Many Masks of Gluten Related Disorders in Children

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Objectives

- Identify clinical, epidemiological, and diagnostic characteristics of celiac disease, wheat allergy, and gluten sensitivity
- Learn the most cost effective means of testing for gluten related disorders
- List similarities and differences in implementing a gluten free diet for the three different forms of gluten-related disorders

Celiac Disease

Celiac Disease

- The most common genetically—induced food intolerance worldwide, with a prevalence around 1% (and growing!)

- An autoimmune condition triggered and sustained by the ingestion of gluten (wheat, rye, barley) in genetically predisposed individuals

- Causes an inflammatory damage of the mucosa of the small intestine resulting in a variety of clinical presentations

- Left untreated may lead to complications and increased mortality

Celiac Disease in London, Year 1938

. 2.—Photograph of five cases of coeliac disease showing the general clinical feature

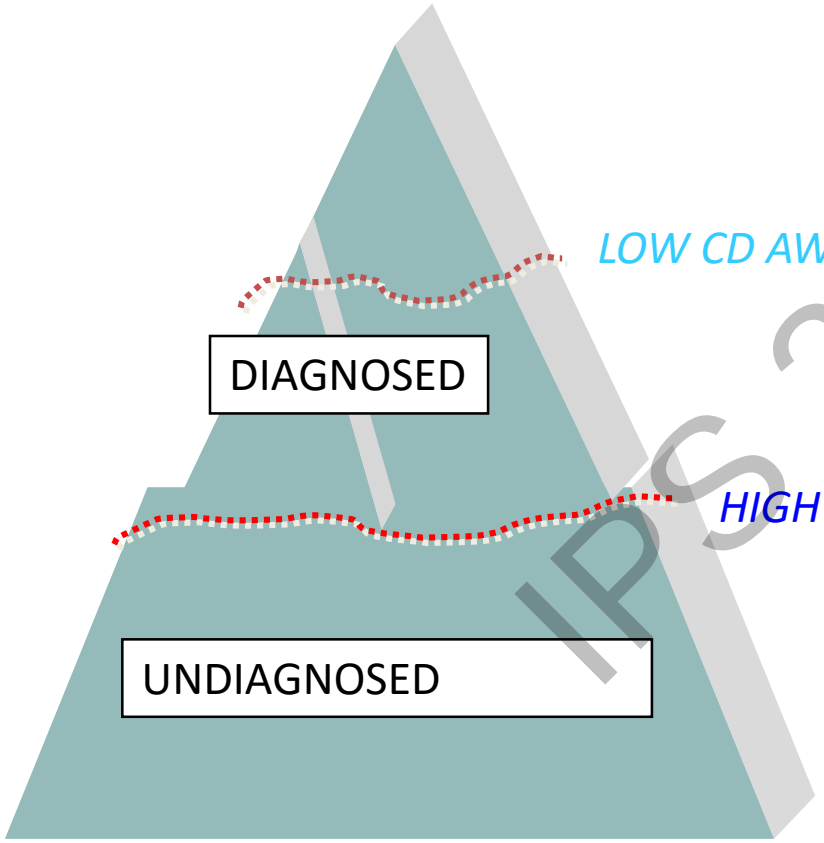
Celiac Disease Prevalence Data

Geographic Area	Prevalence on clinical diagnosis*	Prevalence on screening data
Brasil	?	1:400
Denmark	1:10,000	1:500
Finland	1:1,000	1:130
Germany	1:2,300	1:500
Italy	1:1,000	1:184
Netherlands	1:4,500	1:198
Norway	1:675	1:250
Sahara	?	1:70
Slovenia	?	1:550
Sweden	1:330	1:190
United Kingdom	1:300	1:112
USA	1:10,000	1:133
Worldwide (average)	1:3,345	1:266

*based on classical, clinical presentation

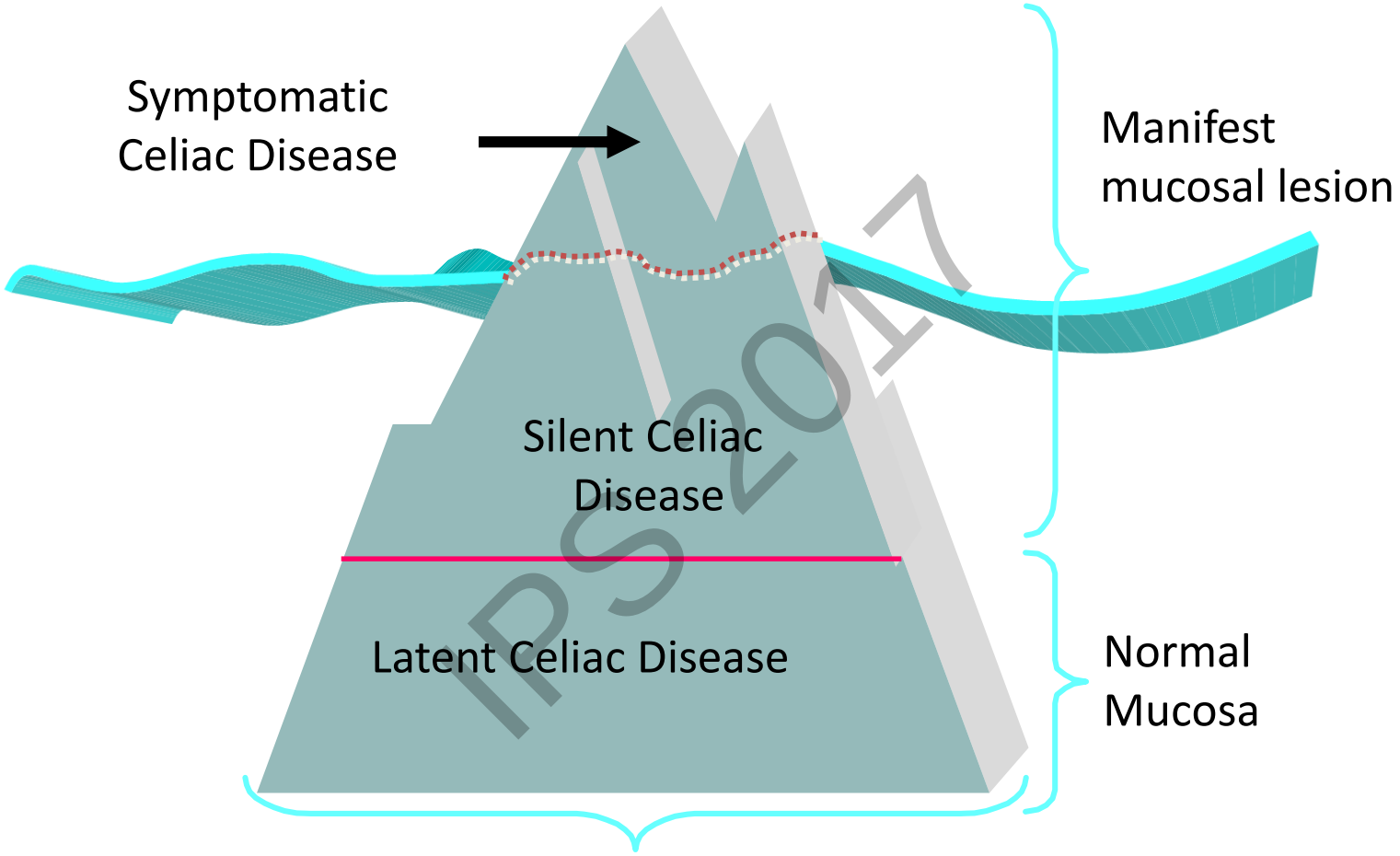
Fasano & Catassi, *Gastroenterology* 2001; 120:636-651.

