Mind, Mood & Food Webinar Series

Presented by the Center for Mind-Body Medicine and hosted by Kathie Madonna Swift, MS, RDN, LDN.
Leaky Gut: Fact or Fantasy?

Presented by:
Sheila Dean, DSc, RDN, LDN, CCN, CDE, IFMCP
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Disclosure

• Co-founder of the Integrative and Functional Nutrition Academy™
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• IFNA™ offers the IFNCP™, Integrative and Functional Nutrition Certified Practitioner Advanced Practice Credential
Learning Objectives

• Describe the relationship between food exposure (i.e. gluten) and intestinal permeability
• Explain the relationship between intestinal permeability and inflammation
• Discuss the relationship between inflammation and the spectrum of chronic disease
• Identify a medical nutrition therapy (MNT) based treatment plan
“Leaky gut” = Intestinal permeability
The Big Picture

Trigger → intestinal permeability - aka “leaky gut”

Leaky gut → Immune/Inflammatory response

Immune/inflammatory response → Chronic disease
Intestinal permeability – a new target for disease prevention and therapy

Stephan C Bischoff¹, Giovanni Barbara², Wim Buurman³, Theo Ockhuizen⁴, Jörg-Dieter Schulzke⁵, Matteo Serino⁶, Herbert Tilg⁷, Alastair Watson⁸ and Jerry M Wells⁹
<table>
<thead>
<tr>
<th>Table 1 Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intestinal barrier</strong></td>
</tr>
<tr>
<td><strong>Intestinal permeability</strong></td>
</tr>
<tr>
<td><strong>Normal intestinal permeability</strong></td>
</tr>
<tr>
<td><strong>Impaired intestinal permeability</strong></td>
</tr>
</tbody>
</table>

Source: Bischoff, et al BMC Gastroenterology, 2014 (see previous slide)
Learning Objectives

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Depiction of immunological mechanisms underlying gluten intolerance and its immunopathological consequences.

Source: http://glutensensitivity.net/VojdaniDiagrams.htm#HG
We now recognise that the functional state of the tight junction, once considered a static parameter, is in reality incredibly dynamic. Epithelial tight junctions open and close all the time in response to a variety of stimuli. These include dietary state, humoral or neuronal signals, inflammatory mediators, mast cell products, and a variety of cellular pathways that can be usurped by microbial or viral pathogens.
Zonulin is the only physiologic modulator of intercellular tight junctions described so far that is involved in the trafficking of macromolecules and therefore in tolerance/immune response balance. When the zonulin pathway is deregulated in genetically susceptible individuals, autoimmune disorders can occur.
“TID” triggers of intestinal permeability

- Toxins
- Infection
- Dietary proteins
Glyphosate, pathways to modern diseases II: Celiac sprue and gluten intolerance

Anthony SAMSEL 1 and Stephanie SENEFF 2
1 Independent Scientific Consultants, Duxbury, MA 01826, USA
2 Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA, USA

ABSTRACT
Celiac disease, and more generally, gluten intolerance, is a growing problem worldwide, but especially in North America and Europe, where an estimated 5% of the population now suffers from it. Symptoms include nausea, diarrhea, skin rashes, macrocytic anemia and depression. It is a multifactorial disease associated with numerous nutritional deficiencies as well as reproductive issues and increased risk to thyroid disease, kidney failure and cancer. Here, we propose that glyphosate, the active ingredient in the herbicide Roundup®, is the most important causal factor in this epidemic. Fish exposed to glyphosate develop digestive problems that are reminiscent of celiac disease. Celiac disease is associated with imbalances in gut bacteria that can be fully explained by the known effects of glyphosate on gut bacteria. Characteristics of celiac disease point to involvement in many cytochrome P450 enzymes, which are involved with detoxifying environmental toxins, activating vitamin D3, catalyzing vitamin A, and maintaining tryptophan production and sulfate supplies to the gut. Glyphosate is known to inhibit cytochrome P450 enzymes. Deficiencies in iron, cobalt, molybdenum, copper and other metals associated with celiac disease can be attributed to glyphosate’s strong ability to chelate these elements. Deficiencies in tryptophan, tyrosine, methionine, and selenomethionine associated with celiac disease match glyphosate’s known depletion of these amino acids. Celiac disease patients have an increased risk to non-Hodgkin’s lymphoma, which has also been implicated in glyphosate exposure. Reproductive issues associated with celiac disease, such as infertility, miscarriages, and birth defects, can also be explained by glyphosate. Glyphosate residues in wheat and other crops are likely increasing recently due to the growing practice of crop desiccation just prior to the harvest. We argue that the practice of “ripening” sugar cane with glyphosate may explain the recent surge in kidney failure among agricultural workers in Central America. We conclude with a plea to governments to reconsider policies regarding the safety of glyphosate residues in foods.

