as celiac disease. Therefore, the aim of this study is to investigate the CXCR3, CXCL10 and CXCL11 genes expression in celiac patients compare with healthy control in the Iranian population.

Methods
In this case-control study, biopsy specimens were collected from 71 celiac patients (28 male and 43 female, mean age: 32.4±7.54) and 90 control subject (39 male and 51 female, mean age: 34.41±9.47) during 2016. The total RNA was isolated, specific primer pairs were designed and mRNA expression of CXCL10, CXCL11 and CXCR3 genes were investigated using Real-Time PCR based SYBER Green method.

Results
Based on relative quantification method, the mRNA levels of CXCL10, CXCL11 and CXCR3 expression levels were significantly higher in duodenal biopsies of celiac patients compared with healthy controls in the study population (p= 0.03, p= 0.02, p=0.01 respectively).

Conclusion
The CXCR3/CXCL10/CXCL11 signaling axis is over activated in the small intestinal mucosa in patients with CD compared with the control, and this finding explains the specific enrollment of the main cell populations that infiltrate the epithelium. This result suggests that these genes may be used as diagnostic marker in the early stage of CD.

Keywords
Celiac disease, intraepithelial lymphocytes, chemokine

P056

Study of the microbiota composition in adult celiac disease

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Background
The gut microbiota largely contributes to the normal development and function of mucosal immunity, intestinal epithelial cell proliferation, and metabolic pathways. Growing evidence support a role for dysbiosis in the pathogenesis and clinical picture of chronic inflammatory conditions, including celiac disease (CD), due to expansion of gut pathobionts with a parallel decline of mutualistic bacteria. The aims of this study were to obtain a comparative metagenomic picture of salivary, duodenal and fecal microbiota composition in adult CD patients, and to assess whether the eventual dysbiosis differs among different clinical settings.

Methods
We enrolled four groups of CD patients: 10 potential, 20 active, 20 treated, and 10 refractory, and 20 controls with dyspepsia. For each patient and control, we collected salivary, duodenal mucosa, and fecal samples that underwent to: DNA extraction and quantification (Qiagen), PCR production of 16S rRNA amplicons and sequencing libraries, high-throughput sequencing of libraries on Illumina MySeq platform (BMR Genomics). Bio-informatic analyses were performed on raw sequencing data. The corresponding Operational Taxonomic Units (OTU) tables were produced.

Results
After polishing raw sequences, the mean number of high-quality reads was: 55603 for feces, 103616 for saliva, 59514 for biopsies. OTU tables show that the mean number of bacterial OTUs at 97% homology level, corresponding to the number of bacterial species, is: 151 for feces, 286 for saliva, 212 for biopsies. Preliminary β-diversity analyses suggest compositional differences in bacterial consortia in terms of reduction of Firmicutes and increase of Proteobacteria at level of Phyla, while a reduction of Veillonella and an increase of Neisseria Genera were observed in both salivary and mucosal samples of CD patients in comparison to controls.

Conclusion
This study clearly shows the presence of dysbiosis in adulthood CD and the similarity between salivary and mucosal data opens the route for a non-invasive diagnostic assessment.

P057

A clinical trial to dissect the transcriptional programme of gluten-specific T cells

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Background
Coeliac disease (CD) is caused by an inappropriate immune response to gluten found in wheat, rye and barley as a network-building component in these cereals.

Several types of T cells are involved in CD: Pathogenic CD4+ Th1 cells recognizing gluten epitopes presented by HLA-DQ2 or -DQ8, which are of central importance in the pathogenesis and intraepithelial lymphocytes (IEL), composed of CD8+ αβ T cells and γδ T cells that induce tissue damage.

Aim
We aim to study the specific activation of disease driving gluten-specific CD4+ Th1 cells by examining the activation pathways which can then be used to track down potential therapeutic targets for CD. Additionally, we will also study the frequency of all gut-homing T cells and their response in blood after gluten challenge.

Methods
CD patients on a gluten-free diet undergo gluten challenge for 3 days with gluten-containing cookies. Blood samples are taken prior and 6 days after challenge. Gluten-specific CD4+ T cells are stained and isolated for transcriptome analysis using HLA tetramers. Quantification of CD8+ αβ T cells, γδ T cells and gluten-specific CD4+ T cells is also done.

Results
We are in the preliminary stage of the project. In a first round of experiments, we are collecting and analysing data from four CD patients challenged with gluten for 3 days to investigate the transcriptome of gluten-specific CD4+ Th1 cells. Data from the first patient indicate an efflux of gluten-specific T cells (0.4 % of CD4+ cells on baseline vs. 8.3 % on day 6) into the blood, but stable levels of CD8+ cells after gluten challenge.

After having identified differentially expressed molecules, we will include more subjects in the gluten challenge for functional studies on gluten-specific CD4+ Th1 cells.

P058

Celiac disease-associated Human Leukocyte Antigens DQ2.5, DQ2.2, and DQ8 are reliably detected by a new multiplex real-time PCR Assay: CeliaSCAN

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Background
Celiac Disease is an autoimmune disease caused by an inappropriate immune response to dietary gluten, found in wheat, rye, and barley and some strains of oats.

Ninety percent of patients with celiac disease express the HLA-DQ2.5 heterodimer. Of the remaining 10% most carry the HLA-DQ8 or HLA-DQ2.2 heterodimers. Absence of these heterodimers is a very strong negative predictor of celiac disease.

Methods
CeliaSCAN, a TubaScan Ltd. product, is an easy to use multiplex real-time PCR assay with melting curve analysis that combines speed (30 samples in 1.5 hrs) and accuracy. This innovative assay has been validated in 96-well plate format (only 3 reactions / sample) on the Roche LightCycler®480 and the ABI Prism®7500 series. CeliaSCAN detects the presence and absence of HLA-variants encoding the HLA-DQ2.5, HLA-DQ2.2, and HLA-DQ8 heterodimers and is able to distinguish HLA-DQ2.5 heterozygotes from HLA-DQ2.5 homozygotes (highest genetic risk for celiac disease).

Human interpretation of data is unnecessary since output files are automatically and instantly translated into individual and batch reports via an online software tool (ClinicaGeno, UK).

Results
Positive and negative EDTA-blood samples from VUMC (n=85 MMI+20 CC) and Reinier Haga MDC (n=61) were genotyped for HLA-DQA1 and HLA-DQB1 by SSCP/HD method at VUMC. These samples were then genotyped with CeliaSCAN at its centers. The results were fully concordant (n=166).

Conclusion
CeliaSCAN is an easy to use multiplex real-time PCR assay with melting curve analysis that combines reliability, speed and accuracy. Larger studies testing the clinical validity of CeliaSCAN for CD patients, their offspring and patients with associated autoimmune diseases in diverse populations are ongoing.

SESSION 3: PATHOGENESIS – I

P059

New markers for celiac disease: anti-neo-epitope human and microbial transglutaminases

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Aim
Microbial transglutaminase (mTg) and human tissue Tg (tTg) complexed to gliadin peptides present neo-epitopes. Antibodies against these complexes are called tTg neo-epitope and mTg neo-epitope.

Reliability of antibodies against the non-complexed and complexed forms of both transglutaminases to reflect intestinal damage and to diagnose the pediatric Celiac Disease (PCD) was compared.

Methods
95 PCD patients, 99 normal children (NC) and 79 normal adults (NA) were tested using the following ELISAs detecting IgA, IgG or both IgA+IgG combined: tTg (for in house research use only), AESKULISA® tTg New Generation (tTg neo-epitope (tTg-neo)), AESKULISA® mTg (RUO) and AESKULISA® mTg neo-epitope (mTg-neo, RUO). Marsh criteria were used for the degree of intestinal injury.

Results
All anti-mTg-neo and anti-tTg-neo levels were higher (p mTg-neo IgA+IgG > tTg-neo IgG = mTg-neo IgG > tTg-neo IgA> tTg-neo IgA+IgG. Taken together, mTg-neo IgG and tTg-neo IgA & IgA+IgG correlated best with intestinal pathology (r=0.5633, r=0.6165 & r= 0.6492; p<0.0001, p<0.0001 & p<0.0001 respectively).

Conclusion
The complexed forms of both transglutaminases exhibited a higher OD activity and better reflected intestinal damage in PCD, compared to the non-complexed forms. mTg is immunogenic in children with CD and by complexing to gliadin its immunogenicity and pathology reflection is enhanced.

P060

Mucosal immune effector and regulatory T cells in adult patients with treatment naive celiac disease

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Background
Celiac disease (CeD) is an immunological jigsaw. Tightly regulated mucosal immunity is crucial for protection against luminal microflora and tolerance to dietary proteins. Loss of circulating regulatory T cell function has recently been shown as the cause behind loss of mucosal tolerance. The aim of this study was to analyze the immune effective and regulatory T cell populations in mucosal biopsies of different modified Marsh grades.

Methods
In this cross section study a total 234 duodenal biopsies [D2 & D3] (132 control & 102 treatment naïve CeD) were included. Mucosa infiltrating lymphocytes as well as the intra-epithelial lymphocytes (IELs) were examined by dual immunohistochemical staining (IHC) for CD20, CD3:CD4, CD3:CD8, CD4:FoxP3, CD8:FoxP3 and TCRαβ: TCRγδ cells. The density of these mucosa infiltrating lymphoid cells were correlated with modified Marsh grades. The study was approved by Institutional Ethics Committee.

Results
In this cohort both CD3+ IELs and CD20+ B cells in lamina propria were found to rise in a linear pattern with increasing modified Marsh grades. Serum anti-tTG titer also showed a linear increasing pattern with Marsh grades. Densities of both CD4+ T cells in lamina propria and CD8+γδ intra-epithelial T cells were significantly more in biopsies of treatment naïve CeD, than in controls. While the CD8+FoxP3+ iTreg cells were found to be significantly upregulated, the CD4+FoxP3+ Treg cells were found deficient in biopsies of CeD, than in control biopsies.

Conclusion
Lack of immune suppressive CD4+FoxP3+ Treg cells in duodenal biopsies of treatment naïve CeD cannot be compensated by upregulated weakly suppressive CD8+FoxP3+ iTreg cells, contributing to loss of mucosal tolerance in CeD. Densities of both T cells and B cells increases proportionate to the histological disease severity in duodenal mucosa. Though, both TCRγδ and TCRαβ are present in duodenal mucosa in CeD, TCRγδ+ IELs were predominant.

P061

Densities of IL-4+ cells and of TCR d + cells in the intestinal mucosa are discriminating factors between potential and overt coeliac disease

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Background
Coeliac disease (CD) is characterized by a variable combination of gluten-dependent symptoms, genetic factors, specific antibodies and enteropathy. Most patients show a variable degree of enteropathy (overt CD), but a minority shows absence of villous atrophy despite the presence of CD-specific autoantibodies (potential CD). We investigated the cytokine profile and the phenotype of intestinal T cells from children affected by overt versus potential CD.

Methods
Cell phenotype (on unstimulated cells) and cytokine production patterns (by intracytoplasmic staining after PMA/Ionomycin stimulation) were analysed by flow cytometry, in both gluten-raised T cell lines (TCLs) and freshly isolated mucosal cells. Jejunal biopsies were obtained from 19 overt CD (mean age 5.1 yrs), 16 potential CD patients (8.5 yrs) and 12 non-CD children (4.2 yrs). Statistical analysis was performed using a paired Student t-test (p< 0.05).

Results
An increased number of CD3 TCR γδ+ cells, mainly CD4CD8 double negative cells, was found in TCLs from overt CD patients compared to potential CD (p<0.004) subjects. A higher fraction of IL-4 producing cells, mainly CD4+ cells, was detected in TCLs from children with potential CD (p<0.0007). Ex vivo analysis on freshly isolated intestinal cells confirmed the significant increased frequency of TCR γδ+ cells in gut mucosa of children with villous atrophy (p<0.02). However, a higher percentage of TCR γδ+ cells was detected in potential CD compared to healthy mucosa of non-CD controls (p<0.04). An increased expansion of IL-4 producing CD4+ T cells was found in biopsies from potential CD compared to overt CD patients (p<0.05).

Conclusion
Our study confirms in CD patients an expansion of TCR γδ+ T-cells, particularly in subjects with enteropathy. The transition to villous atrophy seems to be characterized by a dramatic disappearance of IL4+ cells. These findings may offer biomarkers useful to characterize the different stages of CD.

P062

Functional analysis of CD4+CD8aa double positive and gammadelta T-cells in the duodenal lamina propria of celiac disease patients

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Background
Active celiac disease (ACD) is characterized by intraepithelial lymphocytosis accompanied by a change in composition. This change involves a relative increase in gammadelta and decrease in CD4+CD8aa double positive T-cells (DPT). Murine intestinal DPT produce Th2 cytokines providing B-cell help and produce immunoregulatory IL-10. The function of gammadelta T-cells is not yet clear, they may exert both immunosuppressive and immune stimulatory effects.

Aim
Aim of this study was to elucidate whether proportion of, and cytokine production by LPL derived DPT and gammadelta T-cells is changed in CD. These data may provide clues regarding the function of both cell types.

Methods
Patient groups (n=5-9 per group): ACD, CD on GFD and controls. The ratio of different subsets in IEL was determined in a diagnostic set-up by flow-cytometry. The LPL fraction was isolated separately for this study. DPT, gammadelta T-cells and conventional CD4+ and CD8+ T-cells were isolated by FACS sorting. Upon polyclonal stimulation, cytokine production of the different subsets was determined using a multiplex assay. Frequencies and cytokine production in the different groups were analyzed by the Mann-Whitney U test.

Results
In a historic cohort of patients (67 controls, 75 ACD, 93 GFD) we retrospectively confirmed the decrease of DPT among IEL in ACD and CD patients on a GFD, as well as the increased proportion of gammadelta T-cells in both CD groups. This difference was not apparent in the LPL fraction of the patients analyzed in this study. Preliminary results suggest that the cytokine profile of the DPT resembles the profile of CD4+ conventional T-cells and that cytokine production by gammadelta T-cells is relatively low.

Conclusions
DPT show the highest similarity to CD4+ T-cells and gammadelta T-cells are poor cytokine producers. Final analyses of cytokine production in all samples and comparison among patient groups is currently in progress and will be presented.

P063

Resistance of gluten immunogenic peptides (GIP) to heat elimination in a homelike environment. Lessons for cross contamination prevention.

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Background
Verify effective elimination of Gluten Immunogenic Peptides (GIP) by home cooking techniques.

Methods
Batches of samples of gluten containing flour, potatoes, and potatoes plus flour matched to controls were tested. Each batch was cooked in laboratory by use of electric stove, gas stove, oil deep fryer, induction stove and water bath and was cooked at temperature range from 91-233°C (196-452 F) for 5 up to 30 minutes. GIP content was tested by GlutenTox® Sticks (IKT-5340 Biomedal Diagnostics) based on antibody G12.

Results
On gas stove was necessary to keep 233 °C (451 °F) for 10 minutes to have absence of GIP detection. In range 190-200°C (374-392°F) incubation for 30 minutes was needed to have absence of GIP detection. Tests in temperatures below 190°C (374°F) showed presence of GIP at 10 and 20 minutes.

On induction stove temperature up to 246°C (475°F) for 6 minutes was needed to have negativity to GIP. Lower temperature ranges in spite of extended time up to 30 minutes were unable to get negative GIP. In oven processing never was got negative GIP signal, in spite of processing up to 210°C (410°F) and extended

incubation time up to 45 minutes. Samples processed on electric stove, water bath and deep frying showed presence of GIP in all ranges of time and temperature.

Conclusion
It is not realistic the elimination of gluten (GIP) at home kitchen by heat as temperatures higher that 200°C (392°F) are needed. Extended processing time is no compatible with conventional recipes. Fat processing over 200 is link with toxic metabolites generation which may be harmful. Use of oven or deep frying without proper cleaning may transfer GIP to meals when previously gluten containing meals were processed in these appliances.

P064

Characterization of IgM antibody response to gluten in non-celiac wheat sensitivity

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Background
Some individuals experience a range of symptoms in response to ingestion of gluten-containing food, without the characteristic serological or histological evidence of celiac disease. The condition is referred to as non-celiac gluten or wheat sensitivity (NCWS). Recent studies reveal a state of systemic immune response to gluten and microbial antigens in conjunction with a compromised intestinal epithelium in individuals with NCWS. Previous work has demonstrated the elevation of not only IgG antibody to gliadin similar to that found in celiac disease, but also IgM isotype response in NCWS. Here, we aimed to characterize the IgM antibody response to a native gliadin extract comprising of α, β, and ω gliadin, as well as to the p57-89 peptide fragment of α2-gliadin that contains celiac disease-specific B and T cell epitopes, and the p31-43 fragment of α9-gliadin shown to trigger innate immune responses.

Methods
Study participants included NCWS patients selected according to the Salerno criteria, patients with biopsy-proven celiac disease, and healthy controls. Antibody reactivity in serum was examined by the enzyme-linked immunosorbent assay (ELISA).

Results
Individuals with NCWS, but not celiac disease patients, exhibited elevated IgM antibody response to native gliadin in comparison with healthy controls (p=0.018). Levels of IgM to p57-89 gliadin were not significantly different between NCWS and celiac disease patients. However, IgM antibody response to p31-43 gliadin was significantly greater in NCWS individuals than in celiac disease patients (p<0.001).

Conclusion
Our data demonstrate an enhanced IgM response to gluten in NCWS that is suggestive of a different mechanism of B cell activation and epitope reactivity in comparison with celiac disease. The results may have implications for understanding the mechanism and identifying biomarkers of NCWS.

P065

Analysis of immunotoxic peptides from dietary gluten in human urine

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Background
Celiac disease is driven by consumption of dietary gluten. To date, our knowledge of immunotoxic peptides derived from gluten has emerged primarily from *in vitro* analyses. In most cases, gluten peptides are recognized by HLA-DQ2 or - DQ8 restricted inflammatory Th1 cells. Despite the key role that these peptides play in celiac disease pathogenesis, there is little knowledge of their absorption, metabolism, and excretion characteristics. Furthermore, not a single chemically-defined gluten peptide has ever been identified *in vivo* in the human circulatory system. Here, we sought to identify the sequences of specific peptides derived from dietary gluten circulating *in vivo* through analysis of human urine samples.

Methods
By utilizing samples from a celiac disease patient on a gluten-free diet before and after oral challenge with dietary gluten, we developed a method to identify gluten peptides in urine. Briefly, the protocol involves depletion of urinary proteins followed by untargeted proteomic analysis. Using hits obtained from the gluten-positive urine sample, we then carried out a targeted analysis in the urine of 20 volunteer urine donors.

Results
We have identified the sequences of 22 unique gluten peptides in human urine. In our pilot study of 20 individuals, we found that approximately half of the samples were positive for at least one gluten peptide. Interestingly, some of the identified peptides have previously been reported to be T-cell epitopes or stimulators of the innate immune response in celiac disease, whereas others are novel peptides whose immunopathological roles are unexplored.

Conclusion
Our results provide the first examples of specific peptides from dietary gluten that enter systemic circulation in humans. We are currently performing fundamental studies on their immunotoxicity and are analyzing the pharmacokinetics of their absorption and excretion. Finally, through a clinical collaboration, we are evaluating their potential utility as non-invasive biomarkers of celiac disease status.

P066

Expression of Amylase-Trypsin Inhibitor (CM3) Gene in Wheat During Grain Development

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Background
While gluten peptides are responsible for celiac disease, the amylase trypsin inhibitors (ATI) have also been implicated in the pathogenesis of gluten-related disorders. Among several of ATIs, ATI-CM3 is known to be highly immunogenic. These are data to suggest that ancient diploid wheats are is less immunogenic. We explored the ATI-CM3 gene expression in the diploid, tetraploid and hexaploid wheat.

Methods
In order to study the genome specific gene expression of ATI-CM3 in the grains of wheat progenitors, durum and bread wheat, 5 genotypes (AA: *T. monococcum*; BB: *Ae. Speltoides*; DD: *A. squarossa*: AABB: *T. durum* variety PDW233-durum; AABBDD: *T. aestivum* variety PBW343-bread wheat) were included. Developing grain samples were collected at 2, 3, 4 and 5 weeks after anthesis (WAA). RNA was isolated from all the samples and converted to cDNA. Gene expression of ATI CM3 was studied using real time PCR (q-PCR) using gene specific primers.

Results
Negligible expression of ATI-CM3 was found in diploid progenitors in all the four stages of seed development in comparison to the durum and bread wheat. When the expression was compared between bread and durum wheat, it was higher in the bread wheat during 2&3WAA, whereas it was higher in durum during 4&5WAA. Individual genotypes showed a different trend of gen expression. While *Ae. squarossa*, and bread wheat showed a gradual reduction in the expression of ATI-CM3 towards the grain maturity, there was evidence of gradual increase in the expression towards grain development in *T. monococcum, Ae. Speltoides* and durum wheat.

Conclusion
This is the first study to show that the expression of specific immunogenic ATI is almost nil in the wheat progenitors in comparison to cultivated wheat. We further aim to characterize different types of ATIs in the different wheat genotypes and develop a high throughput method to quantify them

SESSION 4: PEDIATRIC CELIAC DISEASE

P067

Long-term health and quality of life in adult celiac disease patients diagnosed in childhood because of clinical suspicion or by screening

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Background
Celiac disease affects 1-2% of population, but due to diverse clinical presentation most patients remain unrecognized. Diagnostic efficiency could be improved by screening of at-risk groups, but long-term benefits of this approach are unclear. To clarify this issue, we compared large cohorts of adult patients diagnosed in childhood either because of clinical suspicion or by screening.

Methods
A questionnaire about current health and lifestyle, adherence to gluten-free diet (GFD) and follow-up of celiac disease was sent to 564 adults with a childhood diagnosis. Further, they fulfilled validated Gastrointestinal Symptom Rating Scale (GSRS) and Psychological General Well-Being (PGWB) surveys for symptoms and quality of life. Diagnostic and other relevant medical data were confirmed from patient records.