The Size of the Submerged Iceberg is Decreasing in Many Countries Due to Active Case-Finding



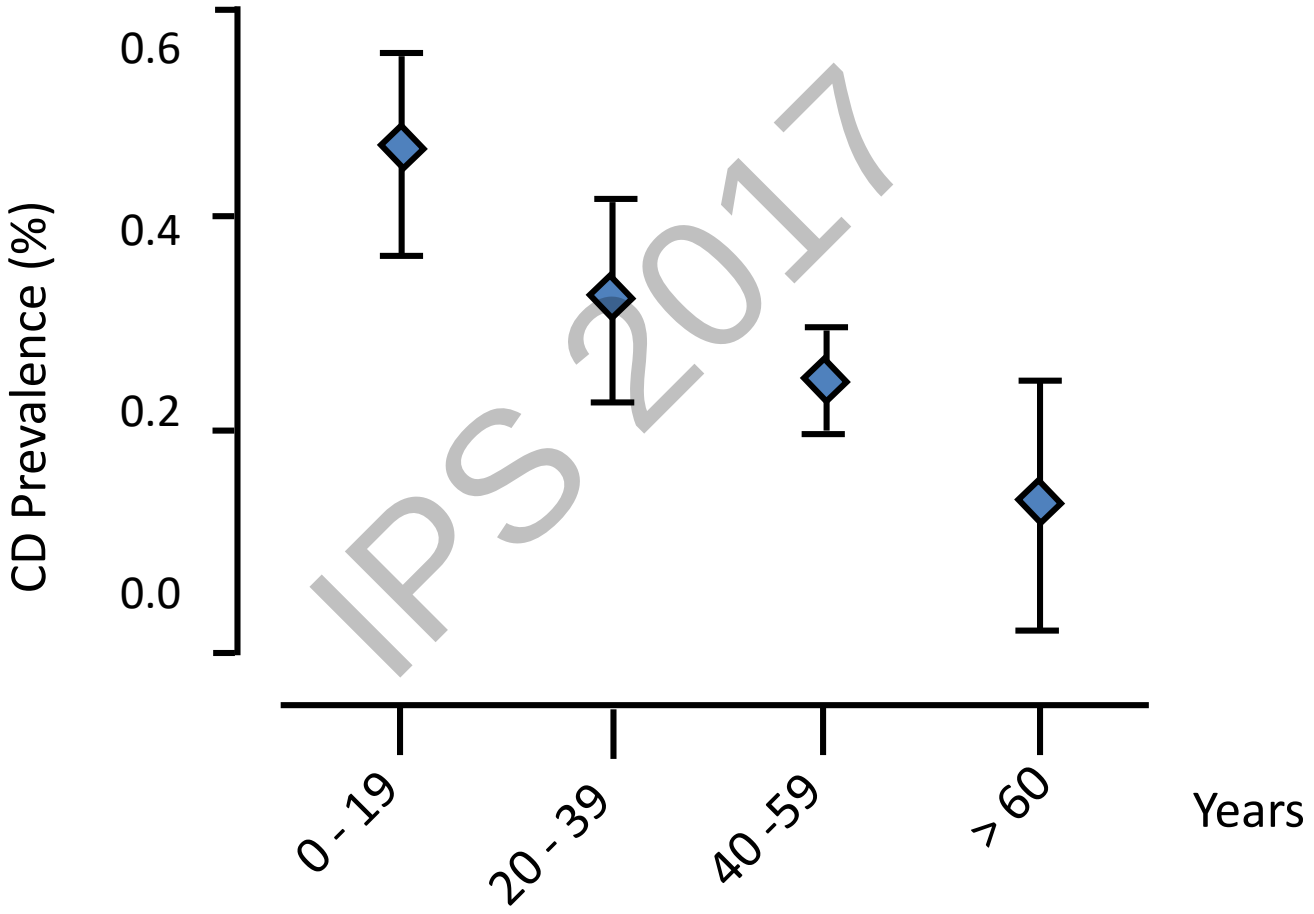
Even an intensive policy of Celiac Disease case-finding will leave at least 50 % of celiacs without a diagnosis.

The Celiac Iceberg

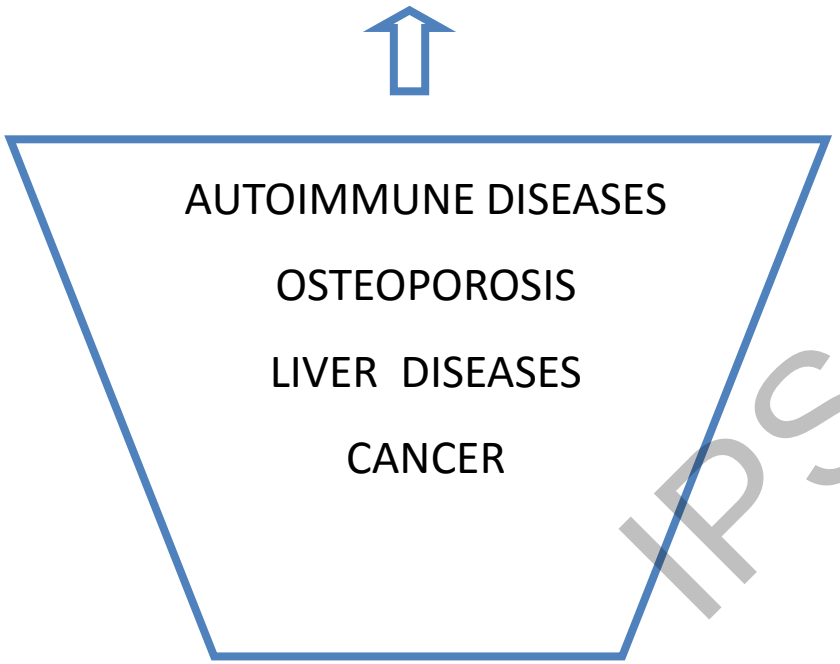


Genetic susceptibility: - DQ2, DQ8
Positive serology

Where Have The Aging Celiacs Gone?



