

Gluten Sensitivity: Real or Not
 (People Shall Not Live by Bread Alone..)



Alessio Fasano, M.D.
 Mucosal Immunology and Biology Research Center
 And Center for Celiac Research
 Massachusetts General Hospital, Boston MA - U.S.A.




Conflict of Interest

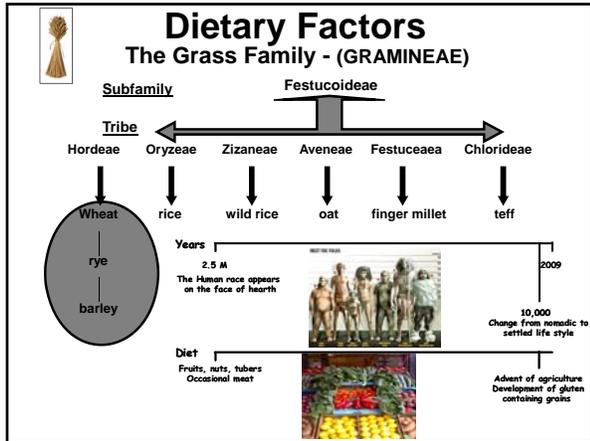
In the past 12 months, I have had the following relevant financial relationships with the following manufacturer of any commercial product(s) and/or provider(s) of commercial services discussed in this CME activity:

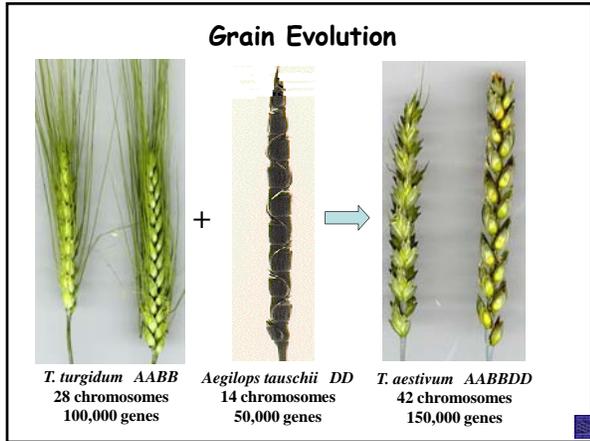
ALBA THERAPEUTICS, CO-FOUNDER AND STOCK HOLDER

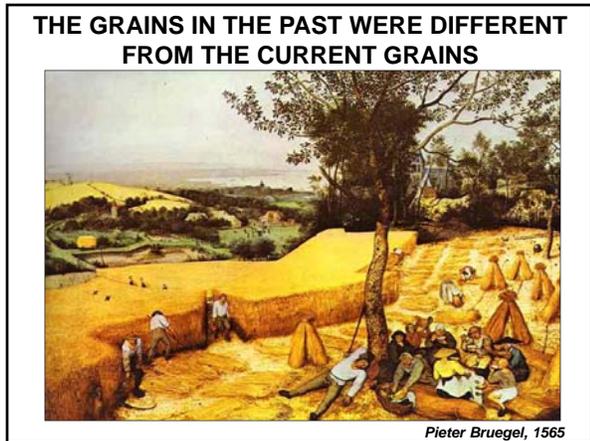
I will not discuss any product from Alba Therapeutics in my presentation. I do not intend to discuss an unapproved or investigative use of a commercial product or device in my presentation.