Results
Altogether 235 (42%) adults completed the questionnaires. At diagnosis, screen-detected patients (n=49) were older (11.3 vs 8.8 yr, p=0.016) and had less symptoms (44% vs 85%, p<0.001) and poor growth (17% vs 51%, p<0.001) than clinically detected patients (n=186). They also had a trend to have less often total villous atrophy (18% vs 32%, p=0.075) and anemia (18% vs 32%, p=0.072). The groups did not differ in gender, current age (median 26.5 vs 27.1 yr, p=0.245), time from the diagnosis, self-experienced health or concern about health, clinical symptoms, strict GFD (74% vs 80%, p=0.161), lifestyle restrictions caused by GFD, presence of celiac disease-related complications, physical activity, fertility or GSRS and PGWB scores. However, screen-detected patients smoked less (4% vs 15%, p=0.037) and had more often celiac disease in relatives (78% vs 58%, p=0.011).

Conclusions
Diagnostic approach and presentation of celiac disease in childhood do not seem to affect the long-term health outcomes or attitude towards the disease in adulthood. Lack of difference in the dietary adherence and lifestyle restrictions gives further

support for active screening and early diagnosis of celiac disease.

P068

Celiac disease is the most common endoscopic diagnosis in children presenting with anemia irrespective of other symptoms

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Background
Digestive diseases are major cause of anemia in children. We aimed to explore the diagnostic yield of gastrointestinal endoscopy in children presenting with anemia with or without other intestinal symptoms.

Methods
Medical records of 1146 consecutive children who underwent gastroscopy were analyzed. Only cases with a first diagnostic endoscopy and known hemoglobin status at that time were included for further analyses (n=737). All results were compared between anemic and non-anemic patients. Furthermore, the long-term prognosis of subjects without diagnosis in the primary endoscopy was inspected.

Results
Altogether 222 (30%) children had anemia. Concurrent colonoscopy was performed in 41% of anemic and 34% of non-anemic patients. Poor growth (13% vs. 6%, p=0.021) and blood in feces (22% vs. 9%, p<0.001) were more common in children with anemia, whereas they had less often abdominal pain (55% vs. 68%, p=0.002), reflux (10% vs. 17%, p=0.010) and dysphagia (1% vs. 5%, p=0.013). Final diagnosis was reached in 77 % of anemic and 52% of non-anemic children (p<0.001). The most common diagnoses in the anemia group were celiac disease (28%), ulcerative colitis (19%) and Crohn's disease (11%). In 30 children anemia was the sole indication for upper gastrointestinal endoscopy; of these 13 had celiac disease, 2 ulcerative colitis, 1 Crohn's disease, 2 H. pylori and 1 gastrointestinal stromal tumor. From the patients who did not get a diagnosis in primary endoscopy only 5 out of the 41 children presenting with anemia and other symptoms and none of the 11 with anemia only developed any disease in a follow-up of up to 10 years.

Conclusion
Anemia increases the likelihood of organic disease at gastrointestinal endoscopy. Celiac disease is the most common single diagnostic entity in children presenting with anemia irrespective of the presence or absence of other symptoms.

P069

Comparison of utility of anti tTG and anti DGP antibodies in monitoring dietary adherence in children with Coeliac disease on gluten free diet

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Background
Non compliance is a major problem in management of Coeliac Disease in children and adolescents. Some studies have been done to explore the utility of anti tTG and anti DGP antibody tests in monitoring dietary compliance but there are conflicting reports from adult and paediatric patients.

Methods
A cohort of 42 newly diagnosed coeliac disease patients (positive coeliac serology and suggestive duodenal biopsy) were started on GFD and followed monthly till one year. Their serum anti tTG IgA and anti DGP IgG levels were measured at diagnosis and at 3, 6 months and one year of follow up. The patients were categorized into good adherent and non-adherent. The ability of anti tTG and anti DGP to identify non adherent patients was explored by ROC curve analysis.

Results
The decline in mean anti tTG Antibody levels from the baseline in two groups (good adherence Vs non adherence) were (92.93 Vs 32.52) at 3 months, (137.8 Vs 56.49) at 6 months and (136.55 Vs 85.76) at 12 months. The difference between two groups was statistically significant with p value of 0.004 at 3 months, 0.000 at 6 months and 0.020 at 12 months respectively. It was found that difference in mean decline in DGP levels in two groups were (73.67 Vs 34.47) significant at 3 months (p value 0.008) but was not significant at 6 months (109.56 Vs 81.44) and at 12 months (134.23 Vs 105.13).

Conclusions
Decline in mean anti tTG Ab and anti DGP Ab levels was observed at the end of one year of follow up. The fall in anti tTG Ab levels was better associated with the degree of adherence than the anti DGP Ab levels.

P070

Calculation of the incidence of disease and the familial frequency of HLA genotype in the high risk, first degree relatives in North Indian celiac patients

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Background
Study was designed to calculate the incidence of celiac disease in high risk first degree relatives of an index & to evaluate the frequency of HLA type DQ2 & DQ8 alleles in children with celiac disease and as well as in their FDR.

Methods
A total of 528 cases (112 index cases and 416 first degree relatives) were enrolled. Disease state was confirmed by serology, duodenal histopathology studies & HLA typing.

Results
A total of 112 index cases were enrolled and categorized into classical & non classical types with 68 (60.71%) & 44 (39.28%) cases. Out of 416 first degree relatives screened, 78 subjects shown a high serology (18.7%). A total of 28 brothers & 26 sisters were positive for serology& underwent duodenal Biopsy, out of which 10 subjects (4 brothers and 6 sisters) showed a normal villous pattern. Forty subjects (24 brothers and 16 sisters) showed total villous atrophy belonged to Marsh 3b & 3c grade and 4 subjects (sisters) refused biopsy. Out of 7 mothers & 13 fathers who were positive for serology 5fathers refused & rest underwent D2biopsy, showed scattered histopathology pattern consistent to Marsh 3a, 3b & 3c grade. DQB1*0201 allele was present in 430 (81.44%) cases & DQA1*0501allele was present in 400 (75.76%).The combined presence of DQB1*0201&DQA1*0501 as DQ2 heterodimer were found in 354 (67.05%) high risk subjects. A total of 52 (9.85%) subjects found negative for HLA type DQ2.The collective presence of HLA type DQ8 (DQA1*0301& DQB1*0302) was found in 69(13%) subject.

Conclusion
Our study shown 19% incidence of CD in high risk asymptomatic FDR group and the data is in corroboration with western pattern of disease manifestation. Only 9.8% of the FDR were negative for HLA DQ2. Frequency of HLA DQ8 alleles were found very low. Our study, strongly recommends serology screening followed by HLA typing as of vital importance because FDR may be detect in the silent phase of disease or as a potential celiac.

P071

Lane-Hamilton Syndrome: Atypical presentation of celiac disease

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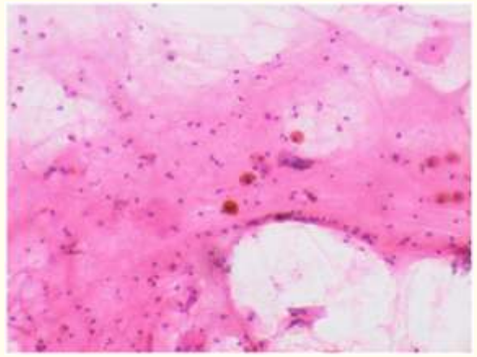
Background
Association of CD with idiopathic pulmonary hemosiderosis (IPH) is known as Lane-Hamilton syndrome which is a rare condition. His association with celiac disease could be due to the fact that both entities share a common pathogenic immune pathway.

Case: A 14 years old non-smoker adolescent boy presented with complaints of intermittent hemoptysis associated with cough and history of progressive pallor for last 5 months. On admission he had severe pallor with respiratory distress. Investigations showed severe anemia (Hb 2 gm/dl). Chest radiograph demonstrated bilateral lower zone alveolar type opacities. A contrast-enhanced computed tomography scan of the chest revealed scattered ground-glass opacities predominantly in both lower lobe and fibrosis with bronchiectatic changes seen in bilateral upper lobes. All laboratory work-up for diffuse alveolar hemorrhage (DAH) were negative. Pulmonary function tests showed restrictive pattern. In sputum examination, smear of sputum showed occasional squamous cells, few neutrophils and hemosiderin-laden macrophages (HLM) enmeshed in mucous, suggesting the possibility of intra-alveolar hemorrhage. The presence of bilateral ground-glass haziness and iron deficiency anemia, along with HLM in sputum examination with exclusion of other causes confirmed the diagnosis of IPH. Positive serology, presence of scalloping in second part of duodenum and modified Marsh grade 3a histological finding in duodenal biopsy was consistent with diagnosis of CD. A final diagnosis of Lane-Hamilton syndrome (CD with IPH) was made. Child was initially managed with blood transfusions and put on gluten-free diet (GFD). Pulmonary symptoms were completely recovered after few days. Hemoglobin at 2 months follow up was normal with complete disappearance of previous radiological findings in chest X-Ray.



Conclusion
A high index of suspicion for celiac disease should be kept in patients of pulmonary hemosiderosis, especially with disproportionately severe anemia despite having no gastrointestinal symptoms and vice-versa.

P072

Celiac disease in children with moderate to severe iron deficiency anemia: A Hospital based study

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Aim
To evaluate the proportion of children with moderate to severe iron deficiency anemia who have celiac disease as the etiologic factor.

Methods
This cross-sectional analytical study was conducted among 152 children aged 1 to 12 years of age with moderate to severe iron deficiency anemia [mean (SD) Hb 7.7 (1.80) g/dL). These children were compared with 152 children without anemia [mean (SD) Hb 12.2 (0.74) g/dL]. Serum IgA-tissue transglutaminase levels were performed in both cases and controls. All children with positive serology underwent upper gastrointestinal endoscopy and duodenal biopsy. The biopsy finding of Marsh grade 3 was considered positive for celiac disease.

Results
16 (10.5%) cases and 3 (2%) control patients had positive serology for celiac disease (*P*= 0.007). Six (3.94%) children with iron deficiency anemia and none of the children without anemia had biopsy features suggestive of celiac disease. None of the patients diagnosed as celiac disease had associated gastrointestinal problems.

Conclusion
Children with moderate to severe anaemia have an OR of 5.33 (95% CI 1.52 to 18.67) of having a positive serology for tTG. Nutritional anemia remains the dominant cause of anemia in India. In the North Indian scenario, CD accounts for only 4% of children presenting with moderate to severe anemia.

PO73

Scoping the literature: Reframing of food-related activities in pediatric celiac disease

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Background
Daily life with celiac disease (CD) presents unique challenges among children and adolescents and can affect children's activities, participation and quality of life (QOL). Activities and participation are components of the International Classification of Functioning, Disability and Health–Children and Youth (ICF-CY) framework presented by the World Health Organization. The aim was to conduct a scoping review of CD literature that describes food-related activities following the ICF-CY concepts and to illuminate gaps in knowledge.

Methods
A scoping review method was selected to synthesize the breadth and depth of knowledge on the topic. The Pubmed, CINAHL, PsycINFO and Web of Science databases were searched for publications between January 2006 and June 2016, to answer the research question "What is known about the ICF-CY *activities* and *participation* concepts and QOL among children and adolescents with CD concerning daily food-related activities?" Data including age, study objectives, methods, evaluation tools and food-related activities were charted.

Results
Twenty-three peer-reviewed publications met the inclusion criteria for the study. Food-related activities were identified and classified by the ICF-CY coding system within the concepts of activities and participation. The literature review exposed food-related activities that spread across seven of the nine ICF-CY activities and participation chapters.

Conclusion
Activities and participation characteristics were not the original focus of the reviewed articles. Reframing the literature with these ICF-CY concepts presents a different point of view of the daily food-related activities. Capturing the everyday situations through a different lens than they were originally seen through can enable deeper understanding of activity demands, limitations and challenges. Better understanding of functioning while adhering to a gluten-free diet and participating in daily food-related activities, may be valuable and can lead to adapted assessments and interventions. Suitable interventions can improve daily functioning, promote health, quality of life and well-being of children and adolescents with CD.

PO74

Understanding actual daily challenges of children and adolescents with celiac disease

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Background
The gluten-free diet can be challenging in everyday life with celiac disease (CD) and adherence among children and adolescents in particular is often inadequate. Activities and participation, components of the World Health Organization's International Classification of Functioning, Disability and Health–Children and Youth (ICF-CY) framework, are crucial in the context of children with CD. Understanding engagement characteristics in daily activities, due to the dietary limitations, provides insight to tailor support, to encourage adherence and promote well-being. The aim was to develop and validate the Celiac Disease-Children's Activity Report (CD-Chart) to explore the daily experiences of children and adolescents with CD.

Methods
Based on previously conducted focus groups, the CD-Chart incorporates nine food-related activities, measured by six dimensions: frequency, preference, preparation, involvement, help, and self-determination. The CD-Chart was administered to 126 children and adolescents aged 8-18, diagnosed with CD for over six months and a matched control group of 30 children and adolescents without CD. Participants with CD also completed the validated Children's Leisure Assessment Scale (CLASS).

Results
The CD-Chart items showed adequate internal reliability as measured by the preference dimension (α=0.80). An independent-samples t-test indicated that the preparation scores were significantly higher for the CD group (M=0.899, SD=0.060) than scores of the control group (M=0.004, SD=0.023); t (38)=76.25, p <0.001. Factor analysis defined between activities in and out-of-home. A significant difference was found in the preference level for CD-Chart food-related activities and other leisure activities measured by the CLASS, t (125)=-5.80, p <0.001.

Conclusion
The CD-Chart is a reliable and valid tool that contributes to characterizing the participation in food-related activities while managing the gluten-free diet among children and adolescents with CD. These characteristics together with additional tools can be integrated into developing intervention goals to promote dietary adherence, effective self-management, and HRQOL of children and adolescents with CD.

PO75

An A-gliadin undigested peptide, activated the INF-alpha pathway in enterocytes by interfering with the endocytic trafficking

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Background
The enteropathy in Celiac Disease (CD) is due the adaptive and to the innate immune response to gliadin peptides. Gliadin peptide P31-43 activates innate immune response and interferes with vesicular trafficking. Type 1 interferons (INFs) and viral infections play a role in CD pathogenesis. In this paper we investigated the role of P31-43 in the activation of the INF-α pathway.

Methods
Small intestinal biopsies of CD patients both with active disease on gluten containing diet (GCD) and in remission phase of the disease on a gluten free diet (GFD) and controls were analyzed before and after culture with P31-43. The levels of toll like receptor 7 (TLR7), myeloid differentiation primary response 88 (MyD88), myxovirus resistance protein 1 (MxA) and nuclear factor-κB (NF-κB) proteins and INF-α mRNA in intestinal biopsies and CaCo-2 cells were analyzed by western blot and quantitative PCR analysis, TLR7/MyD88 complex by immuno-precipitation and by si-TLR7 and si-MyD88. Silencing of growth factor-regulated tyrosine kinase substrate (si-HRS) allowed to study the endocytosis.

Results
In celiac small intestinal biopsies INF-α pathway was activated by P31-43. In CaCo-2 cells P31-43, like loxorubine (LOX) a viral ligand for TLR7, activated the TLR7/INF-α/NF-kB pathways through MyD88)/TLR7 complex formation; P31-43 cooperated with LOX to activate the INF-α pathway. Alteration of the vesicular trafficking "per se", induced by si-HRS, activated the TLR7 and the INF-α pathways.

Conclusion
An undigested gluten peptide was able to activate TLR7 and INF-α pathway by mimicking and potentiating the activity of a TLR7 ligand. Delay of the maturation of intracellular early vesicles was central to the activation of the TLR7 pathway.

PO76

Prevalence and HLA status of potential CD: data from an Italian pediatric cohort

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Background
The term potential celiac disease (PCD) can be used for people with normal small intestinal mucosa who are at increased risk of developing celiac disease (CD) as indicated by positive CD serology. Evidences regarding a specific genetic pattern of PCD is still scanty. From November 2013 to May 2017, 202 children underwent duodenal and bulbar biopsies to confirm CD. All these patients did not fulfil the ESPGHAN 2012 criteria for omitting biopsies.

Methods
All 202 patients displayed positive anti-transglutaminase and anti-endomysial antibodies. Upper GI endoscopy was always performed under general anesthesia. Two biopsies were taken from the bulb and at least 4 from the duodenum. All samples were oriented and sent to the same expert GI tract pathologist. Specimens were graded according to the Marsh-Oberhuber criteria. All individuals were typed

for DRB1, DQA1, and DQB1 genes by sequence-specific primer–polymerase chain reaction (SSP-PCR) from a commercial kit (EUROSPITAL).

Results
Of 202 patients, we found 13 (6.4 %) patients with PCD and 191 with overt CD. Of these 13 PCD patients (M:6; F:7), 7 had suggestive symptoms for CD and 6 were started on a gluten-free diet. As regards PCD genetic pattern, six patients (46%) were DQ2 heterozygous, 2 patients (15%) had only DQB1*02, 2 patients (15%) were both DQB1*02 and DQ8 positive, 2 patients (15%) were DQ8 heterozygous and 1 patient (7.7%) was both DQ2 and DQ8 positive.

Conclusion
In our cohort, the prevalence of potential CD (6.4%) seems lower than in other studies. Heterozygosis for DQ2 is the most representative genetic pattern in our patients with PCD.

PO77

Neuroendocrine differons in celiac disease in children

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Background
The actuality of our study is determined by the frequency of celiac disease in Saint-Petersburg. The morphological differential diagnosis of this disease is very difficult. One of the characteristics of the mucosal state of duodenal mucosa is its neuroendocrine activity, which is provided by the enteroendocrine cells synthesizing neuropeptides and chromogranins, in particular, chromogranin A (CgA), ghrelin and serotonin.

Methods
The aim of our study was to determine the markers of these products in the duodenal mucosa in children with celiac disease and duodenitis of various etiology. We studied 40 distal duodenal biopsies, obtained by fibrogastroduodenoscopy in children aged 6 to 17 years old with morphologically verified chronic gastroduodenitis (CGD).

Results
The first group included children with celiac disease, the second group with Helicobacter pylori infection, the third group with giardiasis, and the fourth (the control group) children with reliably excluded above listed diseases and preserved duodenal mucosa without morphological features of duodenitis. The expression levels of Chromogranin A (Abcam 1: 400), Serotonin (Abcam 1:50), Ghrelin (Abcam 1: 100) were determined immunohistochemically. The intensity of the reaction was evaluated by two parameters - the relative area of expression and the optical density.

Conclusion
We believe that the increased expression of ghrelin, serotonin and chromogranin A plays an important role in the mechanisms of duodenum structure disorders in celiac disease. As to Helicobacter pylori duodenitis, we found a decrease of the level of all markers, whereas no significant change of the mentioned markers content was found in giardiasis. We believe that these results will help to differentiate celiac disease etiologically.

PO78

Autoimmune Gastritis in children with celiac disease

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Aim
To determine the prevalence of autoimmune gastritis in children with celiac disease, comparing enzyme-linked immunosorbent assay (ELISA) and indirect immunofluorescence reaction (IIFR).

Methods
155 children of both sexes at the age of 3 to 17 years were examined. The study involved 78 children with different clinical forms of celiac disease (CD). 72 children with chronic gastritis and excluded celiac disease were a control group.

All patients underwent a same examination: histological examination of gastric biopsies, histological verification of H. pylori infection and biopsy urease test.

Results
In both groups of children chronic gastritis was diagnosed. Helicobacter pylori infection was verified in the majority of patients in both groups (53.7% and 55.9% p> 0,05).

Anti- H+/K+ ATPase antibodies were common in both groups with no statistically significant difference (8.8% and 6.25%, p> 0.05), but only in the group with celiac antibodies combined with gastric atrophy (2.9% and 0%, p <0.01). Anti-Intrinsic Factor antibodies were presented only in the control group (0% and 6.8%, p <0.01) and weren't combined with atrophy. APCA identified with IIFR were detected only in patients with celiac disease (4.54% and 0%, p <0.01) and were associated with gastric atrophy.

Conclusion
Thus, the ELISA detected APCA with no evidence of gastric atrophy in both groups. This requires additional examination to confirm or to exclude the diagnosis of autoimmune gastritis. IIFR displayed complete concurrence of immunological and histological criteria of autoimmune atrophic gastritis, including the lack of association with H. pylori infection. This may indicate a systemic autoimmune process in celiac disease. The prevalence of autoimmune gastritis in children with celiac disease according to IIFR is 4.54% or 1:22.

PO79

Gluten Immunogenic Peptides as marker to monitor Gluten-Free Diet compliance in paediatric celiac disease

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Background
Treatment for celiac disease (CD) is a lifelong strict gluten-free diet (GFD). Patients should be followed-up with dietary interviews and serology as CD markers to ensure adherence to the diet. None of these methods offer an accurate measure of dietary compliance. Our aim was to evaluate the measurement of gluten immunogenic peptides (GIP) in stools as a marker of GFD adherence in CD paediatric patients.

Methods
We performed a prospective, nonrandomized, multicenter study including 64 CD patients. Fecal GIP, anti-tissue transglutaminase (anti-tTG) IgA and anti-deamidated gliadin peptide (anti-DGP) IgA antibodies were measured during basal and follow-up visits at 0, 6, 12 and 24 months. Correlations between GIP and serum antibodies were conducted by Cochran's and Friedman tests.

Results
62 patients (97%) had detectable GIP levels in stools during basal visit, whereas 20.3% of the patients were found to have positive GIP after consumption of a GFD. Dietary transgressions were more frequent in children over 8 years of age, being 46.1% of them repeatedly. However, anti-tTG IgA remained in high concentrations in 48, 34 and 20% of the patients at 6, 12 and 24 months of follow-up, respectively, against the 13, 4.5 and 0% in anti-DGP in each of the follow-up controls mentioned. Both serological methods showed discordance with GIP (p<0.05).

Conclusion
GIP detection in stools reveals limitations of traditional serological methods for monitoring GFD, since these antibodies can take several months or even years to decrease after initiation of the GFD. Therefore, fecal GIP could be a useful tool: i) during the diagnosis of CD, to ensure that a sufficient amount of gluten has been ingested to allow a correct CD diagnosis; ii) during treatment and evolutionary control, the monitoring of short-term and long-term GFD compliance; and iii) during the differential diagnosis of unresponsive CD from dietary non-compliance.

