Gluten Free Society

Educating Patients and Doctors About Gluten

Dr. Peter Osborne

Presents…

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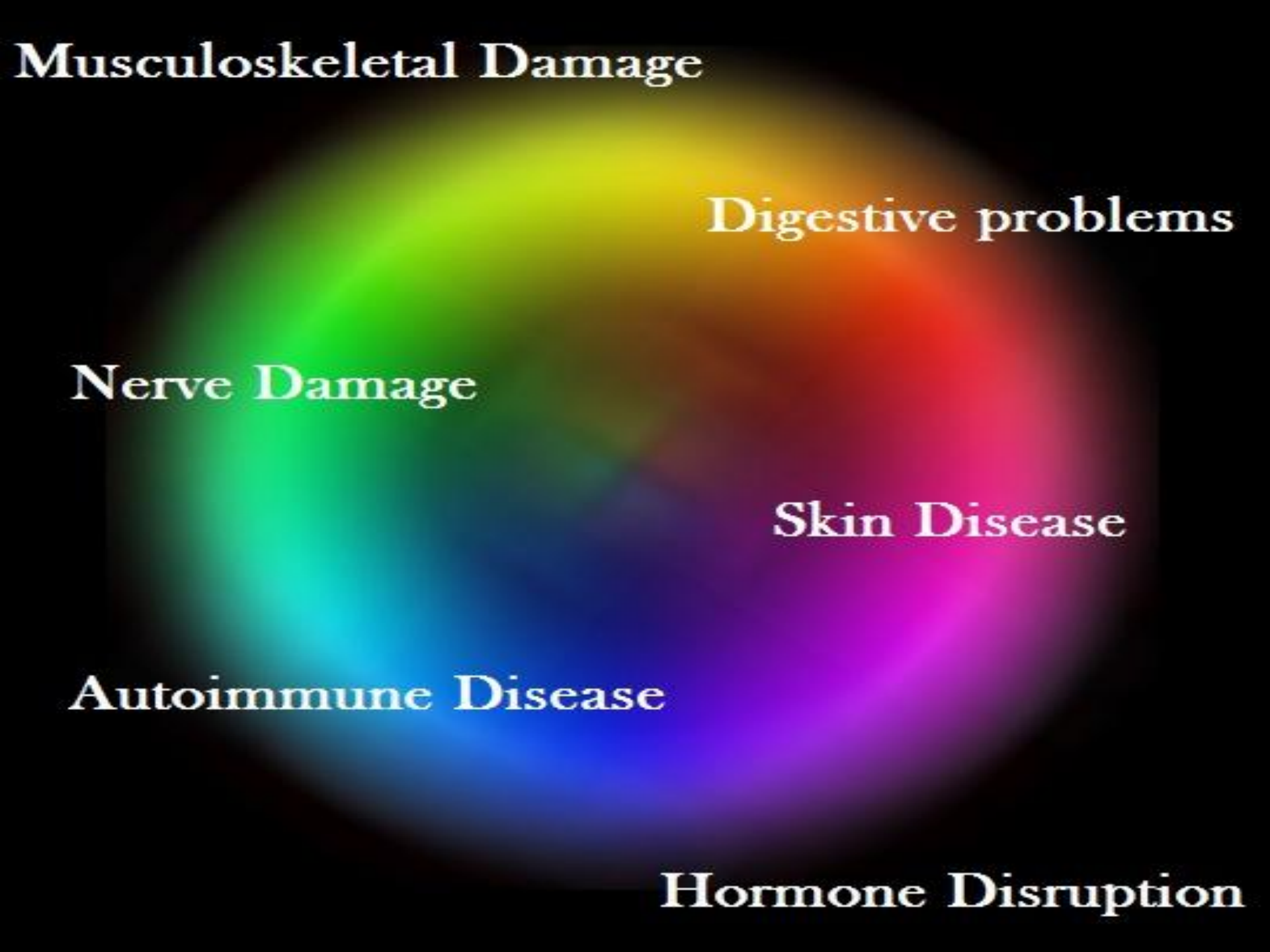
Educating Patients and Doctors About Gluten

Glutenology


Musculoskeletal Damage
Digestive problems
Nerve Damage
Skin Disease
Autoimmune Disease
Hormone Disruption

You must first arm yourself with knowledge!

The most important thing to remember is this:

Celiac disease and gluten intolerance are not the same thing.

Gluten Sensitivity ≠ Celiac Disease

Science Finally Confirms Gluten Sensitivity

A new double blind, randomized, placebo controlled study published in the *American Journal of Gastroenterology* confirms the presence of gluten sensitivity in the absence of celiac disease. This is the first study of its kind confirming the existence of gluten intolerance in the absence of celiac disease.

Source:

Am J Gastroenterol. 2011 Jan 11.

- Gluten Sensitivity has traditionally been used synonymously with Celiac disease because that has been the focus of research.
- These terms have been created in the medical literature to separate Celiac Disease from Gluten Sensitivity
  - Non-Celiac Gluten Sensitivity – Dr. Marsh
  - Gluten Syndrome – Rodney Ford, M.D.

Unpublished data from Dr. Kenneth Fine, laboratory director at Enterolab, speculates that one in three have some degree of gluten intolerance!

Classic Symptoms

Clinical symptoms of Celiac disease taught in graduate school are extreme weight loss, diarrhea, stomach pain, bloating, and vomiting.

In actuality symptoms can be and usually are systemic and we now know that different people respond in different ways.

On Celiac vs. Gluten Sensitivity

"Recent studies are showing the gluten sensitivity may be much more common than previously thought. It may, in fact, be a separate disease entity that involves different organs and different mechanisms than celiac disease. While there is no doubt that the condition exists, the lack of definite criteria for a diagnosis has resulted in a skeptical attitude on the part of many doctors." He goes on to say: **"The acceptance of gluten sensitivity as a valid condition has evolved."**

– **Dr. Peter Green -** Director of The Celiac Disease Center at Columbia University

On Celiac vs. Gluten Sensitivity

60-70% of those who think they have celiac disease and seek help from his research center are actually gluten sensitive – they do not have celiac disease.

Communication from Dr. Alessio Fasano – University of Maryland Celiac Research Center

Courtesy of Dr. Vikki Petersen (Author of the Gluten Effect)

Historical landmarks relating to digestive illnesses (references in process to be posted at www.glutensensitivity.net history page)

BC	The book of Exodus refers to related general and digestive symptoms in reference to bread and grains.
100 AD	Comment describing celiac symptoms in ancient medical literature
300 AD	Comment and description by Aretaeus, refers to "Coeliac disease", meaning "abdominal".
1855	Dr. Gull Guy's Hospital Reports, symptoms described symptoms of gluten intolerance.
1887	Dr. Samuel Gee, "We must never forget that what the patient takes beyond his power to digest does harm."
1850's+	Bechamp-Pasteur debate re: microbiology/vaccines. Continues for many years. Bechamp's predictions fulfilled.
1850's+	Processed flour, sugar and commercially canned vegetables and milks become more widely available with industrialization.
1900	Coronary Heart disease is no more than 10% of annual cause of death from all causes. Butter consumption 18 lbs/person
1908	Drs. E
1910	Myoca
1911	Crisco
1914	Dr. Pa
	Th
1921-51	Holt re
1922	Dr. Ro
1930	Myocardial infarction is responsible for no more than 3000 deaths in 1930.
1932	Dr. B.B. Crohn speaks of "new intestinal disorder" he calls "regional ileitis", now called Crohn's Disease.
1939	Dr. Weston A. Price publishes his 10 year travel research "Nutrition and Physical Degeneration", detailing his comparisons of health and diets of isolated cultures with "modern" societies, and related butter and soil fertility studies.
1940-50	Dr. Willem Dicke notices certain patients' digestion improves during grain shortages in Holland during World War 2. Their illnesses relapse when grain is again available. This turns attention to gluten grains.
1949	Drs. Sidney and Merrill Haas successfully treat 600 cases of "celiac disease" with the Specific Carbohydrate Diet.
1950	Butter consumption has dropped in the US from 18 lbs/person in 1900 to 10 lbs/person per year, 1950's. Hydrogenated vegetable oils replace butter. Coronary heart disease is now the leading cause of death, 30%.
1951	Drs. Haas publish "The management of Celiac Disease" in 1951, focusing on certain complex dietary sugars and starches.
1952	University of Birmingham tests ten children and concludes that gluten, not starch is the culprit. The new focus on gluten widens the number of foods allowed, but few patients meet the diagnostic criteria and recognized symptoms are narrow, mainly wasting diarrhea and failure to thrive in children. They are diagnosed with "gluten induced celiac disease" via early blood and later newly developed capsule biopsy testing. USA doctors are taught that "celiac disease" is rare and they will likely never see a case. Most practitioners don't think of it, so most gluten induced celiac patients *and* those who might have responded to a carbohydrate based approach alike fall by the wayside.
1950-60s	Numerous researchers perform studies finding benefit in saturated animal fats and tropical oils vs. disturbing results from inexpensive hydrogenated vegetable oils.
1960	The American Heart Association launches the Prudent Diet (replace red meat, eggs on TV networks based on the "lipid hypothesis" amid an era of protests from lipid researchers and heart specialist Dr. Paul Dudley White. "I began my practice as a cardiologist in 1921 and I never saw an MI patent until 1928. Back in the MI free days before 1920, the fats were butter and lard and I think that we would all benefit from the kind of diet that we had at a time when no one had ever heard the word corn oil."
1960	Myocardial infarction claims 500,000 lives in 1960.
1960	Margot Shiner and Cyrus Rubin separately invent a small bowel biopsy capsule facilitating dx of small bowel diseases.

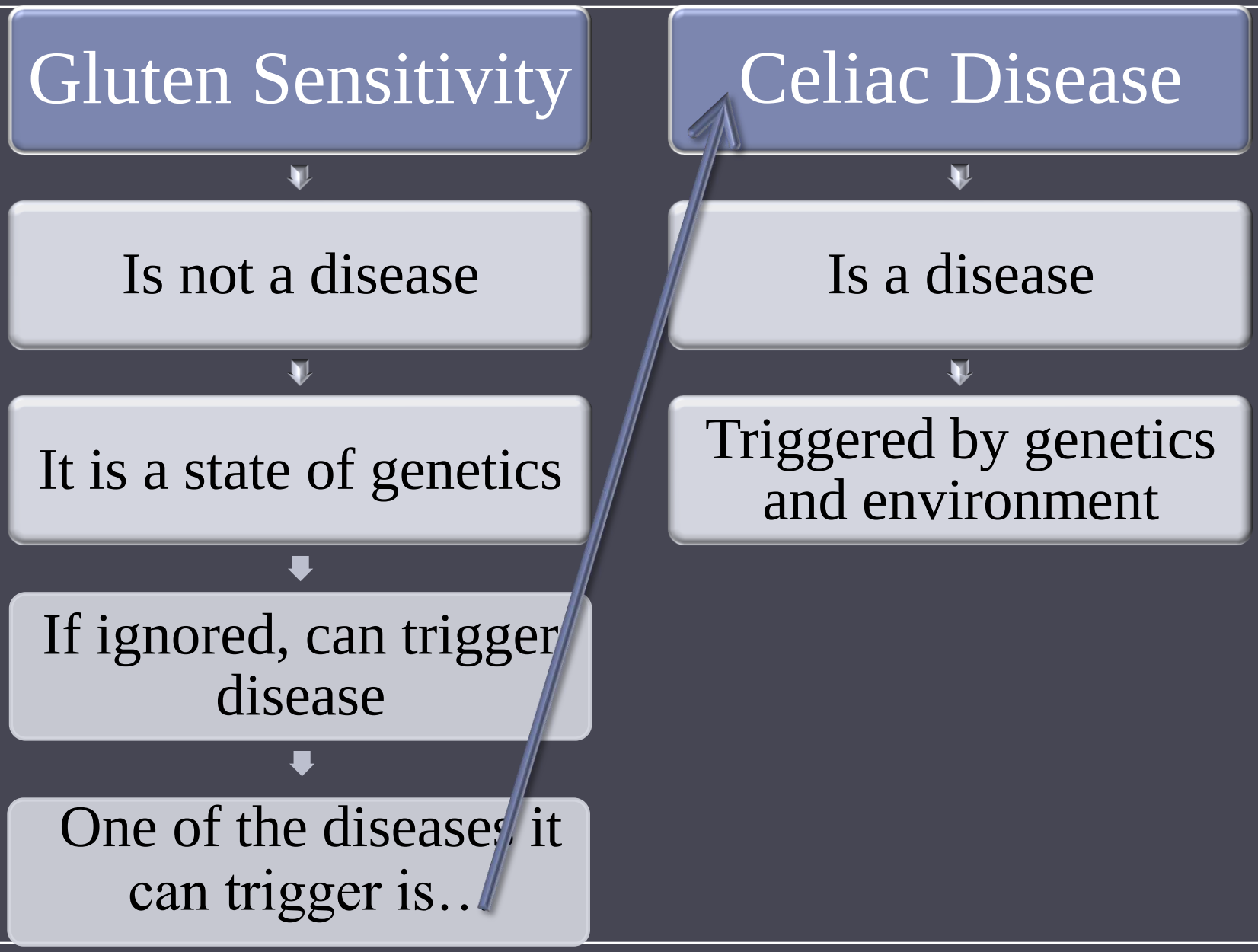
oil, animal tallow, lard

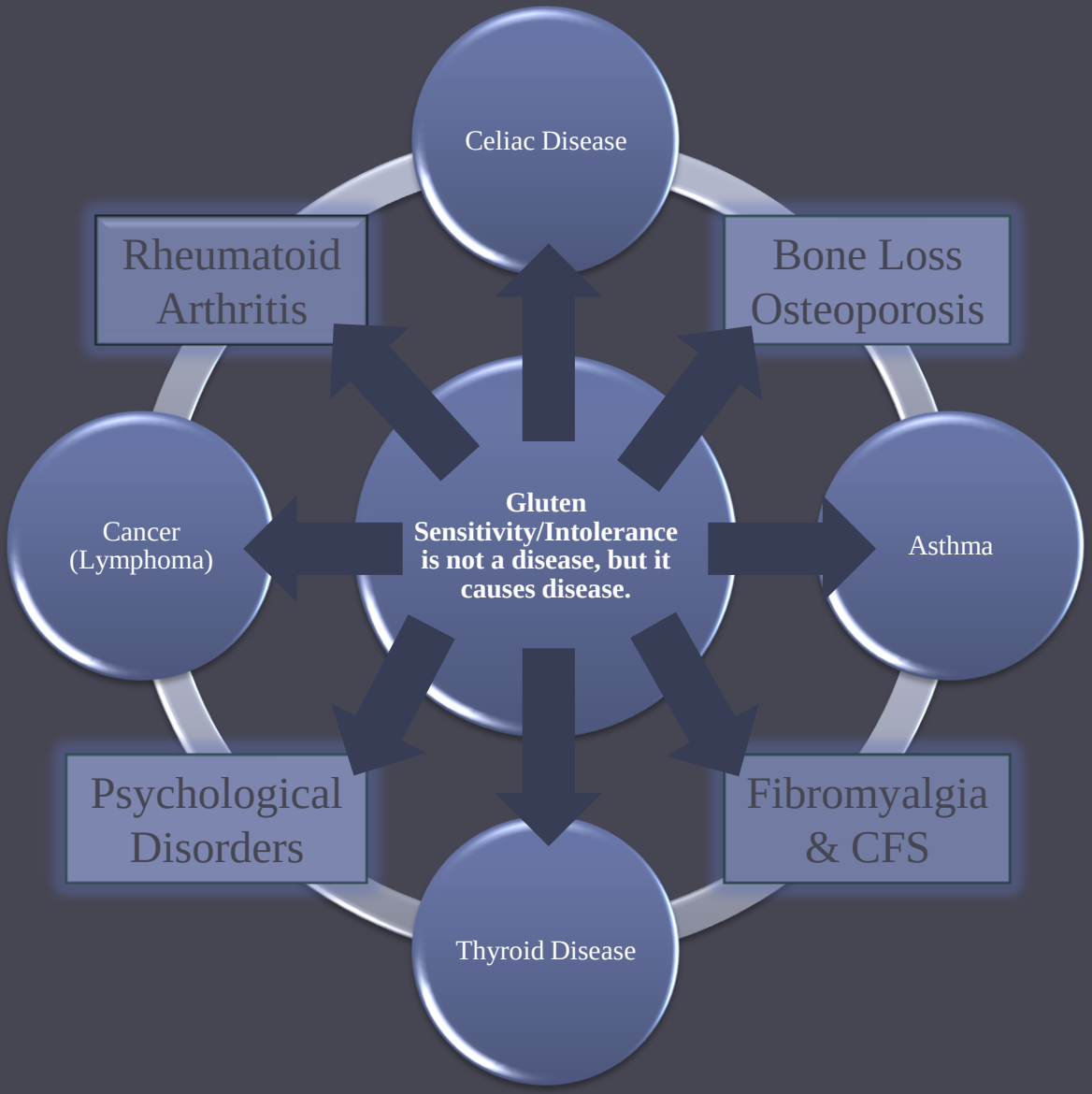
as a long shelf life.

at Harvard U.

tes for better nutrition.