KEY WORDS: celiac, sprue, gluten, glyphosate, food, cytochrome P450, deficiency
Glyphosate Testing now available

GLYPHOSATE
GENERAL
Glyphosate is the world’s most widely produced herbicide and is the primary toxic chemical in Roundup™, as well as in many other herbicides. In addition, it is a broad-spectrum herbicide that is used in more than 700 different products from agriculture and forestry to home use. Glyphosate was introduced in the 1970s to kill weeds by targeting the enzymes that produce the amino acids tyrosine, tryptophan, and phenylalanine. The enzymes of many bacteria are also susceptible to inhibition by this chemical, thus altering the flora of many animals. Usage of glyphosate has since amplified, after the introduction of genetically modified (GMO) glyphosate-resistant crops that can grow well in the presence of this chemical in soil. In addition, toxicity of the surfactant commonly mixed with glyphosate, polyoxyethyleneamine (POEA), is greater than the toxicity of glyphosate alone (1). In addition, in 2014 Enlist Duo™, a herbicide product which contains a 2,4-dichlorophenoxyacetic acid (2,4-D) salt and glyphosate, was approved for use in Canada and the U.S. for use on genetically modified soybeans and genetically modified maize, both of which were modified to be resistant to both 2,4-D and glyphosate. 2,4-D has many toxic effects of its own and can be measured in the GPL-TOX test.
“TID” triggers of intestinal permeability

- Toxins
- Infection
- Dietary proteins
“This finding supports the view that IP increases during the course of protozoan infections which cause damage to the intestinal wall while non-pathogenic protozoan infections have no effect on IP. The increase in IP in patients with *B. hominis* brings forth the idea that *B. hominis* can be a pathogenic protozoan.”
these studies show for the first time that LPS causes an increase in intestinal permeability.
When the finely tuned zonulin pathway is deregulated in genetically susceptible individuals, both intestinal and extraintestinal autoimmune, inflammatory, and neoplastic disorders can occur.
Increased circulating zonulin in children with biopsy-proven nonalcoholic fatty liver disease

Lucia Pacifico, Enea Bonci, Lidia Marandola, Sara Romaggioli, Stefano Bascetta, Claudio Chiesa