PO80

Milk powder and gluten intake on the risk of celiac disease during early childhood: a Swedish case control-study

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Background
Instant porridge and cereal milk drinks containing milk powder and gluten are common in infant diet. While it is hypothesized that large amounts of gluten consumed early in life may affect celiac disease risk in genetically susceptible children, little is known about milk powder.

Aim
The aim of this study was to investigate whether intake of milk powder before 2 years of age increases the risk for celiac disease in early childhood.

Methods
In TEDDY, children at increased risk for type 1 diabetes and celiac disease are screened for celiac disease using tissue transglutaminase autoantibodies (tTGA).

In the Swedish TEDDY site, we conducted a 1-to-3 nested case-control study of 207 celiac disease cases and 621 controls matched for sex, birth year, and HLA genotype. Intakes of milk powder and gluten in grams and grams per kg bodyweight was estimated from a 24-hour recall at 3 months, and 3-day food records at ages 6, 9, 12, 18 and 24 months.

Results
Intake of milk powder was not associated with risk of celiac disease at last intake prior to disease onset (OR=1.00; 95% CI=0.99-1.01; p=0.937), sum of all intakes (OR=1.001; 95% CI=0.998-1.004; p=0.662) or at any given time. In contrast, the gluten intake was directly associated with celiac disease when estimated in grams (OR=1.09; 95% CI=1.03-1.16; p=0.004) and grams/kg (OR=2.78; 95% CI=1.38-5.62; p=0.004) prior to seroconversion of tTGA. This was also true for total gluten intake in grams (OR=1.03; 95% CI=1.01-1.06; p=0.021) and grams/kg (OR=1.38; 95% CI=1.03-1.84; p=0.029) prior to seroconversion of tTGA.

Conclusion
Intake of milk powder during the first 2 years of life was not associated with risk of celiac disease in genetically susceptible children. In contrast, this study confirmed that high amounts of gluten in infant diet seemed to increase the risk of celiac disease in early childhood.

PO81

Intraepithelial lymphocytes: At Diagnosis and after gluten challenge

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Background
Celiac Disease is an immune-mediated response to the ingestion of wheat, rye or barley in genetically predisposed individuals. There are typical gastrointestinal symptoms associated with celiac disease, such as abdominal pain, constipation, diarrhea or other extra-intestinal symptoms. The surveillance of celiac disease is 1:133 in the general population. In pediatrics it is thought to be 1:104. The gold standard for diagnosis of celiac disease is a small intestinal biopsy to identify specific histology findings while maintaining a regular diet. Celiac disease may be patchy thus multiple biopsy should be completed recommending 4 biopsy should be obtained from the 2nd / 3rd portion of the duodenum and the at least two from the bulb. Characteristic findings include intraepithelial lymphocytes, elongated crypts, decreased villous/crypt ratio, partial to total villous atrophy. Marsh-Oberhuber classification is utilized for diagnosis of Celiac disease. The following case study describes a patient (AG) who had abnormal Tissue transglutaminase IgA antibody and Marsh 1 intestinal biopsy on a regular diet. After normalization of the celiac panel on a gluten free diet. Our patient proceeded with a gluten challenge with flour with subsequent elevation of the celiac panel. The purpose of this was to report outcome in our patient.

PO82

Pediatric Celiac Disease and Eosinophilic Esophagitis: Outcome of Dietary Therapy

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Background
The coexistence of celiac disease (CeD) and eosinophilic esophagitis (EoE) in pediatric patients has been increasingly recognized over the last decade. Therapeutic options for these patients are limited, consisting of a gluten-free diet for remission of CeD and dietary eliminations and/or swallowed topical corticosteroids for EoE. In the current study we have endeavored to assess the outcomes of therapeutic dietary interventions in a cohort of pediatric patients with CeD and EoE.

Methods
Pediatric patient records obtained from the University of Chicago Celiac Center Database from August 2008 to July 2013 were reviewed. Information was collected on patients with concomitant CeD and EoE regarding age, gender, dates of diagnoses, presenting symptoms, length of symptoms prior to diagnosis, familial and personal atopic history, dietary therapy, and esophageal histologic response to dietary therapy.

Results
A total of 350 records of CeD patients were reviewed. Among them, 22 had a confirmed diagnosis of CeD and EoE with a prevalence rate of 6.3%, well above that expected in the general population for either disorder. In 18 patients (82%) CeD and EoE were diagnosed simultaneously; while in 4 (18%), CeD diagnosis preceded that of EoE. Ultimately, 19 patients (86%) became asymptomatic and/or had normal esophageal histology following dietary elimination of gluten and other common food allergens.

Conclusion
To our knowledge, this is the first study to assess the histologic outcome of EoE-associated esophageal eosinophilia in response to dietary management of pediatric patients with concomitant CeD and EoE. While few children with CeD and EoE may respond solely to a gluten-free diet, the majority will require additional dietetic eliminations for adequate esophageal histologic response.

PO83

The Prevalence of Mental Health Concerns in Children with Celiac Disease

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Background
Mental health comorbidities are associated with higher medical care utilization and costs for adults and children (Wright, 2016; Doupnik, 2016). In adults, celiac disease (CD) is linked to poorer quality of life (Barratt, 2011), higher perceived burden (Shah, 2014), and elevated symptoms of major depression, anxiety, panic, suicide (e.g., Ludvigsson, 2011), and eating disorders (Mårild, 2017). However, in children with CD, the prevalence of mental health comorbidities is not well studied and could substantially impact the effectiveness of medical care. This study aimed to review existing research examining mental health concerns in pediatric CD.

Methods
A literature review was conducted in Scopus using the following initial key words: "celiac" and at least one of the following: "psychopathology", "psychiatric", "psychosocial", or "emotional". Inclusion criteria required publications to be peer-reviewed, published in English, electronically available, inclusive of child participants, and examining celiac disease (broader studies were included). Additional publications were accessed and reviewed from the references provided by initially identified publications.

Results
Twenty-four publications worldwide were identified as relevant for the current review of pediatric literature on mental health in CD. These consisted of 12 observational studies (prevalence rates, screening for celiac disease, or validating measures), 8 case-control studies, 3 qualitative studies, and 1 clinical trial. Publications were heterogeneous in symptoms examined, methodology, and population characteristics. Nineteen publications detected elevated mental health concerns (e.g., behavior disorders, depression and anxiety, or quality of life) and/or improvement with CD treatment, although 5 studies found no differences.

Conclusion
Very few studies have been published on the prevalence of mental health concerns in pediatric celiac disease. This is concerning, as preliminary evidence indicates that celiac disease may be associated with increased mental health comorbidities. We propose to prioritize more high-quality prevalence research to assess the need for mental health services in celiac disease treatment.

PO84

Problems in ensuring adherence to gluten free diet in children with celiac disease.

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Background
The only treatment for children with celiac disease is strict, life-long adherence to a gluten-free diet (GFD). It is important to document the problems faced by parents in order to maintain strict compliance to GFD.

Aim
To identify problems affecting adherence to GFD in children with celiac disease on follow-up in a Pediatric Gastroenterology Clinic catering to urban poor population; and to study their growth and hematological outcomes.

Methods
We approached 30 children, and enrolled 22 children (age <14 yr) with biopsy- and serology-confirmed celiac disease on GFD for at least 3 months. We interviewed parents about the problems faced in maintaining their child's adherence to GFD. Weight (to nearest 100 g) and height (to nearest 1 mm) were measured for all included children, and hemoglobin and IgA-tTG were measured. Pre- and post-treatment anthropometry Z-scores, hemoglobin and tTG levels were compared in enrolled children using paired Student-t test.

Results
The median (IQR) duration of diagnosis of celiac disease was 20.5 (13.5, 31.5) months. 31% of children ingested gluten once in five days before enrolment, and 77% (17/22) ingested gluten more than once in a month. More than half of the parents had difficulty in availing GFD. Two-thirds (68%) of the parents thought that the price of ingredients used to make GFD was unreasonable. More than 50% of parents avoided travelling and going to the restaurants due to non-availability of such food. Weight-for-age Z-score, hemoglobin and IgA-tTG significantly improved. Height-for-age Z-score and BMI Z-score also improved but not significant statistically.

Conclusion
Most families belonging to urban poor strata face the problems in adherence to GFD. Ignorance, poverty and lack of social support are the main problems faced by these parents. The growth patterns and nutritional status, though improved, remain suboptimal despite GFD.

PO85

Can degree of celiac serological marker elevation predict severity of histological changes?

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Background
Current guidelines state that the diagnostic gold standard for celiac disease is a duodenal biopsy. The usual approach is to perform serological screening in patients with suspected celiac disease and if indicated, confirmed by intestinal biopsy. The primary aim of this study is to determine the association between symptoms, serological markers (3X,6X and 9X upper limit) and the histological findings among patients with a new diagnosis of celiac disease.

Methods
This is a retrospective single center study. Patients who had celiac serology screen and confirmed histology (2006-2016) were enrolled. Patient symptom data including abdominal pain, short stature, anemia, weight loss, constipation was noted. Celiac markers including total IgA, tTG IgA/IgG, Gliadin IgA/IgG, and Endomysial IgA/IgG data was collected. Histological specimen will be recalled and the pathologist determined a histological score using the modified Marsh classification. The pathologist is blinded. Mean SD of tTG IgA were compared to category of Marsh score using Analysis of Variance (ANOVA).

Results
The main symptoms included abdominal pain (44%), short stature (21%), weight loss (18%), constipation (15%) and anemia (2%). The frequency of Marsh Criteria included 1 for Marsh 2, 9 for Marsh 3a, 26 for 3b, and 3 for 3c. The mean of TTG IgA serology was 91 (normal <4) and range of TTG IgA serology from 14-206. Preliminary analysis of 39 patients with complete data reveals no correlation between elevation of TTG IgA and Marsh Criteria (p 0.58).

Conclusion
Study showed that a lack of significant association between degree of serological markers and severity of histological changes. Therefore serological markers cannot be used to assess the severity of mucosal damage in patient Celiac disease.

We hope to obtain more data correlation between symptoms, serology and histology, as we continue to expand our sample size, with goal of N of 150.

SESSION 5: EPIDEMIOLOGY

P086

The influence of smoking on the severity of celiac disease in adults: a retrospective study at Georges Pompidou European Hospital

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Background
The influence of tobacco consumption on the expression of celiac disease (CD) is unknown. The objectives of this study were to investigate the effects of tobacco consumption on the severity of CD at diagnosis, the age at diagnosis, and on occurrence of complicated forms of CD.

Methods
A retrospective study was conducted at European Georges Pompidou Hospital, Paris. Among 596 patients with a diagnosis of CD, followed between 2000 and 2014, those diagnosed during adulthood with available smoking data were included. Severity criterions collected at the time of diagnosis were the presence of typical digestive symptoms, anemia, hypoalbuminemia, bone demineralization and total villous atrophy. Those criterions were compared between smokers, non smokers and former smokers using chi-square test. Age at CD diagnosis was compared using Kruskal-Wallis test. Through logistic regression, occurrence of complicated forms of CD such as refractory sprue or intestinal lymphoma was compared according to smoking status, adjusting for age at diagnosis, sex, presence of typical digestive symptoms and hypoalbuminemia.

Results
259 patients were included, comprising 59 (22.8%) active smokers, 146 (56.4%) non-smokers, and 54 (20.8%) former smokers at the time of CD diagnosis. The proportions of typical digestive symptoms, anemia, hypoalbuminemia, bone demineralization and total villous atrophy were similar, regardless of the smoking status (N.S). The median age at CD diagnosis was 31 years for active smokers, 38 years for non-smokers and 47.5 years for former smokers, p<0.001. Among the smokers, 22% had a complicated form of CD compared with 13.9% in non-smokers and 18.9% in former smokers, p=0.348.

Conclusion
This study does not show any significant difference in CD severity at diagnosis or occurrence of complicated forms depending on the smoking status. Tobacco appears to impact the age of CD diagnosis, with a younger age of diagnosis in active smokers.

P087

Intake of gluten in Indian patients with celiac disease and their first-degree relatives: A pilot study

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Background
Gluten free diet (GFD) is the only known effective treatment for patients with celiac Disease (CeD). Wheat-based food is the staple food in Northern part of India; we wanted to know about the gluten ingestion pattern in patients with CeD (pre- diagnosis) and their healthy first-degree relatives (FDRs).

Methods
Eighty patients with CeD and their FDRs (n=100) were interviewed. Patient's pre-diagnosis and their FDR's present consumption of gluten containing 54 food items were recorded using a semi-quantitative food frequency questionnaire by a trained dietitian. All the recipes were standardized to calculate the amount of wheat used. Per day consumption of wheat and its products (wheat flour, *maida,* semolina, vermicelli, breads, pasta, noodles and confectionaries) was calculated based on frequency (range: daily to once/year) and amount of food items consumed. Wheat protein/day was determined from Indian Food Composition Tables (2017) and amount of gluten/day was calculated as amount of wheat protein × 0.80.

Results
Before the diagnosis of CeD, the daily wheat consumption in patients was 244.6±120.7 gm/day and calculated gluten intake in them was 19.3±9.6gm/day. Male patients had significantly higher gluten intake than females (25.2±10.5 vs 16.5±7.9 gm/day, p<0.001). Gluten intake in male adolescent patients (12-18 years) was lower than those more than 18 years of age (17.5±7.1 vs 28.2±10.2 gm/day, p=0.019), however there was no difference in females patients. Wheat intake in the FDRs was 283.8±109.6 gm/day and calculated gluten intake in them was 23.2±9.8 gm/day. The gluten intake in male FDRs (n=52) was higher than that in female FDRs (26.6±7.8 gm/day vs 19.5±10.5 gm/day, p<0.001). Interestingly, the gluten intake in CeD patients (pre-diagnosis) was lower than that in FDRs (p=0.008).

Conclusion
The gluten intake in patients with CeD, before the diagnosis, is approximately 20 gm/day. Healthy FDRs ingest even higher amount of gluten/day.

P088

Bone mineral density in adult patients with untreated coeliac disease

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Background
Celiac disease, as a malabsorptive disease, may disturb absorption of minerals and micronutrients leading to decrease bone mineral density. In this study, we assessed bone mineral density of patients with newly diagnosed coeliac disease in Iran.

Methods
Between 2007 and 2016, 248 adult new cases of celiac disease were registered in Research Institute for Gastroenterology and Liver Diseases, Tehran, Iran. These patients referred to rheumatology ward to undergo bone densitometry. All had no history of gluten free diet. Bone density Z- score was evaluated for lumbar spine, and femoral neck using dual X-ray absorptiometry.

Results
248 patients with mean age of 31.2±8.6 years (range: 18-44 years), including 104 men and 144 women, were studied. Most patients (73.4%) had body mass index (BMI) less than 25 kg/m2.mean (±standard deviation) of Z- score was -1.06±1.43. 194 (78.2%) had Z- score in normal range. Osteopenia and osteoporosis were reported in 47 (19%) and 7 (2.8%) patients, respectively. There was no significant difference between Z- score of femoral neck and lumbar spine. Low BMI subjects, females, and those who had gastrointestinal symptoms had lower Z- score.

Conclusion
As most patients had normal bone density, bone mineral densitometry is not routinely advised, but it could be considered in selected cases, especially subjects with low BMI.

P089

The correlation between endoscopy manifestations and pathology outcome for diagnosis of celiac disease

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Background
Celiac disease (CD) is one of the most common genetically based disease. Histological confirmation of the characteristic small bowel changes is considered the gold standard to diagnosis of CD in adult patients with positive antibody testing. The aim of this study was to determine the correlation between endoscopy manifestations and pathology outcome for diagnosis of celiac disease.

Methods
In this retrospective study 295 consecutive adult patients with CD who were referred to celiac disease

department from May 2007 through December 2016 were enrolled into the study. Endoscopic features of these patients were compared with their histopathological findings according to the Marsh classification.

Results
295 patients including 147(49.8%) female and 148(50.2%) male with mean age of 46.7±15.5 years were included. No significant correlation was shown between the age and gender of patients (p>0.05). Most patients with Marsh 1 and 2 had a normal endoscopy features. However, 10% of those with Marsh III showed more severe damage at endoscopy including scalloping (83%) and nodularity (17%). The result showed there is no significant differences between endoscopy manifestations and pathology outcome of celiac disease (p=0.277).

Conclusion
Our results indicated that endoscopy manifestations are not specific for CD diagnosis, and patients with symptoms associated with the disease regardless of endoscopic features should be undergo biopsies sampling.

Keywords: Marsh classification, endoscopy features, Celiac disease

PO90

Wheat allergy and wheat protein sensitization in an out - patients population screened for CD

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Background
Gluten-related disorders have emerged as an epidemiologically relevant phenomenon with a global prevalence that is estimated 5%; the prevalence of CD is of approximately 1:100 individuals. Epidemiological studies reports a prevalence of wheat allergy (WA) in American population of around 0.4% until 0.6%.

Method
The diagnosis of WA is classically based on skin prick tests (SPT) and in vitro specific Immunoglobulin E (sIgE) assays as first-level diagnostics tools. However, they are affected by a low predictive value. After exclusion of celiac disease, the patients that reported reactions after a few hours of ingestion of gluten, underwent allergologic workup consists of: skin prick tests for foods including wheat (Alk-abello), LTP (lipid transfer protein) (peach Alk abello), alpha amylase, wheat flour, barley, corn, rice, grass pollen, histamine and patch test for allergy to nickel. We have used the ImmunoCAP™ assay, whereas the alpha-amylase/trypsin inhibitor (Tri a aA/ TI) is only available in the microarray ISAC™ assay. The sIgE to omega-5 gliadin assay is highly reliable and now widely used to identify the patients with WDEIA.

Results
We visited during 2016, 423 (312 F) patients: between a total of 104(24%) patients with history of reaction immediate and not immediate after ingesting gluten, we found a total of 19 (16.8%) with wheat protein reaction, 14 (12.3%,9 F) with sensitization and 5 (4.5%,4F) with WA (1.5%). These percentages are higher than that reported in the literature.

Conclusion
On the basis of our results, we underline that the non - celiac patients with reactions to wheat / gluten, need undergo a complete allergologic pathway to verify the real presence/ absence of wheat protein allergy.

PO91

A screening study to identify celiac disease in patients from risk group

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Background
It is necessary to pay close attention to early detection of celiac disease among asymptomatic patients with different autoimmunity disorders.

Aim
Active detection of Celiac patients among the adult population of Moscow, at risk, to establish the true prevalence of celiac disease and other types of hypersensitivity to gluten.

Methods
The blood sampling from 77 people who have expressed a desire to pass the examination. Performed immunological tests identified antibodies to tissue transglutaminase, gliadin by ELISA using commercial reagents (Orgentec Diagnostics GmbH) and specific IgE (to gluten, wheat, rye, barley, oats) in this group. A completed application form, developed in the Department of pathology of the intestine and takes into account the main clinical and anamnestic data and physical examination data.

Results
None of the patients were not revealed specific IgE to gluten, wheat, rye, barley, oatmeal. High levels of IgA AGA were detected in 4 patients that made up 5.2%, and elevated levels of IgG AGA were detected in 5 patients, which was 6.5%. Of the 77 patients, one diagnosed with selective IgA immunodeficiency. In this patient, the values of 0.02 AGA IgA, tTG IgA 0.007. One patient recorded an increased level of tTG IgA-250 IU / l, IgG tTG Of 15.8 IU / l, and also recorded increased values of IgA AGA 24,3 U / l, AGA IgG Of 38.7 U / l, which is 1.3%. In this patient the diagnosis of Celiac disease was proven by biopsy (Marsh-3C)

Conclusion
The frequency of Celiac disease in patients from risk group (with autoimmune disorders) was 1.3%.

PO92

Frequency of celiac disease in gastroenterological patients

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Aim
To investigate the frequency of celiac disease among patients with gastroenterological disorders.

Methods
A total 318 gastroenterological patients which treated in Central Research Institute for Gastroenterology (Moscow Clinical Scientific Center) were examined. The patients' age was 18 to 74 year (mean 51.5±16.4 years). Immunoglobulin A (IgA) and immunoglobulin G (IgG) anti-gliadin antibodies (AGA), immunoglobulin A (Ig A) and immunoglobulin G (Ig G) anti-tissue-transglutaminase antibodies (anti-tTG) were determined. In case, when the level of AGA and anti-tTG were high, the esophagogastroduodenoscopy with duodenal biopsy was performed.

Results
Forty-one of the 318 patients were found to have higher level of AGA (12.9%); out of them IgA AGA were in 17 (5.35%) patients and IgG AGA were also in 17(5.35%). Elevated levels of both antibodies (IgA AGA and IgG AGA) were seen in 7 (2.2%) patients. Overall, the detection rate of increased AGA level was 12.9%. The antibodies were more commonly higher in patients with liver diseases (21.8%) and in those with inflammatory bowel diseases (21.6%). Both IgA anti tTG, IgG anti-tTG, IgA AGA and IgG AGA were detected in 6 (1.9%) of 318 patients. The diagnosis of celiac disease was verified by duodenal histological examination in 3 (0.94%) of the 318 patients.

Conclusion
The celiac disease detection rate in gastroenterological patients was 0.94%.

PO93

Autoimmune diseases and associated conditions in children and adults with celiac disease

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Background
Celiac disease (CeD) is associated with other autoimmune diseases (AID) and conditions, but the prevalence and related predictive factors for these comorbidities of CeD have not been fully explored.

Methods
Data obtained from 1,090 participants with biopsy-reported CeD enrolled in the iCureCeliac® Patient Registry were used to analyze the variety and frequency of previously associated AID and conditions, as well as their relationship to gender, age, and race/ethnicity. Diagnoses of autoimmune diseases and associated conditions were obtained from self-reported iCureCeliac® data.