Increased Overall Mortality In Adult Life



ORIGINAL INVESTIGATION

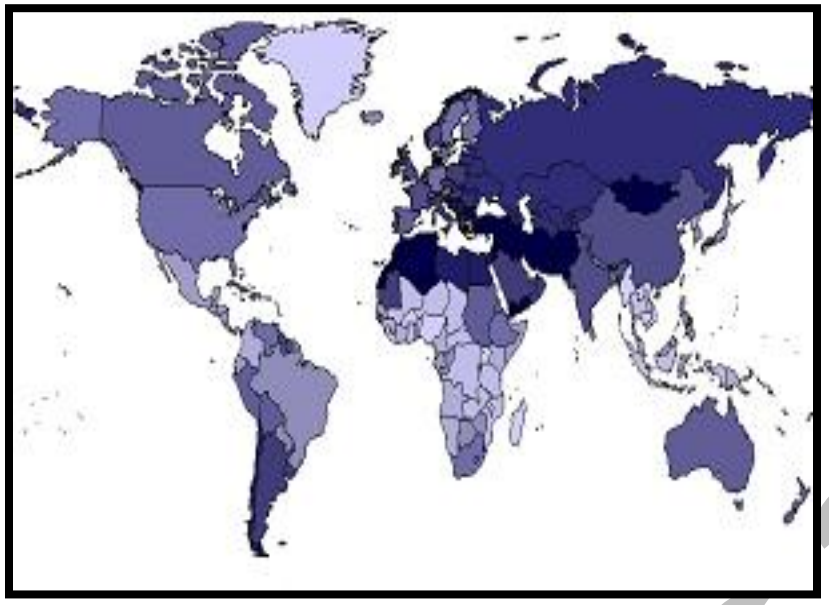
Causes of Death in Patients With Celiac Disease in a Population-Based Swedish Cohort

Ulrike Peters, PhD, MPH; Johan Askling, MD; Gloria Gridley, MS; Anders Ekbom, MD, PhD; Martha Linet, MD

Mortality in patients with coeliac disease and their relatives: a cohort study

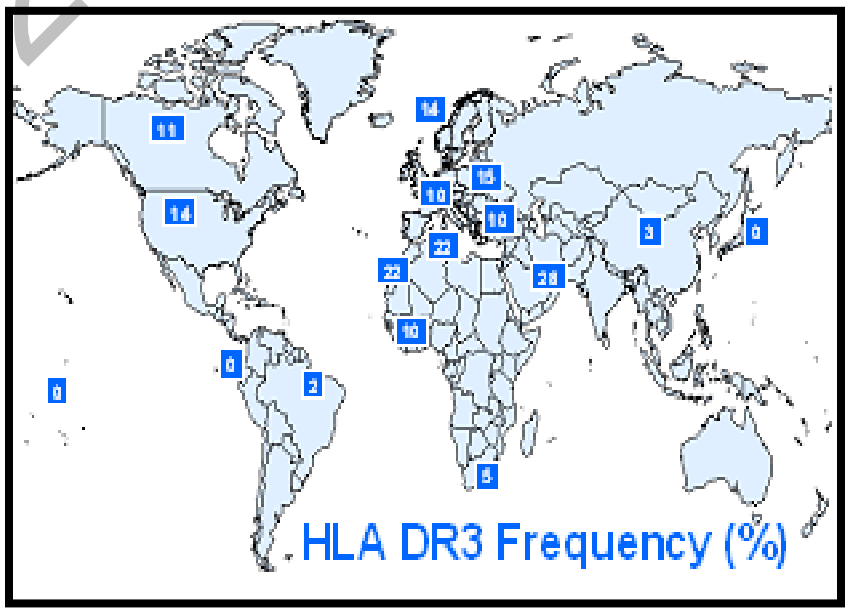
Giovanni Corrao, Gino Roberto Corazza, Vincenzo Bagnardi, Giovanna Brusco, Carolina Ciacci, Mario Cottone, Carla Sategna Guidetti, Paolo Usai, Pietro Cesari, Maria Antonietta Pelli, Silvano Loperfido, Umberto Volta, Antonino Calabrò, Maria Certo, for the Club del Tenue Study Group

Risk Factors



The Grains

The Genes



Celiac Disease in Developing Countries

- Worldwide circulation of gluten-containing food could cause epidemics of Celiac Disease
- Largely underestimated (e.g. along the “silk road”)
- Typical symptoms and stunting (nutritional dwarfism)
- Celiac Disease serological markers still reliable
- Formidable treatment difficulties

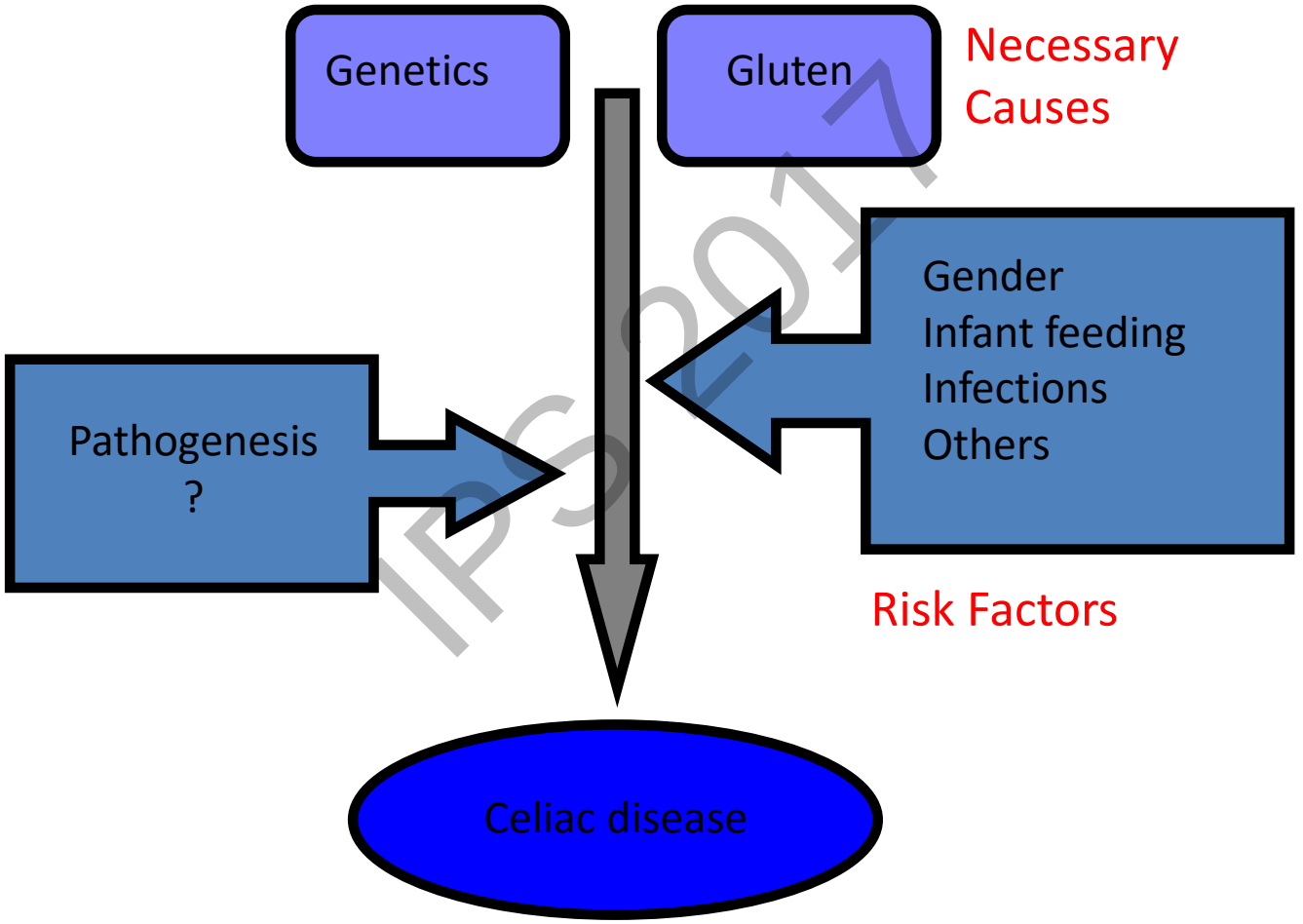
The Global Village of Celiac Disease

- In many areas of the world Celiac Disease is one of the commonest, lifelong disorders affecting around 1% of the general population.
- Most cases escape diagnosis and are exposed to the risk of complications.
- Active Celiac Disease case-finding is needed but mass screening should be considered.
- The impact of Celiac Disease in the developing world needs further evaluation.