Why is the focus primarily on celiac disease?


Gluten Sensitivity
Is not a disease
It is a state of genetics
If ignored, can trigger disease
One of the diseases it can trigger is…
Celiac Disease
Is a disease
Triggered by genetics and environment

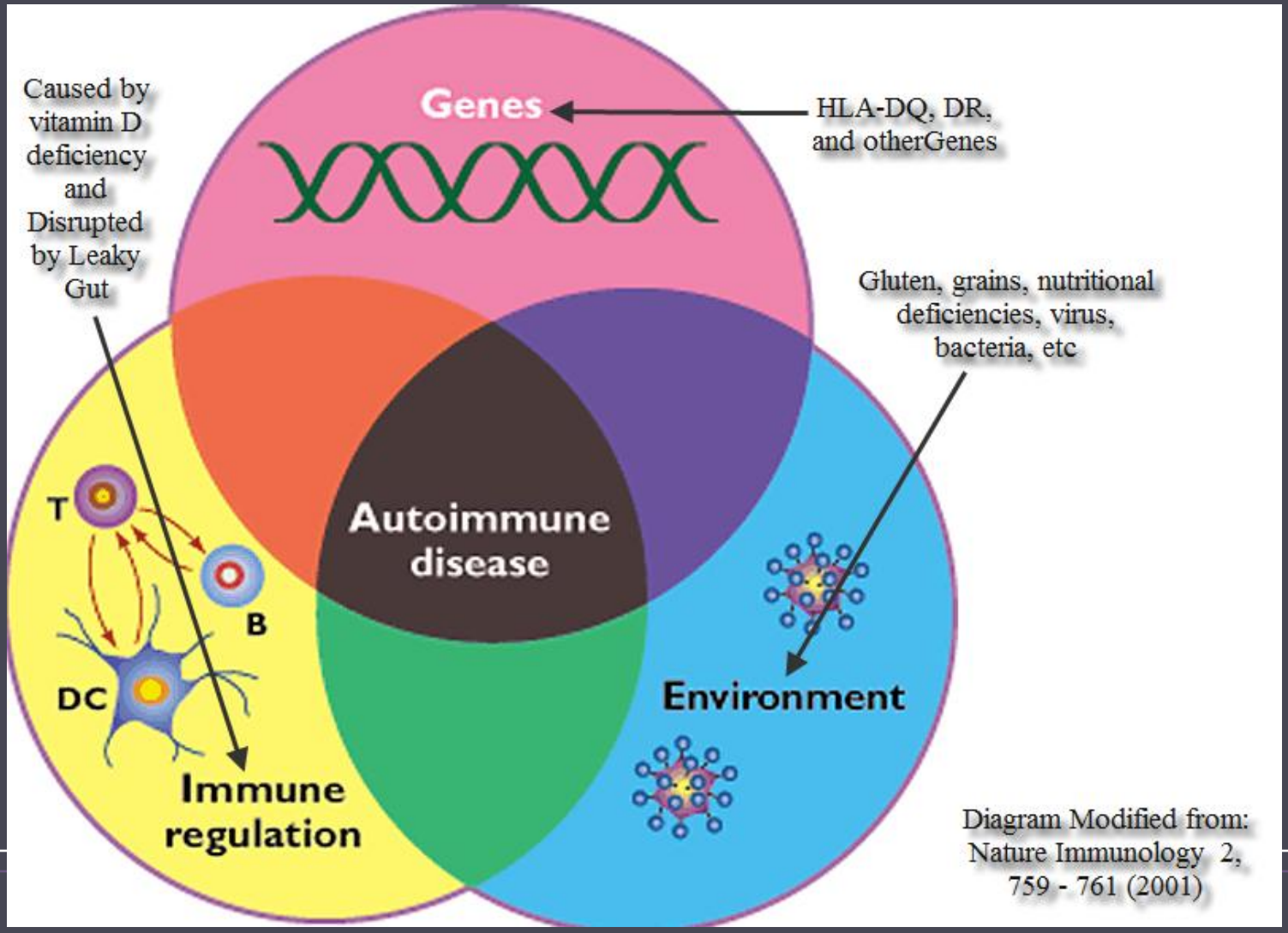

Celiac Disease
Bone Loss Osteoporosis
Asthma
Fibromyalgia & CFS
Thyroid Disease
Psychological Disorders
Cancer (Lymphoma)
Rheumatoid Arthritis
Gluten Sensitivity/Intolerance is not a disease, but it causes disease.

"Gluten sensitivity is a systemic autoimmune disease with diverse manifestations. This disorder is characterised by **abnormal immunological responsiveness to ingested gluten in genetically susceptible individuals. Coeliac disease, or gluten-sensitive enteropathy, is only one aspect of a range of possible manifestations of gluten sensitivity.** Although neurological manifestations in patients with established coeliac disease have been reported since 1966, it was not until 30 years later that, in some individuals, gluten sensitivity was shown to manifest solely with neurological dysfunction."

THE LANCET Neurology

The Lancet Neurology, Volume 9, Issue 3, Pages 318 – 330, March 2010.

All Patients with Autoimmune Disease should be screened for Gluten Sensitivity…



Silent Celiac Disease is Gluten Sensitivity

Table 1. Manifestations of silent celiac disease (predominantly extra-intestinal).

- Dermatitis herpetiformis
- Anemia
- Autoimmune disorders → Hypothyroidism
- Osteoporosis
- Neurological disorders
  - Epilepsy with cerebral calcification
  - Neuropathy
  - Cerebellar ataxia
  - Chorea
- Infertility/subfertility
- Non-alcoholic fatty liver disease
- Unexplained chronic hypertransaminasemia

Clin Med Res. 2007 Oct;5(3):184-92.

BMC Gastroenterology

BioMed Central

Research article

Open Access

Symptoms and signs in individuals with serology positive for celiac disease but normal mucosa

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Abstract

Background: Antibody serology is an important tool in the investigation of celiac disease (CD), but does not always correlate with mucosal appearance in the small intestine. Patients with positive CD serology but normal mucosa (Marsh 0) are at increased risk of future CD. In this study we describe a model for identifying and characterizing individuals with normal mucosa but positive CD serology. Such individuals are sometimes referred to as having latent CD.

Methods: The records of ten Swedish pathology departments were used to identify individuals with biopsies indicating normal duodenal/jejunal mucosa. Using the national personal identification number, these data were linked with CD serology data (antigliadin, antiendomysial and tissue transglutaminase antibodies); and we thereby identified 3,736 individuals with normal mucosa but positive CD serology. Two independent reviewers then manually reviewed their biopsy reports to estimate comorbidity. We also randomly selected 112 individuals for validation through patient chart review.

Results: The majority of the 3,736 individuals were females (62%). Children (0–15 years) made up 21.4%. The median number of biopsy specimen was 3. Our review of biopsy reports found that other gastrointestinal comorbidity was rare (inflammatory bowel disease: 0.4%; helicobacter pylori infection: 0.2%). Some 22% individuals selected for patient chart review had a relative with CD. The most common symptoms among these individuals were diarrhea (46%) and abdominal pain (45%), while 26% had anemia. Although 27% of the individuals selected for validation had been informed about gluten-free diet, only 13% were adhering to a gluten-free diet at the end of follow-up.

Conclusion: Individuals with positive CD serology but normal mucosa often have CD-like symptoms and a family history of CD.

Results: 1 to 20 of 252

1. Gastroesophageal reflux symptoms in patients with celiac disease and the effects of a gluten-free diet.
Nachman F, Vázquez H, González A, Andrenacci P, Compagni L, Reyes H, Sugai E, Moreno ML, Smecuol E, Hwang HJ, Sánchez IP, Mauriño E, Ba
Clin Gastroenterol Hepatol. 2010 Jul 2. [Epub ahead of print]
PMID: 20601132 [PubMed - as supplied by publisher]
Related citations

2. Severe iron deficiency anaemia as a manifestation of silent coeliac disease: case report and literature review.
Paul SP, Taylor TM, Barnard P.
J Fam Health Care. 2010;20(2):56-9.
PMID: 20518373 [PubMed - indexed for MEDLINE]
Related citations

3. Silent celiac disease presenting with polyarthritis.
Efe C, Urün Y, Purnak T, Ozaslan E, Ozbalkan Z, Savaşs B.
J Clin Rheumatol. 2010 Jun;16(4):195-6. No abstract available.
PMID: 20511982 [PubMed - in process]
Related citations

4. Implications of gluten exposure period, CD clinical forms, and HLA typing in the association between celiac disease and dental enamel defects in c
study.
Majorana A, Bardellini E, Ravelli A, Plebani A, Polimeni A, Campus G.
Int J Paediatr Dent. 2010 Mar;20(2):119-24.
PMID: 20384826 [PubMed - indexed for MEDLINE]
Related citations

5. Celiac disease in Middle Eastern and North African countries: a new burden?
Barada K, Bitar A, Mokadem MA, Hashash JG, Green P.
World J Gastroenterol. 2010 Mar 28;16(12):1449-57. Review.
PMID: 20333784 [PubMed - indexed for MEDLINE] Free PMC Article Free text

Gluten sensitivity: a many headed hydra

Heightened responsiveness to gluten is not confined to the gut

In a lecture entitled "On the coeliac affection"[1] given in London in 1887 Dr Samuel Gee first described the condition we now refer to as coeliac disease or gluten sensitive enteropathy. With clinical manifestations confined to the gastrointestinal tract or attributable to malabsorption, it was logical to assume that the key to the pathogenesis of this disease resided in the gut. However, focusing diagnostic criteria on the gut (as most physicians still do) has delayed the appreciation of the wider spectrum of gluten sensitivity.

The treatment of coeliac disease remained empirical until 1940-50, when the Dutch paediatrician Willem Dicke noted the deleterious effect of wheat flour on indi-

We have, however, shown that neurological dysfunction can not only precede coeliac disease but can also be its only manifestation.[6] Of even more interest is the demonstration of a high prevalence of circulating antigliadin antibodies (IgG, IgA, or both) in patients with neurological dysfunction of obscure aetiology (57% *v* 5% in neurological controls and 12% in normal controls).[7] Only 35% of these patients had histological evidence of coeliac disease. The remaining 65% have gluten sensitivity where the target organ is the cerebellum or the peripheral nerves, a situation analogous to that of the skin in dermatitis herpetiformis.

In the light of these findings the specificity of

We have, however, shown that neurological dysfunction can not only precede coeliac disease but can also be its only manifestation…The typical clinical expression of a patient with gluten sensitivity where the sole manifestation is neurological is cerebellar ataxia, often with a peripheral neuropathy. Most of these patients will have histologically normal mucosa on biopsy and few or no gastrointestinal symptoms. Both the ataxia and the neuropathy may be reversible with adherence to a gluten free diet.

the concept of latent gluten sensitivity. The term is now used to describe people with a histologically normal small bowel while on a normal diet who at some stage of their lives have had or will have an abnormal small bowel that responds to a gluten free diet.[4]

Also in 1966 Cooke and Thomas-Smith published a paper on neurological disorders associated with adult coeliac disease.[5] Further case reports have since been published, but most are based on patients with coeliac disease who later develop neurological dysfunction, implying that gut disease is a prerequisite.

disorders associated with gluten sensitivity have an HLA genotype in keeping with coeliac disease compared with 25% of the normal population.[8]

Unlike antiendomysium or antireticulin antibodies, antigliadin antibodies are antibodies against the extrinsic causal factor for gluten sensitivity. Antiendomysium antibodies may be more specific for coeliac disease, but no large scale data are available as yet on their specificity or sensitivity in patients with gluten sensitivity where the immunological target organ may be other than the gut.

BMJ 1999;318:1710–1

Gluten-Sensitive Enteropathy (Celiac Disease): More Common Than You Think

sas for Medical Sciences, Little Rock, Arkansas

ommonly called, celiac disease, is an
l intestine that is precipitated by the
ein, in genetically susceptible persons.
the mucosa, resolution of the malab-
ffects of celiac disease. Recent studies
of celiac disease is approximately one
athy commonly manifests as "silent"
erologic tests for antibodies against
ntify most patients with the disease.
s who are at increased genetic risk for
of celiac disease or personal history
hronic diarrhea, unexplained anemia,
arly diagnosis and management are
malabsorption, such as osteoporosis
5,2269-70. Copyright© 2002 American

A patient information handout on celiac disease, written by the author of this article, is provided on page 2269.