Results
Among the 1,090 biopsy-reported iCureCeliac® participants, 91.3% were Caucasian and 82.7% were female, and the majority (44%) of patients were between the ages of 26 and <50 years old. The mean diagnosis age was 34.3 ± 15.2 years, the mean duration of celiac disease was 4.5 ± 6.4 years, and the mean number of years to a celiac disease diagnosis was 7.6 ± 12.2. Of these participants, 37% were diagnosed with at least one additional AID and/or associated condition. The most common AID/associated conditions were irritable bowel syndrome (19.5%), thyroid disease (15.5%), psoriasis (5.3%), ulcerative colitis (3.1%), rheumatoid arthritis (2.5%), and type 1 diabetes (2.1%). Addison's disease was rare (0.2%), as was primary biliary cirrhosis (0.3%), and scleroderma (0.3%). The prevalence of one or more AID/associated conditions was increased in females and older adults.

Conclusion
In the iCureCeliac® Patient Registry, diagnosis of one or more autoimmune diseases/associated conditions in addition to celiac disease is common, particularly in women and older adults. These results have implications for primary care, gastroenterology, and rheumatology practice, and will allow healthcare providers to better predict and manage the additional autoimmune diseases/associated conditions that may develop in patients with celiac disease.

PO94

Global prevalence of celiac disease: Systematic review and Meta-analysis

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Background
Celiac disease (CD) has emerged as a major public health problem worldwide. Once reported from countries with predominant Caucasian population, it is now reported from other parts of world as well. The exact global prevalence of CD is not known. We conducted a systematic review and meta-analysis to estimate the global prevalence of CD.

Methods
We searched Medline, PubMed and EMBASE with the keywords- "celiac disease", "coeliac disease", "tissue transglutaminase antibody", "anti-endomysium antibody" and "prevalence" for studies between January 1991 to March 2016. Each keyword was cross-referenced with "Asia", "Europe", "Africa", "South America", "North America", and "Australia". Diagnosis of CD was based on European Society of Pediatric Gastroenterology, Hepatology and Nutrition guidelines. Of 3843 articles, 96 articles were included.

Results
Pooled global sero-prevalence of CD was 1.4% (95% CI 1.1%, 1.7%) in 275,818 individuals based on positive anti-tissue transglutaminase and/or anti-endomysial antibodies. Pooled global prevalence of biopsy-confirmed CD was 0.7% (95% CI 0.5%, 0.9%) in 138,792 individuals. The prevalence of CD ranged from 0.4% in South America, 0.5% in Africa and North America, 0.6% in Asia to 0.8% in Europe and Oceania. There was remarkable variation in country-wise prevalence of CD ranging from 0.2% (in Tunisia) to 2.4% (in Sweden). The pooled prevalence of CD was higher in females than in males (0.6% vs. 0.4%, P<0.001). Similarly, children had substantially higher prevalence of CD than adults (0.9% vs. 0.5%, P<0.001). The pooled prevalence of CD increased from 0.6% between 1991 and 2000 to 0.8% from 2001 onwards.

Conclusion
CD is a global disease and the global sero-prevalence and prevalence of CD are 1.4% and 0.7%, respectively. The prevalence of CD varies with gender, age and geographic location. The prevalence of CD is increasing over time. There is a need for population-based prevalence studies in many countries.

P095

Allergen Online-Celiac Peptide and Protein Database Update 2017: A bioinformatics tool for assessing potential risks of celiac disease from new dietary proteins in genetically modified organisms and novel foods

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Background
Wheat, barley, rye, and oat are important dietary protein sources used in bread and pasta. Wheat is genetically complex and glutens (gliadins and glutenins) are known to cause celiac disease (CD). Over 1% of the global population is affected, although 30% of us have the cognate MHC Class II DQ2.5 or DQ8 to stimulate CD4+ T cells. Gluten peptides are typically deamidated by intestinal tissue transglutaminase (tTG) which enhances DQ binding. A few peptides are "toxic", causing intestinal inflammation. Safety for patients requires strict avoidance from dietary glutens. Thus regulatory guidelines (CODEX Alimentarius Guidelines, 2003) suggest evaluating any wheat protein transferred to a different crop through genetic engineering (GE) for potential risks of CD. In 2012 the first Celiac Peptide and Protein database was publicly available to allow simple, effective identification of potentially risky proteins. We have now completed and updated.

Rationale
Consumption of glutens from wheat, barley, rye, triticale and oats are known to trigger T cell responses in CD individuals with restricted MHCs. Since reactivity is enhanced by tTG, we include native and deamidated forms of peptides. The 2012 database included 1,016 native, deamidated and a few toxic peptides.

Methods
Original publications were reviewed along with 16 new studies. The authors interpret published data in coming to final conclusions.

Results
Fifteen original peptides were removed due to insufficient evidence. Thirty new peptides were added. One full-length protein sequence was replaced. The full dataset will be posted online in June, 2017 at the public www.AllergenOnline.org/celiachome.shtml. Protein amino acid sequences can be entered to search for exact peptide matches or FASTA alignments to full length proteins with criteria that are predictive of risk (identity scores > 45% identity over 50% protein length, with *E* score of <1 e -15th).

Conclusion
The update provides greater assurance of safety evaluations.

P096

Seroepidemiology of celiac disease in a large cohort of Iranian patients with inflammatory bowel diseases

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Background
Although the incidence of inflammatory bowel diseases (IBD) in Iran has increased, the prevalence of celiac disease (CD) is considerable and around 1% of normal population is infected. There are controversial reports in Iran that patients with IBD are at increased risk of developing CD. Therefore the aim of this prospective study is to evaluate the prevalence of serum celiac antibody in a large cohort of patients with IBD in Iran

Methods
In this cohort study 557 confirmed IBD patients who were referred during 2010-2015 enrolled into the study. 70 (12.6%) had Crohn's disease (40 males), 406 (72.9%) had ulcerative colitis (214 males), and 77 (13.8%) had indeterminate colitis (44 males). Total IgA and IgA tissue transgulaminase antibody were assayed. In cases of IgA deficiency, anti-tTG IgG and were measured

Results
Out of 557 patients anti-tTG Ab was positive in 28 (5%) patients including 20 (71.4%) UC, 4 CD (14.3%) and 4 indeterminate colitis (14.3%). No statistical correlation was detected between study groups. On the other hand 15 subjects were IgA deficient but none were anti-tTG IgG positive.

Conclusion
In contrast with previous studies with lower samples size the prevalence of CD seems to be quite high in Iranian IBD patients. Also our results (in accordance with several other countries) do support routine screening for CD in patients with IBD. All in all, based on the above considerations, both celiac disease and IBD are autoimmune disorders and the associations between them might be due to common susceptibility to a number of genetic and exogenous antigens.

Keywords
Inflammatory bowel diseases, Seroepidemiology, celiac disease

P097

Influence on changing the clinical picture in Montenegro

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Background
The prevalence of celiac disease appears to be increasing quite dramatically during the past few decades. Epidemiological data do document worldwide a true increase in prevalence, with rates doubling approximately every 20 years.

Results
Our work analyzes the clinical picture in the last 20 years on the territory of Montenegro. Data were analyzed over 20 years from 1995 to 2015 year. Our diet is predominantly used wheat flour and products. The introduction of flour in the diet begins early, about 4 months of life, Especially the first 10 years of the analyzed period. In the first ten years from 1995 to 2005 predominantly celiac disease has been shown as chronic diarrhea, weight loss, loss of appetite and malnutrition. In the second period from 2005 to 2015 predominantly low growth, anemia, loss of appetite and vomiting. Our data indicate that at approximately the same percentage is the typical clinical picture in the rural and urban areas. In children on breastfeeding, we saw a later start, after 9 months of life. Children who later manifested symptoms suffered from respiratory infections, and in the last decade they had more frequent bronchoconstriction. Among the patients, there is a greater number of children with natural birth than the cesarean section. A large number of patients come from the urban area caused by increased migration of the population and the development of the country.

Conclusion
We have noted fewer children in the family, regular visits to pediatricians, better information to social networks. Increased number of pediatricians and training of gastroenterologists to recognize early symptoms of the disease is also an important factor in faster diagnostics

SESSION 6: REFRACTORY CELIAC DISEASE

P098

ASCA is a possible new marker for nonresponsive celiac disease

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Background
In nonresponsive celiac disease (NRCD) the symptoms and duodenal damage persists despite a gluten-free diet (GFD). We have previously shown an association between dysbiotic microbiota and persistent symptoms. Furthermore, serum microbial antibodies to Saccharomyces cerevisiae (ASCA),

Pseudomonas fluorescens-associated sequence (I2) and Bacteroides caccae TonB-linked outer membrane protein (OmpW) are gluten-sensitive and present at early stages of CD development. We hypothesized that increased seroreactivity to microbial antibodies is associated with NRCD.

Methods
Serum ASCA, I2 and OmpW were measured in 20 seronegative CD patients with persistent villous damage despite strict GFD (NRCD group). Fifty-eight GFD responsive patients served as CD controls (55 samples on GFD) and 80 blood donors as non-CD controls. Kruskal-Wallis test was used to compare the serum antibody titers between the groups and Dunn-Bonferroni for post hoc pairwise comparisons.

Results
At least one microbial marker was positive in 80% of NRCD patients, in 97% of untreated and 87% of treated CD patients and in 44% of controls. NRCD patients had the highest frequency of ASCA positivity (64% vs 52%, 20% and 0%, respectively) and also significantly higher ASCA IgA (median 14.5 U/ml) and IgG (32.5 U/ml) titers than treated CD patients (7.0 U/ml, 13.0 U/ml) and non-CD controls (4.5 U/ml, 5.8 U/ml). ASCA did not differ between NRCD and untreated CD. The frequencies of I2 and OmpW were lower in NRCD than in untreated CD (65% and 45% vs 86% and 59%, respectively), and I2 titers were higher in NRCD (median absorbance 0.76) and untreated (1.0) and treated (0.83) CD than controls (0.32). OmpW was elevated in untreated (1.1) and treated (0.94) CD patients compared with controls (0.79).

Conclusion
Seropositivity and high titers of ASCA were associated with NRCD and might serve as additional follow-up tool in CD.

P099

Comparison of the reliability of 17 celiac disease associated bio-markers to reflect intestinal damage

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Aim
In view of the increasing importance of serological biomarkers for screening and diagnosing celiac disease (CD), lack of back-to-back comparison, and reliability of isolated or combined antibody test systems to reflect intestinal damage in children with CD, their differential performances were evaluated.

Methods
AESKULISA® Gliadin (AGA), AESKULISA® DGP (DGP), AESKULISA® tTG "New Generation" (Neo-epitope tTG complexed to gliadin= tTG-neo), tTG (for in house research purpose only), AESKULISA® mTg neo-epitope and mTg (RUO). Anti-endomysial antibodies (EMA) were checked by immunofluorescence (AESKUSLIDES® EMA). The results were compared to the degree of intestinal injury, using the revised Marsh criteria.

Results
Most assays were able to discriminate between patients with low and high degree of intestinal damage. Comparing the different correlations between CD associated IgA and IgG antibodies' isotypes, the tTG-neo IgA (r=0.6165, p<0.0001) and tTG-neo check (r=0.6492, p<0.0001) stood out, significantly, as the best indicators of the intestinal damage in CD. EMA-IgA, tTG and DGP check and mTg-neo IgG correlated nicely to the mucosal injury.

Conclusion
It is suggested that tTg-neo IgA/IgG antibodies should be used preferably to reflect intestinal damage during screening and diagnosing childhood CD. EMA-IgA, tTg, DGP checks and mTg-neo IgG titers followed the tTg-neo check performance. mTg-neo IgG presents a new serological biomarker for CD.

P100

Antibodies against neo-epitope tTg complexed to gliadin out performe the uncomplexed anti tTg to follow rheumatic arthritis patients

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background
Rheumatoid arthritis (RA) is a high-risk disease for celiac disease (CD), sharing multiple aspects. IgA-tTG autoantibody is a classical marker for CD, however, it has many false positives. Anti neo-epitope tTG complexed to gliadin is a reliable biomarker for CD and it has never been compared to the IgA-tTG performance and false positivity in naive and treated RA population.

Methods
135 RA adult patients, mean age 55±12.7 years, F/M 1:0.2, respectively, from the ADAPTHERA study cohort, where studied in naïve patients and longitudinally at 3 follow up visits. ADAPTHERA is a network to improve patient care and to find new biomarkers for RA. Patients were tested using the following ELISAs detecting either IgA, IgG or both (IgA+IgG): tTG (for in house research purpose only) and AESKULISA® tTG New Generation (tTG neo-epitope).

Results
In the naïve patients, on the first visit after diagnosis and along the follow up under pharmaceutical therapy, for 3 consecutive visits, the % positivity of the IgA-tTG (Visit 1, 2, 3, 4 , 6.7 %, 3.1 %, 4.6 %, 7.0 %, respectively) was significantly higher than in the tTg-neo antibodies (Visit 1, 2, 3, 4, 2.2 %, 0.8 %, 1.1 %, 2.8 %, respectively, p<0.05).

Conclusion
Determinations of CD associated autoantibodies in naïve and treated RA groups reveal that IgA-tTg is less specific for CD in relation to the lower false positivity of its competitor (anti tTg neo-epitope antibodies) in RA patients' sera. This is also mirrored by IgA-tTG´s higher false positivity rate.

P101

Epitopes of human and microbial transglutaminases are shared by celiac disease sera

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Background
The consumption of microbial transglutaminase (mTg) in Western diet is expanding. mTg shares multiple functional similarities with human endogenous tTg. However, immunogenic comparison of the two enzymes in celiac disease (CD) is lacking.

Methods
Complexing mTg and gliadin results in mTg neo-epitope (mTg neo). The complexes were purified by asymmetric flow field-flow fractionation and confirmed by multi-angle light scattering and SDS-PAGE. Sera of 81 CD patients and 81 healthy controls were analysed using the following ELISAs: AESKULISA® tTG New generation (tTG neo-epitopes) IgA and IgG, AESKULISA® Gliadin IgA and IgG, AESKULISA® DGP IgA and IgG and AESKULISA®s against mTg and mTg neo-epitopes (Research use only (RUO) Kits as IgA and IgG).

Results
Purified mTg-neo IgG and IgA (AUC=0.92, 0.93, respectively) showed an increased immunoreactivity compared to single mTg and gliadin (p<0.001) but similar immunoreactivity to the tTG-neo IgG and IgA ELISA (AUC=0.94, 0.95, respectively). Using a competition ELISA, the mTg neo-epitopes and tTG neo-epitopes have identical outcomes in CD sera both showing a decrease in optical density of 55±6%, (p<0.0002). Sera with high antibody titre (U/ml) against the tTG neo-epitope show also high antibody activities of the mTg neo-epitope and vice versa indicating the presence of similar epitopes within the Tg-gliadin complexes.

Conclusion
mTg and tTG display a comparable immunopotent epitope. mTg neo-epitope IgA and IgG antibodies are immunogenic in CD. If substantiated, it will impact the food industry additive regulation.

P102

Risk for lymphoma and gastrointestinal carcinoma after diagnosis of celiac disease based on a nationwide population-based case-control study

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Background
Celiac disease (CD) usually runs a benign course, but patients are at increased risk to develop various malignancies. To support evidence-based follow-up programs in CD patients, we performed a large population-based study to assess the subsequent risk for malignant lymphoma and gastro-intestinal (GI) carcinoma after a confirmed diagnosis of CD.

Methods
To estimate relative and absolute risks for the development of lymphomas and GI carcinomas, we applied a case-control design. Patients with lymphoma or GI carcinoma (cases) and melanoma or basal cell carcinoma (controls) diagnosed between 1994 and 2014 were retrieved through the Dutch nationwide population-based pathology database (PALGA). Within this series, all individuals with histologically confirmed CD before or within 3 months after the diagnosis of malignancy were identified through PALGA. Odds ratios (OR) were determined using logistic regression analysis with corrections for age and gender.

Results
Of 301,425 cases and 576,971 controls, 349 (0.1%) and 282 (0.05%), respectively, were diagnosed with CD. T-cell lymphoma was associated with a previous diagnosis of CD (OR 35.8 [95% CI, 27.1-47.4]), whereas B-cell lymphoma was not associated. Absolute cumulative risk of T cell lymphoma reaches the risk of colon carcinoma in the general population. However, the majority of the Enteropathy Associated T cell Lymphomas, the most common T cell lymphoma in the CD group, were discovered together with CD. An association was also found between small bowel adenocarcinoma and esophageal squamous cell carcinoma (SCC) and CD (OR 11.9 [95% CI, 8.2-17.2] and 3.5 [95% CI 2.1-5.8]). Colorectal, esophageal and stomach adenocarcinoma and SCC of the anus were not associated with CD history.

Conclusions
The data suggest strongly increased risk for specific malignancies after CD diagnosis. These results

provide detailed information and strong motivation to develop follow-up guidelines for newly diagnosed CD patients, especially diagnosed over 50 years of age.

P103

Systematic review of coeliac disease complications

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Background
Delayed diagnosis of coeliac disease (CD) or poor adherence to a gluten-free diet (GFD) may cause disease complications spanning many physiological systems. Systematic literature reviews (SLRs) previously published on seven classes of complications traditionally associated with CD were updated to determine whether the most current evidence supports their conclusions regarding incidence and outcomes of CD complications.

Methods
Search strategies used by SLRs in bone mineral density (BMD) (Grace-Farfaglia, Nutrients. 2015;7(5):3347-69), bone fracture (Heikkilä et al, J Clin Endocrinol Metab. 2015;100(1):25-34), malignancy (Han et al. Medicine. 2015;94(38):e1612), cardiovascular conditions (Heikkilä et al. Nutr Metab Cardiovasc Dis. 2015;25(9):816-31), pregnancy complications (Saccone et al, Am J Obstet Gynecol. 2016;214(2):225-34), infertility (Lasa et al, Arq Gastroenterol. 2014;51(2):144-50), and mood disorders (Smith and Gerdes, Acta Psychiatr Scand. 2012;125(3):189-93) were replicated in Medline, Embase, the Cochrane Library, and conference abstracts to systematically identify literature published since the original searches and meeting their criteria.

Results
Current studies supported and expanded upon conclusions reached by the source SLRs. CD was associated in both the source SLRs, and in the current update, with higher rates of low BMD, lymphoproliferative cancers, obstetric complications, and mood disorders. It is likely to be associated with an increased risk of bone fractures, and evidence is mixed regarding an association with infertility. CD is associated with a normal or lower risk of cardiovascular disease. There is a lower risk of malignancies among CD patients responsive to a GFD compared to non responders.

Conclusion
Recent publications of complications traditionally associated with CD support findings of prior SLRs and suggest higher risks of these conditions in the CD population. Further research should investigate whether, as with cancer, the risk of other complications of CD is reduced with improved control of celiac disease activity. The inverse relationship between CD and cardiovascular risk should also be explored.

SESSION 7: PATHOGENESIS (PART II)

P104

Gluten immunological side effects are detrimental to human health: the joint aspects

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Background
Evolution is accompanied by enrichment of gluten content in the wheat and today 80% of the proteins are gluten. In parallel, some unwanted effects induced by gluten consumption in non-celiac affected populations are recently described.

Aim
To summarize the literature for gluten consumption and withdrawal effects on autoimmune diseases in general and rheumatoid arthritis (RA) in particular.

Methods
A systematic review was performed, using Medline, Google, and Cochrane Library databases.

Results
Multiple autoimmune conditions respond to gluten free diet (GFD), including RA. Several pathophysiological avenues were described for the detrimental effects of gluten: breach of intestinal tight junction integrity, decrease in viability and apoptosis induction in human cell lines, induction of neutrophil migration, decrease in NKG2D and ligand expression, increase of Th17 cell population, effect on regulatory T-cell subsets, change of innate immunity, change of dendritic cell functions and change of microbiome diversity. The articular tissue transglutaminase and its inflammatory effects, the intestinal peptidylarginine deiminase, the enterocyte's origin of citrulline, the beached tight junction integrity, the arthritis in celiac disease, the enteritis in early RA and the partial response to GFD, are several potential pathophysiological pathways, connecting gluten consumption to RA.

Conclusion
Multiple non-celiac autoimmune diseases and conditions respond, to a variable degree to GFD. The protective mechanisms of GFD are constantly unraveled and involve multiple immunoregulatory pathways. Several pathophysiological pathways can explain the detrimental health effects of gluten consumption in RA.

P105

Comparative genomics of rare duodenal microbes from a celiac disease patient decipher their clinical importance.

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Background
Celiac disease (CD) is an autoimmune disease in which infections are found associated with disease presentations. As a part of large project we recovered some microbes from a CD patient. It was difficult to guess their importance in disease at a point when literature was scarce in defining the virulence behaviour of those microbes.

Methods
By using culture based approaches we could recover 7 total microbes and most of them were recognized to be rare. Therefore, as a preliminary step to uncover the features of microbes, we sequenced the genomes of those rare microbes *Microbacterium oleivorans*, *Janibacter melonis*, *Dietzia cinnemea*, *Methylobacterium populi* and *Mycobacterium immunogenum*. Genome sequences were assembled and further annotated through Rapid annotation using Subsystem Technology (RAST). Further, a comparison of genes was evaluated among genomes of our microbes and genome of *Neisseria flavicans,* an invasive literature searched isolate of CD. Genomic comparison of these CD microbes with their reference strains showed the evolutionary trends that may contribute their pathogenic status and adaptability in host.

Results
Exploration through RAST and their genome insights indicated some microbes possess higher number of virulence determinant genes in comparison to experimentally proved invasive strains of CD i.e. *Neisseria flavicans.* Genes belonging to categories Virulence Disease and defense, membrane transport, iron aquisition system, Phages and prophages were evaluated. Kyoto Encyclopedia of Genes and Genomes (KEGG) further reveal these microbes to have potential of interfering with the host metabolic processes.

Conclusions
Our work also shows the importance of microbial genome sequencing in clinical set up to predict the accurate detection of virulent behaviour of clinical microbes. Our data signifies the importance of rare/new but virulent microbes in health and disease seeking desirable treatments that may modulate the patient's disease conditions.

P106

Wheat gliadin protein induced inflammation and oxidative damage in human cell line.