Pathogenesis

- Genetic predisposition
- Environmental triggers
  - Dietary
  - Non dietary?

Pathogenesis



Genetics

- Strong HLA association
- 90 - 95% of patients HLA-DQ2 – also found in 20 - 30% of controls
  - Most of the remainder are HLA - DQ8
- 10% of patients have an affected first degree relative

Tissue Transglutaminase (TTG)

- Normal gut enzyme released during injury and stabilizes the cross-linking of proteins in granulation tissue
- Role in Celiac Disease
  - Modification of gliadin epitopes
  - Autoantibodies against TTG correlate with active Celiac Disease - ? involved in pathogenesis

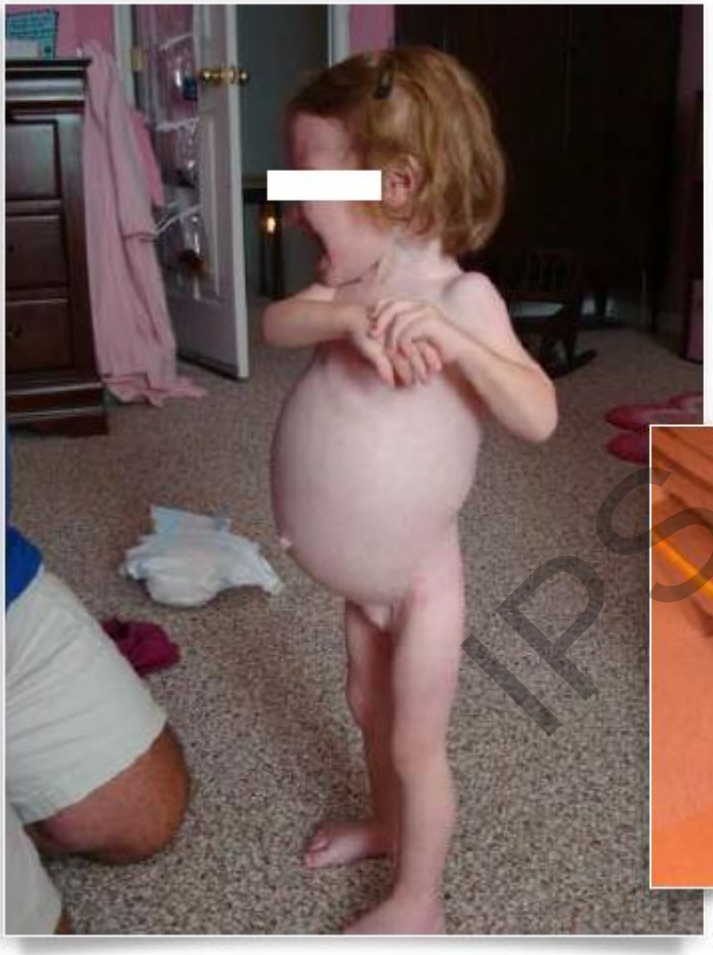
Pathophysiology Sequelae

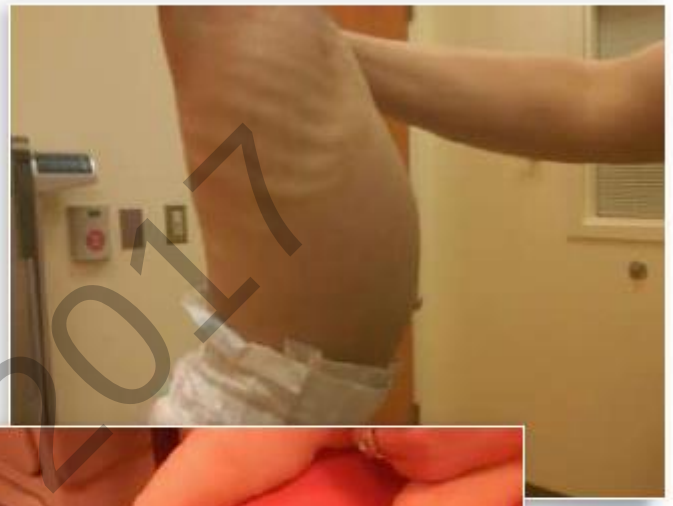
- Malabsorption of nutrients, especially iron, folate, calcium, and vitamin D
- Increased intestinal permeability may permit entry of other toxins which might induce autoimmune diseases

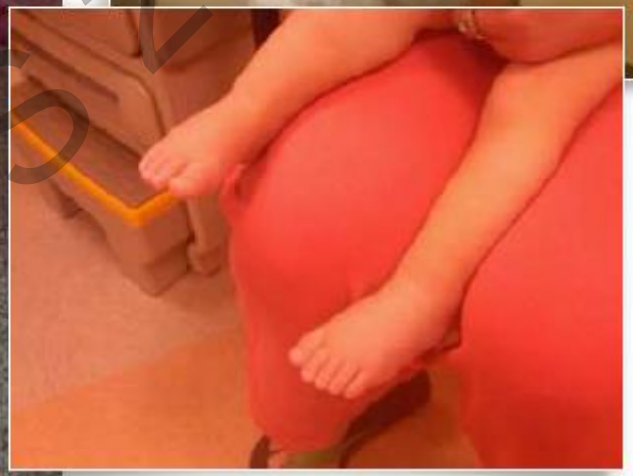
The "Typical" (GI) Presentation

- Diarrhea
- Vomiting
- Failure to thrive or weight loss
- Abdominal bloating/pain
- Constipation

"Typical" Celiac Children







Interlaken ESPGHAN criteria (1979)

1. Small intestinal biopsy: villous atrophy
2. Gluten free diet for 1-2 years
3. Biopsy: normal.
4. Re-introduction of gluten
5. Biopsy: villous atrophy