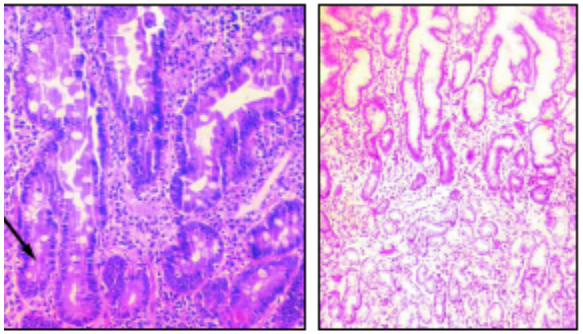
TABLE 2
Symptoms of Celiac Disease and Possible Causes

Symptoms	*Possible causes*
Fatigue, malaise	Anemia, general immune system activation
Weight loss	Nutrient malabsorption
Diarrhea, abdominal pain	Accelerated gastrointestinal tract transit time, steatorrhea, malabsorption
Anemia	Most commonly, iron deficiency; less commonly, vitamin B_{12} and/or folate deficiency
Bone pain	Osteoporosis
Aphthous oral ulcers, glossitis, stomatitis	Vitamin deficiency, "oral" celiac disease
Infertility	Postulated cause: iron, folate, and/or zinc deficiency
Male impotence, decreased libido	Peripheral insensitivity to circulating testosterone
Alopecia areata	Immunologic attack on hair follicles
Dental enamel defects	Demineralization during tooth bud development in children
Hypoglycemia	Delayed absorption of glucose
Gas, flatus, borborygmus	Secondary digestion of sugars by intestinal flora
Seizures, gluten ataxia, central nervous system symptoms	Increased affinity of celiac antibodies for brain vasculature

celiac disease was for-
escribed late in the
ntury, treatment re-
mpiric until the mid-
e 20th century when
improve dramatically
l from their diet. With
ll-bowel biopsy tech-
e was identified as the
usality was established
features of villous flat-

tening, crypt hyperplasia, and increased intraepithelial lymphocytes *(Figure 1)* were shown to normalize after the institution of a gluten-free diet.[1]

In the mid-1960s, an enteropathy strikingly similar to celiac disease was identified in patients with dermatitis herpetiformis. Subsequently, this skin disorder was shown to be a manifestation of gluten-sensitive enteropathy. In the mid-1960s, adult celiac disease was also noted to be associated with numerous neuro-



icrograph of distal duodenal biopsy specimen in a patient with celiac dis-
istic features of crypt hyperplasia (CH), and increased intraepithelial lym-
phocytes (IEL). *(Right)* For comparison, a normal biopsy specimen is shown.

Celiac Disease without Villous Atrophy in Children: A Prospective Study.

“The study provided evidence that children who are EmA positive have a celiac-type disorder and benefit from early treatment despite normal mucosal structure, indicating that the diagnostic criteria for celiac disease should be re-evaluated.”

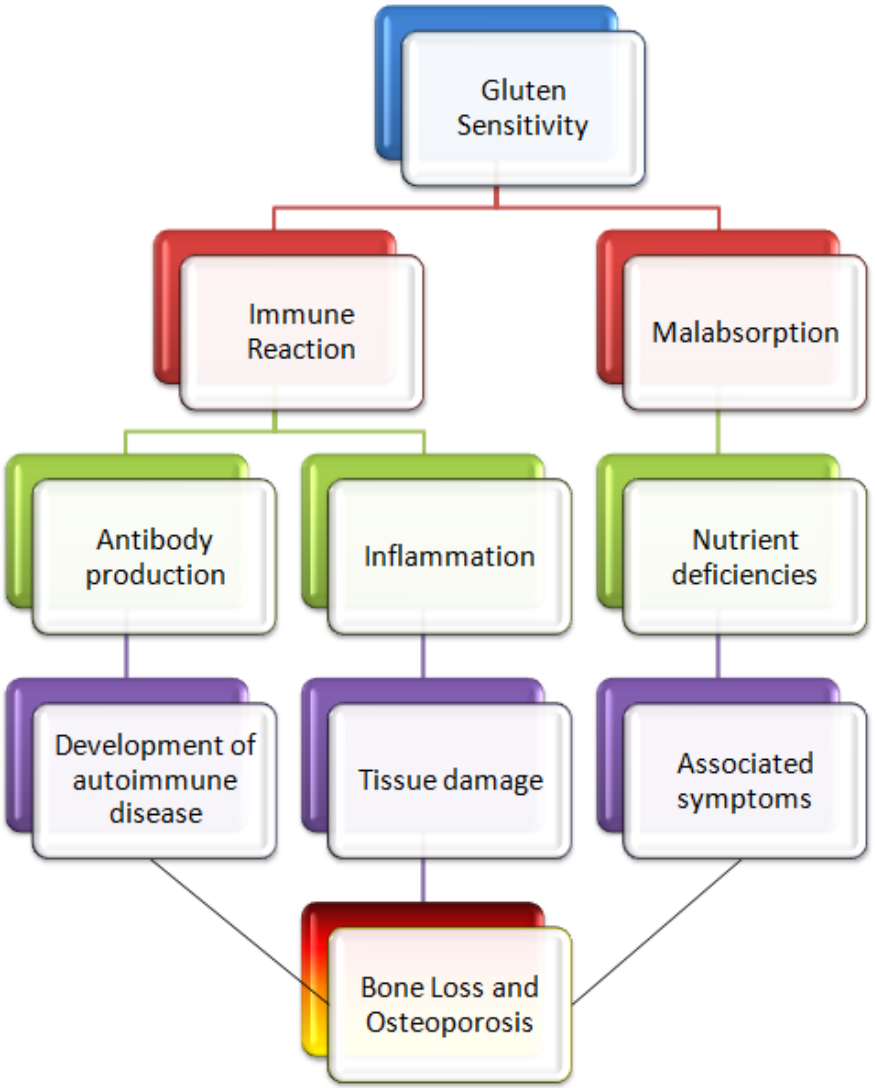
J Pediatr. 2010 Apr 16.

The NEW ENGLAND JOURNAL of MEDICINE

A new report in the *New England Journal of Medicine* identifies antibodies against osteoprotegerin (a protein that prevents bone breakdown) in several patients with celiac disease. This protein is responsible for helping maintain bone density. When it is attacked by the body's immune system, bone loss becomes accelerated contributing to osteoporosis.

N Engl J Med 2009;361:1459-65.

Common Mechanisms of Gluten Induced Damage on Bone Tissue



Symposium on Hepatology and Gastroenterology II

Liver Involvement in Celiac Disease

Giuseppe Maggiore and Silvia Caprai

Department of Reproductive Medicine and Child Development University of Pisa, Gastroenterology and Liver Unit and IsMeTT, University of Pittsburgh Medical Center, Palermo, Italy.

ABSTRACT

"a wide spectrum of liver injuries in children and adults may be related to CD and in particular: (1) a mild parenchymal damage characterised by absence of any clinical sign or symptom suggesting a chronic liver disease and by non-specific histological changes reversible on a gluten-free diet; (2) a chronic inflammatory liver injury of autoimmune mechanism, including autoimmune hepatitis, primary sclerosing cholangitis and primary biliary cirrhosis, that may lead to fibrosis and cirrhosis, generally unaffected by gluten withdrawal and necessitating an immunosuppressive treatment; (3) a severe liver failure potentially treatable by a gluten-free diet. Such different types of liver injuries may represent a spectrum of a same disorder where individual factors, such as genetic predisposition, precocity and duration of exposure to gluten may influence the reversibility of liver damage."

Persistent elevation of serum aminotransferase activity is the most common liver abnormality found in untreated CD.[2] Hagander first in 1977 found that almost 40% of 74 untreated coeliac adult patients showed, at diagnosis, an hypertransaminasemia, in most cases reversible with a gluten free diet (GFD).[3] An histological evaluation,

TABLE. Liver Diseases Associated with Celiac Disease

Reactive hepatitis (*coeliac hepatitis*)
Autoimmune liver disorders
Autoimmune hepatitis
Autoimmune overlap syndrome
Autoimmune (sclerosing) cholangitis
Primary biliary cirrhosis
Non alcoholic fatty liver disease
Acute liver failure
Cryptogenic cirrhosis
Regenerative nodular hyperplasia
Hepatocellular carcinoma

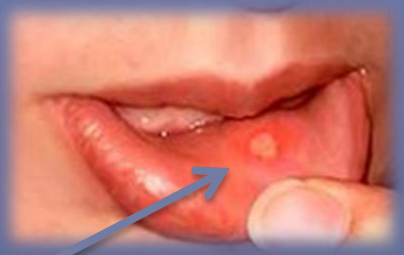
Correspondence and Reprint requests : Prof. Giuseppe Maggiore, Dipartimento di Medicina della Procreazione e della Età Evolutiva, Università di Pisa, Via Roma 67 56100 Pisa-Italy. Fax: +39050 888 622

What?

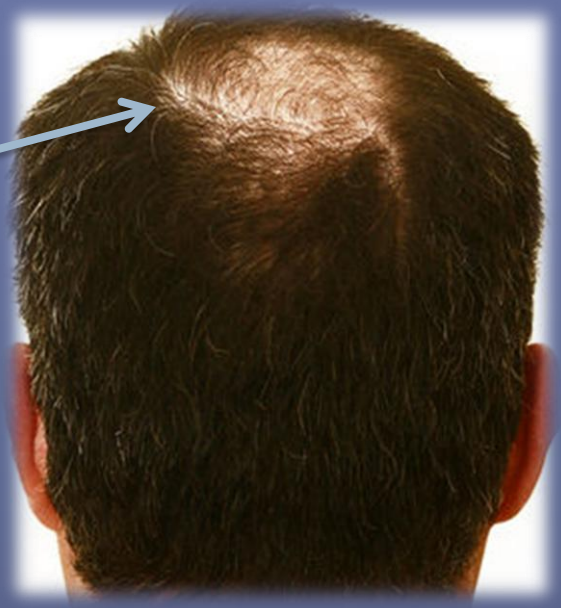
Keep in mind…

Gluten intolerance/sensitivity is not the sole cause of the following diseases. In cases where a person does not have a known cause for their diagnosis, gluten sensitivity should be ruled in or out. Therefore; those with the following conditions should be genetically screened…

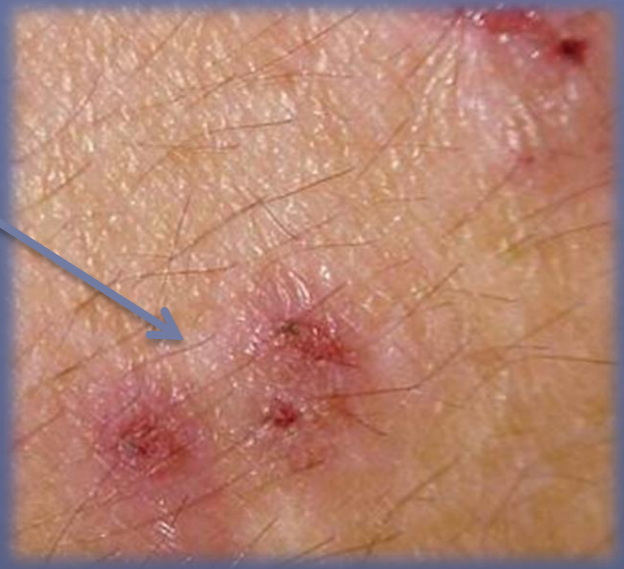
- Angina Pectoris (chest pain/pressure)
- Anorexia
- Immunoglobulinopathies
- Antiphospholipid syndrome
- Anxiety
- Apathy
- Aphthous ulcers and canker sores
- Aortic Vasculitis
- Arthritis
  - Juvenile rheumatoid
  - Enteropathic
  - Psoriatic
  - rheumatoid



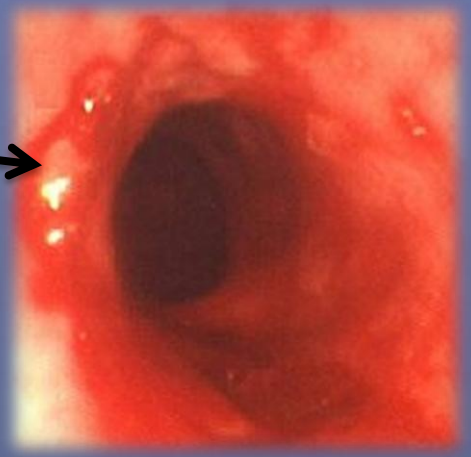
- Abdominal pain and distention
- Spontaneous abortion
- Addison's Disease
- ADHD
- Alopecia (hair loss)
- Anemia
  - Iron deficiency
  - Folate deficiency
  - B-12 deficiency
  - B-6 deficiency
  - Vitamin C deficiency
  - Vitamin E deficiency
  - Copper deficiency



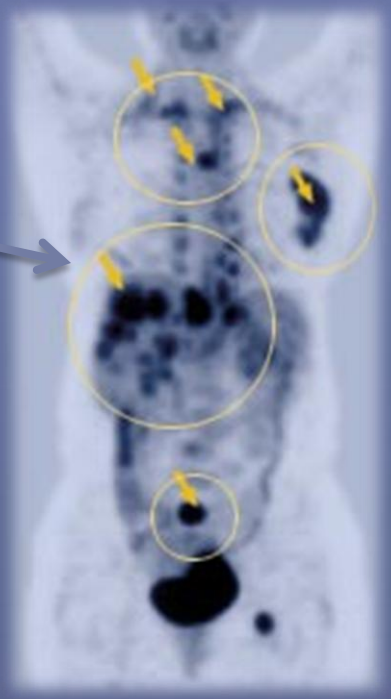
- Ataxia
- Atherosclerosis
- Autism and other learning disorders
- Cholangitis (gall bladder)
- Dermatitis Herpetiformis
- Autoimmune hepatitis
- Polyglandular syndrome
- Thyroiditis (hypothyroidism)
- Bitot’s spots
- Blepharitis
- Abnormal blurry vision



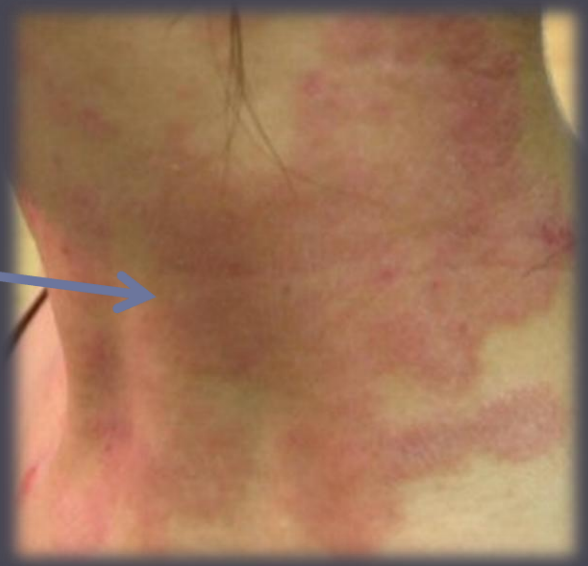
- Bone pain
- Bone fractures
- Cachexia
- Bronchiectasis
- Barrett's Esophagus
- Bronchoalveolitis
- Adenocarcinoma of the intestine
- Small cell esophageal cancer
- Melanoma
- Asthma
- Cardiomegaly
- Cardiomyopathy
- Cataracts
- Cerebral perfusion abnormalities
- Cheilosis
- Chorea
- Coagulation abnormalities
- Crohn's disease
- Ulcerative colitis



- Chronic constipation
- Coronary artery disease
- Diarrhea
- Lymphoma
- Cutaneous vasculitis
- Cystic fibrosis
- Delayed puberty
- Failure to thrive
- Dementia
- Depression
- Dermatomyositis
- Diabetes Mellitus type I
- Down syndrome
- Dysmenorrhea
- Dysgeusia
- Duodenal erosions