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Abstract
In Celiac disease, gluten proteins from wheat and other cereals after deamination by TG2 enzyme, are engulfed by DQ2/8 peptide containing antigen presenting cells. It generating reactive oxygen and nitrogen species in the intestine which leads to inflammation. Chronic inflammation in the small intestine creates avillus condition of mucosa that causes diarrhea and malabsorption. In the present study twelve wheat varieties of diverse origin namely C273, C281, C286, C306, C518, C591, Agra Local, 9D, 8A, Raj4229, HD3027, NP824 (released during 1920 to 2014) were analyzed for their protein (gluten and gliadin) contents using SDS-PAGE. Further the gliadin proteins from these varieties were tested on human colon cancer cell line HCT116 to assess their role in inflammation, oxidative and nitrosative stress. Expression level of different pro-inflammatory cytokines was studied through RT-PCR and other spectrophotometric assays which showed that all the wheat varieties induced high levels of ROS/RNS and MPO activity. These results were further supported by the increase in the expression level of cytokine genes IL-1β and IL15. All these suggest that gliadin from all the wheat varieties used in present work are potential antigen enhancing the level of inflammation irrespective of their year of origin and release.

P107

Evaluation of serum levels of inflammatory cytokines in patients with celiac disease and non-celiac gluten-sensitive individuals compared with the control subjects

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Background
There is increasing line of evidence regarding elevated serum levels of IL-6, IL-8, IL-15, IFNγ, and TNF-α in the patients with active celiac disease (CD). The aim of this study was to evaluate serum levels of inflammatory cytokines in Iranian patients with CD and non-CD gluten-sensitivity compare with healthy individuals.

Methods
A total of 110 CD, 15 non-CD gluten-sensitivity, and 46 healthy individuals (control) were enrolled. Demographic and clinical information of all participants was collected using questionnaire. Serum levels of IL-1, IL-6, IL-8, IL-15 and IFNγ was measured by ELISA and were compared between the groups. The relationship between the levels of cytokines with the severity of mucosal damage and clinical symptoms were assessed.

Results
The mean serum levels of IL-6 in the CD group was significantly higher than control group (P = 0.007). Also, the mean serum levels of IL-8 in the CD group was significantly higher than non-CD gluten-sensitivity group (P = 0.041). However, the levels of IL-1, IL-15 and IFNγ showed no significant differences between the groups (P> 0.05). Statistically significant correlations were observed between the serum level of IFNγ and CD patients with infertility (r = -0.329 and P = 0.031) and abortion (r = -0.429 and P = 0.010). Also, a significant correlation was seen between serum level of IL-6 and patients with bone diseases (r = 0.122 and P = 0.048). No statistically significant correlation was observed between the severity of mucosal damage and studied cytokines.

Conclusion
It seems that the elevation of inflammatory cytokines such as; IL-6 and the chemokine IL-8 is implicated in the pathogenesis of celiac disease and there is no evidences regarding the correlation between the serum level of these cytokines and NCGS.

Key words
Celiac disease, inflammatory cytokines, non-celiac gluten sensitivity, severity of mucosal damage

P108

Non-coeliac Gluten sensitivity and idiopathic Iron deficiency Anemia

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Background
The etiology of Iron deficiency anaemia (IDA) remains unknown in a significant number of patients. Recent studies report the presence of IDA in patients with non-celiac gluten sensitivity (NCGS). The aim of this study was to evaluate the effect of gluten free diet on iron deficiency anemia in patients with NCGS.

Methods
29 patients with nonspecific GI symptoms and IDA of unknown origin (23 [79.3%] female; mean age 30.31±SD=7.783) were studied. The serology, small bowel biopsies and colonoscopy were negative for coeliac disease (CD) and any other malignancies. A gluten free diet (GFD) was recommended and implemented for 6 weeks. The level of Hg, ferritin, serum iron and TIBC were evaluated at the beginning and after 6 weeks gluten free diet. HLA typing was performed according to the Real-time PCR based SYBER Green method.

Results
6.9% of patients were DQ8, 3.4% DQ2 and 89.7% were negative for both of them. After 6 weeks GFD the level of ferritin (P=0.036) and the level of Iron in the study population was significantly increased (p=003).

Conclusion
NCGS seems to represent the etiology of IDA in a number of patients previously called idiopathic. A trial of gluten free diet would be recommended in patients with non-specific gastrointestinal symptoms and negative anaemia workup.

Key words: Celiac disease, iron deficiency anemia, non-celiac gluten sensitivity

P109

Imbalance in splicing of Mcl-1 causes inhibition of apoptosis in Enteropathy-associated T-cell Lymphoma

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Background
Enteropathy-associated T-cell lymphoma (EATL) is a rare extranodal T-cell non-Hodgkin lymphoma arising from aberrant intestinal intraepithelial T-cells (IELs). Outcome of EATL remains poor, despite aggressive therapies. Inhibition of the apoptosis cascade is an important cause of therapy-resistance and contributes to pathogenesis. Myeloid cell leukemia-1 (Mcl-1) is a member of the Bcl-2 apoptosis family and can be alternatively spliced into pro-apoptotic Mcl-1S and anti-apoptotic Mcl-1L. In various hematological malignancies Mcl-1 is deregulated. In the present study, we investigated the expression and functional role of Mcl-1 in EATL.

Methods
mRNA expression of Mcl-1 was detected in laser-capture microdissected tissue sections from twenty EATL patients, healthy donor aberrant IELs and cell line ETL using RT-MLPA analysis. Mcl-1 protein expression was evaluated by western blot analysis and immunohistochemistry. Knockdown of Mcl-1 was performed using siRNA analysis. Interactions of Mcl-1 were investigated with immunoprecipitation. EATL cells were incubated with spliceosome inhibitor Pladienolide-B and caspase activity and apoptosis was determined using flowcytometry.

Results
In EATL patient samples, mRNA expression of Mcl-1L was significantly higher than Mcl-1S expression. Immunohistochemical and western blot analysis also demonstrated increased protein expression of Mcl-1. Knockdown of Mcl-1L increased apoptosis with 40% and enhanced sensitivity of EATL cells to chemotherapeutical agent doxorubicin. Mcl-1L interacted with the pro-apoptotic protein Bak to prevent apoptosis. In EATL patient cells, Mcl-1L/Mcl-1S ratios were evidently higher compared to aberrant IELs of controls. Treatment of EATL cells with Pladienolide-B altered splicing of anti-apoptotic Mcl-1L to Mcl-1S resulting in a decrease in Mcl-1L/Mcl-1S ratios. Additionally, incubation with Pladienolide-B activated caspase-3/7 and caspase-9 and induced cell death in all EATL patient samples and EATL cell line.

Conclusion
We show that Mcl-1 is aberrantly spliced in EATL cells and contributes to inhibition of apoptosis and resistance to chemotherapy. Mcl-1 therefore might be a potential therapeutic target for EATL patients.

P110

The intrinsic apoptosis pathway is inhibited in Enteropathy-associated T-cell lymphoma by downregulation of pro-apoptotic Noxa and can be restored by bortezomib

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Background
Enteropathy-associated T-cell lymphoma (EATL) is a rare intestinal lymphoma that arises from intraepithelial lymphocytes (IEL). Clinical outcome of patients with EATL is very poor, due to chemotherapy-resistance and high relapse rates. Many studies in other types of lymphoma have shown that inhibition of apoptosis intrinsically causes chemotherapy-resistance. In the present study, we investigated if the intrinsic apoptosis pathway is disrupted in EATL and if apoptosis can be restored.

Methods
Laser-capture micro-dissection was applied to twenty frozen EATL samples. IEL of healthy donors (HD) and RCDII patients were isolated from duodenal biopsies by FACS sorting. mRNA and protein expression and functional analyses of the intrinsic apoptosis pathway were determined using RT-MLPA analysis, immunocyto/histochemistry, western blot and siRNA analysis, respectively.

Results
Two EATL groups were identified using unsupervised cluster analysis; both groups showed (very) low expression of pro-apoptotic genes with one group demonstrating concomitant high levels of anti-apoptotic genes. Expression of pro-apoptotic gene Noxa was strikingly downregulated in EATL cells compared to HD IEL and aberrant IEL of RCDII patients. Similarly, almost no protein expression of Noxa was observed in EATL. Functional analyses in EATL revealed that caspase-9 and -3 activation and induction of apoptosis was blocked. Treatment with bortezomib resulted in induction of cell death in all EATL samples tested. The lethal dose varied between 5-15nM after 48 hours of incubation. Bortezomib-induced apoptosis in EATL cells was caspase-9 mediated. mRNA and protein expression analyses showed upregulation of Noxa after exposure to bortezomib. Downregulation of Noxa using siRNA analysis decreased bortezomib-induced apoptosis in EATL cells.

Conclusions
Our study showed that the intrinsic apoptosis pathway is blocked in EATL by downregulation of Noxa. Bortezomib can restore apoptosis by upregulation of Noxa and therefore, it should be considered as a potential therapy in the treatment of EATL patients.

P111

Fructans and not gluten as symptom trigger in self-reported non-coeliac gluten sensitivity

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Background
Non-celiac gluten sensitivity (NCGS) is characterized by symptom improvement after gluten withdrawal in absence of coeliac disease (CD). The entity lacks mechanistic understanding and objective biomarkers which complicate the work up of these patients. Gluten

often coexists with fructans, a type of FODMAP (fermentable oligo -, di-, monosaccharides and polyols).

Aim
We aimed to investigate the effect of gluten and fructans separately in subjects with self-reported gluten sensitivity, where coeliac disease and wheat allergy were excluded.

Methods
In a double-blind crossover challenge in 59 participants who beneficially self-instituted a gluten-free diet and, in whom CD was excluded, participants were randomized to seven days of gluten (5.7 g), fructans (2.1 g) and placebo concealed in muesli bars, each challenge separated with 7 days of washout. Symptoms were measured by Gastrointestinal Symptom Rating Scale IBS version (GSR-IBS). A linear mixed model for analysis was used.

Results
Symptom scores differed significantly between gluten, fructan and placebo challenge for overall GSRS-IBS, mean (SD) 33.1 (13.3), 38.6 (12.3) and 34.3 (13.9), respectively (p=0.04) and for GSRS bloating, 9.3 (3.5), 11.6 (3.5) and 10.1 (3.7), respectively (p=0.004). Fructan scores were significantly higher than gluten score for overall GSRS-IBS (p=0.048) and GSRS bloating (p=0.003). Overall responses to gluten and placebo did not differ (p=0.99). There was no effect of period or sequence.

Conclusion
The study found minimal evidence that gluten is the symptom trigger in participants with self-reported gluten sensitivity. Fructans are more likely the inducer of symptoms in those reporting sensitivity to wheat, rye and barley. The finding raises doubts about the need for a gluten-free diet in these patients and weakens the diagnostic use of the term "NCGS".

P112

Celiac and Helicobacter Heilmannii

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Abstract
Celiac Disease is an immune-mediated response to the ingestion of wheat, rye or barley in genetically predisposed individuals. There are typical gastrointestinal symptoms associated with celiac disease, such as abdominal pain, constipation, diarrhea or other extra-intestinal symptoms. The surveillance of celiac disease is 1-133 and the general population. In pediatrics it is thought to be 1:104. Gold standard for diagnosis of celiac disease is a small intestinal biopsy while maintaining a regular diet. In 2012, the European Society of Gastroenterology, Hepatology and Nutrition guidelines were modified and recommended that a diagnosis of celiac disease can be made without a small biopsy in symptomatic patients with a tissue transglutaminase IgA 10 times the upper limit of normal, positive for HLA DQ 2 and DQ 8. Positive anti-endomysial antibody at the same time tested for the HLA. Proceeding without a small intestinal biopsy may miss other conditions that can be the cause of symptoms such as in the following case.

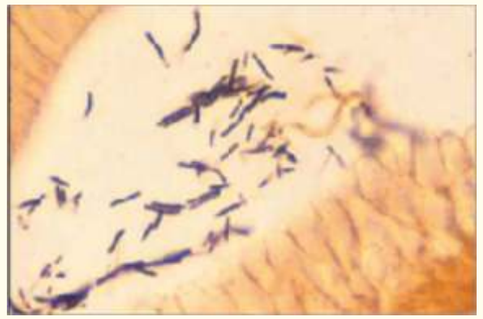

Figure 3) Corkscrew-like appearance of Helicobacter heilmannii (Warthin-Starry stain)

P113

Non-coeliac gluten sensitivity or Irritable bowel (IB); what is the truth?

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Background
Irritable bowel syndrome has been used for decade as a label for a large number of unexplained gastro-intestinal disorders. Discovery of food sensitivity and high rate of symptomatic response to low FODMAP diet has revolutionized the treatment of this condition. The aim of this study was to report the effect of dietary intervention in this group of patients.

Methods
This was a cross-sectional study evaluating 149 patients presenting with IBS symptoms. A strict gluten and lactose free diet (G/LFD) was recommended for 6 weeks to patients fulfilling Salerno criteria to identify non-coeliac gluten sensitivity (NCGS). Hundred and thirty-four from 149 patients were assessed after following a G/LFD. Demographics and presenting symptoms data were recorded.

Results
The ages of 134 study subjects ranged from 8 to 85 years (mean age of 46.41 years ±SD 17.388). Subjects were predominantly female 109 (81.34%) in comparison to male 25 (18.66%). The most prevalent GI symptoms were abdominal pain 109 (81.3%), diarrhoea 88 (66%), bloating 74 (55%) followed by heartburn 54 (40%). Following G/LFD introduction, 72.3% (97/134 cases) improved with a score between 30-100%. The vast majority of this group had an improvement rate close to 100%. Around 22.3% of study population become completely asymptomatic, while 26.87% had a poor response < 30%. Over 50% of these patients didn't require any further follow-up within 12 months.

Conclusion
This prospective study showed that NCGS is the main feature behind the symptoms labeled with IBS. Gluten and lactose free diet have been used as an effective and healthy treatment strategy in treating a large proportion of patients with IBS. No medications were used in treating these patients and the diet strategy was not only more effective but also significantly cost saving with the benefit of adding to life qualities and avoiding long-term side effect of medications.

SESSION 8: TREATMENT OF CELIAC DISEASE

P114

Adjunctive induction therapy with oral effervescent budesonide in newly-diagnosed coeliac disease' results of a pilot, randomized, double-blind, placebo controlled trial

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Background
We aimed to assess (a) whether induction therapy with oral, topically-acting budesonide to the GFD would lead to more frequent and faster healing of the intestinal lesion and greater improvement in symptoms in patients with newly-diagnosed CD and (b) the frequency of early (8-week) healing.

Methods
Participants with newly-diagnosed CD were randomized to 10 weeks of daily effervescent budesonide or placebo. Follow-up endoscopy occurred at weeks 8 and 52. The primary outcome was the proportion of participants achieving mucosal response (Marsh 1 or better) at week 8. Secondary outcomes included: mucosal response at week 52; mucosal remission (Marsh 0) and improvement in villous height to crypt depth ratio (Vh:Cd) at weeks 8 and 52.

Results
A total of 37 participants (73% female; mean age 36±16 (SD) yr) were randomized to budesonide (n=19) or placebo (n=18). Overall, mucosal response and remission was noted in 12 (32%) and 9 (24%) respectively at week 8, and 20 (53%) and 14 (38%) at week 52. Mucosal healing was seen in 6 (37%) receiving budesonide and 5 (28%) receiving placebo (p=0.73). Mucosal remission was more common in those receiving budesonide (n=12, 32%) than placebo (n=3, 17%; p=0.45). A non-significant trend was noted at week 52(n=8, 42% vs. n=6, 33%; p=0.74)). Change in Vh:Cd was non-significantly higher in the budesonide group at week 8 (1.64±1.07 vs. 1.31±0.87) and at week 52 (2.39±1.02 vs. 2.01±1.03). The safety profile of oral effervescent budesonide was acceptable.

Conclusion
Within 8 weeks, complete normalization of histology was seen in one in four participants. When used in conjunction with a GFD, treatment with budesonide in newly-diagnosed CD showed a trend toward improved mucosal healing rates and was well tolerated. The sample size limits conclusions, but permits planning of future well-powered randomized controlled trials of oral formulations of budesonide.

P115

Compliance of gluten free food provided in Melbourne food outlets

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Background
Effective treatment of coeliac disease is contingent upon a strict gluten free diet. Inadvertent gluten exposure while dining out is thought to be common, but has never been formally assessed. This study aimed to investigate the likelihood of gluten exposure in outlets providing gluten free food.

Methods
Food outlets within the City of Melbourne that declared gluten free items on their menu were randomly selected for unannounced site inspections conducted by Environmental Health Officers (EHO) in 2016. Inspections involved sampling gluten free food items for independent analysis of gluten content (Ridascreen® R5 Elisa), and foodservice staff completing a questionnaire assessing knowledge and implementation of gluten free standards. Gluten free was defined as 'no detectable gluten' as per the Food Standards Australia New Zealand code. Data were compared to retrospectively obtained compliance rates of gluten free food samples tested in 2015 and 2014.

Results: From the 127 food outlets, 158 samples were analyzed and 14 (9%) had detectable gluten; five <20 ppm, four 20-80 ppm and three >80 ppm (two were from gluten-containing foods mistakenly provided to the EHO as gluten free). Non-compliance rates had improved, being 28/138 (20%) in 2014 (P=0.005 compared to 2016; chi squared analysis) and 22/151 (15%) in 2015 (P=0.118). Knowledge of gluten free food was generally poor, with 110/123 (89%) of survey responders not correctly identify gluten-containing and gluten-free grains, including 12 not identifying wheat as gluten containing. The only factor associated with non-compliance was a lack of staff training (11/118 compliant versus 2/5 non-compliant, p=0.029) (see Table).

Table. Associations with outlets non-compliant in providing gluten free food

Variable	Non-compliance (%)	P-value	Odds ratio
Knowledge questions all correct	1/12 (8)	0.791	1.33
Knowledge questions not all correct	12/111 (11)		
No staff training	2/5 (40)	0.029	0.154
Staff training	11/118 (9)		
Prohibited claims used	2/16 (13)	0.788	0.802
Prohibited claims not used	11/107 (10)		
Contamination disclaimer used	5/51 (10)	0.909	1.07
Contamination disclaimer not used	7/67 (10)		

Conclusions: Despite improving rates of compliance to provide gluten free menu items, knowledge of gluten and food standards amongst foodservice staff is inadequate and not training staff on gluten free handling practices is associated with gluten contamination.

Conclusion
Despite improving rates of compliance to provide gluten free menu items, knowledge of gluten and food standards amongst foodservice staff is inadequate and not training staff on gluten free handling practices is associated with gluten contamination.

P116

Predictors of adherence to a gluten free diet in Australians and New Zealanders with coeliac disease

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Background
A gluten free diet (GFD) treats coeliac disease (CD), but its efficacy is dependent on strict adherence. A variety of patient factors, some modifiable, may influence maintenance of adherence but these have not been well described at a population level. We aimed to comprehensively assess the patient factors influencing GFD adherence in order to improve treatment outcomes.

Methods
Patients ≥13 years with CD completed an online survey comprising the validated Celiac Disease Adherence Test (CDAT) in addition to data on demographics, details of diagnosis and questions about knowledge of a GFD, including assessment of label-reading skills. Survey data were analyzed for predictors of adherence.

Results
Of 7393 responses, 5604 (76%) completed the CDAT and 3405 (61%) were adherent to a GFD. Multivariate regression analysis showed that education, household income, having a medical condition associated with CD and self-reported symptoms following gluten ingestion were independent predictors of adherence (see Table). Responders who considered themselves to have poor or terrible knowledge in applying a GFD were less likely to identify gluten free foods according to ingredients lists (0/18) compared to those who rated themselves with excellent, good or fair knowledge (2340/5460, 43%; P≤0.001; chi-squared analysis).

Table. Multivariate regression model showing adherence to a GFD and estimated odds ratio (OR) in a CD population

Variable	Adherence n (%)	P-value	OR
Some secondary college or equivalent	38/60 (57)	-	1
Comleted secondary college	1312/2108 (62)	0.725	0.964
TAFE course or equivalent	710/1202 (59)	0.959	1.005
Undergraduate degree	967/1566 (62)	0.089	1.177
Postgraduate degree	772/1175 (66)	0.002	1.335
Annual income < $20,000	172/333 (52)	-	1
Annual income $ 20,000 - $ 50,000	687/1134 (61)	0.052	1.291
Annual income $ 50,000 - $ 100,000	1085/1811 (60)	0.001	1.512
Annual income $100,000 - $ 200,000	1097/1793 (61)	≤0.001	1.695
Annual income > $ 200,000	371/543 (68)	≤0.001	2.238
Diagnosis from symptons	1831/3081 (59)	-	1
Diagnosis from associated medical condition	927/1441 (64)	0.021	1.173
Diagnosis from family screening	245/415 (59)	0.55	1.069
Incidental diagnosis	419/695 (60)	0.797	0.977
No symptoms followint gluten ingestion	521/890 (59)	-	1
Moderate symptoms following gluten ingestion	950/1582 (60)	0.101	1.156
Serve symtoms following gluten ingestion	1235/2013 (61)	0.014	1.235
Unsure of symtoms following gluten ingestion	280/425 (66)	0.005	1.421

Conclusion
Patient income, education and disease phenotype impact adherence to a GFD. Severe symptoms after gluten ingestion and presence of a co-morbidity associate with better dietary adherence, but lower education and lower income do the opposite, suggesting that factors such as cost of gluten-free options influence treatment. Patients who self-report poor knowledge of applying a GFD are less likely to correctly identify gluten-free, but not gluten-containing foods, so may follow an unnecessarily restrictive GFD. Education on how to access affordable and safe food options may improve adherence.

P117

Canadians with celiac disease misinterpret product label information which may lead to unsafe food choices despite allergen labeling laws

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Background
Patients with celiac disease often report challenges reading labels as well as inadvertent gluten exposures. The most common cause of non-responsive celiac disease is gluten exposure.

Aim
To assess whether patients with celiac disease can proficiently assess product labeling to determine if a product is gluten-free.

Methods
The Manitoba Celiac Disease Cohort consists of newly diagnosed adults with elevated TTG and/or EMA antibodies and Marsh III histology, followed for 2 years. At each follow-up visit (6, 12 and 24 months), participants were presented with 25 grocery items from a local supermarket (different items at each visit) and asked to determine whether each was gluten-free based upon labeling information. The Celiac Diet Assessment Tool (CDAT) and Gluten-Free Eating Assessment Tool (GF-EAT) were used to assess gluten-free diet (GFD) adherence.