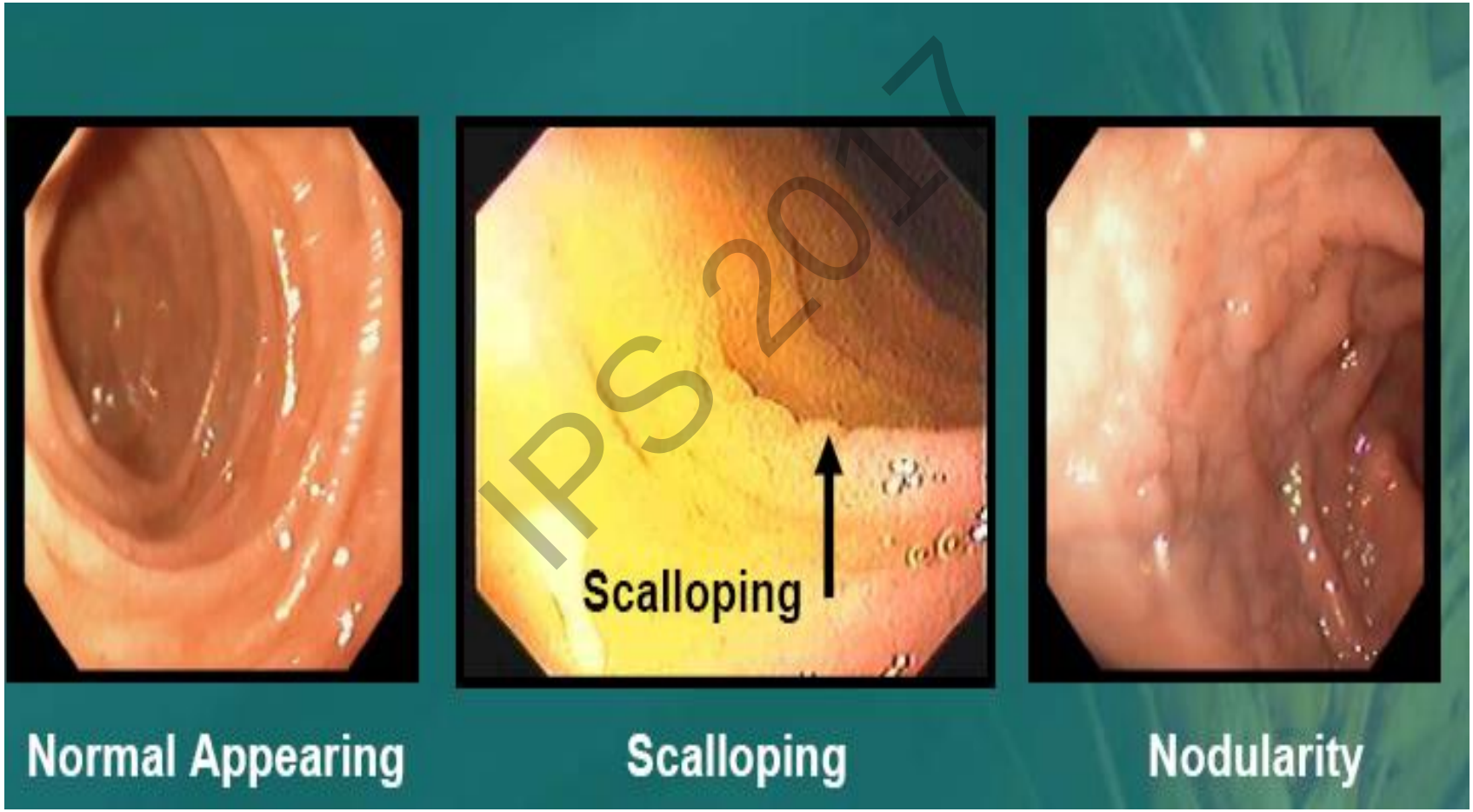
McNeish et al. Arch Dis Childh 1979;54:783

Revised ESPGHAN criteria 1990

1. Small intestinal biopsy: villous atrophy
2. Clinical and serological improvement after 2-3 months
   - No further biopsy
   - Provided age > 2 years