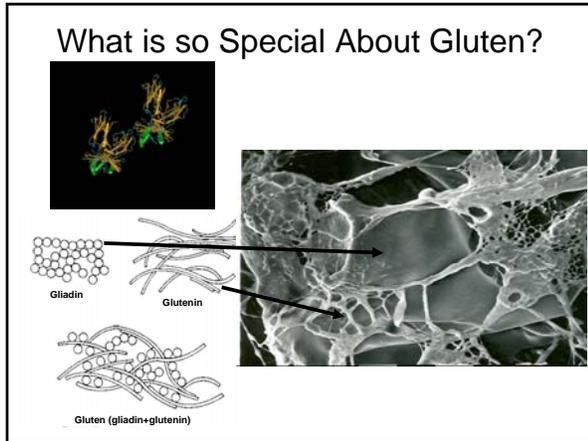
NEWS #1:
Why Gluten is Toxic

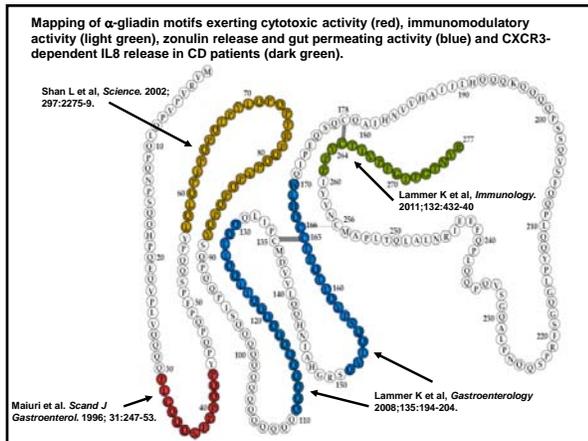


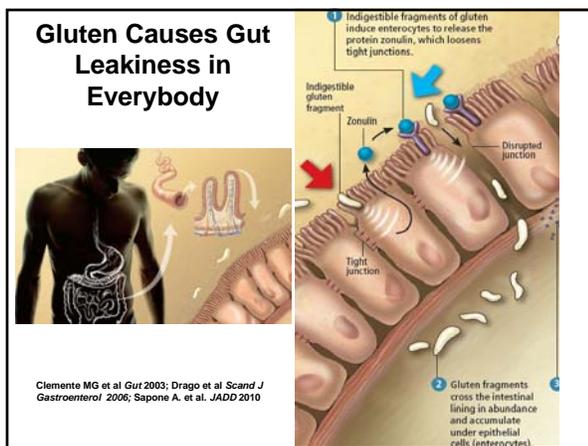












NEWS #2: Not Only Celiac Disease



Gluten Free Market

Low Carb Diet Fat Free Diet Gluten Free Diet



For the American general population adopting a gluten-free diet is becoming an increasingly popular solution. The market for gluten-free food and beverage products grew at a compound annual growth rate of 28 percent from 2004 to 2008, to finish with almost **\$2.6 billion** in retail sales last year. By 2017 the market is expected to reach about **\$ 6.1 billion** in sales.

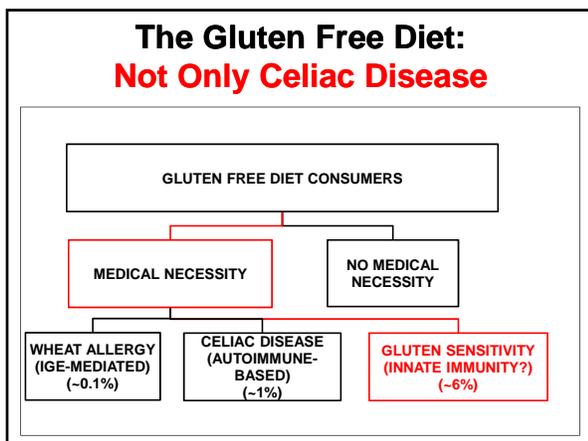
The fact that approximately 3 million Americans suffer from celiac disease and only a fraction of these patients have been diagnosed implies that patients suffering of other forms of proven gluten reaction, including gluten sensitivity and wheat allergy, contribute to this market growth. The rest of the market is filled by people affected by maladies claimed to be affected by gluten exposure, including autism, ADHD, multiple sclerosis, IBS, and ADHD.

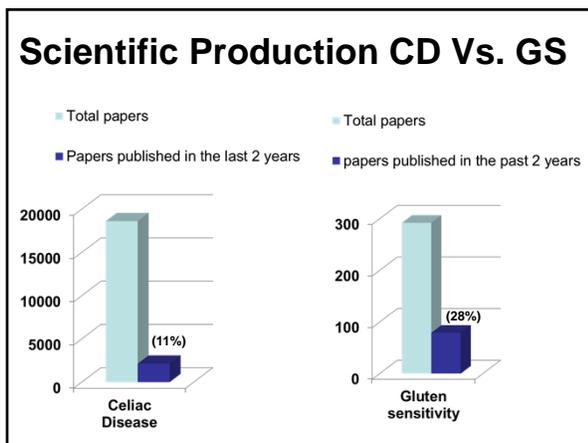
The Fad Factor of the GFD

Lady Gaga goes on gluten free diet

Updated: 2012-08-20 14:45
(Agencies)







Line First, published on February 16, 2012 as 10.1136/gutjnl-2011-301346

Coeliac disease

ORIGINAL ARTICLE

The Oslo definitions for coeliac disease and related terms

Jonas F Ludvigsson,^{1,2} Daniel A Leffler,³ Julio C Bai,⁴ Federico Biagi,⁵ Alessio Fasano,⁶ Peter H R Green,⁷ Marios Hadjivassiliou,⁸ Katri Kaukinen,⁹ Ciaran P Kelly,³ Jonathan N Leonard,¹⁰ Knut Erik Aslaksen Lundin,¹¹ Joseph A Murray,¹² David S Sanders,^{13,14} Marjorie M Walker,¹⁴ Fabiana Zingone,¹⁵ Carolina Ciacci¹⁶