Results: Seventy-eight participants (62% female, mean age 40 years) completed the 24-month study visit, of whom 70 also completed the 6-month assessment and 62 the 12-month assessment. Participants generally reported good adherence (median CDAT score <13 at each time point); however, at 24 months, 73% reported rare gluten exposure (<1/month) on the GF-EAT. Grocery quiz scores were [median (IQR)]: 6 months, 22 (21-23); 12 months, 21 (20-22); 24 months, 18 (18-19). Participants were most likely to make errors with gluten-containing items and least likely to make errors with gluten-free products with explicit "gluten-free" labeling. There were no significant correlations between quiz scores and either TTG antibody levels or standardized diet assessment tools.

Conclusion
Patients who are trying to follow a GFD may not be able to consistently choose appropriate gluten-free foods

based upon product labeling information. The ability to correctly read food labels does not appear to improve with time. Further studies are needed to evaluate whether insufficient label reading skills are associated with villous atrophy.

P118

Prevalence and associated factors of everyday life restrictions caused by long-term treated celiac disease

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Aim
We aimed to evaluate adult patients' experience of living with celiac disease diagnosed in childhood, and identify factors associated with possible everyday life restrictions caused by the disease.

Methods
232 adults (women 69%, median age 27.0 yr) with a childhood diagnosis of celiac disease fulfilled a questionnaire evaluating general health, lifestyle, gluten-free diet (GFD) and long-term follow-up. Further, they completed validated Gastrointestinal Symptom Rating Scale (GSRS) and Psychological General Well-Being (PGWB) surveys for gastrointestinal symptoms and quality of life. Clinical and histological presentations at diagnosis were confirmed from patient records.

Results
Altogether 108 (47%) of the 232 responders felt that celiac disease restricts their daily life. This was experienced especially when eating in a restaurant (72%), traveling abroad (38%) and visiting a friend (30%). Patients reporting restrictions had more often anemia (38% vs 22%, p=0.013) and severe symptoms (16% vs 6%, p=0.047) at diagnosis, whereas they did not differ from those without restrictions in age, gender or other clinical and histological presentation. Current age, time from the diagnosis, general health, presence of co-morbidities, lifestyle, socioeconomic status and presence of celiac disease in relatives were also comparable. There was no difference in specific gastrointestinal symptoms measured by GSRS, but patients considering the disease restrictive reported more overall symptoms than those without restrictions (32% vs 17%, p=0.007). Furthermore, despite strict GFD (78% vs 82%, p=0.770) they experienced adhering to the diet more challenging (somewhat difficult 33% vs 7%, p<0.001) and had significantly lower PGWB vitality scores (median 17 vs 18, p=0.023).

Conclusion
Almost half of patients diagnosed in childhood experienced celiac disease to cause marked restrictions in adulthood. This was associated with current symptoms, lower vitality scores and difficulties to maintain GFD. Patients with severe symptoms and anemia at diagnosis might require special attention and tailored follow-up in these circumstances.

P119

Dietary factors and mucosal immune response in celiac disease patients having persistent symptoms despite a gluten-free diet

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Background
For unexplained reasons, many treated celiac disease patients suffer from persistent gastrointestinal symptoms despite a strict gluten-free diet (GFD) and recovered intestinal mucosa. We investigated the role of dietary factors, distinct small-bowel mucosal immune cell types and epithelial integrity in the perpetuation of these symptoms.

Methods
We compared clinical and serological data and mucosal recovery in 25 symptomatic and 22 asymptomatic celiac patients on a long-term GFD. The density of CD3+ and γδ+ intraepithelial lymphocytes (IELs), CD25+ and FOXP3+ regulatory T cells and CD117+ mast cells, and the expression of tight junction proteins claudin-3 and occludin, heat shock protein 60 (HSP60), interleukin 15 (IL-15) and Toll-like receptors (TLR) 2 and 4 were evaluated in duodenal biopsies.

Results
All subjects kept a strict GFD and had negative celiac autoantibodies and recovered mucosal morphology. The patients with persistent symptoms had lower mean fiber intake (15.2 vs. 20.2 g/day, p=0.028) and density of CD3+ IELs (45.0 vs. 59.3 cell/mm, p=0.045) than asymptomatic patients. There was a similar but non-significant trend in γδ+ IELs (13.5 vs. 17.9, p=0.149). There were no differences between the groups in other parameters measured.

Conclusion
Low fiber intake may predispose to persistent symptoms in celiac disease. The results do not support the idea of innate immunity, epithelial stress or altered epithelial integrity having a marked role in the development of persistent symptoms. A higher number of IELs in asymptomatic subjects may indicate that the association between symptoms and mucosal inflammation is more complicated than previously thought.

P120

Long-term follow-up in patients with celiac disease: predictors and effect on long-term health outcomes

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Background
Current guidelines recommend regular follow-up in celiac disease. However, the actual implementation and effect of the follow-up to long-term health outcomes remains unclear. We explored this issue in a large cohort of adults with celiac disease.

Methods
Altogether 677 patients were enrolled in a nationwide study. Medical data were gathered through interviews and patient records. Current symptoms and quality of life were assessed by validated SF-36, PGWB and GSRS questionnaires and blood samples were drawn for serology. All results were compared between patients with and without long-term (>2 years) follow-up.

Results
Only 15% had long-term follow-up, the median duration being 10 (range 2-38) years. Predictors for the follow-up were immunological (35% vs 24%, p=0.020) and circulatory (20% vs 12%, p=0.010) comorbidities, whereas it was less common in subjects with musculoskeletal (23% vs. 34%, p=0.045) comorbidity and those in not-at-risk group for celiac disease (16% vs. 27%, p=0.025). Demographic data, site of diagnosis, baseline clinical and histological presentation and smoking had no effect. Patients with or without follow-up were comparable in gender, age at diagnosis and at present, adherence and capability to manage gluten-free diet, and current positivity to endomysial antibodies. Questionnaire scores were also similar, but those without follow-up reported more overall symptoms (16% vs. 26%, p=0.043). More than 80% of patients in both groups wished regular follow-up.

Conclusion
Only a minority of patients had regular long-term follow-up. Although the study groups were comparable in most health outcomes, those without follow-up reported more overall symptoms. Based on these results, there is an unmet need for more systematic follow-up policies in celiac disease.

P121

Treatment with gliadin-containing, tolerogenic immune modifying nanoparticles (TIMP-GLIA) antagonizes gliadin hypersensitization in HLA-DQ8 transgenic mice

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Background
In celiac disease (CD), tolerance to gluten proteins from cereals is lost. Tolerogenic immune modifying nanoparticles (TIMP) are effective at restoration of antigen-specific immune tolerance in various autoimmune conditions. The identification of gliadins as the primary epitopes in CD suggests that TIMP containing gliadin (TIMP-GLIA) may serve as a cure. We recently reported that TIMP-GLIA reversed body weight loss, reduced the severity of histological duodenitis and diminished inflammatory cytokine secretion in response to gliadin in an adoptive T cell transfer model of CD in Rag1-/- mice (unpublished). Here, we tested immunomodulatory effects of TIMP-GLIA in HLA-DQ8 transgenic mice, bearing a major human genetic risk factor for CD.

Methods
TIMP-GLIA were administered intravenously 11 and 3 days before immunization of HLA-DQ8, huCD4 transgenic Ab0 NOD mice with gliadin in complete Freund's adjuvant. Ovalbumin-containing TIMP (TIMP-OVA) were used as a treatment control. 14 days later, animals received 1 boost with gliadin in incomplete Freund's adjuvant. Mice were monitored for 28 days post-immunization.

Results
Treatment with TIMP-GLIA (vs. TIMP-OVA) effectively reduced 1) serum anti-gliadin IgG2c titers (ELISA), and 2) both proliferation (BrdU incorporation) and IFNγ, IL-17 and IL-2 inflammatory cytokine secretion (ELISA) by splenocytes restimulated ex vivo with gliadin.

Conclusion
The results demonstrate that treatment with TIMP-GLIA modulates the immune response against gliadin and counteracts Th1 skewing in humanized mice. They support the concept of gliadin-specific immune tolerance induction and treatment of CD with TIMP-GLIA in patients. Collectively, the results from pre-clinical efficacy testing of TIMP-GLIA in celiac animal models support clinical trials of TIMP-GLIA.

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P122

Microbial transglutaminase used in bread preparation at standard bakery concentrations does not increase immuno-detectable amounts of deamidated gliadin

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Background
Gliadin deamidation by tissue transglutaminase is considered as a key factor in celiac disease (CD) pathogenesis. Microbial transglutaminase (MTG) may be used as a processing aid by the food industry, e.g. in gliadin containing bakery products. As MTG is also able to deamidate gliadin, a celiac disease triggering effect of bread prepared with MTG is under discussion. In this study the effect of standard bakery concentrations of microbial transglutaminase in wheat bread preparation on the immunoreactivity of CD patients' sera was investigated.

Methods
Bread samples prepared using different MTG concentrations were processed to extract albumin/globulin, gliadin, and glutenin fractions. The samples were analyzed by immunoblotting using monoclonal antibodies specific to unmodified and/or deamidated gliadin. Further, CD patients' sera were used for characterization of the extracts by immunoblotting.

Results
Using monoclonal antibodies, no differences between control bread and MTG-breads were observed in immunoblotting. Essentially, no gliadin deamidation could be detected at standard bakery MTG concentrations. The recognition pattern obtained after using CD sera for immunoblotting did not reveal differences between control and MTG-treated bread protein extracts.

Conclusion
Our results indicate that MTG-treatment of wheat bread prepared with typical MTG concentrations used in standard bakery processes does not lead to immuno-detectable amounts of CD-immunotoxic deamidated gliadins.

Keywords
Microbial transglutaminase, celiac disease, gliadin, wheat bread

P123

Cystamine dependent decrease of the Mucosal Immune Inflammatory Response in Experimental Model of Celiac Disease

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Background
Celiac disease (CD) is a polygenic, auto-inflammatory disease, activated by the exposure of dietary gluten in individuals with specific genetic background. With the help of a suitable animal model of CD, potential treatments could be administered and their effectiveness determined before clinical trials are conducted. The study intended to evaluate the efficacy of Cystamine (CysN), a multipotent molecule and unique inhibitor of tissue transglutaminase 2 (TG2) in an experimental model of CD.

Method
A total of 36 adult C57BL/6 mice were randomized into 6 groups: *Group 1)* control without treatment; *Group 2)* received polyinosinic: polycytidylic acid (Poly I:C) ; *Group 3*) treated with Poly I:C plus 17.2 mg/ day CysN per o.s for 21 days; *Group 4)* treated with Poly I:C plus 225 mg/kg CysN i.p for 7 days; *Group 5)* treated with cystamine per o.s alone for 21 days; *Group 6)* treated with Cystamine i.p for 7 days. After killing, TG2 activity by immunohistochemistry, expression of Rae-1 (homolog of human MICA) by RT-PCR, interleukin-15 expression by ELISA and histopathology of small intestinal tissue evaluated.

Result
Poly I:C –CysN group developed significantly less severe inflammation compared with the Poly I:C group, associated with decrease TG2 activity, IL-15 levels, Rae-1 expression and lesions.

Conclusion
The study evaluated both the acute and long term effect of CysN on the intestinal inflammation. CysN administered for 21 days showed better results than the CysN administered through intraperitoneal route for 7 days. The study concluded beneficial effect of CysN in the experimental model of CD and strongly advocated its future prospect in the clinical trial.

Keywords
Celiac disease, Animal model, Cystamine, Tissue transglutaminase inhibitor, Drug therapy

P124

Ascorbate attenuates the severity of inflammation in an experimental model of celiac disease

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Background
Celiac disease (CD) is an autoimmune condition, activated by the exposure of dietary gluten in individuals with specific genetic background. With the help of a suitable animal model of CD, potential treatments could be administered and their effectiveness determined before clinical trials are conducted. Ascorbate (Asc) found to inhibit the gliadin-induced expression of IL-15 and hence proved to be useful in CD biopsy explants. Therefore, present study intended to evaluate the effect of Asc in an experimental model of CD.

Method
A total of 36 adult C57BL/6 mice were randomized into 6 groups: *Group 1)* control without treatment; *Group 2)* received the polyinosinic: polycytidylic acid (Poly I:C); *Group 3)* treated with Poly I:C plus 1000 mg/kg/day Asc per o.s for 21 days; *Group 4)* treated with Poly I:C plus 4000 mg/kg Asc i.p for 7 days; *Group 5)* treated with Asc per o.s alone for 21 days; *Group 6)* treated with Asc i.p for 7 days. After killing, TG2 activity by immunohistochemistry, expression of Rae-1 (homolog of human MICA) by RT-PCR, interleukin-15 expression by ELISA and histopathological evaluation of small intestinal tissue were performed.

Result
Poly I:C –Asc group developed significantly less severe inflammation compared with the Poly I:C group, associated with decrease IL-15 levels, Rae-1 expression and lesions.

Conclusion
The study evaluated both the acute and long term effect of Asc on the intestinal inflammation. Asc administered for 21 days showed better results than the Asc administered through intraperitoneal route for 7 days. The study concluded beneficial effect of Asc in the experimental model of CD and strongly advocated its future prospect in the clinical trial.

Key words
Celiac disease, Animal model, Ascorbate, Drug therapy

P125

Assessment of the types, variety and frequency of the alternative Gluten free grains consumption by North Indian Celiac patients' a hospital based study

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Background
Large amount of daily nutrient intake is provided by consumption of grains. Therefore, the choice of alternative grains (grains which are gluten-free) not only predisposes a Celiac individual to insufficient nutrient intake but also an unbalanced diet. For appropriate dietary counselling and planning, it is imperative to know the grain components of the diet. Our study aimed to get an insight into the types, variety and frequency of consumption of alternative grains by the Celiacs and the reasons for avoidance of certain grains.

Methods
A descriptive cross-sectional survey was conducted on 50 patients with an established diagnosis of CD. Patients aged 5 years and above, following a GFD for at least 6 months were recruited from the specialized clinic. A close ended multiple choice type questionnaire was used for the assessment of grain consumption pattern i.e. types and frequency of grains consumed and reasons for avoiding specific grains. Fourteen different grains were studied.

Results
Among the subjects, twenty six were females (52%) and 24 were males (48%). Mean age was 13 years (range 5 -50 years). The two most commonly consumed grains were White rice and Bengal gram. Many nutritious gluten-free grains were avoided by the participants due to either lack of awareness or concerns about the high cost. Ragi, Buckwheat and Amaranth were the three least commonly consumed alternative grains. Most participants who avoided Ragi (74%), Buckwheat (34%) and Amaranth (88%) did so because they have never heard of it". Seventy six percent of the participants reported Brown rice and 34% reported Buckwheat to be "too expensive" as the reason for not consuming these grains.

Conclusion
Many nutritious alternative grains are not consumed by Celiacs because of lack of awareness and concerns about their high cost. Therefore, increasing awareness about nutritious gluten-free grains is necessary to improve nutrients intake among Celiacs.

P126

Liver dysfunction in patients with celiac disease and effect of gluten free diet on them.

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Background
With its wide spectrum of manifestations, celiac disease (CeD) is known to affect liver in many forms including asymptomatic increase in transaminases, autoimmune liver diseases, cirrhosis of liver and vascular disorders. We, in a prospective study, evaluated consecutive patients with CeD for liver dysfunction and the response to gluten-free diet (GFD) in them.

Methods
146 adult treatment naïve patients with CeD were screened prospectively for liver dysfunction using liver

function tests, ultrasound, fibroscan, and colour doppler. They were evaluated extensively for etiology of the liver disease. Liver dysfunction was defined if the patients had any or more of the following: increase in transaminases more than one and half times the normal value, altered echotexture of liver on ultrasound or presence of cirrhosis.

Result
Liver dysfunction was found in 24 (16.4%) patients. Mean age of these patients was 27.8 ±1.5 years (16, 66.6% males). Serum ALT or AST were elevated in 18 (12.3%) patients and 6 (4.1%) had cirrhosis. The aetiology of liver dysfunction was found in 5 (hepatic venous outflow tract obstruction in 2, alcohol, drug-induced and chronic hepatitis B in one each) and in 19 the liver dysfunction remained cryptogenic. Eighteen patients underwent liver biopsy as part of diagnostic workup, which showed features suggestive of autoimmune hepatitis in 3, and rest 15 (with persistently elevated transaminases) the features were non-specific such as mild chronic inflammation, occasional spotty necrosis, mild ballooning ,steatosis and focal lipofuscin deposition. ALT/AST normalized in 11(73.3%) of them with gluten-free diet over a mean follow up of 16±1.3 weeks.

Conclusion
Overall liver dysfunction was found in 16.4% of patients. Elevated transaminases, in majority (73.3%), normalized with GFD.

P127

Is education increasing the knowledge of patients with celiac disease?

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Background
Education plays an important role in raising awareness of patients. Therefore increased awareness in patient's leads to better manage the diseases. The aim of this study was to investigate the effects of education on increasing the knowledge of patients with celiac disease in Iranian population.

Method
This cross-sectional study was conducted on 88 celiac patients who were participated to the second national educational meeting for patients in September, 2016. For each patient, the data of pre-test and Post-test were collected using questionnaire. During the meeting information regarding epidemiology, diagnosis and treatment of celiac disease was educated. The questionnaire was consisted of 11 questions about the epidemiology, diagnosis and treatment of celiac disease was completed by participants. The data were analyzed using SPSS version 20.

Result
Of 88 participants, 65 (73.9%) were women and 45 (51.1%) were educated.
According to the results, except for awareness of cross contamination with gluten, the education sections had significantly effects on increasing the knowledge of patients with celiac disease for epidemiology, diagnosis and treatment (p=0.001).

Conclusion
The result of this study showed that specific meetings and training sessions can increase the knowledge of CD patients in treatment, diagnosis and have an important role to understanding gluten free and gluten-containing products. Raise the awareness of patients directly can reduce the cost of disease and improve the quality of patient's life.

Keyword: Celiac disease, awareness, patients

P128

Assessment of knowledge of diagnosis and treatment of celiac disease among specialists

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Background
Specialists as the main therapist group may play crucial role in the diagnosis and treatment of celiac disease. Therefore, training and ensuring capabilities is important. In this respect, the aim of this study is to assess the knowledge of specialists of diagnosis and treatment celiac disease.

Methods
The population was specialists graduated from Iranian Medical Sciences Universities that participated in the Gastroenterology congress across the country. Data was collected using a questionnaire and its reliability was confirmed using test-retest (r = 91.6%). The total score obtained from this questionnaire was 150 with the classification of participants to the following categories: excellent group: 113- 150 points, good: 79-112, average: 39-78 and poor less than 38. Since the diagnosis and treatment of celiac disease is the responsibility of specialists, the minimum required educational need was determined based on a score of less than 113. The collected data were analyzed using descriptive and inferential statistics.

Results
Out of 250 participants, 132 questionnaires were returned (Response rate = 52.8%). The mean age of the participants was 42.67 years (SD = 7.9 years) and the majority of them were male (63.6%). Only 12.1% and 9.8% of specialist have got the excellent score for diagnosis and treatment respectively. Average score of participants who had less than three years' experience was significantly higher than others (P≤0.05).

Conclusion
It may conclude that specialists have had performance gap and around 90% needed training based on the principles of instructional design in order to improve their knowledge and skills to do and practice their assigned tasks. Therefore, development of training packages according to the principles of instructional design is suggested.

Keywords
Celiac disease, specialists, need assessment.

P129

The physicians' opinion to introduce the target group for effective celiac disease management

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Background
Lack of physician awareness on atypical celiac disease is common but not evaluated before. The aim of this study was to assess the physicians' awareness on celiac disease diagnosis and management.

Method
In this cross-sectional study, 50 general practitioners, 50 internists and 50 consultants completed the survey during 2016. The data regarding the work experiences, education, place of work, demographic characteristics and specific questions regarding introduce the target group for effective CD management were collected using a questionnaire. The results were analyzed using SPSS software.

Results
Of the 150 study population (92 men (65.2%)) with mean age 40.67±10.7, 49% had over 10 years work experience, 48% were in the public hospital, 30% in public and private hospital, 19% in the private hospital and 3% were looking for work. According to the physician's opinion most people who need education regarding the diagnosis, treatment and follow-up of celiac disease are including general practitioners (56.8%), general population (47.7%), health care workers (20.5%) and internists (15.2%) respectively.

Conclusion
The results of this study indicate that increase awareness in the general practitioners as well as general population is suboptimal and require attention and adjustment.

P130

The ancient wheat species Triticum monococcum elicits a reduced in vivo inflammatory response: implication for celiac disease prevention

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Background
There is an increasing interest to find wheat varieties with null or low toxicity suitable for treatment or prevention of celiac disease. T. monococcum, a diploid (AA genome) ancient wheat, is a promising species for the low content of gluten epitopes and the high *in vitro* digestibility. However, very little is known on the *in vivo* immunogenicity of T. monococcum for celiac patients.

Methods
We used a short (3 days) wheat challenge (SGC) to assess the *in vivo* immunostimulatory properties of gluten from T. monococcum (*ID331 cultivar*) and hexaploid wheat T. aestivum (*Sagittarium cultivar*). Seventeen celiacs (aged 6-14yrs) in remission participated to the study and consumed for 3 days 3 sandwiches with common (N=7) and ID331 wheat (N=10), containing approximately 12 gr of gluten/die. Immune-reactivity was assessed by counting by ELISPOT at day6 peripheral blood IFN-γ-secreting cells against whole gliadin and dominant gliadin peptides. Furthermore, the expression level of inflammatory cytokines/receptors (IL-12A, IL-15, IL-18RAP, INF-γ) was detected by real-time PCR on peripheral mononuclear cells.

Results
A higher number of IFN-γ-secreting cells was detected in peripheral blood in response to both gliadin and peptides in the group challenged with common wheat compared to the group fed with monococcum gluten ($p<0.05$). Similarly, an increased mRNA expression for IL12A and INFγ was detected in the group challenged with hexaploid gluten compared to monococcum ($p<0.05$). No differences were observed for IL-15 and IL-18RAP mRNA expression between the two groups (p=ns).