Lucia Pacifico, Sara Romaggioli, Stefano Bascetta, Department of Pediatrics and Child Neuropsychiatry, Sapienza University of Rome, 00161 Rome, Italy
Enea Bonci, Lidia Marandola, Department of Experimental including zonulin, inflammatory and metabolic parameters, and MRI for measurement of HFF and visceral adipose tissue.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No NAFLD (n = 40)</th>
<th>NAFLD (n = 40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>11.10 (3.1)</td>
<td>11.10 (3.1)</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>25 (62.5)</td>
<td>25 (59.5)</td>
<td>0.5600</td>
</tr>
<tr>
<td>BMI-SD score</td>
<td>2.10 (0.32)</td>
<td>2.15 (0.50)</td>
<td>0.0270</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>92 (12)</td>
<td>97 (12)*</td>
<td></td>
</tr>
<tr>
<td>Abdominal fat</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visceral adipose tissue, cm²</td>
<td>284 (217-502)</td>
<td>447 (337-676)</td>
<td>0.0040</td>
</tr>
<tr>
<td>Subcutaneous adipose tissue, cm²</td>
<td>1648 (1301-2503)</td>
<td>1828 (1629-2471)</td>
<td>0.2200</td>
</tr>
<tr>
<td>Hepatic fat fraction</td>
<td>1.5% (1.0%-3.0%)</td>
<td>16.0% (10.0%-30.0%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>81 (52-114)</td>
<td>96 (68-149)</td>
<td>0.0490</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>154 (142-185)</td>
<td>149 (130-179)</td>
<td>0.1100</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td>49 (43-54)</td>
<td>45 (37-53)</td>
<td>0.3100</td>
</tr>
<tr>
<td>Aspartate aminotransferase, U/L</td>
<td>25 (11)</td>
<td>34 (26)</td>
<td>0.0370</td>
</tr>
<tr>
<td>Alanine aminotransferase, U/L</td>
<td>26 (17)</td>
<td>50 (43)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>γ-glutamyl transferase, U/L</td>
<td>15 (8)</td>
<td>23 (12)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>85 (6)</td>
<td>83 (8)</td>
<td>0.3300</td>
</tr>
<tr>
<td>2-h glucose, mg/dL</td>
<td>94 (13)</td>
<td>93 (14)</td>
<td>0.8700</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>11 (8-15)</td>
<td>20 (15-28)</td>
<td>0.0010</td>
</tr>
<tr>
<td>2-h insulin, μU/mL</td>
<td>35 (23-63)</td>
<td>67 (29-107)</td>
<td>0.0070</td>
</tr>
<tr>
<td>Fasting C peptide, pmol/L</td>
<td>780 (576-887)</td>
<td>1075 (816-1302)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>HOMA-IR values</td>
<td>2.24 (1.80-3.17)</td>
<td>4.11 (2.95-6.67)</td>
<td>0.0030</td>
</tr>
<tr>
<td>WBISI</td>
<td>5.84 (3.16-6.87)</td>
<td>2.57 (1.58-5.36)</td>
<td>0.0020</td>
</tr>
<tr>
<td>HbA1c</td>
<td>5.0% (0.32)</td>
<td>5.4% (0.47)</td>
<td>0.0170</td>
</tr>
<tr>
<td>HSCRP, ng/L</td>
<td>1800 (1000-3200)</td>
<td>2000 (1500-4325)</td>
<td>0.0490</td>
</tr>
<tr>
<td>Zonulin, ng/mL</td>
<td>3.31 (2.05-4.63)</td>
<td>4.23 (3.18-5.89)</td>
<td>0.0090</td>
</tr>
</tbody>
</table>

1Matched variables. Results are expressed as n (%), mean ± SD, or median (IQR). BMI-SDS: Body mass index-standard deviation score; HDL-C: High-density lipoprotein cholesterol; HOMA-IR: Homeostasis model assessment of insulin resistance; WBISI: Whole-body insulin sensitivity index; HbA1c: Haemoglobin A1c; HSCRP: High-sensitive C reactive protein; NAFLD: Nonalcoholic fatty liver disease.
ZOOM IN TO KNOW IF WHEAT IS THE SOURCE OF YOUR PROBLEMS

THE WHEAT ZOOMER

Your celiac blood test came out negative but you still do not feel well. Want to find out why?

ORDER NOW
### Final Report Date:
05-06-2016 15:08

### Specimen Collected:
11-30-2015

### Accession ID:
1512010000

### Specimen Received:
12-01-2015 00:00

<table>
<thead>
<tr>
<th>Last Name</th>
<th>First Name</th>
<th>Middle Name</th>
<th>Date of Birth</th>
<th>Gender</th>
<th>Physician ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>TESTNAME</td>
<td>PATIENT</td>
<td>VIBRANT</td>
<td>1994-10-10</td>
<td>Female</td>
<td>999994</td>
</tr>
</tbody>
</table>

### HLA Type Tested

<table>
<thead>
<tr>
<th>HLA Type</th>
<th>Results</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>DQ2.2</td>
<td>NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>DQ2.5</td>
<td>NEGATIVE</td>
<td></td>
</tr>
<tr>
<td>DQ7</td>
<td>POSITIVE</td>
<td></td>
</tr>
<tr>
<td>DQ8</td>
<td>POSITIVE</td>
<td></td>
</tr>
</tbody>
</table>

Patient is at risk for developing celiac disease.