Walker-Smith et al. Arch Dis Child 1990;65:99

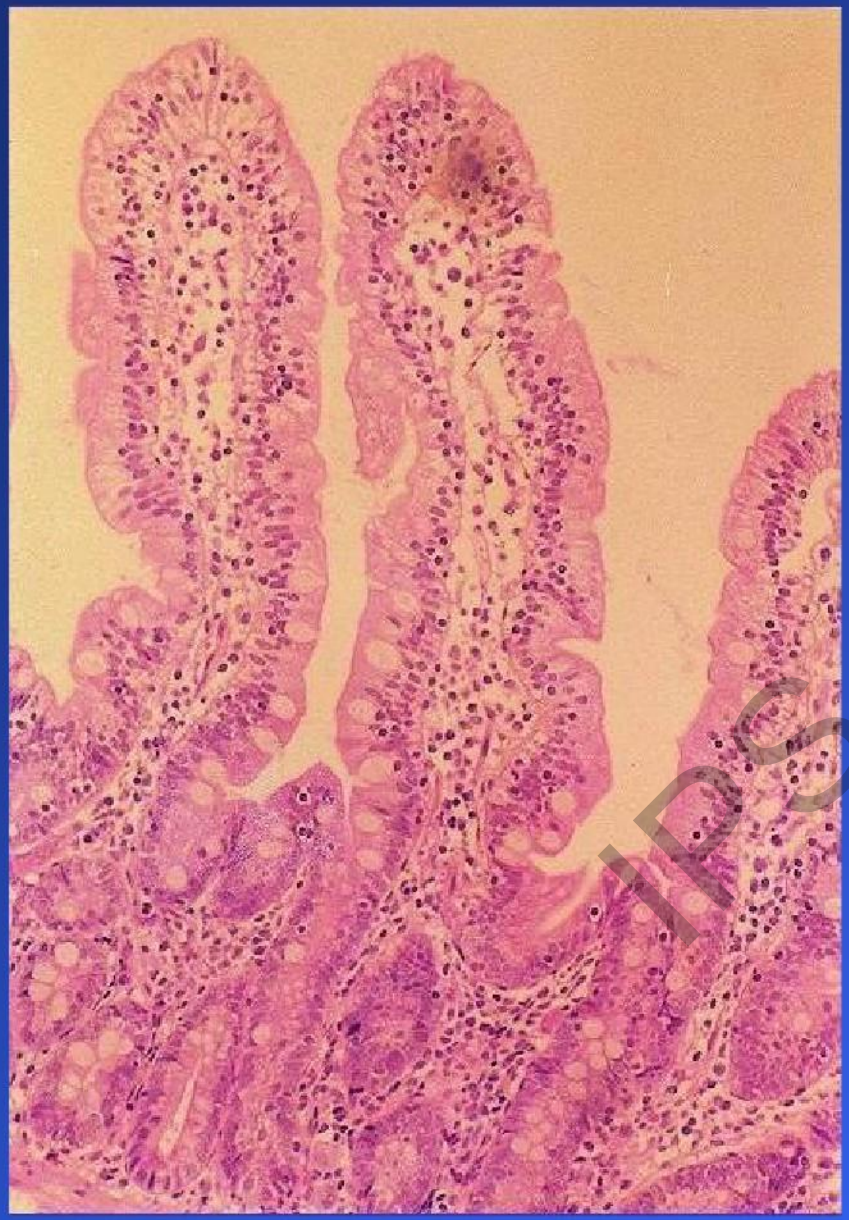
Endoscopic Findings

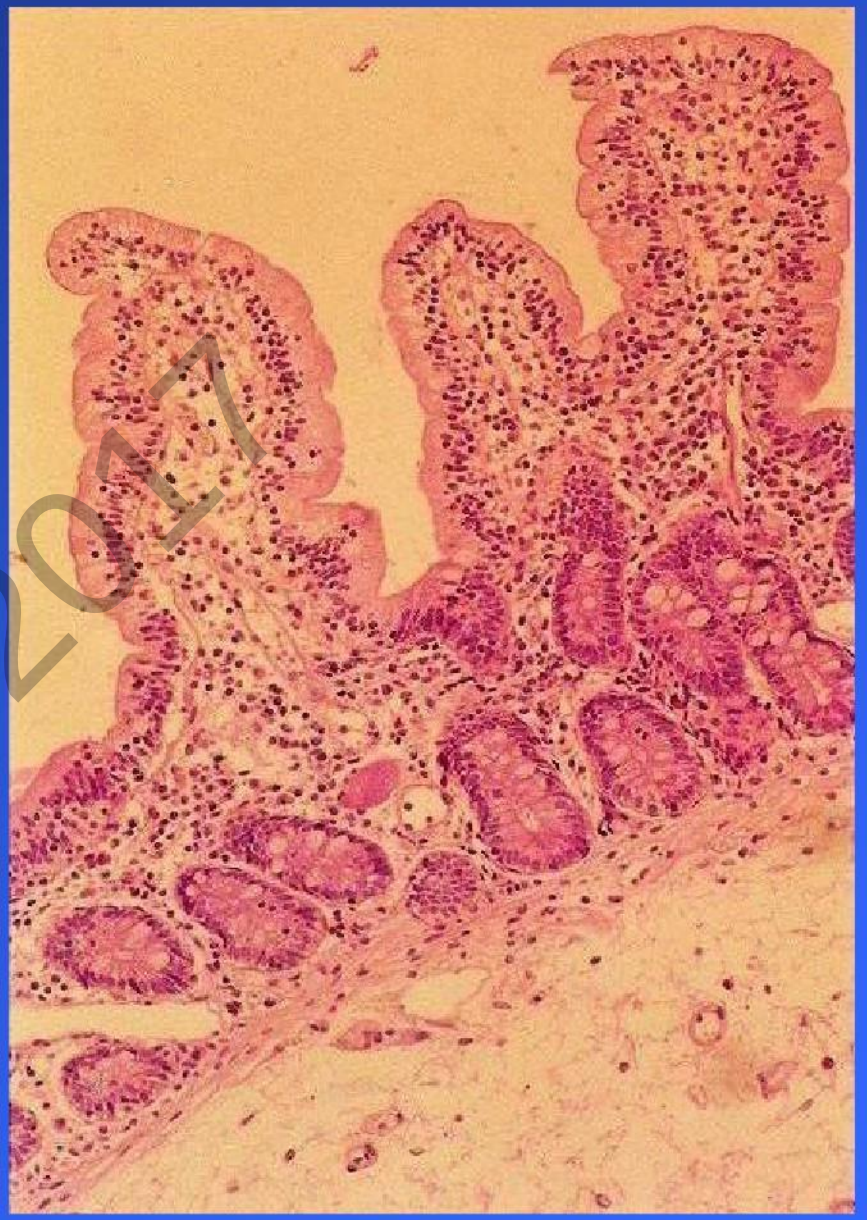


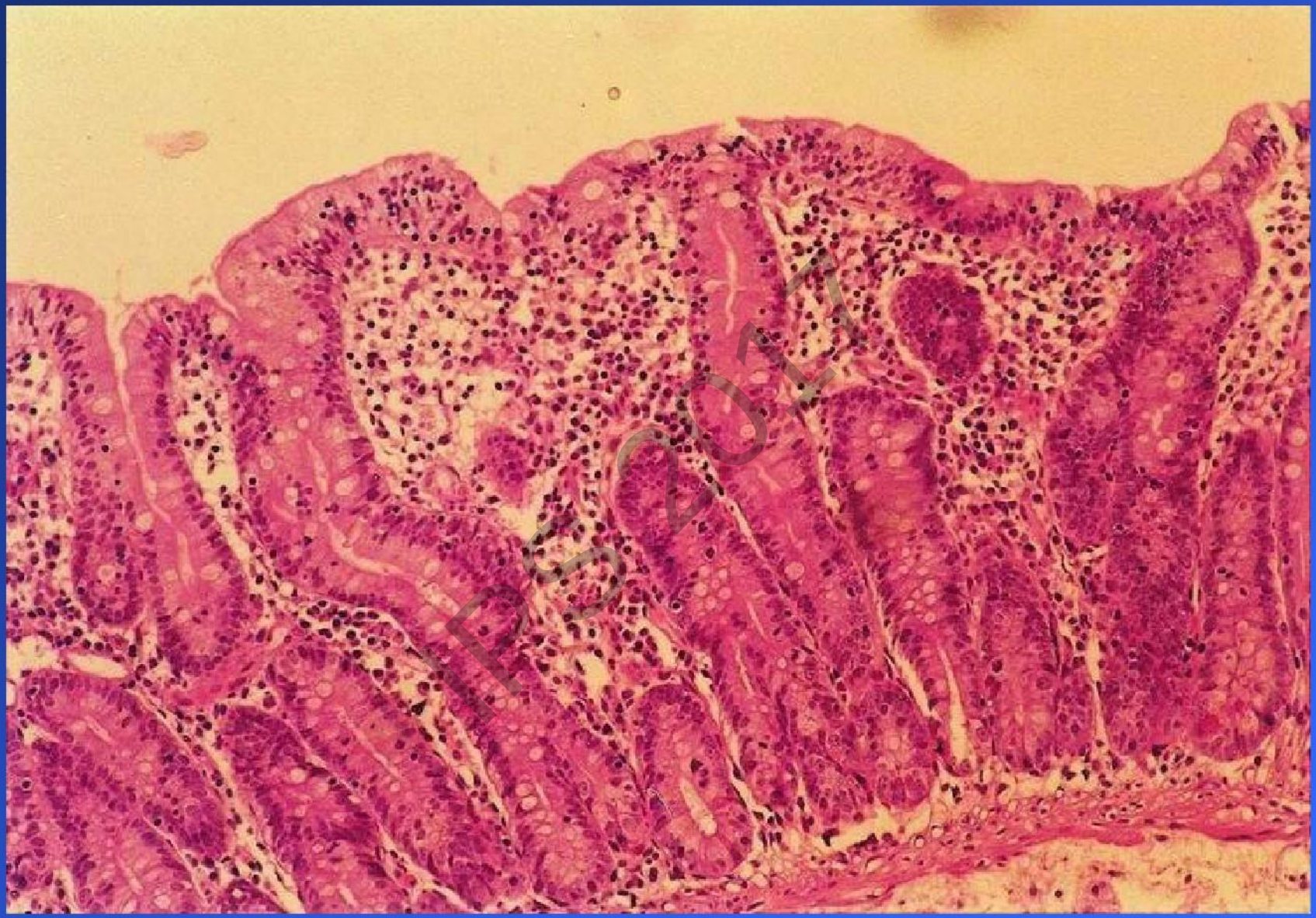
Intestinal biopsy

- Histologic changes
  - mucosal atrophy
    - Marsh classification
      - type 0: preinfiltrative phase
      - type 1: infiltrative phase
      - type 2: infiltrative-hyperplastic phase
      - type 3 (a, b, c): destructive phase
      - type 4: atrophic-hypoplastc phase
    - villous atrophy, crypt hyperplasia, IEL count

Marsh MN. Gluten, major histocompatibility complex, and the small intestine. A molecular and immunobiologic approach to the spectrum of gluten sensitivity ('celiac sprue'). Gastroenterology 1992.
Oberhuber G, et al. The histopathology of coeliac disease: time for a standardised report scheme for pathologist. Eur J Gastroenterol Hepatol 1999.