Conclusion
Diploid wheat showed a reduced *in vivo* capability to recruit from the intestinal mucosa gliadin-specific T cells and to stimulate the production of inflammatory cytokines, compared to common hexaploid cereal in celiacs. Although T. monococcum is a cereal not suitable for the diet of celiacs, it could still have a role in strategies aimed to prevent celiac disease in at risk subjects.

P131

Management of (suspected) celiac disease by general practitioners: a qualitative approach

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Background
General practitioners (GPs) play a key role in detecting and diagnosing celiac disease (CD). However, data about GP management of (suspected) CD patients are sparse. The aim of this study was to provide insights in the management of GPs regarding diagnosis, treatment and follow-up of CD.

Methods
We conducted a qualitative study using semi-structured in-depth interviews of Dutch GPs with more than 5 years' experience using purposive sampling for selection. The amount of GPs interviewed depended on when data saturation was reached. We applied content analysis to the semi-structured interviews.

Results
Seven GPs were interviewed of whom five females. Analysis of the interviews resulted in three main themes: "CD suspicion", "CD diagnosis" and "Treatment and follow-up of CD". Most GPs considered vague gastrointestinal symptoms and diarrhea as presentation of CD. All GPs mentioned the importance of antibodies in CD diagnosis, although some started a gluten-free diet as first diagnostic tool. Some GPs reported that CD diagnosis could be based on antibodies only without referring to secondary care and/or duodenal biopsy analysis. The majority of the GPs mentioned no role for primary care physicians in the follow-up of CD and noticed the important role for dieticians in CD management.

Conclusion
A variety exists among GPs how to diagnose CD properly and how to perform follow-up. There are some indications that guidelines are not always followed by GPs, which may affect the CD detection rate.

P132

No need for routine laboratory checks for nutritional deficiencies in follow up of coeliac disease. Symptom based diagnostics and DEXAs are sufficient.

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Background
In coeliac disease, gluten-free diet enables mucosal healing, restoring mucosal function and preventing complications. However, gluten-free products that may contain less vitamins and micronutrients pose a risk for ongoing deficiencies. For follow up of patients, guidelines recommend routine blood checks for deficiencies and associated diseases and Dual Energy X-ray Absorptiometry (DEXA)-scans.

Aim
We aim to assess the expediency of these guidelines by evaluating the yield of these screening tests. Is screening needed in follow up or should patients be tested according to symptoms?

Methods
A retrospective analysis of medical files of all follow up patients with coeliac disease attending the Rijnstate Hospital in 2014 with respect to blood tests, DEXA-scans and related symptoms or signs of abnormalities.

Results
We analyzed 250 patients with a median follow-up of 7.8 (1-22) years. At diagnosis, we found anemia in 24.4%, iron deficiency in 38%, folic acid deficiency in 22.6% and vitamin B12 deficiency in 15.9%. All deficiencies recovered within 1-2 years with or without supplements. In patients with normal baseline values routine screening found two cases of mild asymptomatic anemia, one autoimmune thyroid disease and one type 1 diabetes. Osteoporosis and osteopenia were present in 23.3% and 35% at diagnosis. In most patients bone mineral density (BMD) improved or stabilized during follow up, 8% deteriorated.

Conclusion
The frequency of asymptomatic, coeliac-related anemia, nutritional deficiencies and/ or associated autoimmune disorders is very low in patients with normal values at diagnosis. We do not recommend routine screening during follow-up in these patients. Osteopenia and osteoporosis are frequent in follow up of coeliac disease and need clinical attention. Therefore, we recommend follow-up DEXA-scans.

P133

Modifying or deleting celiac disease epitopes in gliadin proteins of bread wheat using mutagenesis and gene editing technologies

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Background
Wheat grains contain gluten proteins that harbour immunogenic epitopes, which can trigger Coeliac disease in genetically predisposed humans. Wheat mutagenesis offers alternatives to modify or delete gliadin immunogenic epitopes, preventing binding to immune cells in Coeliac patients. Two mutagenesis approaches, not currently regulated as genetically modifying techniques, were deployed to alter or remove gliadin epitopes in bread wheat grains.

Methods
CRISPR/Cas9 technology, a site directed gene editing technique, was applied to precisely cut DNA of gliadin-coding genes in order to trigger mutations altering or removing their immunogenic domains. Four CRISPR/Cas9 constructs cutting α-gliadin or/and γ-gliadin genes at one or more sites were designed and transformed into bread wheat.

Gamma irradiation methods, a random mutagenesis technique, was used to remove large DNA fragment in plants, enabling deletion of entire gene families. An existing gamma-irradiated bread wheat population was analyzed for its potential gliadin gene copies deletions. The initial screening for gliadin mutants was done using Acid-PAGE, comparing the gliadin protein profile of grains of offspring plants to that of the wild type grain.

Results
Mutant CRISPR/Cas9 and gamma-irradiated lines have been identified. Mutants showed fewer bands, indicating the absence of synthesis of some gliadins, or additional smaller bands, which may be associated with truncated gliadin proteins likely missing the epitope domain. The DNA of mutant lines identified will be analyzed in detail by next generation sequencing.

Conclusion
We delivered proof of principle that mutagenesis technologies can be used on bread wheat in order to reduce celiac disease epitopes in the gluten. Mutagenesis technologies can be used on bread wheat in order to alter gliadins or reduce their expression. These results constitute an initial step towards the creation of gluten-safer wheat with lower gliadin immunogenicity, yet retaining glutenins conferring bread backing abilities.

P134

Rapid urine home test for gluten free diet monitoring

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Introduction
The only effective management of celiac disease is adherence to a strict gluten free diet (GFD). There is no reliable method to confirm adherence to the GFD or to ascertain whether symptoms may be due to gluten exposure. Celiac serology and dietary questionnaires show poor correlation with gut mucosal recovery.

To address this need, we developed a lateral flow immunoassay (LFIA) to detect gluten immunogenic peptides (GIP) in urine. Urine GIP have high correlation with gut mucosal damage in celiac disease. Our goal was to simplify the LFIA method so that it could be used at home, and to validate the test, establishing its performance characteristics.

Methods
Urine samples (n=317) from volunteers under different gluten exposure conditions were analyzed in a central laboratory with the simplified urine GIP LFIA. The samples included expected positive-control random urine samples from healthy volunteers following a non-standardized gluten-containing diet (GCD) who had ingested gluten in the previous 16 hours (n=110), expectedly negative random samples from celiac patients on a reportedly strict GFD (n=180) and lastly, first morning samples from healthy subjects on a GFD after the administration of 0.5g of gluten a day -i.e., a moderate gluten challenge- (n=27).

Results
GIP were detected in 100 out of 110 samples of volunteers on a GCD whereas no GIP were detected in 179 out of 180 samples from patients on a GFD. GIP were detected in 24 of the 27 samples collected from volunteers ingesting 0.5g.

The diagnostic sensitivity of the test was 91% and the specificity 99%. The positive and negative predictive values were 99% and 95% respectively. The sensitivity for the detection of the ingestion of 0.5g of gluten was 89%.

Conclusion
The rapid urine gluten test is highly specific and sensitive to assess adherence to GFD and gluten exposure in celiac patients.

P135

Gender differences in dietary habits of celiac people

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Background
Specific nutritional assessment becomes necessary to equilibrate a gluten-free diet (GFD) due to food restriction promoted by the diet. Adult women and men can develop a different feeding pattern to face nutritional requirements. The aim of this study was to evaluate nutritional status and dietary habits of adult celiac population taking into account the gender gap.

Methods
Adult celiac people (46 women and 12 men) following GFD for more than 1 year were recruited (19-71 years). 24-hour food recall of 3 days and a food frequency questionnaire were collected. Anthropometric parameters were measured.

Results
Body Mass Index (BMI) was significantly higher in men (24.6±3.7 m/kg2) than in women (21.6±2.4m/kg2). A third of men were overweight (16.6%) or obese (16.6%) while only a 6.5% of women showed overweight and none were obese. Celiac women had lower BMI values than general population. Macronutrient contribution to energy consumption was unbalanced for all participants, but differences were found between genders: men showed increased fat and protein intake (43.0% and 18.9% respectively) and reduced carbohydrate consumption (38.1%) than women. Fibre ingestion was also higher (20.2 *vs* 16.4 g) in male participants. Concerning food habits, cereal-based food intake was very low in all participants, particularly in men, who none of them fulfilled recommendations. Whereas the half of celiac men accomplished daily vegetables recommendations, only around a third of women did it. Celiac men reflected a lower intake of pulses than women. Excessive meat consumption was observed in all participants, but men ate more servings per week.

Conclusion
Celiac men were further from a healthy diet than women, and this could contribute to observed higher BMI values. Gender is an important aspect to take into account during nutritional education for celiac people.

P136

The implementation of European regulation for gluten-free rendered foodstuffs increase their safety

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Background
The interest for gluten-free (GF) products and consequently the production have increased during the last years in Europe. Gluten contamination on GF rendered products has represented an important problem of food safety, and thus specific regulations have been defined for this foodstuff. CODEX STAN 118-2008 and Regulation (EC) No. 41/2009 allowed the inclusion of food information by the statements "gluten-free" (<20 mg/kg) or for "very low gluten" (<100 mg/kg) foods. More recently, the regulation (EU) No. 1169/2011 (Date of effect: 2014/12/13) that requires the declaration of cereals containing gluten even in unpackaged foodstuffs, and Regulation (EU) No. 828/2014 were implemented. The aim of this study was to determine the effectiveness of these standards on the absence of gluten in GF rendered products.

Methods
GF- claimed cereal-based foods (flours, breads, pasta, bakery...) (n=2614) were analyzed from 2004 to 2016 in order to measure the gluten contamination and two subgroups were distinguished: 1) gluten-free-labeled products (GF-L) - using a label mark (n: 1652) - and 2) reportedly gluten free, but not certified products (GF-NC) (n: 962). Gluten content was analyzed by R5 based ELISA sandwich method.

Results
From 2004 to 2008, before any regulation was implemented, 13% of GF-NC samples and 5% of GF-L were gluten-positive (gluten content > 20 mg/kg). Nevertheless, during 2009 and 2014 these percentages decreased to 6% and 1.5% respectively. From 2014 onwards, after regulation (EU) No. 1169/2011 was set, the amount of positive samples was reduced even more to 1.8% in GF-NC and 1.3% in GF-L samples.

Conclusion
GF-L have been safer than GF-NC over the years, reaching similar results nowadays. European Regulations have been effective in terms of gluten control for GF rendered products, especially in GF-NC. Cereal-based foods are more reliable products for the celiac population.

P137

Lactobacillus plantarum Heal9 and Lactobacillus paracasei 8700:2 suppress ongoing celiac autoimmunity in children at genetic risk for developing celiac disease

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Background
Strains of *Lactobacillus (L.) plantarum* and *L. paracasei* have in different ways reduced pro-inflammatory responses in animal models. The present study tested the hypothesis that a mixture of these two strains can modify the autoimmune response in children with moderately elevated levels of tissue transglutaminase autoantibodies (tTGA) on a gluten-containing diet.

Methods
Eighty-nine children carrying any of the risk haplotypes HLA-DQ2 and/or DQ8 who were detected with moderately elevated tTGA levels in a prospective screening for celiac disease were invited to participate in a double blind placebo controlled randomized clinical trial. Of those 89 children, 79 (88.8%) children accepted participation (43 females, 36 males) at median 4.5 (range 3-7) years of age. Forty (50.6%) children received *L.plantarum* Heal9 and *L.paracasei* 8700:2 (total dose 1010 CFU/day; probiotic group) and 39 (49.4%) received maltodextrin (placebo). Blood samples were drawn at baseline and after 3 and 6 months of intervention. tTGA were analyzed using radiobinding assays and peripheral blood lymphocytes by flow cytometry. Wilcoxon rank sum test tested differences between groups and Wilcoxon signed rank test differences within groups with nominal two-sided p-values.

Results
In the probiotic group, levels decreased after 6 months for IgA-tTGA (mean -107.0U/mL; p<0.05) and IgG-tTGA (mean -84.7 U/mL; p=0.06), whereas in the placebo group levels increased for IgA-tTGA (mean +25.0 U/mL; p<0.05) and IgG-tTGA (mean +56.2 U/mL; p<0.01). After 6 months, changes in percentage between groups were found for NK-cells (p<0.05), NKT-cells (p<0.01) and for naïve CD4+ T-cells (p<0.05). The percentage of CD4+CD25+Foxp3+ T-cells tended to increase over time in the placebo group, albeit not significantly (p=0.08).

Conclusion
L.plantarum Heal9 and *L.paracasei* 8700:2 showed suppressing effects on celiac autoimmunity in children on gluten-containing diet. This indicated that certain *Lactobacillus*-strains can hamper celiac autoimmunity in at HLA-risk individuals, suggesting a possible preventive application of probiotics in celiac disease.

P138

A study of cognitive dysfunction in Coeliac disease and the impact of strict adherence to a gluten free diet.

Hadjivassiliou M[1], Pyser C[1], Sanders D[1], Venneri A[1], Tooth C[1]

[1] *Royal Hallamshire Hospital, United Kingdom*

Background
Limited published reports suggest that patients with CD may suffer from cognitive deficits. To investigate this further we performed a cross-sectional study to establish if such cognitive deficits are present at diagnosis and after treatment with a GFD.

Methods
Over the last 20 years a number of patients with CD and cognitive complaints have been referred and assessed by the Clinical Neuropsychology Service. This clinical experience led to the development of a cognitive assessment protocol. This study consecutively recruited 19 patients with newly diagnosed CD, 40 patients with a diagnosis of CD for at least 5 years and 21 healthy controls. All participants underwent a 2 hour cognitive assessment.

Results
Serological results indicated 16 patients adhered strictly to GFD and 19 patients did not. Five patients from the established CD group were excluded from the analyses because of uncertainty about correct initial diagnosis of CD.

The groups were matched for years of education, estimated pre-morbid intellectual abilities, anxiety and depression scores. The Newly Diagnosed and Control groups were also matched for age, but younger than the 2 established diagnosis groups.

Significant group effects were seen for Block Design, Trail Making part B, Immediate and Delayed visual recall. Immediate visual recall was impaired in Newly Diagnosed CD patients compared to the Control Group. Additional differences between the CD Adherent group and the Control Group were seen in block design and matric reasoning. Increasingly marked differences were seen between the CD Non-adherent group and the Control Group.

Conclusion
This study indicates a cognitive impact of CD in patients presenting with GI symptoms. The extent of this depends on time since diagnosis and GFD status. There was trend evidence supporting the protective value of maintaining a GFD. A longitudinal investigation of patients with newly diagnosed CD would significantly improve the methodology.

P139

Pain in gluten neuropathy: does gluten free diet have a role to play?

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Background
Peripheral neuropathy is a common neurological manifestation of gluten sensitivity. This study looked at the prevalence and effect of gluten free diet (GFD) on pain in patients with gluten neuropathy. We also investigated its impact on patients' mental status.

Methods
Between 10/2015 and 01/2017 all consecutive patients attending a specialist gluten/neurology clinic, were invited to participate. Pain was assessed via the DN4 questionnaire and the visual analogue scale (VAS). Overall Neuropathy Limitations Scale (ONLS) was used to assess the severity of neuropathy.

The Mental Health Index (MHI-5) was used to measure participants' mental health status.

Results
Fifty five patients (74.5% males) with gluten neuropathy were recruited, age range 45 to 88 years (mean 70.0±9.8 years). Twenty-nine patients (52.7%) were on a strict GFD (Biagi score 3 or 4).

Symmetrical sensorimotor axonal neuropathy was the commonest form of neuropathy (69.1%), followed by sensory ganglionopathy (29.1%) and mononeuritis multiplex (1.8%). The ONLS score ranged from 1 to 7 (mean 3.2±1.8).

Pain was present in 35 patients (63.6%). Pain intensity ranged from 0 to 7 (mean 2.6±2.3) and the maximum intensity ranged from 2 to 10 (mean 7.0±2.3). In 10 patients (18.2%) pain was the first manifestation of PN. Comparison between groups of painful and not painful neuropathy did not show significant differences regarding age, gender, neuropathy severity or neuropathy type. Patients on a gluten free diet were less likely to suffer from pain (70% versus 42.9%, p=0.052). Patients with pain had significantly worse mental health status based on the MHI-5 score (76.6±13.6 versus 85.8±9.6, p=0.01).

Conclusions
Pain is very prevalent in gluten neuropathy and has a significant effect in patients' mental health status. Strict gluten free diet has been shown to improve the neuropathy and this study shows significant reduction in the prevalence of pain for those patients on GFD.

P140

Peer Mentorship Social Groups for Children with Celiac Disease

Weisbrod V[1], Kerzner B[1], Mcmahon J[1], Stern L[1], Hashiguchi L[1], Safra L[1], Potomac R[1]

[1] *Children's National Health System, United States*

Background
To help families newly diagnosed with celiac disease build a strong gluten-free support community, our Celiac Disease Program at Children's National launched the Gluten-Free Buddies Program in late 2016. The goals of the program include: offering children with celiac disease the opportunity to meet other kids managing a gluten-free diet and engaging in peer mentorship activities; securing a meeting place that offers safe gluten-free food options; providing a trained facilitator to help children navigate difficult issues; and allowing parents of the children to meet one another and providing support for issues parents may encounter.

Methods
With the help of two motivated 12-year-old patients, our team designed bi-monthly activities for children ages 4 to 12. Activities included: gluten-free cooking classes; a bouncy-house pizza party; food-themed pottery painting; decorating lessons from gluten-free bakery owners; and dinner outings. Enrollment fees ranged from free to $25 depending on the nature of the activity. Complimentary services are paid by philanthropic support for our Celiac Disease Program.

Results
During the first six months of offering activities, 74 children participated in a Gluten-Free Buddy activity. Initial feedback from participants was uniformly positive, however concerns were consistently raised about the wide range of ages at each event, as well as the lack of availability for teenagers.

Conclusion
To address the concerns, moving forward our CDP will separate the Gluten-Free Buddy activities into three distinct groups: ages 4-6, ages 7-12, and teen ages 13-18. The youngest group will participate in parent/child activities, while the older groups will interact just with a facilitator while their parents meet in a nearby location. Future event plans include additional cooking classes, a baseball game, a trip to the National Zoo, a family picnic, and a visit to a waterpark accompanied by a gluten-free BBQ.

P141

A Comprehensive Digital Resource Center for Gluten-Free Diet Education

Weisbrod V[1], Mcmahon J[1], Stern L[1], Hashiguchi L[1], Kerzner B[1]

[1] *Children's National Health System, United States*

Background
Successful management of a gluten-free diet (GFD) can be significantly challenging for patients newly diagnosed with celiac disease. There are an abundance of resources available on the Internet and via mobile applications, but few are developed maintained by respectable medical institutions. Many applications offer conflicting advice for GFD management and can leave patients feeling confused and overwhelmed as they begin the GFD. To streamline high-quality GFD information, our Celiac Disease Program (CDP) launched a mobile application – The Celiac Disease & Gluten-Free Diet Digital Resource Center. All materials contained within the app were developed and are maintained by a multidisciplinary team including a dietitian, GF nutrition expert, doctor, nurse and chef.

Methods
To build our mobile platform, we partnered with the developer BuildFire. Using their digital platform, we designed an app with six education plugin modules including: Resource Materials; Classes & Events; Education & Cooking Videos; Gluten-Free Recipes; News Digest; and a monthly Podcast. Users can also learn about our CDP team, contact us and share the app. The app is free to download via the iTunes Store and Android Marketplace. Patients visiting our Children's National multidisciplinary CDP Clinic are enrolled at their initial appointment with our education director.

Results
During the first 14-days post-release, there were an average of 91 active users per day. Users accessed an average of 3.76 plugins per app open. The most viewed plugins were Resource Materials (26.8%), Education & Cooking Videos (13.6%), Gluten-Free Recipes (13.2%), Classes & Events (8.8%), and News Digest (8.5%).

Conclusion
Developing a platform to bundle our CDP educational materials has simplified the process of providing information to patients and families. Over the next 12 months, our CDP will continue to track how users engage with the materials and use the information to guide development of future educational tools.

P142

Innovative approaches to gluten-free diet education for children and families

Weisbrod V[1], Stern L[1], Mcmahon J[1], Hashiguchi L[1], Kerzner B[1]

[1] *Children's National Health System, United States*

Background
As the only treatment for celiac disease (CD), proper gluten-free diet (GFD) education is imperative at first diagnosis. Historically, printed manuals were provided in our clinic for GFD education. Anecdotal interactions showed patients needed more than one modality to properly adjust to the GFD. In response, our Celiac Disease Program (CDP) developed multiple educational tools to offer children with CD, their families, and the larger GF community in our region. The interventions were developed by a multidisciplinary team and were aimed at addressing ways in which different populations are best educated.

Methods
The tools offered include: recurring nutrition education and cooking classes; mobile app; series of web-based videos; monthly podcast series; printed handbooks; grocery store simulation game; monthly newsletter; annual GFD Education Day; and regularly scheduled peer-mentorship groups. At initial diagnosis, patients and families are informed about the various offerings and provided with printed materials. Classes and group activities are promoted through flyers handed out in the GI clinic, email communication, and community outreach. Enrollment fees range from free to $25 depending on the nature of the activity. Complimentary services are paid by philanthropic support.

Results
In 2016, our CDP held 41 nutrition education and cooking classes with a total of 1,157 participants. Our CDP produced 10 web-based educational videos that were viewed 2,466 times as of the time of abstract submission. The 2016 GFD Education Day had 1,812 attendees and the peer-mentorship groups had 26 to 35 attendees per event. Initial feedback from participants was consistently positive.

Conclusion
The initial success of the interventions has led to plans for continuation and expansion of the programs. In 2017 we began a systematic assessment to quantitate the impact of the various programs by measuring factors including pre-and-post knowledge, practices, and compliance with GFD. Results will be available later this year.

P143

Depression modifies the association between gluten-free diet adherence and symptoms in patients with celiac disease: analysis of a patient powered research network

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Background
In patients with celiac disease, the effect of depression on the relationship between somatic symptoms and dietary adherence is not well understood. We used a newly created patient powered research network (iCureCeliac®) to explore the effect that depression has on patients' symptomatic response to a gluten-free diet (GFD).