### Leaky Gut Panel

<table>
<thead>
<tr>
<th>Test Name</th>
<th>In Control</th>
<th>Moderate</th>
<th>High Risk</th>
<th>In Control Range</th>
<th>Moderate Range</th>
<th>High Risk Range</th>
<th>Previous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zonulin (ng/mL)</td>
<td>&lt;10.0</td>
<td></td>
<td></td>
<td>&lt;=45.3</td>
<td>45.4-55.3</td>
<td>&gt;=55.4</td>
<td>&lt;10.0 08/20/2015</td>
</tr>
<tr>
<td>Anti-Zonulin IgG</td>
<td>0.60</td>
<td></td>
<td></td>
<td>&lt;=0.94</td>
<td>0.95-1.05</td>
<td>&gt;=1.06</td>
<td>0.77 08/20/2015</td>
</tr>
<tr>
<td>Anti-Zonulin IgA</td>
<td>0.05</td>
<td></td>
<td></td>
<td>&lt;=0.94</td>
<td>0.95-1.05</td>
<td>&gt;=1.06</td>
<td>0.20 08/20/2015</td>
</tr>
<tr>
<td>Anti-Actin IgG</td>
<td>0.31</td>
<td></td>
<td></td>
<td>&lt;=0.94</td>
<td>0.95-1.05</td>
<td>&gt;=1.06</td>
<td>0.67 08/20/2015</td>
</tr>
<tr>
<td>Anti-Actin IgA</td>
<td>0.73</td>
<td></td>
<td></td>
<td>&lt;=0.94</td>
<td>0.95-1.05</td>
<td>&gt;=1.06</td>
<td>0.09 08/20/2015</td>
</tr>
<tr>
<td>LPS IgG (U/ml)</td>
<td>&lt;6.3</td>
<td></td>
<td></td>
<td>&lt;=60.0</td>
<td>60.1-80.0</td>
<td>&gt;=80.1</td>
<td>&lt;6.3 08/20/2015</td>
</tr>
<tr>
<td>LPS IgM (U/ml)</td>
<td>&lt;6.3</td>
<td></td>
<td></td>
<td>&lt;=38.3</td>
<td>&gt;=38.4</td>
<td>&gt;=38.4</td>
<td>&lt;6.3 08/20/2015</td>
</tr>
</tbody>
</table>
ADVANCED INTESTINAL BARRIER ASSESSMENT: PROFILE 5150 (PLASMA)

**DAO (Diamine Oxidase)**
- **Patient Result:** 46.0 ng/ml
- **Reportable Range:** 10.0-36.0 ng/ml

**Zonulin**
- **Patient Result:** 0.92 ng/ml
- **Reportable Range:** <3.0 ng/ml

**Histamine**
- **Patient Result:** 1.62 ng/ml
- **Reportable Range:** 0.1-3.1 ng/ml

**DAO: Histamine Ratio**
- **Result:** 28

A high DAO:Histamine ratio suggests that there is sufficient DAO present to degrade any free histamine. A low ratio, on the other hand, may be indicative of histamine intolerance. The lower the ratio, and particularly the closer it gets to 1, the stronger that indication.
Doctor's Data offers scores of distinct tests across key categories:

- Allergy & Immunology
- Bloodspot
- Cardiovascular
- Clinical Microbiology
- Endocrinology
- Environmental Exposure/Detoxification
- Nutritional
- Toxic & Essential Elements

**Doctor's Data now offers**

*Metabolomic Profiles and Zonulin testing!*
Zonulin Test Summary

Sample Type/Collection/Stability/Shipping

It is recommended that patients refrain from taking probiotics for 14 days and antibiotics for 28 days prior to sample collection or as directed by the healthcare provider.