ABSTRACT
Objective The literature suggests a lack of consensus on the use of terms related to coeliac disease (CD) and gluten.
Design A multidisciplinary task force of 16 physicians from seven countries used the electronic database PubMed to review the literature for CD-related terms up to January 2011. Teams of physicians then suggested a definition for each term, followed by feedback of these definitions through a web survey on definitions, discussions during a meeting in Oslo and phone conferences. In addition to 'CD', the following descriptors of CD were evaluated (in alphabetical order):

Significance of this study

What is already known on this subject?

- There is a lack of consensus on the use of terms related to coeliac disease (CD) and gluten.
- Variability in the use of terminology has led to difficulty when comparing and evaluating clinical studies and research findings.

What are the new findings?

- The panel reached agreement on the definition

BMC Medicine impact factor 5.75

Search: this journal for

Articles Authors Reviewers About the journal My BMC Medicine

Opinion Highly accessed Open access

Spectrum of gluten-related disorders: consensus on new nomenclature and classification

Anna Sapone^{1,2}, Julio C Ball³, Carolina Ciacci⁴, Zsuzsanna Dolinsek⁵, Peter HR Green⁶, Marius Hadjiyavdimou⁷, Katri Vuolteenaho⁸, Kameron Rostiani⁹, David S Sanders¹⁰, Michael Schumann¹¹, Heiner Tibirica¹², Danilo Villalta¹³, Umberto Volta¹⁴, Carlo Catassi^{15,16} and Alessio Fasano^{1*}

* Corresponding author: Alessio Fasano a.fasano@bmc.com

Some interesting statistics (updated September 7th, 2012):

- Published February 7th, 2012;
- Total number of download since published: 68169 (second all time);
- #4 most popular paper of the month (2,614 downloads);
- #2 Paper of the year;
- Average downloads/month: 3787;
- Most frequent health care professionals to download the paper: pediatricians, primary care physicians and lab professionals.

Case Presentation: Diagnosis of Gluten Sensitivity

Description of the Case

AJ 19 y old F

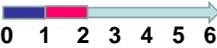
0 1 2 3 4 5 6

- 6 months history of:
 - Recurrent abdominal pain (mainly epigastric)
 - Heartburn

Suspecting GERD, pt was placed on PPI, but no resolution of symptoms.

One month after the onset of GERD symptoms pt developed headaches, dizziness, numbness of fingers, paresthesia, gradual reduction of legs' muscle strength that forced her on a wheelchair.

Description of the Case



Suspecting neurological cause, patient underwent to:

- MRI
- Evoked potentials

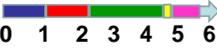
Both resulted negative

Other diagnoses that were considered include:

- Lyme disease;
- Epstein Barr Virus
- Pernicious Anemia
- Lupus

All were ruled out

Description of the Case



Because of the persistence of GERD symptoms pt underwent to an EGD reported as normal (including duodenal biopsy that showed only increased IEL). She was also screened for CD and tested negative

Despite negative results, pt decided to embrace a GFD

- Within 3 weeks her GI symptoms resolved
- Within 2 months her neurological symptoms also improved. Six month after implementation of the GFD she was able to walk with the assistance of a cane. Twelve months later she regained completely her walking function.

Gluten Sensitivity: Definition

Cases of gluten reaction in which both allergic and autoimmune mechanisms have been ruled out (diagnosis by exclusion criteria)

- Negative immuno-allergy tests to wheat;
- Negative CD serology (EMA and/or tTG) and in which IgA deficiency has been ruled out;
- Negative duodenal histopathology;
- Presence of biomarkers of gluten immune-reaction (AGA+);
- Presence of clinical symptoms that can overlap with CD or wheat allergy symptomatology;
- Resolution of the symptoms following implementation of a GFD (double blind)

Gluten Sensitivity:
What is the Magnitude of the Problem?
The CFCR Experience (2004-2010)

- Nr. of the patients seen at the CFCR clinic: **5,896**
- Nr. of patients fulfilling criteria for GS: **347**
- Prevalence in our cohort: **1:17 (6%)**
- Symptoms:
 - Abdominal pain: 68%
 - Eczema and/or rash: 40%
 - Headache: 35%
 - "Foggy mind": 34%
 - Fatigue: 33%
 - Diarrhea: 33%
 - Depression: 22%
 - Anemia: 20%
 - Numbness legs/arms/fingers: 20%
 - Joint pain: 11%