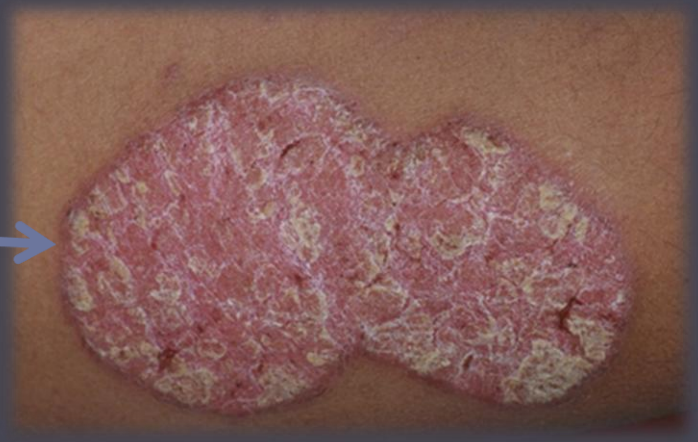
- Edema
- Eczema
- Dysphagia
- Epilepsy
- Spontaneous nose bleeds
- Erythema nodosum
- CFS
- Growth retardation
- Mental retardation
- Secondary food allergy response
- Blood in the stool
- Gastric bloating
- Grave’s disease



- Bleeding gums
- Hair loss
- Heartburn
- H. pylori infection
- Hives
- NAFL
- Malnutrition and nutritional deficiencies
- Infertility
- Hypogonadism
- Hypoglycemia
- Hypospleenism
- Thrombocytopenia
- Impotence
- Osteoporosis
- Insomnia
- IBS
- Keratomalacia

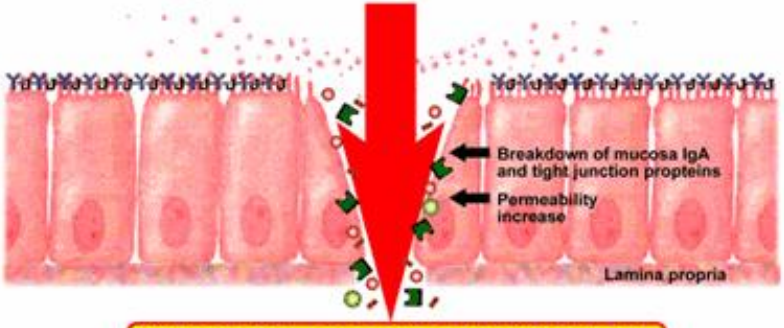
- Lactose intolerance
- Loss of smell
- Non Hodgkin lymphoma
- Early menopause
- Migraine headache
- Multiple sclerosis
- Muscle wasting
- Myopathy
- Obesity
- Osteomalacia
- Osteopenia
- Parathyroid carcinoma
- Pancreatic insufficiency

- Polymyositis
- PMS
- Biliary cirrhosis
- Psoriasis
- Dermatitis
- Sjogren’s syndrome
- Short stature
- Scleroderma
- Steatorrhea
- Spina bifida
- SLE
- Tremors
- Parkinson’s disease
- Glossitis
- Vitiligo
- Vomiting
- Vaginitis
- UTI



Factors affecting mucosal immune system resulting in intestinal barrier dysfunction, autoimmunity and nervous system abnormalities

Dietary Proteins & Peptides | Antibodies | Drugs & Xenobiotics | Physical Stress | Infections | Cytokines | Neurotransmitters | Enzymes



INTESTINAL BARRIER DYSFUNCTION

FOOD ALLERGY & INTOLERANCE

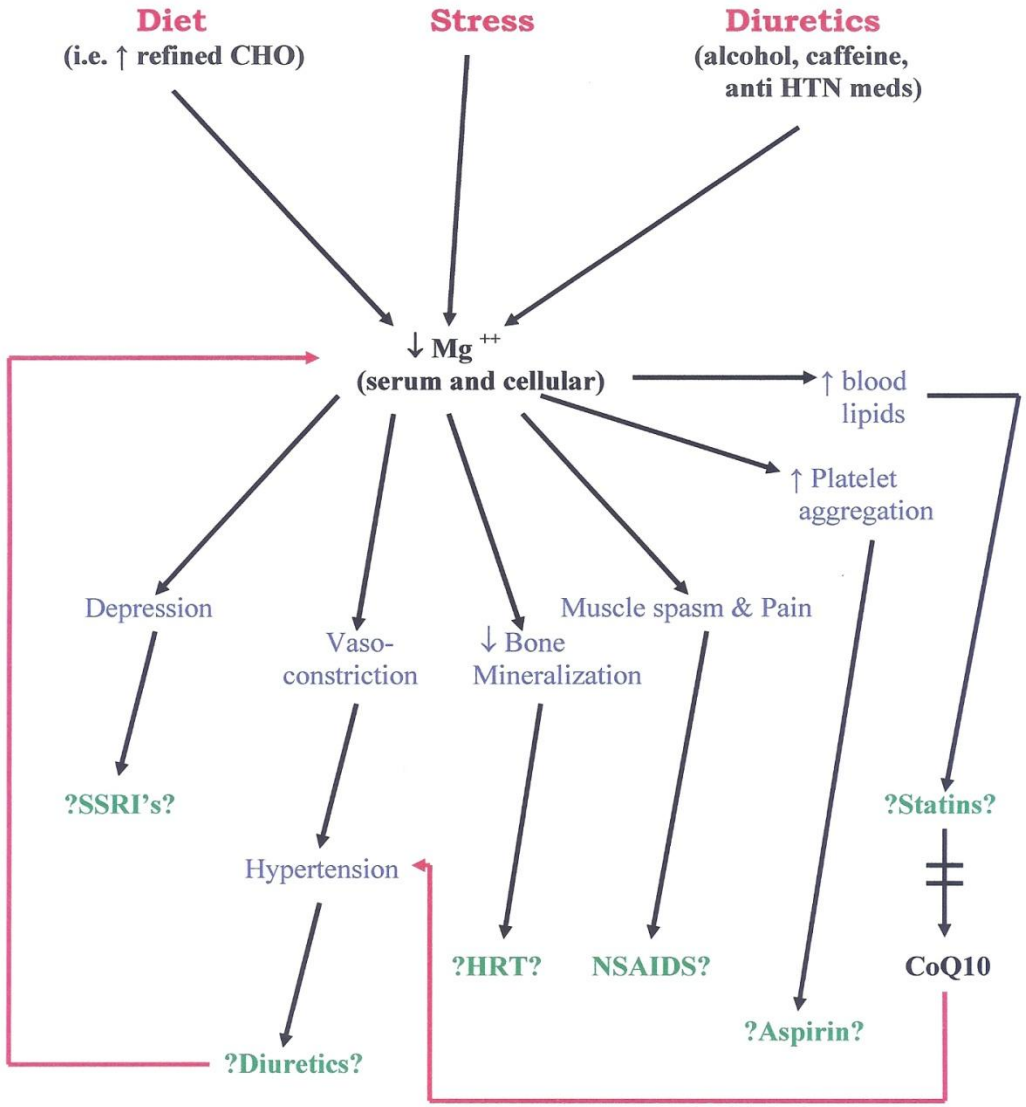
IMMUNE SYSTEM ABNORMALITIES

AUTOIMMUNITY

INFLUENCE ON THE BLOOD-BRAIN BARRIER AND NEUROAUTOIMMUNITY

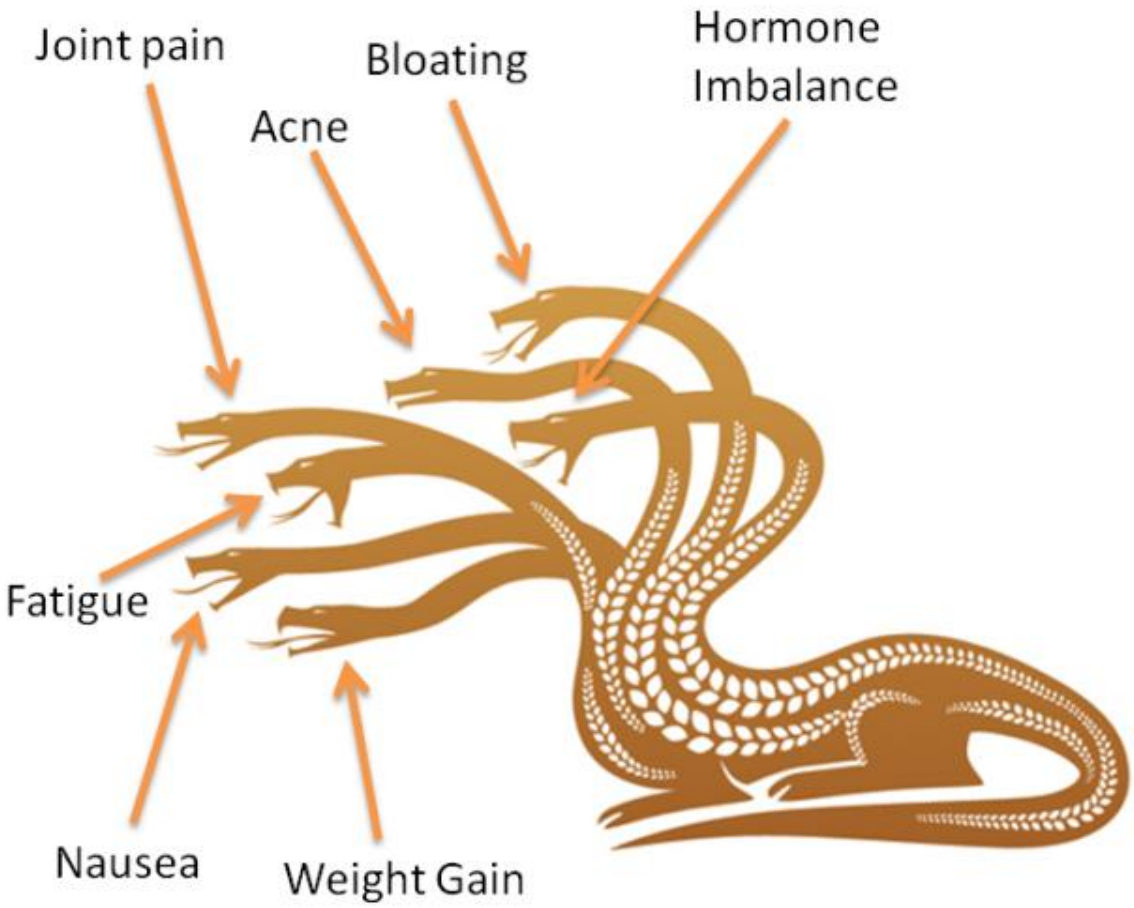
Aside from physical stress, gluten has been shown to contribute to all of these mechanisms...

Diagram 1 – Possible Mechanisms and Consequences of Magnesium Deficiency



SSRI – Selected Serotonin Reuptake Inhibitors
HRT – Hormone Replacement Therapy
NSAIDS – Non steroidal Anti-Inflammatory Drugs

The Gluten Sensitivity *HYDRA*



Treating these symptoms with medicine does not resolve the origin of a patient's problem…

What is Gluten?

- Gluten is a mixture of proteins found in all grains. It is composed of two primary subfractions:
  - Prolamines
  - Glutelins
- The prolamine gliadin is the most studied piece of gluten in the medical literature as it relates to celiac disease.

The Prolamine Fraction of Proteins in Grains

Grain	Prolamine	% Total Protein
Wheat	Gliadin	69
Rye	**Secalinin**	**30-50**
Oats	Avenin	16
Barley	**Hordein**	**46-52**
Millet	Panicin	40
Corn	**Zien**	**55**
Rice	Orzenin	5
Sorghum	**Kafirin**	**52**
Teff	Penniseiten	11

Lab Tests Focusing on Alpha Gliadin is Flawed

Sci Transl Med 21 July 2010:
Vol. 2, Issue 41, p. 41ra51
DOI: 10.1126/scitranslmed.3001012

‹ Prev | Table of Contents | Next ›

RESEARCH ARTICLE

Comprehensive, Quantitative Mapping of T Cell Epitopes in Gluten in Celiac Disease

Jason A. Tye-Din[1,2,3,*], Jessica A. Stewart[1,*], James A. Dromey[1,*], Tim Beissbarth[1,*†], David A. van Heel[4], Arthur Tatham[5], Kate Henderson[6], Stuart I. Mannering[1,‡], Carmen Gianfrani[7], Derek P. Jewell[8], Adrian V. S. Hill[9], James McCluskey[10], Jamie Rossjohn[6] and Robert P. Anderson[1,3,§]

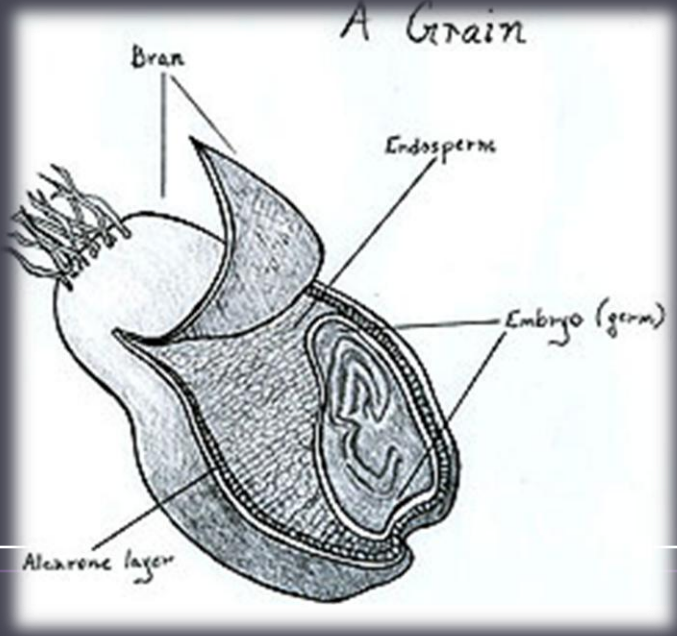
"Unexpectedly, a sequence from ω-gliadin (wheat) and C-hordein (barley) but not α-gliadin was immunodominant regardless of the grain consumed. "

Celiac disease is a genetic condition that results in a debilitating immune reaction in the gut to antigens in grain. The antigenic peptides recognized by the T cells that cause this disease are incompletely defined. Our understanding of the epitopes of pathogenic $CD4^+$ T cells is based primarily on responses shown by intestinal T-cells in vitro to hydrolysates or polypeptides of gluten, the causative antigen. A protease-resistant 33-amino acid peptide from wheat α-gliadin is the immunodominant antigen, but little is known about the spectrum of T cell epitopes in rye and barley or the hierarchy of immunodominance and consistency of recognition of T-cell epitopes in vivo. We induced polyclonal gluten-specific T cells in the peripheral blood of celiac patients by feeding them cereal and performed a comprehensive, unbiased analysis of responses to all celiac toxic prolamins, a class of plant storage protein. The peptides that stimulated T cells were the same among patients who ate the same cereal, but were different after wheat, barley and rye ingestion. Unexpectedly, a sequence from ω-gliadin (wheat) and C-hordein (barley) but not α-gliadin was immunodominant regardless of the grain consumed. Furthermore, T cells specific for just three peptides accounted for the majority of gluten-specific T cells, and their recognition of gluten peptides was highly redundant. Our findings show that pathogenic T cells in celiac disease show limited diversity, and therefore suggest that peptide-based therapeutics for this disease and potentially other strongly HLA-restricted immune diseases should be possible.