Stool samples should be refrigerated immediately after collection and shipped with cold icepacks to Salveo Diagnostics. Zonulin is stable for up to 4 days at room temperature.

Description/Background Information

Zonulin - the “Gatekeeper” of Intestinal Permeability
“TID” triggers of intestinal permeability

Toxins

Infection

Dietary proteins
Just the basics: What is gluten?

* Gluten is a mixture of proteins found in wheat and related grains, including all their species and hybrids. It is composed of two primary subfractions:
  * Prolamines
  * Glutelins
The Prolamine Fraction of Proteins in Grains

<table>
<thead>
<tr>
<th>GRAIN</th>
<th>PROLAMINE</th>
<th>% TOTAL PROTEIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wheat</td>
<td>Gliadin</td>
<td>69</td>
</tr>
<tr>
<td>Rye</td>
<td>Secalinin</td>
<td>30-50</td>
</tr>
<tr>
<td>Oats</td>
<td>Avenin</td>
<td>16</td>
</tr>
<tr>
<td>Barley</td>
<td>Hordein</td>
<td>46-52</td>
</tr>
<tr>
<td>Millet</td>
<td>Panicin</td>
<td>40</td>
</tr>
<tr>
<td>Corn</td>
<td>Zien</td>
<td>55</td>
</tr>
<tr>
<td>Rice</td>
<td>Orzenin</td>
<td>5</td>
</tr>
<tr>
<td>Sorgum</td>
<td>Kafirin</td>
<td>52</td>
</tr>
</tbody>
</table>

Source: http://www.nutramed.com/celiac/gluten.htm
Figure 1 Proposed new nomenclature and classification of gluten-related disorders.

Gliadin, zonulin and gut permeability: Effects on celiac and non-celiac intestinal mucosa and intestinal cell lines.


Abstract

OBJECTIVE: Little is known about the interaction of gliadin with intestinal epithelial cells and the mechanism(s) through which gliadin crosses the intestinal epithelial barrier. We investigated whether gliadin has any immediate effect on zonulin release and signaling.

MATERIAL AND METHODS: Both ex vivo human small intestines and intestinal cell monolayers were exposed to gliadin, and zonulin release and changes in paracellular permeability were monitored in the presence and absence of zonulin antagonism. Zonulin binding, cytoskeletal rearrangement, and zonula occludens-1 (ZO-1) redistribution were evaluated by immunofluorescence microscopy. Tight junction occludin and ZO-1 gene expression was evaluated by real-time polymerase chain reaction (PCR).

RESULTS: When exposed to gliadin, zonulin receptor-positive IEC6 and Caco2 cells released zonulin in the cell medium with subsequent zonulin binding to the cell surface, rearrangement of the cell cytoskeleton, loss of occludin-ZO1 protein-protein interaction, and increased monolayer permeability. Pretreatment with the zonulin antagonist FZI/0 blocked these changes without affecting zonulin release. When exposed to luminal gliadin, intestinal biopsies from celiac patients in remission expressed a sustained luminal zonulin release and increase in intestinal permeability that was blocked by FZI/0 pretreatment. Conversely, biopsies from non-celiac patients demonstrated a limited, transient zonulin release which was paralleled by an increase in intestinal permeability that never reached the level of permeability seen in celiac disease (CD) tissues. Chronic gliadin exposure caused down-regulation of both ZO-1 and occludin gene expression.