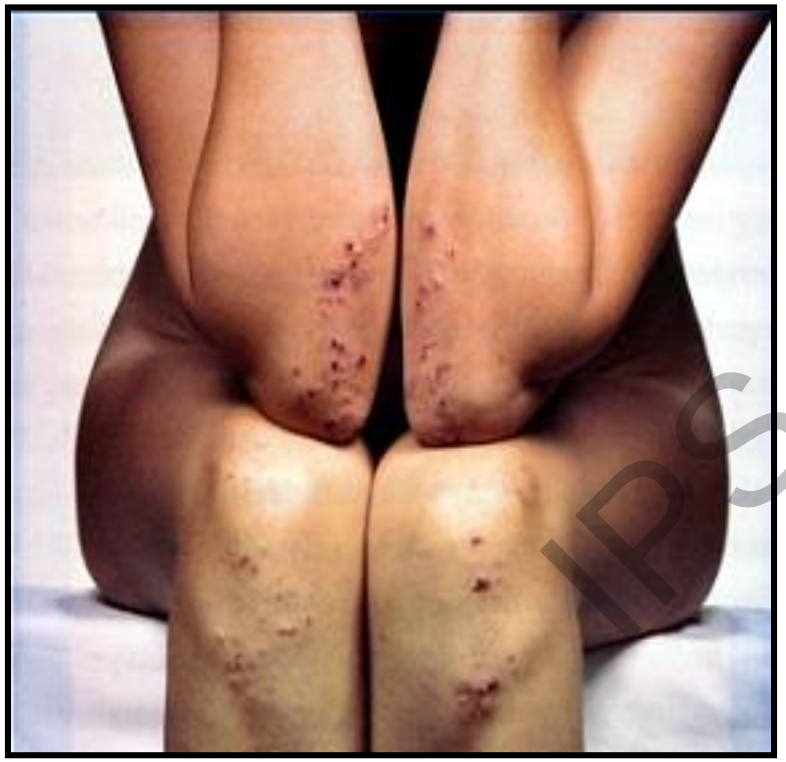




The Main Atypical (Extra-GI) Presentations

- Dermatitis Herpetiformis and other skin disorders
- Short Stature *(15% of our pts!)*
- Delayed Puberty
- Dental enamel hypoplasia
- Osteopenia
- Iron-deficient anemia resistant to oral Fe
- Liver and biliary tract disease (High transaminases)
- Arthritis
- Neurological problems
  - Headaches
  - Peripheral Neuropathy
  - "Gluten Ataxia"
- Fatigue
- Behavioral changes/Psychiatric Disorders
- Reduced female fertility or pregnancy adverse events

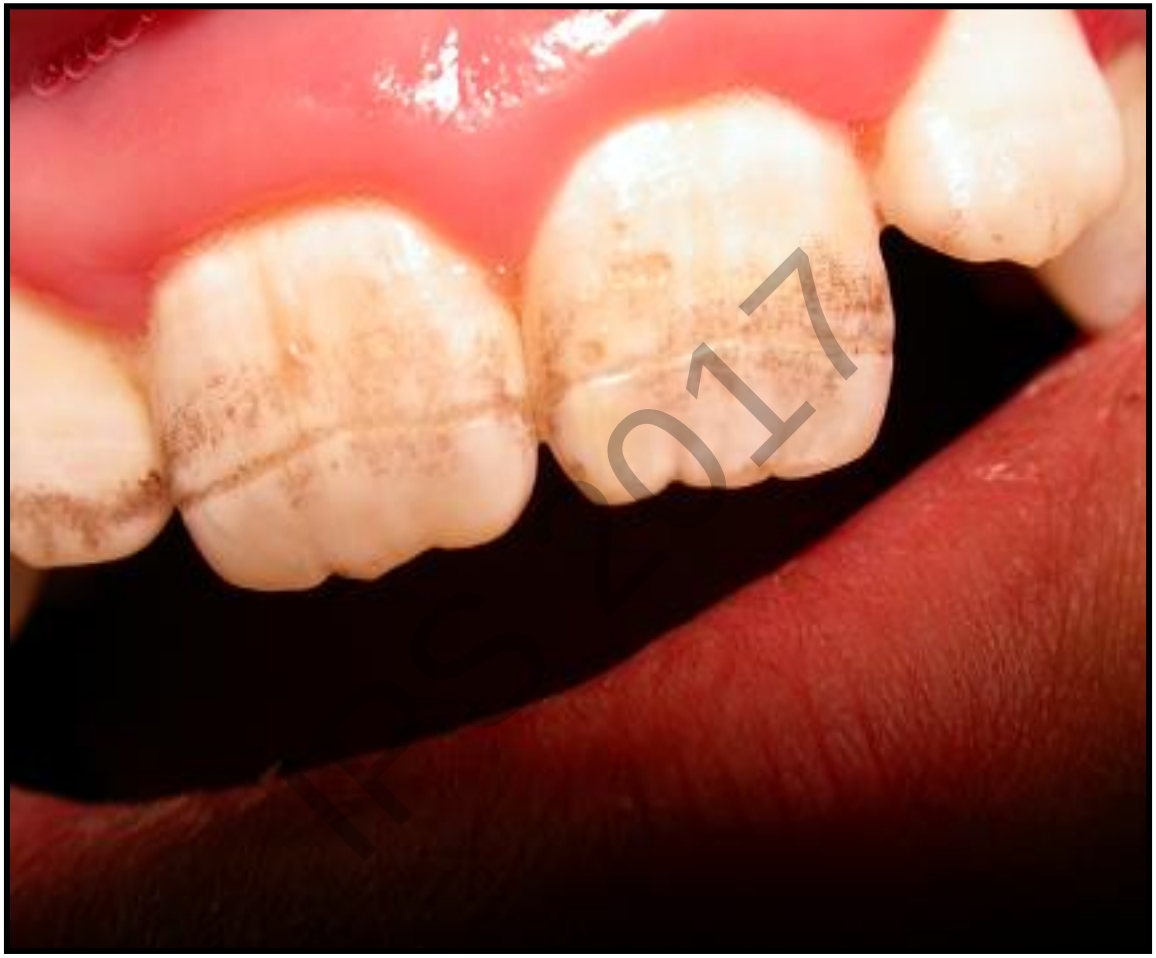
Dermatitis Herpetiformis



- Erythematous macule > urticarial papule > tense vesicles
- Severe pruritus
- Symmetric distribution
- 90% no GI symptoms
- 75% villous atrophy
- Gluten sensitive