Prolamine Definition

- Any of a class of simple proteins soluble in alcohol and usually having a high proline and glutamine content, found in the grains of cereal crops such as wheat, rye, barley, corn, and rice.
- Prolamines are further subclasified into:
  - alpha, beta, gamma and omega fractions
  - Alpha and beta gliadins are the most well studied in relation to celiac disease.

Grains are the seeds of grass. The seed has a bran casing, a starchy endosperm which contains 90% of the protein (including gluten), and a small germ nucleus which is the plant embryo, waiting to grow. Any flour made from the starchy endosperm contains prolamines and is potentially toxic to the grain sensitive/intolerant person.



Excerpt from:

"Nutrition Therapy"

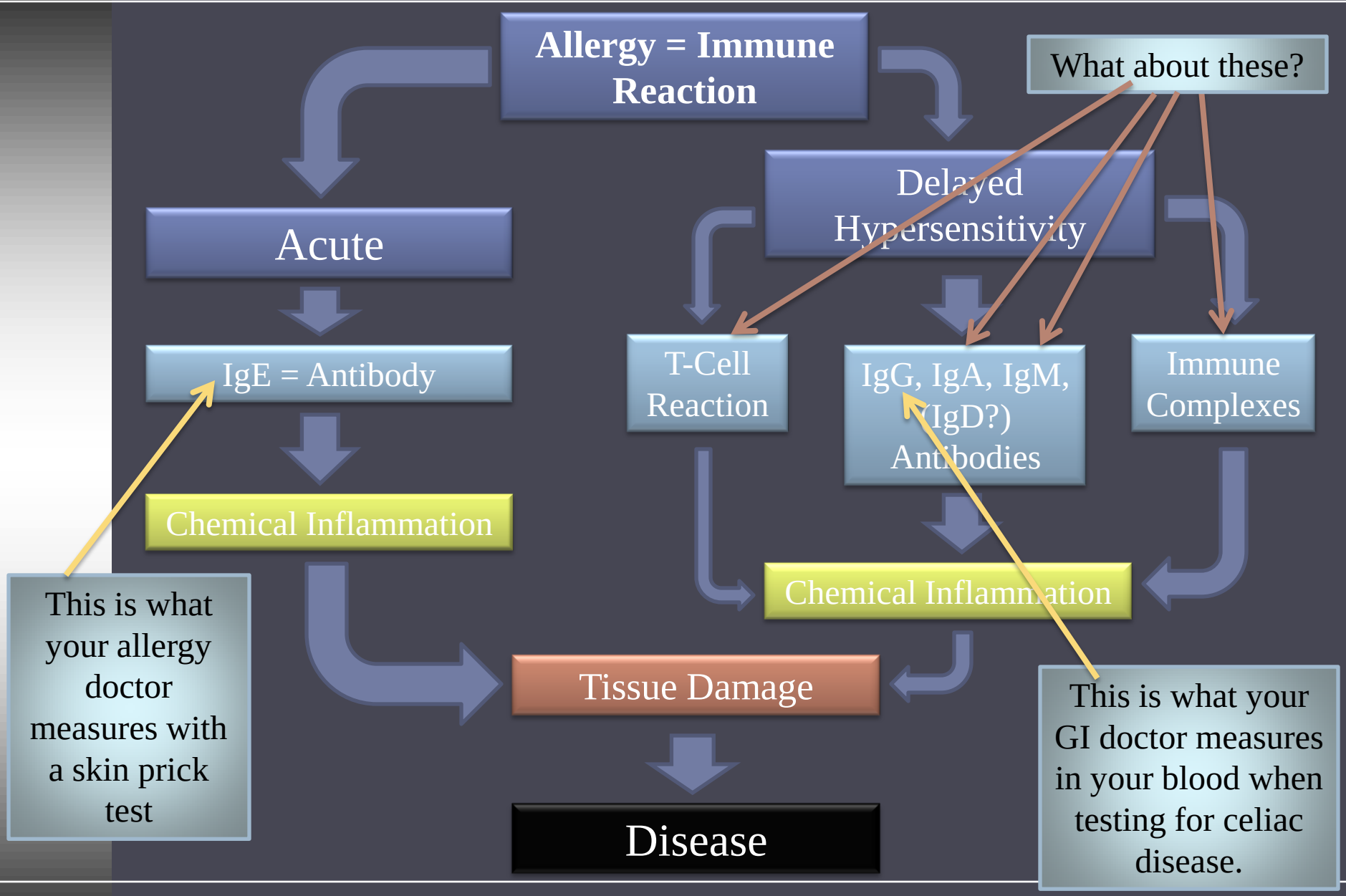
by Stephen J. Gislason, MD

What is Gluten Sensitivity?

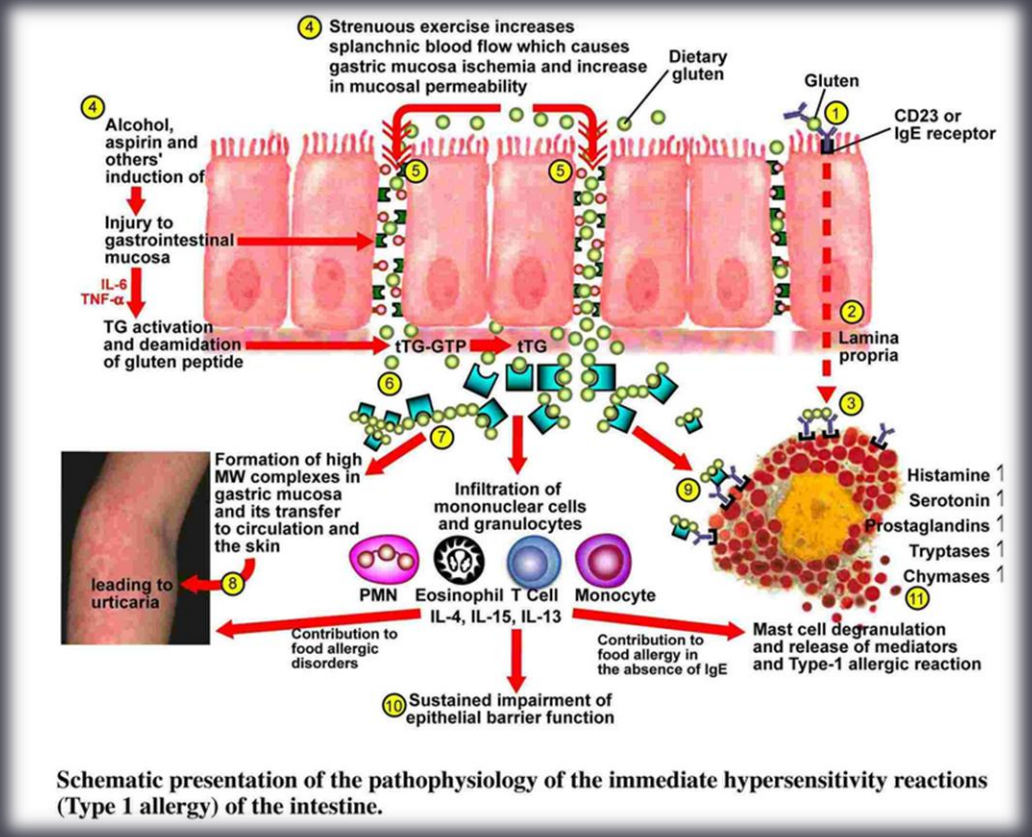
- The current yet antiquated definition is as follows:
  - Gluten sensitivity is an immune reaction to the protein gluten found in *wheat*, barley, and rye. The definition sometimes includes oats & sometimes does not. This definition is often times incorrectly used synonymously with celiac disease.
  - Why is it inconsistent?
  - What about those with non celiac symptoms?
  - What about other gluten containing grains?

Definitional Differences

- **Gluten Allergy** is typically considered to be an allergy (immune mediated response).
- **Gluten intolerance** is considered to be an inability to tolerate gluten (immune and non immune mediated).
- **Gluten Sensitivity** is a mesh of the above two terms.
- **Celiac Disease** is an autoimmune disease of the small intestine caused by gluten induced damage.


Allergy = Immune Reaction
What about these?
Acute
Delayed Hypersensitivity
IgE = Antibody
T-Cell Reaction
IgG, IgA, IgM, (IgD?) Antibodies
Immune Complexes
Chemical Inflammation
Chemical Inflammation
This is what your allergy doctor measures with a skin prick test
Tissue Damage
This is what your GI doctor measures in your blood when testing for celiac disease.
Disease

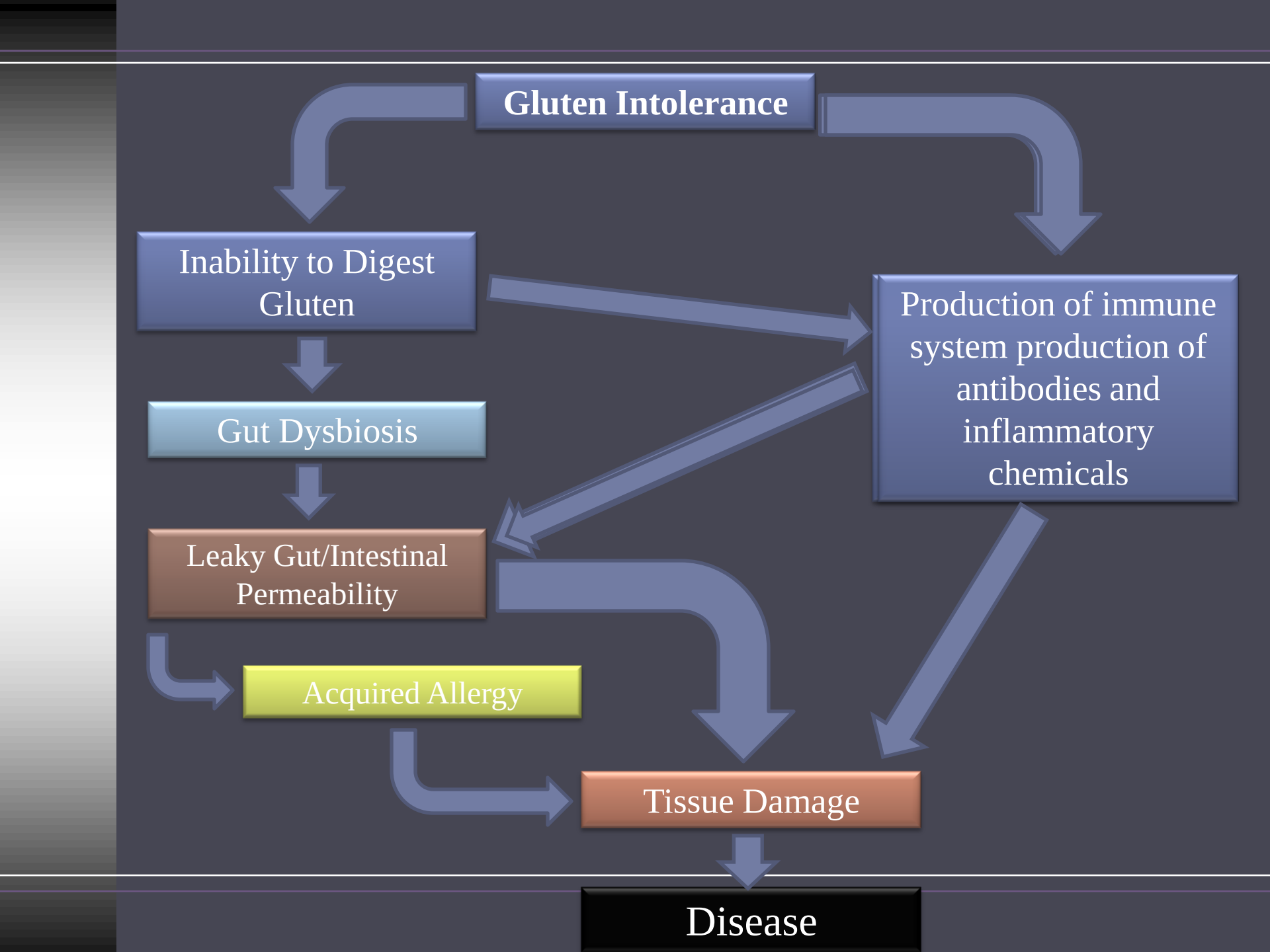
True Allergy Reaction to Gluten (IgE)

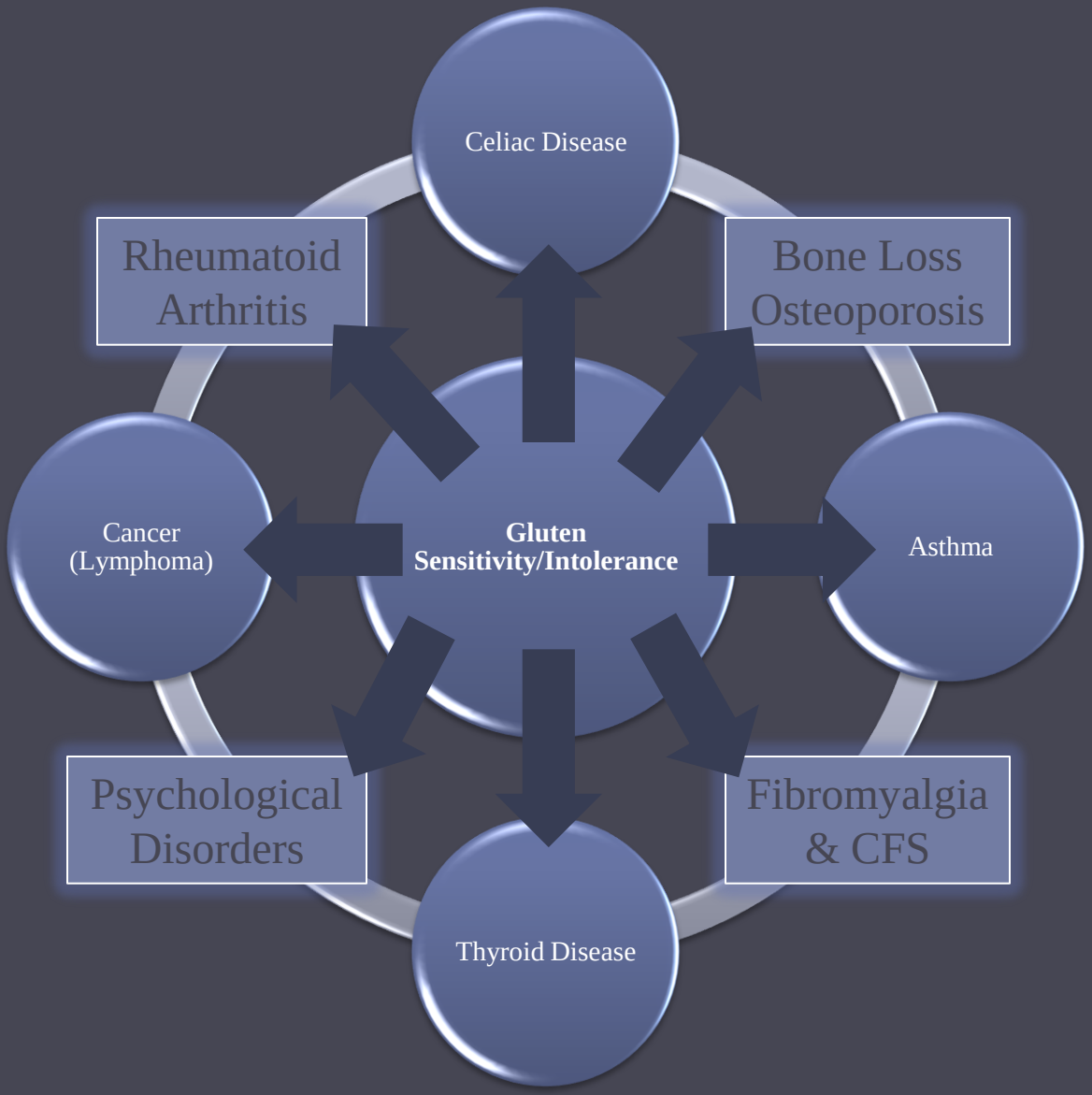


Schematic presentation of the pathophysiology of the immediate hypersensitivity reactions (Type 1 allergy) of the intestine.