CONCLUSIONS: Based on our results, we concluded that gliadin activates zonulin signaling irrespective of the genetic expression of autoimmunity, leading to increased intestinal permeability to macromolecules.
How many know or suspect a sensitivity to gluten?
There is an emerging problem encountered in clinical practice of patients complaining of gluten-related symptoms despite the absence of diagnostic markers for CD, such as negative coeliac serology and normal duodenal biopsies.
These patients pose a clinical dilemma to healthcare professionals and in the past have been described as belonging to a ‘no man’s land’ due to the diagnostic uncertainty.
“Please...tell me more about this imaginary fence.”
Ok, so should I go gluten free?
Google Search Term Popularity: "Celiac Disease" Versus "Gluten Free"

It appears that a GFD in both coeliac and non-coeliac subjects could produce similar, potentially adverse changes in the microbiota solely on the basis of a marked reduction in intake of naturally occurring fructans which have prebiotic action.
Effects of a gluten-free diet on gut microbiota and immune function in healthy adult human subjects

Giada De Palma, Immacolata Nolli, Maria Carmen Collado and Yolanda Sanz

Research Council (CSIC), P.O. Box 71, 46980 Burjassot, Valencia, Spain

(Delivered 10 May 2009—Revised 4 April 2009—Accepted 4 April 2009—First published online 11 May 2009)

...Therefore, the GFD led to reductions in beneficial gut bacteria populations and the ability of faecal samples to stimulate the host’s immunity. Thus, the GFD may constitute an environmental variable to be considered in most Celiac patients for its possible effects on gut health.

Integrated microbiota—Gut function—Celiac disease

GFD: gluten-free diet; IRP: immunoreactive peroxidase; IGF: insulin-like growth factor; IL: interleukin; MHC: major histocompatibility complex; MM: multiple myeloma; NK: natural killer cell; NOD: non-obese diabetic; Peyer’s patches; SCF: staphylococcal enterotoxin F; TNF: tumour necrosis factor; TGF: transforming growth factor; FBS: fetal bovine serum; PBS: phosphate-buffered saline; SAS: standard amino acid; TMA: trinitrophenylated myelin basic protein.
Provision of gluten-free but prebiotic-rich foods and/or a supplement of fructan-type prebiotics could avoid this situation and, in so doing, provide important support to the intestinal microbiota as well as important nutritional guidance for the coeliac patient.
A large number of human intervention studies have been performed that have demonstrated that dietary consumption of certain food products can result in statistically significant changes in the composition of the gut microbiota in line with the prebiotic concept. Thus the prebiotic effect is now a well-established scientific fact.

As a result of the research activity that followed the publication of the prebiotic concept 15 years ago, it has become clear that products that cause a selective modification in the gut microbiota's composition and/or activity(ies) and thus strengthens normobiosis could either induce beneficial physiological effects in the colon and also in extra-intestinal compartments or contribute towards reducing the risk of dysbiosis and associated intestinal and systemic pathologies.
The use of probiotics seems to reduce the inflammatory response and restore a normal proportion of beneficial bacteria in the gastrointestinal tract.
<table>
<thead>
<tr>
<th>DIVERSITY ASSOCIATION</th>
<th>RELATIVE ABUNDANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGHER</td>
<td>PATIENT RESULTS</td>
</tr>
<tr>
<td>LOWER</td>
<td>HEALTHY COHORT</td>
</tr>
</tbody>
</table>

**INFECTION**
- Calprotectin
- Fecal Lactoferrin
- EPX
- Fecal secretory IgA

**INFLAMMATION**
- Fecal Fats (Total)

**INSUFFICIENCY**

**IMBALANCE**
- PP Bacteria
- Beneficial Bacteria
- n-Butyrate
- Beta-glucuronidase

**Phylum**
- Veillonellaceae Phylum
- Firmicutes Phylum
- Bacilli Phylum
- Eubacteriaceae Phylum
- Proteobacteria Phylum
- Actinobacteria Phylum
- Bacteroidetes Phylum
The grain with two faces
Conclusions: Increased intestinal permeability after gliadin exposure occurs in ALL individuals.
wheat also provides substantial amounts of a number of components which are essential or beneficial for health, notably protein, vitamins (notably B vitamins), dietary fiber, and phytochemicals..
Learning Objectives