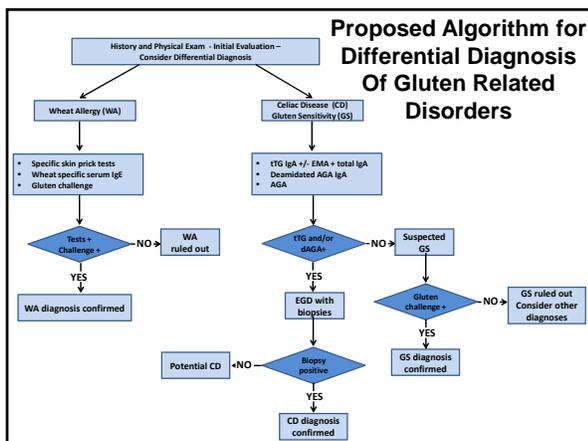
Gluten Sensitivity and IBS

[Cell Mol Immunol](#). 2013 Aug 12. doi: 10.1038/cmi.2013.28. [Epub ahead of print]
Non-celiac gluten sensitivity: questions still to be answered despite increasing awareness.
 Volta U, Caio G, Tovoli F, De Giorgio R.

Abstract
 Recently, the increasing number of patients worldwide who are sensitive to dietary gluten without evidence of celiac disease or wheat allergy has contributed to the identification of a new gluten-related syndrome defined as non-celiac gluten sensitivity. Our knowledge regarding this syndrome is still lacking, and many aspects of this syndrome remain unknown. Its pathogenesis is heterogeneous, with a recognized pivotal role for innate immunity; many other factors also contribute, including low-grade intestinal inflammation, increased intestinal barrier function and changes in the intestinal microbiota. Gluten and other wheat proteins, such as amylase trypsin inhibitors, are the primary triggers of this syndrome, but it has also been hypothesized that a diet rich in fermentable monosaccharides and polyols may elicit its functional gastrointestinal symptoms. The epidemiology of this condition is far from established; its prevalence in the general population is highly variable, ranging from 0.63% to 6%. From a clinical point of view, non-celiac gluten sensitivity is characterized by a wide array of gastrointestinal and extraintestinal symptoms that occur shortly after the ingestion of gluten and improve or disappear when gluten is withdrawn from the diet. These symptoms recur when gluten is reintroduced. Because diagnostic biomarkers have not yet been identified, a double-blind placebo-controlled gluten challenge is currently the diagnostic method with the highest accuracy. Future research is needed to generate more knowledge regarding non-celiac gluten sensitivity, a condition that has global acceptance but has only a few certainties and many unresolved issues.

Cellular & Molecular Immunology advance online publication, 12 August 2013; doi:10.1038/cmi.2013.28.

| Differential Diagnosis Between CD, GS, and WA | | | |
|---|--|---|--|
| | Celiac Disease | Gluten Sensitivity | Wheat Allergy |
| Time interval between gluten exposure and onset of symptoms | Weeks-Years | Hours-Days | Minutes-Hours |
| Pathogenesis | Autoimmunity (Innate+ Adaptive Immunity) | Immunity? (Innate Immunity?) | Allergic Immune Response |
| HLA | HLA DQ2/8 restricted (~97% positive cases) | Not-HLA DQ2/8 restricted (50% DQ2/8 positive cases) | Not-HLA DQ2/8 restricted (35-40% positive cases as in the general population) |
| Auto-antibodies | Almost always present | Always absent | Always absent |
| Enteropathy | Almost always present | Always absent (slight increase in IEL) | Always absent (eosinophils in the lamina propria) |
| Symptoms | Both intestinal and extra-intestinal (not distinguishable from GS and WA with GI symptoms) | Both intestinal and extra-intestinal (not distinguishable from CD and WA with GI symptoms) | Both intestinal and extra-intestinal (not distinguishable from CD and GS when presenting with GI symptoms) |
| Complications | Co-morbidities Long term complications | Absence of co-morbidities and long term complications (long follow up studies needed to confirm it) | Absence of co-morbidities. Short-term complications (including anaphylaxis) |



Diagnosis of Gluten Sensitivity

Take Home Messages:

- **Gluten Sensitivity is not rare;**
- **Gluten Sensitivity cannot be distinguished from Celiac Disease purely on the clinical basis;**
- **Gluten Sensitivity can present with vague, non-specific symptoms;**
- **A gluten free diet can be considered only when other forms of gluten reactions and other causes of pt's symptoms have been ruled out;**
- **Listen to your patient!!!**