Common Acute Food Allergy Reactions

- Hives- itching, burning and swelling of the skin
- Eczema – redness and small blistering of skin
- Bronchitis
- Asthma
- Coughing
- Sneezing
- Diarrhea
- Colic
- Vomiting or excessive spitting up


Gluten Intolerance
Inability to Digest Gluten
Production of immune system production of antibodies and inflammatory chemicals
Gut Dysbiosis
Leaky Gut/Intestinal Permeability
Acquired Allergy
Tissue Damage
Disease


Celiac Disease
Bone Loss Osteoporosis
Asthma
Fibromyalgia & CFS
Thyroid Disease
Psychological Disorders
Cancer (Lymphoma)
Rheumatoid Arthritis
Gluten Sensitivity/Intolerance

Diagnosing Gluten Sensitivity

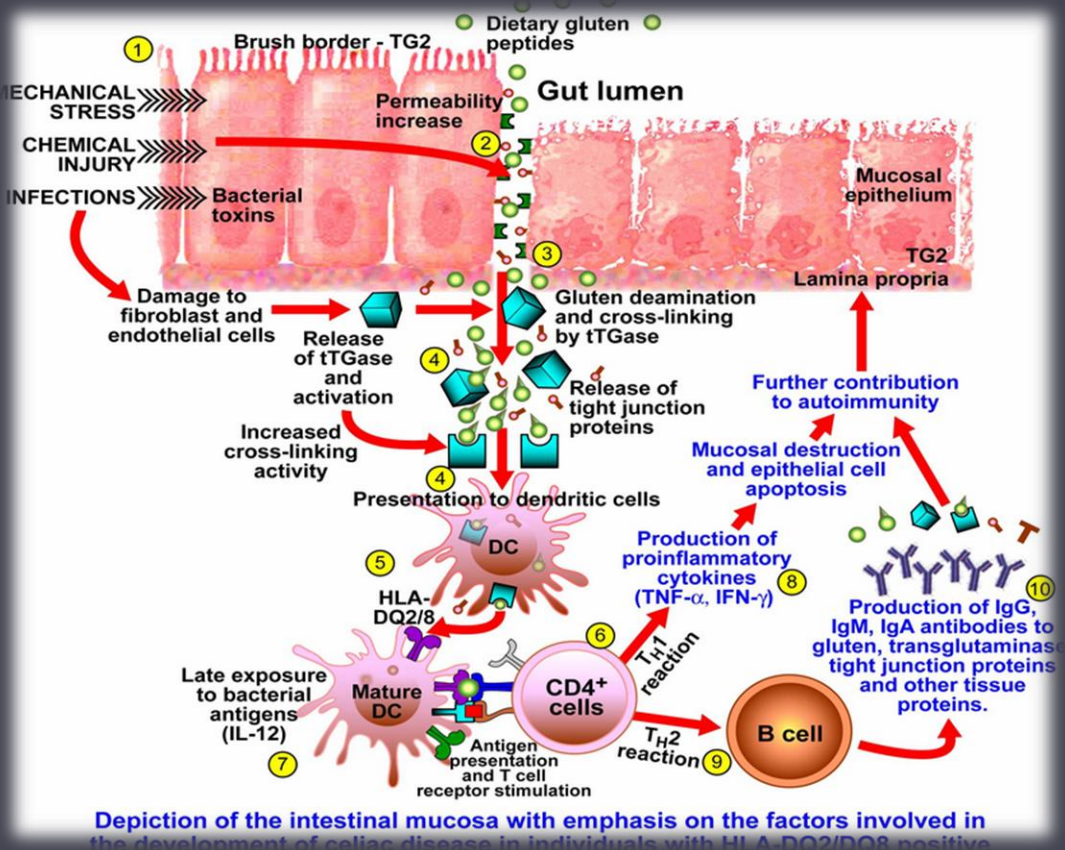
- Blood tests
  - Non specific
  - High tendency towards false negative
- Biopsy
  - Only diagnostic for celiac disease
  - Not an accurate representation of the entire intestine or of extra intestinal damage
- Genetics
  - Very accurate for identifying potential to react to gluten
- Stool tests
  - More accurate than blood but still limited to gliadin
- Predictive antibody testing
  - in development
  - Used to monitor more than diagnose

Old School vs. *New School*

1. Celiac disease is the only manifestation of gluten sensitivity
2. Intestinal biopsy is the gold standard for diagnosis of celiac disease
3. Antibody blood tests are used for gliadin
4. Extraintestinal manifestations of celiac disease are rare

1. Celiac is a rare manifestation of gluten sensitivity
2. HLA-DQ testing with clinical symptoms is the gold standard for gluten sensitivity recognition
3. Extraintestinal manifestations of gluten intolerance are a major cause of missed diagnosis in developed nations worldwide.

Genetic Influence on the Gut Response



Gut 1995; 37: 766–776

Gluten specific, HLA-DQ restricted T cells from coeliac mucosa produce cytokines with Th1 or Th0 profile dominated by interferon γ

E M Nilsen, K E A Lundin, P Krajči, H Scott, L M Sollid, P Brandtzaeg

Abstract

Coeliac disease is precipitated in susceptible subjects by ingestion of wheat gluten or gluten related prolamins from some other cereals. The disease is strongly associated with certain HLA-DQ heterodimers, for example, DQ2

mRNA was analysed semi-quantitatively by slot blotting and polymerase chain reaction (PCR). All TCC were found to secrete interferon (IFN) γ, often at high concentrations (>2000 U/ml); some secreted in addition interleukin (IL) 4, IL 5, IL 6, IL 10, tumour necrosis factor (TNF), and transforming growth factor (TGF) β. The last TCC thus displayed a Th0-like cytokine pattern. However, other TCC produced IFN γ and TNF but no IL 4, or IL 5, compatible with a Th1-like pattern. In conclusion, most DQ8 restricted TCC seemed to fit with a Th0 profile whereas the DQ2 restricted TCC secreted cytokines more compatible with a Th1 pattern. The TCC supernatants induced upregulation of HLA-DR and secretory component (poly-Ig receptor) in the colonic adenocarcinoma cell line HT-29.E10, most probably reflecting mainly the high IFN γ concentrations. This cytokine, particularly in combination with TNF α, might be involved in several pathological features of the coeliac lesion. The characterised cytokine profiles thus

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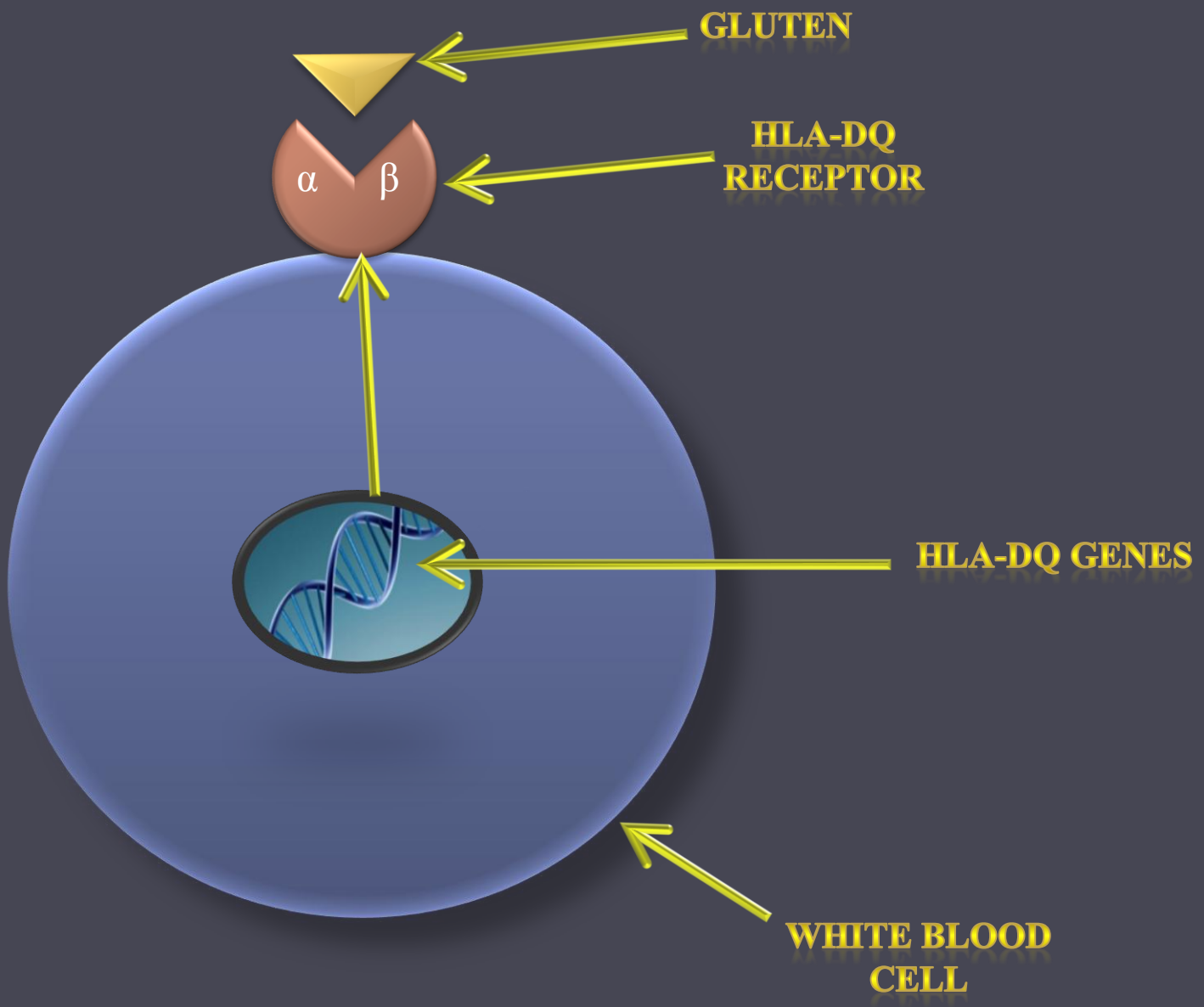
Coeliac disease or gluten sensitive enteropathy is a proximal small intestinal disorder characterised by various degrees of crypt cell hyperplasia and villous atrophy.[1 2] The result is malabsorption and often diarrhoea. The disease is precipitated in susceptible subjects by ingestion of cereal proteins, particularly

immunopathology of the mucosal lesion has not been elucidated. Gluten challenge of treated patients (that is, previously taking a gluten free diet) induces systemic as well as mucosal immune activation.[7–12] Hyperactivation of mucosal T cells seems to be an important feature of the disease.[11] It has been speculated that local generation of various cytokines may contribute to increased permeability and damage of the epithelium,[13 14] upregulation of epithelial HLA class II and secretory component or polymeric immunoglobulin receptor expression,[15–18] as well as expansion and terminal differentiation of mucosal B cells.[19] All these phenomena are seen in the active coeliac lesion.

Gluten responsive T cell clones (TCC) were recently established[20–22] from coeliac mucosa challenged with gluten peptides in vitro.[12] Such TCC were obtained from two patients with the major disease susceptibility haplotype HLA-DR3, -DQ2 and from one with the HLA-DR4, -DQ8 haplotype. All clones were T cell receptor (TcR)α/β^+, $CD2^+$, $CD3^+$, $CD4^+$, $CD8^-$, and the predominant T cell restriction was exerted by the disease suscepti-

All TCC were found to secrete interferon (IFN) y, often at high concentrations (>2000 UIml); some secreted in addition interleukin (IL) 4,IL 5, IL 6, IL 10, tumour necrosis factor (TNF), and transforming growth factor (TGF) P. The last TCC thus displayed a ThO-like cytokine pattern. However, other TCC produced IFN y and TNF but no IL 4, or IL 5, compatible with a Thl like pattern.


GLUTEN
HLA-DQ
RECEPTOR
α
β
HLA-DQ GENES
WHITE BLOOD
CELL

The Gluten Positive Genes

- HLA-DQa1 Gene
  - 0505 (DQ2)*
  - 0501 (DQ2)*
  - 0301 (DQ8)*
- HLA-DQβ1 Gene
  - 0201 (DQ2)*
  - 0202 (DQ2)*
  - 0302 (DQ8)*
  - 03xx (DQ3)
  - 01xx (DQ1)
  - 05xx (DQ1)
  - 06xx (DQ1)

Gluten sensitivity related to HLA alleles other than HLA-DQ2 or DQ8

***Am J Gastroenterol* 2000;95:1974-1982.**

High prevalence of celiac sprue-like HLA-DQ genes and enteropathy in patients with the microscopic colitis syndrome.

Fine KD, Do K, Schulte K, Ogunji F, Guerra R, Osowski L, McCormack J.

OBJECTIVE: Celiac sprue is associated with specific HLA-DQ genes (mainly DQ2). Because there are epidemiological and histopathological similarities between celiac sprue and microscopic colitis, we hypothesized that these syndrome may share an HLA genetic predisposition and pathogenesis. METHODS: The HLA-DQ genes of 25 patients with celiac sprue, 53 patients with the microscopic colitis syndrome, and 429 normal controls were typed and compared. Serum was analyzed for antigliadin and antiendomysial antibodies. Small intestinal biopsies were analyzed for signs of histopathology. RESULTS: HLA-DQ2 or DQ1,3 (the latter as DQ1,7,DQ1,8, or DQ1,9) were seen more frequently in both patient groups relative to controls. In patients with the microscopic colitis syndrome, serological tests for celiac sprue were weakly positive in 17%; mild inflammation of the small intestine without villous atrophy was present in 43%, and inflammation plus partial or subtotal villous atrophy was present in 27%. CONCLUSIONS: A shared set of predisposing HLA-DQ genes account for the epidemiological overlap of celiac sprue and microscopic colitis. Mild to moderate mononuclear cell inflammation of the small intestine, often accompanied by partial or subtotal villous atrophy, is frequent in patients with the microscopic colitis syndrome. Although further studies will be necessary to determine if this enteropathy is induced by dietary gluten, we speculate that the small intestinal but not colonic histopathology in patients with microscopic colitis is caused by immunological gluten sensitivity.