Methods
We identified 519 adults with biopsy-diagnosed celiac disease who answered questions pertaining to symptoms (Celiac Severity Index [CSI]), GFD adherence (Celiac Dietary Adherence Test [CDAT]), and a 5-point, scaled question regarding depressive symptoms.

Results
Among 519 patients, 86% were female and the mean age was 41. Of these 519 patients, 46% indicated that they "somewhat," "quite a bit," or "very much" felt depressed because of their disorder. Depression had a weak-to-moderate correlation with both worsened symptoms (r=0.35, p <0.0001) and poorer GFD adherence (r=0.25, p <0.0001). There was a stronger correlation between worsened symptoms and poorer GFD adherence (r=0.6, p <0.0001). In those with a positive depression screen, there was a moderate correlation between worsening symptoms and worsening dietary adherence (r=0.5, p <0.0001) whereas in those without depression, the correlation was stronger (r=0.64, p <0.0001).

Conclusion
We found a moderate correlation between more severe celiac disease symptoms and depression and a weaker correlation between poor adherence to a GFD and depression. Notably, in patients with a positive depression screen, correlation between poorer adherence and increased symptoms was weaker, suggesting effect modification. Therefore, the presence of depression may mask the relationship between inadvertent gluten exposure and symptoms.

P144

Definition of the purity protocol for producing gluten-free oats

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Background
Several oat processors in the U.S. and Canada operate under what is referred to as a Purity Protocol for the provision of gluten-free oats. This term is derived from a Health Canada position statement which indicated that pure oats, which they defined as oats that are harvested, transported, stored, processed and manufactured under Good Manufacturing Practices (GMPs) to minimize the presence of gluten, can safely be consumed by some persons with celiac disease. While proprietary definitions of the appropriate GMPs have been used in industry for many years, no independent definition of the requirements to make a Purity Protocol claim has been published.

Method
This presentation provides a consensus definition of the Purity Protocol requirements based on input from the four largest Purity Protocol oat processors in North America.

Conclusion
This definition provides transparency to gluten-free consumers and allows for auditing of Purity Protocol claim.

P145

The celiac patient antibody response to conventional and gluten-removed beer

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Background
Enzymatic digestion, or hydrolysis, has been proposed for treating gluten-containing foods and beverages to make them safe for persons with celiac disease (CD). There are no validated testing methods that allow the quantification of all the hydrolyzed or fermented gluten peptides in foods and beverages that might be harmful to CD patients, making it difficult to assess the safety of hydrolyzed products. This study examines an ELISA-based method to determine whether serum antibody binding of residual peptides in a fermented barley-based product is greater among active-CD patients than a normal control group, using commercial beers as a test case.

Method
Sera from 31 active-CD patients and 29 non-celiac control subjects were used to assess the binding of proteins from barley, rice, traditional beer, gluten-free beer, and enzymatically treated (gluten-removed) traditional beer.

Results
In the ELISA, none of the subjects' sera bound to proteins in the gluten-free beer. Seven active - CD patient serum samples demonstrated immunoglobulin A (IgA) binding to a barley extract, compared to only one non-celiac control subject. Of the seven active-CD patients who had an IgA binding response to barley, four also responded to traditional beer, and two of these responded to the gluten-removed beer. None of the non-celiac control subjects' sera bound to all three beer samples.

P146

The use of visual examination for determining the presence of gluten containing grains in gluten-free whole commodities

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Background
The adventitious presence of wheat, rye, barley and related gluten-containing grains (GCG) in other cereals, beans, pulses, legumes and seeds presents a major risk for manufacturers and consumers of gluten-free foods. These commodities can share many steps of the supply chain with GCG, including being grown in the same fields, harvested with the same equipment, transported on the same vehicles, stored in the same facilities and processed in the same mills. Current methods for detecting GCG in other commodities include the use of ELISA and lateral flow methods, but because of the large particle size of the materials, large sample volumes and sample numbers are required. Grinding these samples to obtain representative sub-samples for testing can be challenging as gluten tends to aggregate in clumps rather than distribute uniformly in flour. This study proposes the use of visual counts of GCG within other commodities as a complementary method to detect gluten in non-gluten whole commodities.

Method
This study proposes a threshold for the allowable number of GCG per kilogram of non-GCG, with the goals of meeting the GFCO threshold of 10 ppm and minimizing gluten exposure to the gluten-free consumer. The study also outlines sampling plans and acceptance criteria using operating characteristic (OC) curves to demonstrate the risks to the public as well as the producer. Finally, the study examined data from two oat producers to demonstrate the feasibility of meeting the proposed threshold with current processing techniques.

Results
Data from two independent oat producers indicates that the proposed threshold is attainable, and can be met consistently over growing seasons.

Conclusion
This threshold and the sampling plans proposed in this study can be applied across any whole commodity, and provide an additional quantitative measure of gluten contamination in gluten-free grains, seeds, beans, pulses and legumes.

P147

Evaluation of the importance of education on the gluten free diet in patients with celiac disease

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[2]*Thomas Jefferson University Hospital, United States*

Background
The only current treatment for celiac disease (CeD) is the gluten-free diet (GFD) which requires major lifestyle changes. The NIH recommends patient education as a key element in effective CeD management. Studies have shown that patients are frequently dissatisfied with the information provided by physicians. This study reports Celiac Dietary Adherence Test scores for adult patients seen at Jefferson both before and after receiving an educational packet, as compared to community patients with CeD, who did not receive the packet. This packet, developed in collaboration with the advocacy organization, Beyond Celiac, includes detailed information on: the GFD, lifestyle changes, counseling for family members, and other associated conditions.

Methods
Study cohort comprises 75 patients followed at Jefferson upon diagnosis with CeD, 56 of which completed the survey after receiving the CeD educational packet, as well as 58 community patients that completed the survey during a first-round send-out, and 48 of which completed the survey on a follow-up send-out. Age and sex were similar in both groups. All participants completed the online survey anonymously.

Results
In the Jefferson patients, the mean CDAT score increased by 27.9, from 9.413 to 37.34 ($p < 0.001$, 95% CI). The mean CDAT score increased by 7.15, from 32.897 to 40.417 ($p=0.0002$; 95% CI 3.23 to 11.05) in community patients. Using the Fisher's exact test, the difference in the results of the two groups is statistically significant ($p<0.01$).

Conclusion
Patient education in addition to clinical follow-up is essential in treating patients with CeD. The significant increase in GFD adherence in patients who received the educational packet in comparison to the patients who did not receive the packet emphasizes the importance of patient education and follow-up. The difference in the baseline scores CDAT scores between Jefferson and community patients may reflect disparities in access to educational resources.

P148

Alternative grain intake among teenagers with celiac disease: a prospective cross sectional study

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Background
The only treatment for Celiac Disease (CeD) is lifelong adherence to a gluten-free diet (GFD), but nutritional intake on a GFD can be deficient. Inclusion of whole gluten-free grains other than white rice could correct this deficiency, as processing decreases nutrient content. The present study examines consumption of whole, processed and alternative grains.

Methods
We performed a cross sectional study of thirty 13-17 year olds with biopsy-confirmed CeD on a GFD. Dietary intake was assessed using three 24hr multiple pass recalls over a one month period, focusing on whole or processed products containing brown rice, buckwheat, quinoa, millet, amaranth, oats, teff, or sorghum. Level of processing was assessed with a modified version of the NOVA food classification.

Results
Among the 30 teenagers, 86.7% reported consuming at least one alternative grain product over three days of intake; 43.3% reported unprocessed or minimally processed alternative grain products, 83.3% reported ultra-processed products, 16.7% reported processed products. Across 88 recall days (two missing recalls), the mean number of alternative grain products consumed was 1.3; the maximum was 4 (reported on two occasions). Among the 117 instances of alternative grain consumption the primary grain sources were brown rice (73.5%) and oats (22.2%). Top unprocessed

or minimally processed products were brown rice and cooked oats. Top processed and ultra processed products were gluten free breads (e.g., Udi's breads, bagels), cold cereals (e.g., Cheerios, Chex), and granola-type bars (e.g., Kind Bars).

Conclusion
Although alternative grains were found in most teens' diets, sources were primarily processed or ultra-processed foods containing brown rice and oats. Gluten-free grains such as buckwheat, quinoa, millet, amaranth, teff, and sorghum were consumed infrequently and rarely as a whole grain. Teenagers may benefit from nutrition education to promote fiber and nutrient rich alternative gluten-free grains in their diet, particularly in their natural form.

P149

Effect of a tailored, culturally competent, celiac disease awareness program on referral rates from a strict Orthodox Jewish Community

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Background
In the United States, Celiac Disease (CD) educational programs have largely been singular and homogenous with one distinct message. However, with a diverse population made up of various cultural and racial groups, a more tailored and multi-pronged approach may be more effective. The primary objective was to assess if a tailored community outreach program for CD education and awareness would increase patient referral rates from a specific cultural group.

Methods
The number of CD-specific referrals from the zip code 08701 from May 2009 to April 2013 was retrospectively retrieved from electronic billing records at the Children's Hospital of Philadelphia (CHOP).

The multi-pronged outreach program, initiated in May 2011, was tailored towards a nearby strict-Orthodox Jewish community. The program included:

1. Assessment of barriers to screening for CD with community pediatricians followed by specific tailored education

2. Creation of an expedited appointment pipeline for patients referred from the trained community pediatricians

3. Development of culturally specific resources and support for diagnosed patients

Results
In the two years prior to the introduction of the outreach program (May 2009-April 2011), 11 unique patients from zip code 08701 were seen for CD at CHOP. In the subsequent two years (May 2011-April 2013), 69 patients were seen. The Celiac Center at CHOP saw a 6.27-fold increase in unique patients from zip code 08701 after implementation of the community outreach program.

Conclusion
Tailoring education to a specific cultural group can have an impact as seen with the 6.27-fold increase in patients seen after implementation of the program. While this program was tailored specifically to the Orthodox Jewish community, the methods may be translated to other communities. The success lies in the model of taking education to nontraditional settings and developing trust and respect in a community. Future studies should implement this strategy in other populations to assess generalizability.

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Gutowski	E		75
Haak	S	10	
Hadjivassiliou	M	7	85
Haere	P		36
Haghbin	M		31,45
Hagopian	W	8,13	
Hajifathali	A		70
Hakansson	A		84
Halmos	EP		74
Hashiguchi	L		38,86,87
Hauptmann	M		67
Heijmans	R		47
Heil	A		78
Henriksen	C		71
Hermine	O	14	
Heydari	F		69
Hijmering	N	13	70,71
Hilmer	A		50
Hils	M		78
Hiltunen	P		52
Hinterleitner	R	15	
Hlywiak	K		90
Hoggard	N	7	
Hoie	O		36
Hooda	U		29
Hosiynee	M		32
Hosking	P		73
Huhtala	H		65,76,77
Humaidan	P	12	
Hussien	H		20
Iltanen	S		65
Ilus	T		76
Iqbal	A		28,79
Isabel	C		57
Ismail Ali	J		73
Iverson	G		88
Jabri	B	9,15,16	
Jagannathan	N		24
Jain	A		28
Jain	R		52
Janowski	R		89
Jansen	T		82
Jensen	T	12	
Jeremias	P		47,66,67
Jhajharia	A		41
Jhamb	I		25
Jinga	M		21
Joelson	A		87
Joshi	A		28
Jouanin	A		83
Kalinina	E		56
Kapoor	S		52
Kapur	D		79

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Kaukinen	K		21, 51, 52, 65, 76, 77
Kaur	G		69
Kaushik	M		51
Kelly	C		39, 63
Kerzner	B		38, 86, 87
Khadgawat	R		28, 29
Khanna	G		24
Khater	S	14	60
Khosla	C	6, 9, 16	50
Kim	S	9	
Kivela	L		21, 51, 76
Knowles	S		74
Kochhar	R		25, 26, 27, 30, 69, 78
Koirala	S		46
Kokhaee	P		45
Koletzko	S		22
Koning	F	9, 13	64
Konopka	E		37
Kooy Winkelaar	Y	9	
Korponay Szabo	I		22
Koshki	K		64
Kotru	M		54
Krawitz	S		89
Krischer	J	8, 13	
Krishnareddy	S	10	
Kroger	S		21
Krol	E		49
Kumar	L	6	
Kumar	T		43
Kumar	P		52
Kumazawa	Y		78
Kupfer	S	15	
Kupper	C		88
Kurada	S		39
Kurppa	K	8, 13	51, 52, 57, 65, 76, 77
Kutum	R		43
Lahdeaho	M		76
Laitinen	A	8	
Lamprea Moruno	M		49
Lania	G	11	55
Lapin	S		56
Larretxi	I		83, 84
Lasa	A		83, 84
Laurikka	P		76
Laurila	K		21
Lavin	P		40
Lebwohl	B		87
Lebwohl	B	10	89
Lee	H	8, 13	57
Lee	A		89
Leffler	D		39, 63, 68
Leigh	F		83
Leinonen	H		76
Lejeune	T	9	
Leon	F		83
Leonard Puppa	E		59
Lerner	A		47, 66, 67

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Lernmark	A	8, 13	57
Lesko	K		88
Lewis	S	10	
Lhermitte	L	14	
Lhospice	F	14	
Li	X		50
Limongelli	M	10	
Lindfors	K	8	52, 76
Lionetti	E	12	34
Liu	E	8	
Lomash	A		52
Lombardo	C		46
Lundin	K		36, 39, 46, 71
M Hard af Segerstad	E		57
Macfaul	G		73
Macintyre	E	14	
Madhotra	R		73
Maglio	M	11	55
Mahler	M		40
Maiorano	G		41
Maiti	P		25
Majsiak	E		37
Makharia	GK	6, 7	22, 24, 27, 28, 29, 34, 43, 48, 51, 60, 63, 79
Maki	M		21, 51, 65, 76
Malamisura	B	10	
Malamut	G	14	21, 60
Malhotra	A		60
Malik	R		27
Malik	A		30
Mamone	G		80
Manchanda	V		54
Mandal	P		51
Mandile	R	11	
Mantha	A		69
Marchesini	A	12	
Marietta	E	9	
Martinez	O		84
Massitti	M	10	
Matthias	T		47, 66, 67, 68
Mayilraj	S		69
Mckiernan	D		88
Mcmahon	J		86, 87
Mearin	LM		22, 35
Mearns	E		68
Medhi	B		26, 27, 78
Mehtab	W		60
Meijer	C	13	70, 71
Meresse	B	14	
Meri	S		77
Messing	M		77
Meyer	S		54
Miele	E	10, 11	
Miller	S		77
Milo J	J		40
Minelle	I		71
Miranda	J		83, 84
Mirfeizi	Z		42

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Mishra	A		26, 27, 43, 48
Mockler	D		59
Moesbergen	L	13	70, 71
Mohaghegh	H		80
Mohaghegh Shalmani	H		60
Mohebalian	A		44
Moleski	S		89
Molin	G		84
Molina	T	14	
Monachesi	C	12	
Monje	J		49
Montuori	M		55
Mora	B		55
Moradi	A		31, 45
Morkrid	L		36
Morre	S		47
Mosanen Mozafari	H		32
Muir	J		71
Mukerji	M		43
Mulder	C	13	40, 49, 67, 70, 71, 82
Mullan	B		74
Munoz Suano	A		83
Munozsuano	A		57
murray	J	6, 9, 16	
Nakhcha	I		34, 35, 42
Nanayakkara	M	11	55
Narang	M		54, 59
Nasyrov	R		56
Natarajan	R		54
Navarro	V		83
Nayak	B	6	
Neidhoefer	S		66
Newland	C		58
Newnham	E		73
Ng	A		89
Nichols	M		90
Nijeboer	P		67
Nijhawan	S		26, 41
Nikzamir	M		61
Norman	G		40
Norris	J	13	57
Not	T	8	
Nouri Hosseini	G		32
Novikova	V		56
Ohsam	J		78
Oittinen	M		76
Opri	R		33
Oralewska	B		37
Oscarsson	E		84
Oudejans	J	13	71
Overbeek	L		67
Padhye	L		58
Pahuja	A		59
Palanski	B		50
Palpacelli	A	12	
Pandey	T		27
Pandey	R		43

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Panelli	S		46
Papa	A		62
Parfenov	A		62, 63
Parr	A		73
Pasternack	R		78
Patton	T		58
Pekki	H		77
Pena	S		47
Perry	T		88
Perumal	R	7	
Petersen	J	9, 15	
Picascia S	S		48, 81
Pizzuti	A		55
Podojil	J		77
Polanco	I		22
Polipalli	S		52
Popp	A		21
Potomac	R		86
Pourhoseingholi	M		44, 45, 61
Pouyet	L	14	
Prabu	O		30
Prager	K		67
Prakash	S	6	
Prasad	K		25, 78
Puri	A		54
Pyser	C		85
Qiao	S	15	36
Rad	N		31, 64
Radersma	M	13	70, 71
Radersma	M		70
Radovic	S		65
Rai	A		43
Rajabpourborj	S		42
Ramadass	B		22
Ramakrishna	BS		22
Ramlauhansen	C	12	
Ramteke	P		24
Rana	S		30
Rao	D	7	85
Rapaccini	G		62
Rawat	R		24
Rayner	M		57
Reid	H	9, 15	
Reijm	M	13	47, 49
Reizis	B	10	
Repo	M		52
Revnova	M		56
Rewers	M	8, 13	
Ribes Koninckx	C		22
Rigaux	L		75
Ripoll	O	12	
Rismantab	S		31
Rodriguez Herrera	A		49, 57, 83
Rohatgi	S		52
Rolfsen	K		71
Romano	A		62
Roovers	L		35, 82

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Rosenblum	S		54
Rossjohn	J	9,15	
Rostami	K		31,44,45,61,64,69,70,73,80,81
Rostami Nejad	M		31,44,45,61,64,69,70,73,80,81
Russell	A		20
Ryee	M		38
Saavalainen	P		65
Sabelnikova	E		38,62,63
Sadeghi	A		31,45,61,64,70,80,81
Safra	L		86
Sahl	C		77
Saini	S		27,43
Sainsbury	K		74
Salamone	D	10	
Salmi	T		76
Sanders	D	7	85
Santarlasci	V		48
Santosh	B	7	
Sarma	P		26,27,78
Sarna	V		36,39,46,71
Sarrgiannis	P	7	
Sarrigiannis	P		85
Scapaticci	S	11	
Scattolo	N	12	
Schaart	J		83
Schiepatti	A		41,46
Sealey Voyksner	J	6,16	40
Segura	V		57
Selvarajah	J		73
Semrad	C		
Senler	T		82
Shah	D		54,59
Shahrokh	S		64
Shanmugarajah	P	7	
Shapovalova	N		56
Sharma	U		24
Sharma	S		30
Sharma	P		43
She	J	8,13	
Shea	L		77
Shepherd	S		73
Sherine	K		21
Shetty	S	7	
Shouche	Y	7	
Shums	Z		40
Sibon	D	14	
Sidappa	P		25
Silvester	J		75
Simon	E		83,84
Singh	A	6	24,26,27,28,29,34,43,58,51,78,79
Singh	K		25
Singh	R		26,78
Singh	P		27,63
Singh	I		29
Singh	S		43
Singh	T		43
Singh	N		60

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Sinha	S		25,26,30,51
Sircar	S		28
Sjoholm	I		57
Skodje	G		39
Smamir	R		22
Smeets	L		47
Smith	S		88
Smulders	M		83
Snir	O		46
Snyder	J		38
Sollid	L	15	36,39,46
Soni	S		28,29
Sotka	A		52
Sousa	C		57,83
Sowa	P		89
Srinivasan	P		22
Srivastava	A		29
Steinhoff	J		90
Stencel Baerenwald	J	15	
Stephen	R		88
Stern	L		38,86,87
Strand	T		63
Sturton	W		89
Syage	J	6,16,	40
Szajewska	H		22
Taavela	J		21
Tagaya	Y	16	
Taylor	A		68
Tetteh	A		64
Thapa	B		26,27
Ting	Y	15	
Tooth	C		85
Toppari	J	8,13	
Trevisan	M	12	
Trinquand	A	14	
Trojanowska	I		37
Troncone	R	8,10,11	22,48,55,61
Trovato	C		55
Tyagi	B		51
Tye Din	JA		20,74
Uhde	M	10	50
Upadhyay	D		24
Upadhyay	S		69
Urquiaga	M		39
Uusitalo	U	13	57
Vadola	V		48
Vaiphei	K		25
Valenta	R		22
Valitutti	F		55
Van Bergen	J	13	
Van De Water	J	13	70,71
Van Der Horst	H		82
Van Der Laan	J		82
Van Der Werf	J		47
Van Genugten B	B		78
Van Gils	T		49,82
Van Leeuwen	F		67

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Van Wunnik	P		47
Vanbergen	J	9	
Veierd	M		71
Venneri	A		85
Venugopal	G		22, 63
Verhage	J		35
Verkarre	V	14	
Verma	A	6, 7, 12	24, 29, 34, 48
Verma	R		58, 72, 909
Viitasalo	L		65
Villafuerte Galvez	J		39
Virtanen	S	13	57
Vishnubatla	S		24
Visser	R		83
Vitale	S		48
Volta	U		33, 50
Von Hoogstraten	I		40
Voorhees	K		89
Wahab	P		82
Walker	J		75
Wallington	E		83
Wang	S		20, 39
Wanjari	S		26
Webster	R		74
Weisbrod	V		38, 86, 87
Weiten	D		75
Wessels	M		35, 82
Williams	L		20, 39
Wise	J		64
Wolf	R		89
Yadav	R		27
Yadav	A		39
Yadav	P		79
Yang	J	13	57
Yokoyama	K		78
Yoo	J		89
Zabolotsky	A		89
Zagroba	M		37
Zali	M		44, 45, 69, 70, 80, 81
Zanoni	G		33
Ziegler	A	8, 13	
Zindal	G	6	
Zis	P	7	85
Zuehlke	S		46
Zuffada	M		41
Zurenski	M	9	
Zybert	P		89
Zylberberg	H		87

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