• Describe the relationship between food exposure (i.e. gluten) and intestinal permeability

• Explain the relationship between intestinal permeability and inflammation

• Discuss the relationship between inflammation and the spectrum of chronic disease

• Identify a medical nutrition therapy (MNT) based treatment plan
The increase in intestinal permeability is most likely caused by inflammation-induced paracellular permeability, rather than ischemia-mediated enterocyte damage.
Specific gut bacteria seem to serve as lipopolysaccharide (LPS) sources and several reports claim a role for increased intestinal permeability in the genesis of metabolic disorders.... In Asian Indians who are considered highly insulin resistant, the circulatory LPS levels, LPS activity, and ZO-1 were significantly increased in patients with type 2 diabetes and showed positive correlation with inflammatory markers and poor glycemic/lipid control.
Recent studies investigating the underlying mechanisms involved in disease development in diabetes point to the role of the dysregulation of the intestinal barrier. Via alterations in the intestinal permeability, intestinal barrier function becomes compromised whereby access of infectious agents and dietary antigens to mucosal immune elements is facilitated, which may eventually lead to immune reactions with damage to pancreatic beta cells and can lead to increased cytokine production with consequent insulin resistance.
It is recognized that a chronic low-grade inflammation and an activation of the immune system are involved in the pathogenesis of obesity-related insulin resistance and type 2 diabetes. Systemic inflammatory markers are risk factors for the development of type 2 diabetes and its macrovascular complications. Adipose tissue, liver, muscle and pancreas are themselves sites of inflammation in presence of obesity. An infiltration of macrophages and other immune cells within the adipose tissue and postprandial glucose levels may result in a population shift from an anti-inflammatory to a pro-inflammatory state. Interleukin-1β is implicated in the development of the NLRP3 inflammasome. This suggests that type 2 diabetes and to examine various mechanisms underlying this relationship. If type 2 diabetes is an inflammatory disease, anti-inflammatory therapies could have a place in prevention and treatment of type 2 diabetes.
“Research results seem to be very promising and indicate the possibility of improved clinical outcomes in some patients with schizophrenia by modifying diet, use of probiotics, and the implementation of antibiotic therapy of specific treatment groups.”
Learning Objectives

• Describe the relationship between food exposure (i.e. gluten) and intestinal permeability
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Healing Leaky Gut with the 4R GI Restoration Protocol

1. Remove
   a. Toxins
   b. Infection
   c. Dietary triggers

2. Replace
   a. HCL
   b. Digestive enzymes

3. Reinoculate
   a. probiotics

4. Repair
   a. Glutamine/SCFAs
   b. Fish oils
   c. curcumin

Source: Institute for Functional Medicine
What to consider eliminating:
- Gluten (r/o celiac disease first, if possible)
- Dairy
- Corn? Soy? Grains? animal protein?
- Refined sugar
- Infection
- Toxins (alcohol, preservatives, smoking, stress)

What to consider adding:
- Betaine HCL, broad spectrum digestive enzymes
- Probiotics/prebiotics/fermented foods
- Glutamine (dose low and go slow)/zinc carnosine
- Methylated nutrients (B2, B6, folate, B12, CoQ10)
- Omega-3 fish oils
- Fiber rich foods/prebiotics
- Antioxidant/phytochemical rich foods (i.e. fresh fruits and vegetables, seeds, nuts, legumes, etc.)
Once you have a good history, test results etc., you can formulate the rest of your Nutrition Care Plan

Image source: www.IFNAcademy.com
Key Takeaways

• Impaired intestinal permeability is a real phenomenon that is part of the “3 legged stool” that leads to autoimmunity.

• Triggers can include toxins, infection, diet (TID).

• Impaired intestinal permeability can be healed using the 4R protocol.
Presenters from left to right: Alessio Fasano, MD; Sheila Dean, DSc, RDN, Andrea Scaramuzza, MD
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thank you
More questions?
Contact me via www.IFNAcademy.com
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