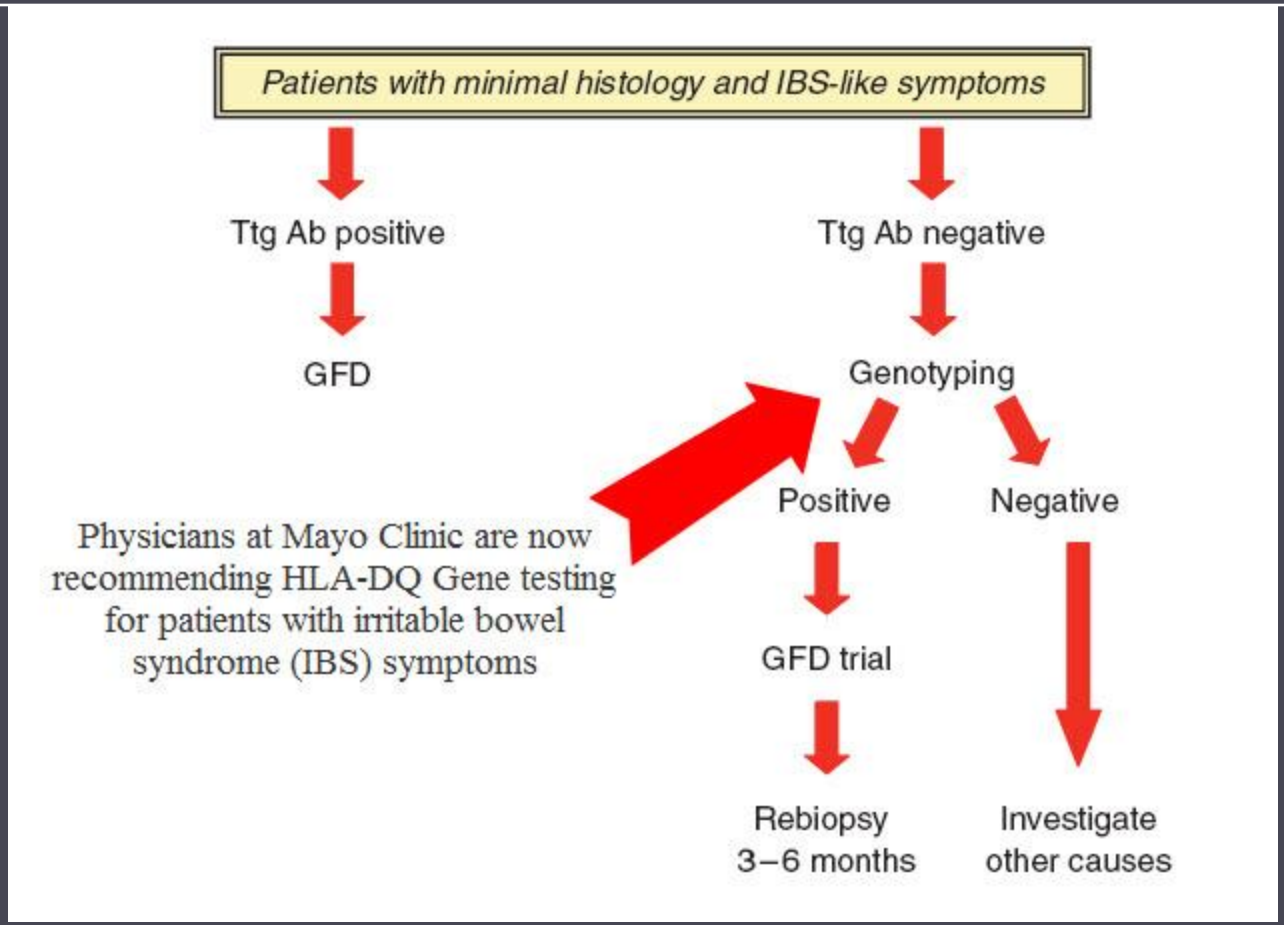
Gluten ataxia in perspective: epidemiology, genetic susceptibility and clinical characteristics.

Brain. 2003 Sep;126(Pt 9):E4; 685-691

Hadjivassiliou M, Grunewald R, Sharrack B, Sanders D, Lobo A, Williamson C, Woodroofe N, Wood N, Davies-Jones A.
Department of Neurology, The Royal Hallamshire Hospital, Sheffield, UK. m.hadjivassiliou@sheffield.ac.uk

We p… …nd sugg… …e have ther… …familial atax… …nd twer… spin… …ble cere… …nstitute of N… scre… …14%), 54 out … …(12%) in th… …e diffe… …< 0.0001 and P < 0.003, respectively). The clinical characteristics of 68 patients with gluten ataxia were as follows: the mean age at onset of the ataxia was 48 years (range 14-81 years) with a mean duration of the ataxia of 9.7 years (range 1-40 years). Ocular signs were observed in 84% and dysarthria in 66%. Upper limb ataxia was evident in 75%, lower limb ataxia in 90% and gait ataxia in 100% of patients. Gastrointestinal symptoms were present in only 13%. MRI revealed atrophy of the cerebellum in 79% and white matter hyperintensities in 19%. Forty-five percent of patients had neurophysiological evidence of a sensorimotor axonal neuropathy. Gluten-sensitive enteropathy was found in 24%. HLA DQ2 was present in 72% of patients. DQ1 accounts for 20% of the gluten ataxia patients. Gluten ataxia is therefore the single most common cause of sporadic idiopathic ataxia. Antigliadin antibody testing is essential at first presentation of patients with sporadic ataxia.

Gastrointestinal symptoms were present in only 13%. MRI revealed atrophy of the cerebellum in 79% and white matter hyperintensities in 19%. Forty-five percent of patients had neurophysiological evidence of a sensorimotor axonal neuropathy. Gluten-sensitive enteropathy was found in 24%. HLA DQ2 was present in 72% of patients. **DQ1 accounts for 20% of the gluten ataxia patients.** Gluten ataxia is therefore the single most common cause of sporadic idiopathic ataxia.



References:

1. *Am J Gastroenterl* 2009;104:1587-94.
2. *J Gastrointestin Liv Dis* 2006. 15;3:221-25

Fortification of Grain?

In the United States, manufacturers of cereals, rices, breads and other grains are federally required to fortify their products with the mineral iron and several B vitamins. In 1943 the government mandated that grain products be fortified with niacin, riboflavin, thiamine and iron, while 1998 saw folate added to this list of nutrients. The addition of these nutrients into everyday products was undertaken to reduce the incidence of beriberi, pellagra, birth defects and other issues.

Traditional Gluten Free Diets Fail

Researchers give the traditional gluten free diet an ***F...***

In this study **only 8% of the patients recovered** from intestinal damage while following *a traditional gluten free diet.*

After a median 16 months GFD, 38 (8%) patients had histological 'normalization', 300 (65%) had 'remission' with persistent intraepithelial lymphocytosis, 121(26%) had 'no change' and 6 (1%) had 'deterioration'.

Source:

Aliment Pharmacol Ther. 2009 Jun 15;29(12):1299-308. Epub 2009 Mar 3.

Why are Gluten Free Diets Failing to Heal So Many Patients?

A recent study published in the *American Journal of Gastroenterology* finds that more than 30% of patients with celiac disease following a gluten free diet fail to exhibit recovery of intestinal damage after 5 years on a gluten free diet.

> **Mucosal recovery was absent in a substantial portion of adults with CD after treatment with a GFD. There was a borderline significant association between confirmed mucosal recovery (vs. persistent damage)**

Source:

The American Journal of Gastroenterology , (9 February 2010)

Let's take a closer look:

1. The Cardinal Rule – One cannot achieve or maintain health eating unhealthy foods.
2. Processed and packaged food is not healthy regardless of whether or not the label claims to be gluten free.
3. Eating unhealthy foods leads to poor health (I know, this should be a no brainer).
4. Many over the counter packaged foods contain cross contamination of gluten
5. Many "gluten free" products contain other types of grain based glutens that have not been adequately studied to be safe for those with gluten sensitivity (see video tutorial #1 for more on this).
6. Most processed "gluten free" products contain genetically modified grains, high amounts of sugar, and are devoid of any significant nutrient density.

Gluten Free Whiplash

Going gluten free can be a saving grace for many. However; a common clinical manifestation called ***Gluten Whiplash*** occurs for many who do not go TRUE gluten free.

The Gluten Whiplash Effect **typically occurs 3-6 months after starting a gluten free diet. Let me explain. When one initially goes gluten free, a state of dietary distress and confusion sets in. Many limit their diets to an extreme because they are not quite sure what to eat. The typical gluten free diet learning curve takes 8-12 weeks. This is because one must spend enough time educating themselves about acceptable products, restaurants, etc. During this time, the body starts to heal and most people do very well noticing dramatic improvements in their health.**

Once the learning curve is conquered, people tend to gravitate toward the processed, packaged "gluten free" food items. People tend to get lazy and make the choice of convenience over health. BIG MISTAKE! This is where *Gluten Whiplash* tends to set in.

Modern Wheat Breeding Increases Celiac Disease Occurrence?

New research claims that the toxicity of wheat gluten potentially worsened by cross breeding different strains…

> **suggests that modern wheat breeding practices may have led to an increased exposure to CD epitopes**

Source:

Theor Appl Genet. 2010 Jul 28.

1. Genetic manipulation of grains – no long term research has been done on safety, yet we assume these foods are OK contrary to common sense. Many studies show these foods to be dangerous.
2. The pervasive use of grains in the food supply. Almost all packaged foods contains grain either as a main ingredient or an agent to alter food texture, viscosity, etc. More grain exposure = more people reacting to grain.
3. The use of herbicides, pesticides, fungicides, etc. Much like genetically modified foods, these chemicals are used under the assumption that they are safe.
4. Over use of antibiotics. Although life saving if one has a bacterial infection, the over utilization of these drugs contributes to a change in the normal healthy gut flora thus weakening the immune system. Additionally, we feed them to chickens, pigs, cows, and fish that are being raised for human food consumption.
5. Anti-acid medications. Nexium, Tums, Prilosec, Rolaids, and more, these drugs suppress acid in the stomach. Acid suppression weakens the immune system and leads to wide spread malabsorption of nutrients.
6. Non steroidal anti-inflammatory medications (NSAIDS). These medications contribute to the destruction of the gastric and intestinal lining thus weakening immunity and predisposing one to intestinal permeability (leaky gut syndrome)
7. Medications in general. Many OTC and prescription medications contain grain based adhesives. Sick from gluten? Take this pill (with gluten in it) and you will get better?!?
8. Grain is cheap food. The government subsidizes grain making it much less expensive to use as a staple food.
9. Commercialization. Everywhere you look, there is a billboard, TV commercial, nutritionist, Food Guide Pyramid, etc telling us how healthy whole grains are.
10. Degradation of the eduction system. Public schools focus on teaching students how to pass standardized tests. Nutrition and physical education are given minimal time in the classroom. Many of those teaching nutrition do not lead by example thus devaluing the lesson. The nutrition basics taught focus on a Food Guide Pyramid based in grain.

What about corn?

"Maize prolamines had low but definite activity even though maize is reported to be harmless"

Gut, 1983, 24, 825-830

GUT
An International Journal of Gastroenterology and Hepatology

Clin. exp. Immunol. (1979) 35, 147–148.

Antibodies to maize in patients with Crohn's disease, ulcerative colitis and coeliac disease

TABLE 1. Incidence of maize and wheat antibodies in patients with Crohn's disease, ulcerative colitis and coeliac disease

Group	Number	Maize antibody positive	Significance*	Wheat antibody positive	Significance*
Crohn's disease	33	11 (33%)	$P = 0{\cdot}037$	19 (58%)	$P = 0{\cdot}000035$
Ulcerative colitis	18	9 (50%)	$P = 0{\cdot}0054$	9 (50%)	$P = 0{\cdot}0027$
Total inflammatory bowel disease	51	20 (39%)	$P = 0{\cdot}0061$	28 (55%)	$P = 0{\cdot}000014$
Coeliac disease	36	16 (44%)	$P = 0{\cdot}0032$	21 (58%)	$P = 0{\cdot}000017$
Coeliac disease off GFD†	22	10 (45%)	$P = 0{\cdot}0079$	15 (68%)	$P = 0{\cdot}0000094$
Coeliac disease on GFD†	14	6 (43%)	$P = 0{\cdot}0307$	6 (43%)	$P = 0{\cdot}018$
Controls	41	6 (14%)	—	5 (12%)	—

* Patients *vs* controls (probabilities estimated either by the Chi-square test with Yate's correction or Fisher's exact test, as appropriate).

† GFD = Gluten-free diet.

"It is of interest that patients with coeliac disease on a gluten-free diet had a lower incidence of wheat, but not of maize, antibodies when compared with those patients not on a diet."

wheat and maize antibodies but in general there was no correlation between the two. In addition,

Correspondence: Professor R. Wright, Professorial Medical Unit, Level F, Centre Block, Southampton General Hospital, Southampton.

0099-9104/79/0010-0147$02.00

3754 J. Agric. Food Chem. 2009, 57, 3754–3759
DOI:10.1021/jf802596g

JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY
ARTICLE

Bovine Milk Caseins and Transglutaminase-Treated Cereal Prolamins Are Differentially Recognized by IgA of Celiac Disease Patients According to Their Age

Francisco Cabrera-Chávez,[†] Ofelia Rouzaud-Sández,[§] Norberto Sotelo-Cruz,[#] and Ana M. Calderón de la Barca*[,†]

[†]Departamento de Nutrición y Metabolismo, Centro de Investigación en Alimentación y Desarrollo, A. C., Carretera a la Victoria Km 0.6, P.O. Box 1735, Hermosillo 83000, Mexico, [§]Departamento de Investigación y Posgrado en Alimentos, Universidad de Sonora, Hermosillo, Mexico and [#]Hospital Infantil del Estado de Sonora, Hermosillo, Sonora, Mexico

The prevalence of celiac disease (CD) has increased worldwide, which could be related to some dietary proteins in infant regimens and/or new food processes, affecting CD-predisposed infants and older children or adults differentially. IgA reactivity to human and bovine caseins, as well as yogurt caseins

mTG treatment increased reactivity to wheat and maize prolamins in patients with celiac disease…

Celiac disease (CD) is an enteropathy triggered by dietary proteins of wheat gluten and related cereals, which has increased to an estimated worldwide prevalence of 1−2% (*1*). Among the causes for the increase in the incidence of CD could be the use of infant formula feeding instead of breastfeeding and the early introduction of cereals in the diet, which have been related to the earlier onset of CD (*2*). Additionally, in recent decades, cereal food technology has changed to fast processes by which proteins are not degraded during manufacture, which could initiate or exacerbate CD in predisposed individuals (*3*). Another change related to CD (*4*, *5*) is the increasing industrial use of microbial transglutaminase (mTG) for improving functional properties of dairy and bakery products (*6*).

CD is characterized by the presence of antibodies against gluten peptides, especially after deamidation by the tissue transglutaminase (tTG), which is also the autoantigen (*7*). Therefore, it was not rare that immunoreactivity of IgA from CD patients' to gluten proteins increased after mTG treatment (*4*, *5*). In addition, some other dietary proteins, such as milk caseins and maize zeins, induced in a contact probe an inflammatory reaction in the CD mucosa of 50% of the patients (*8*) and were recognized by IgA antibodies from other

*Corresponding author [telephone + 52 (662) 289 24 00; fax + 52 (662) 280 00 21; e-mail amc@ciad.mx].

ing the induction of inflammation as an early step that allows gliadins to cross the intestinal barrier in CD-predisposed individuals, and it might initiate the cascade of autoimmune reactions (*10*).

Although CD onset can appear at any age, there are some differences in the immune responses among infants and older children or adults. In young children, the cellular immune response is against amino acid sequences, which are not substrates for tTG, whereas in older children and adults, deamidation of the sequences by tTG increases the response (*11*). In a previous study (*5*), we found that reactivity of serum IgA from a 16-year-old celiac patient to gliadins increased after treatment with mTG, whereas the IgA reactivity of a 2.9-year-old patient was the same against gliadins, whether it was mTG-treated or not.

There are also age-related differences in CD manifestations. In children under 2 years old, CD is characterized by diarrhea and abdominal distension, whereas abdominal pain is more common in children older than 2 years old (*12*). Atypical features (e.g., affecting other organ systems) occur in patients with later onset of the disease (*13*). Additionally, D'Amico et al. (*14*) found that the onset of CD symptoms was mainly in the first to second year for nonbreastfed children, whereas it was in the second to third year for exclusively breastfed children. Therefore, we hypothesized that reactivity of serum IgA from CD patients, which is a manifestation of the immune

 Published on Web 3/16/2009

ELSEVIER

Nutrition 25 (2009) 715–716

NUTRITION

www.nutritionjrnl.com

Research letter

Bovine milk intolerance in celiac disease is related to IgA reactivity to α- and β-caseins

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Abstract — Celiac disease is an autoimmune disease triggered mainly by ingestion of wheat gluten proteins. However, some other dietary proteins, such as those of cow's milk, induce celiac disease–like symptoms in some patients with celiac disease. Different approaches have been done to detect the component responsible for this problem, including the possibility of gluten peptides present in cow's milk.

Keywords: Bovine caseins; Immunoglobulin A reactivity; Celiac disease

In a recent issue of *Nutrition* [1], intolerance to bovine milk of some patients with celiac disease (CD) was reported to not be due to the presence of epitopes from wheat gluten. In the excellent work by Dekking et al. [1], the investigators did not detect gluten proteins or peptides in bovine milk from cows fed diets containing large amounts of wheat. Thus, it was demonstrated that the symptoms seen in patients with CD after cow's milk consumption are not related to gluten proteins in bovine milk coming from wheat-

"the serum IgA response of patients with CD to bovine milk could be related to gliadins and caseins sharing epitopes recognized by antigliadin IgA antibodies, as previously proposed."

caseins was performed [4]. Gels were stained with Coomassie blue or electrophoretically transferred to nitrocellulose membranes. After transfer, immunodetection of antigens on nitrocellulose membranes was carried out [5]. Membranes were incubated overnight with a sera pool from 14 patients diagnosed with CD, followed by incubation with rabbit anti-human IgA, and an extra incubation with alkaline phosphatase–conjugated goat anti-rabbit antibodies. Alkaline phosphatase activity was developed.

Figure 1 shows the gliadins (Fig. 1A, lane 2) and bovine caseins (Fig. 1B, lane 2) electrophoretic patterns and their respective immunodetections with serum IgA from patients with CD (lane 3 for gliadins in Fig. 1A and lane 3 for caseins in Fig. 1B). As expected, there was a clearly different electrophoretic mobility for the two protein types. In Figure 1A, lane 2, gliadins had a molecular weight from 40 and 28 kDa (Fig. 1B, lane 3), but not κ-casein near 30 kDa. The minority fraction of caseins, κ-casein, has the higher antigenicity for milk-intolerant individuals [7]. Therefore, the IgA immunoreactivity found against α- and β-caseins is not attributable to antigenicity.

Previous studies [2,3] have demonstrated a reaction to caseins, although these were mixtures of α-, β-, and κ-caseins and probably other milk proteins; however, a distinctive identification had not been done. It has been published that there is a high homology of some peptides in bovine β-casein to the gluten peptide, mainly with the amino acid

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"The observation that corn gluten challenge induced an abnormal NO reaction in some of our patients with CD is intriguing as maize is considered safe and is recommended as the substitute cereal in a gluten free diet."

Gut 2005;54;769-774

"The allergens in rice, corn, millet and buckwheat should be better studied before they can be recommended as alternatives for cereal allergic children."

Clin Exp Allergy. 1995 Nov;25(11):1100-7.

JPGN Journal of Pediatric Gastroenterology and Nutrition

"High titres were also found when coeliac sera were tested against wheat glutenins, albumins, and globulins, as well as against barley, oats, and maize prolamines"

J Pediatr Gastroenterol Nutr. 1987 May Jun;6(3):346-50.

Polizzi A, Finocchiaro M, Parano E, et al. Recurrent peripheral neuropathy in a girl with celiac disease. *J Neurol Neurosurg Psychiatry*2000;68:104-105.

In this case, corn flakes triggered her symptoms!

Journal of
NEUROLOGY, NEUROSURGERY
& PSYCHIATRY with Practical Neurology

Recent Studies on Rice…

Mehr S, Kakakios A, Frith K, et al. Food Protein Induced Enterocolitis Syndrome: 16 year experience. *Pediatrics* 2009;123(3):

"Causative foods for the 35 children were rice (*n* = 14), soy (*n* = 12), cow's milk (*n* = 7), vegetables and fruits (*n* = 3), meats (*n* = 2), oats (*n* = 2), and fish (*n* = 1). In the 66 episodes, vomiting was the most common clinical feature (100%), followed by lethargy (85%), pallor (67%), and diarrhea (24%). A temperature of <36°C at presentation was recorded for 24% of episodes."

Mehr S, Kakakios AM, Kemp AS. Rice: a common and severe cause of food protein induced enterocolitis syndrome. *Arch Dis Child* 2009;94(3):220-3.

Gluten Aside. Isn't Grain Supposed to Be Healthy?

- The food guide pyramid recommends up to 11 servings per day with 50% coming from whole grain sources.

Isn't Grain Supposed to Be Healthy?

- The seeds are sprayed with fungicides and insectisides.
  - Xenoestrogens which effect hormone balance and contribute to many diseases (breast cancer, endometriosis, fibrocystic breasts)

Isn't Grain Supposed to Be Healthy?

- The seeds are doused with hormones to aid in growth
- The grains are stored in bins sprayed with additional pesticides
- Drying of the grain causes damage to it's proteins
- Processing adds…
  - Dough conditioners
  - Preservatives
  - Soy flour
  - Extrusion creates acrylamide
  - Hydrogenated oils

Nutrient Properties of Grains

- Poor source of protein leads to inadequate growth (archeological fossil records show reduction in stature and osteoporosis with the introduction cereal grain based diets)
- Low in EPA and DHA
- Contain Anti-nutrients
- Contain Autoimmune inducing peptides for genetically susceptible individuals

Hormonal influences linked to obesity

- Much like sugar, Grains cause insulin excess…
  - Tells the body to store fat
  - Prevents muscle building
  - Reducing vitamin C uptake into white blood cells
  - Causes magnesium loss
    - Leads to cyclical hypertension (muscle constriction
  - Sodium retention and excess
    - Contributes to congestive heart failure

What about infant cereals?

So What Do I Eat?

Meat – any variety is ok. You must consider the source of the animal. In the case of animal based foods you are not what you eat, you're what you eat eats!

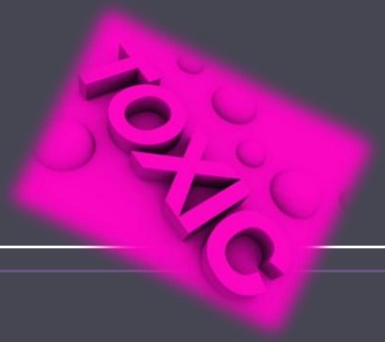
- Beef – should come from grass fed animals.
- Fish – Should be wild caught not farm raised.
- Poultry and eggs – should be free range organic

- Dairy
  - Only from grass fed (grazing animals). Raw dairy from a reputable farm is recommended.
- Fruits and Vegetables
  - Any organic variety that you are not allergic to.
- Nuts, non grain seeds, and beans
  - Any organic variety that you are not allergic to.
- Processed food including processed food labeled “gluten free” are better left avoided.

Gluten contamination of grains, seeds, and flours in the United States: a pilot study.

"Twenty-two inherently gluten-free grains, seeds, and flours not labeled gluten-free were purchased in June 2009 and sent unopened to a company who specializes in gluten analysis. All samples were homogenized and tested in duplicate using the Ridascreen Gliadin sandwich R5 enzyme-linked immunosorbent assay with cocktail extraction… **Nine of 22 (41%) samples contained more than the limit of quantification**, with mean gluten levels ranging from 8.5 to 2,925.0 ppm. Seven of 22 samples (32%) contained mean gluten levels >/=20 ppm and would not be considered gluten-free under the proposed FDA rule for gluten-free labeling. **Gluten contamination of inherently gluten-free grains, seeds, and flours not labeled gluten-free is a legitimate concern."**

J Am Diet Assoc. 2010 Jun;110(6):937-940.



If the following terms are found on the food label or ingredient list the food should be avoided:

- Malt
- Wheat
- Gluten
- Barley
- Rye
- Oats
- Teff*
- Sorghum*
- Buckwheat***
- Amaranth***
- Quinoa***
- Spelt*
- Rice*
- Corn or maize*
- Millet*
- Triticale (wheat hybrid)*

Processed foods are not recommended!

- Textured vegetable protein **
- Hydrolyzed plant protein **
- Extenders and binders **
- Hydrolyzed vegetable protein **
- Modified Food Starch**
- MSG**
- Natural Flavors**

*These grains are classically considered gluten free, but are not recommended on a TRUE gluten free diet.

** These items are only found in processed food items.

*** These items are technically not grains, but are at high risk for cross contamination and not recommended on a TRUE gluten free diet unless verification can be obtained. These pseudo cereals are also very high in glutamic acid and should be discouraged as substitutes for patients with neurological symptoms.

Additional Recommendations

Because gluten sensitivity has been shown to cause malabsorption of vitamins, minerals, and other nutrients, it is recommended that you see your doctor to be tested for nutritional deficiencies. Spectracell labs has the most comprehensive and scientifically advanced test available. You can visit their website @ www.spectracell.com to find physicians in your area capable of performing the testing for you.

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LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
4724 Sweetwater Blvd
Suite 102
Sugar Land, TX 77479-
USA

Name: [redacted]
Gender: Female DOB: 09/30/1970

Accession Number: K49200
Requisition Number: 382057

Date of Collection: 06/07/2011
Date Received: 06/08/2011
Date Reported: 06/17/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Folate Asparagine Oleic Acid Calcium

Gluten sensitivity, migraine headaches, and chronic fatigue

John F. Crawford, Ph.D.
Laboratory Director

CLIA# 45D0710715

SPECTRACELL LABORATORIES

LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
4724 Sweetwater Blvd
Suite 102
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USA

Name: [redacted]
Gender: Female DOB: 07/24/1950

Accession Number: K59843
Requisition Number: 378167

Date of Collection: 08/01/2011
Date Received: 08/02/2011
Date Reported: 08/11/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Calcium Zinc Spectrox

Irritable Bowel Syndrome, Gluten Sensitivity

John F. Crawford, Ph.D.
Laboratory Director

CLIA# 45D0710715

SPECTRACELL LABORATORIES

LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
4724 Sweetwater Blvd
Suite 102
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USA

Name [redacted]
Gender: Female DOB: 07/22/1954

Accession Number: K59076
Requisition Number: 382063

Date of Collection: 07/27/2011
Date Received: 07/28/2011
Date Reported: 08/08/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Pantothenate Biotin

Antibiotic induced waisting, muscle pain, IBS (diarrhea)

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Laboratory Director

CLIA# 45D0710715

SPECTRACELL LABORATORIES

LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
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Suite 102
Sugar Land, TX 77479-
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Name: [redacted]
Gender: Female DOB: 11/14/1953

Accession Number: K55373
Requisition Number: 337236

Date of Collection: 07/07/2011
Date Received: 07/08/2011
Date Reported: 07/19/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Zinc
Spectrox
Magnesium
Selenium
Vitamin E

This patient was diagnosed with the following:

Gluten Sensitivity
Hypothyroidism
Type II Diabetes

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Laboratory Director

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LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
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Name: [redacted]
Gender: Female DOB: 12/13/1978

Accession Number: K51283
Requisition Number: 382064

Date of Collection: 06/15/2011
Date Received: 06/16/2011
Date Reported: 06/27/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Vitamin B1	Vitamin B2	Vitamin B3	Vitamin B6
Folate	Glutamine		

This gluten sensitive patient was diagnosed with PCOS, obesity, and chronic muscle pain.

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Laboratory Director

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LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
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Name: [redacted]
Gender: Female DOB: 09/16/1993

Accession Number: K47855
Requisition Number: 382050

Date of Collection: 05/31/2011
Date Received: 06/01/2011
Date Reported: 06/10/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Vitamin B12 Serine Asparagine Oleic Acid
Spectrox

Gluten Sensitivity - Chronic anemia, IBS, muscle pain, and intermittent fainting

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Laboratory Director

CLIA# 45D0710715

SPECTRACELL LABORATORIES

LABORATORY REPORT

Account Number: 191473

Peter Osborne , D.C.
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Suite 102
Sugar Land, TX 77479-
USA

Name: [redacted]
Gender: Female DOB: 05/25/1978

Accession Number: K58594
Requisition Number: 398244

Date of Collection: 07/25/2011
Date Received: 07/26/2011
Date Reported: 08/04/2011

Summary of Deficient Test Results

Micronutrient analysis (WBC) determined the following deficiencies:

Vitamin B3 Vitamin B6 Folate Coenzyme Q-10

Before seeing me, this patient was diagnosed with idiopathic peripheral neuropathy, depression, hypothyroid, and migratory joint pain.

John F. Crawford, Ph.D.
Laboratory Director

CLIA# 45D0710715

Additional Recommendations

Gluten can cause leaky gut syndrome. Because of this, many people develop additional food allergies. Measuring for food allergies is an important next step to help to determine what other dietary exposures are contributing to disease.

ELISA/ACT Biotechnologies LLC

Have Family Members Genetically Tested!

For more information and for physician affiliate inquiries:

Contact Dr. Osborne or visit

www.GlutenFreeSociety.org