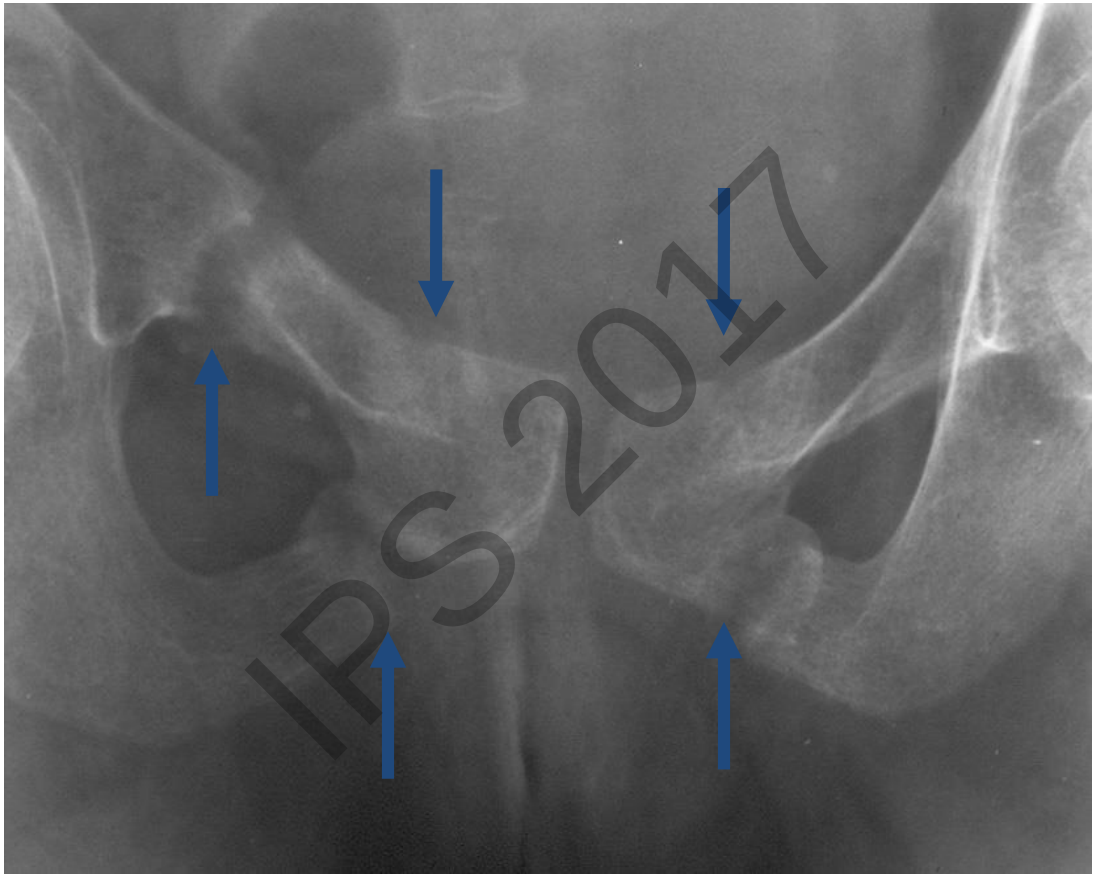
Garioch JJ, et al. *Br J Dermatol*. 1994;131:822-6.
Fry L. *Baillieres Clin Gastroenterol*. 1995;9:371-93.
Reunala T, et al. *Br J Dermatol*. 1997;136-315-8.

Dental Enamel Defects



Involve the secondary dentition
May be the only presenting sign of Celiac Disease

Osteoporosis



Low bone mineral density improves in children on a gluten-free diet.

Short Stature/Delayed Puberty

- Short stature in children / teens:
  - ~10% of short children and teens have evidence of celiac disease
- Delayed menarche:
  - Higher prevalence in teens with untreated Celiac Disease

Fe-Deficient Anemia Resistant to Oral Fe

- Most common non-GI manifestation in some adult studies
- 5-8% of adults with unexplained iron deficiency anemia have Celiac Disease
- In children with newly diagnosed Celiac Disease:
  - Anemia is common
  - Little evidence that Celiac Disease is common in children presenting with anemia

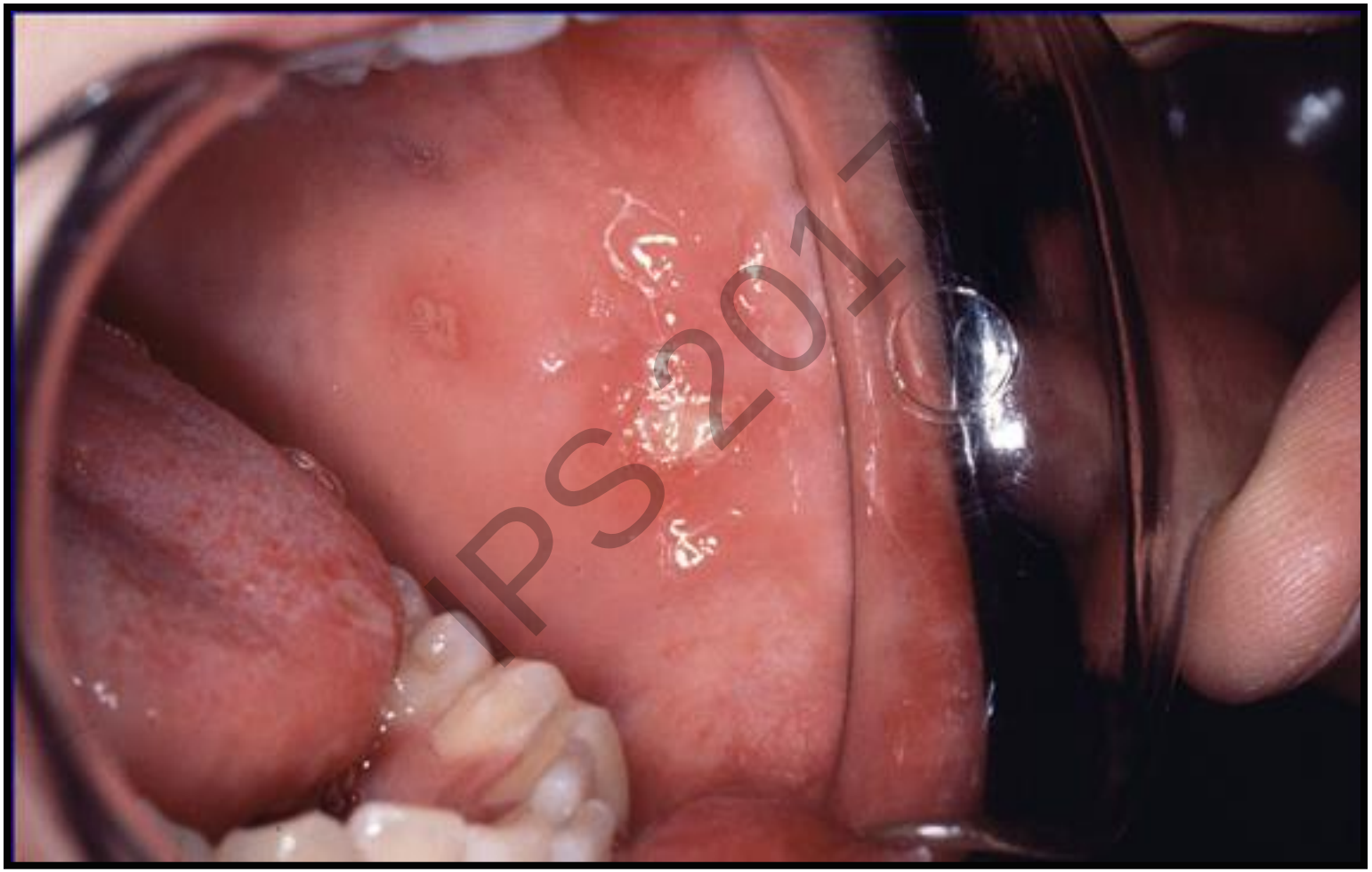
Hepatitis

- Some evidence for elevated serum transaminases (ALT, AST) in adults with untreated Celiac Disease
  - Up to 9% of adults with elevated ALT, AST may have silent Celiac Disease
  - Liver biopsies in these patients showed non-specific reactive hepatitis
  - Liver enzymes normalized on gluten-free diet

Arthritis and Neurological Problems

- Arthritis in adults
  - Fairly common, including those on gluten-free diets
- Juvenile chronic arthritis
  - Up to 3% have Celiac Disease
- Neurological problems
  - Epilepsy with cranial calcifications in adults
  - Evidence for this condition in children with Celiac Disease is not as strong

Recurrent Aphtous Stomatitis



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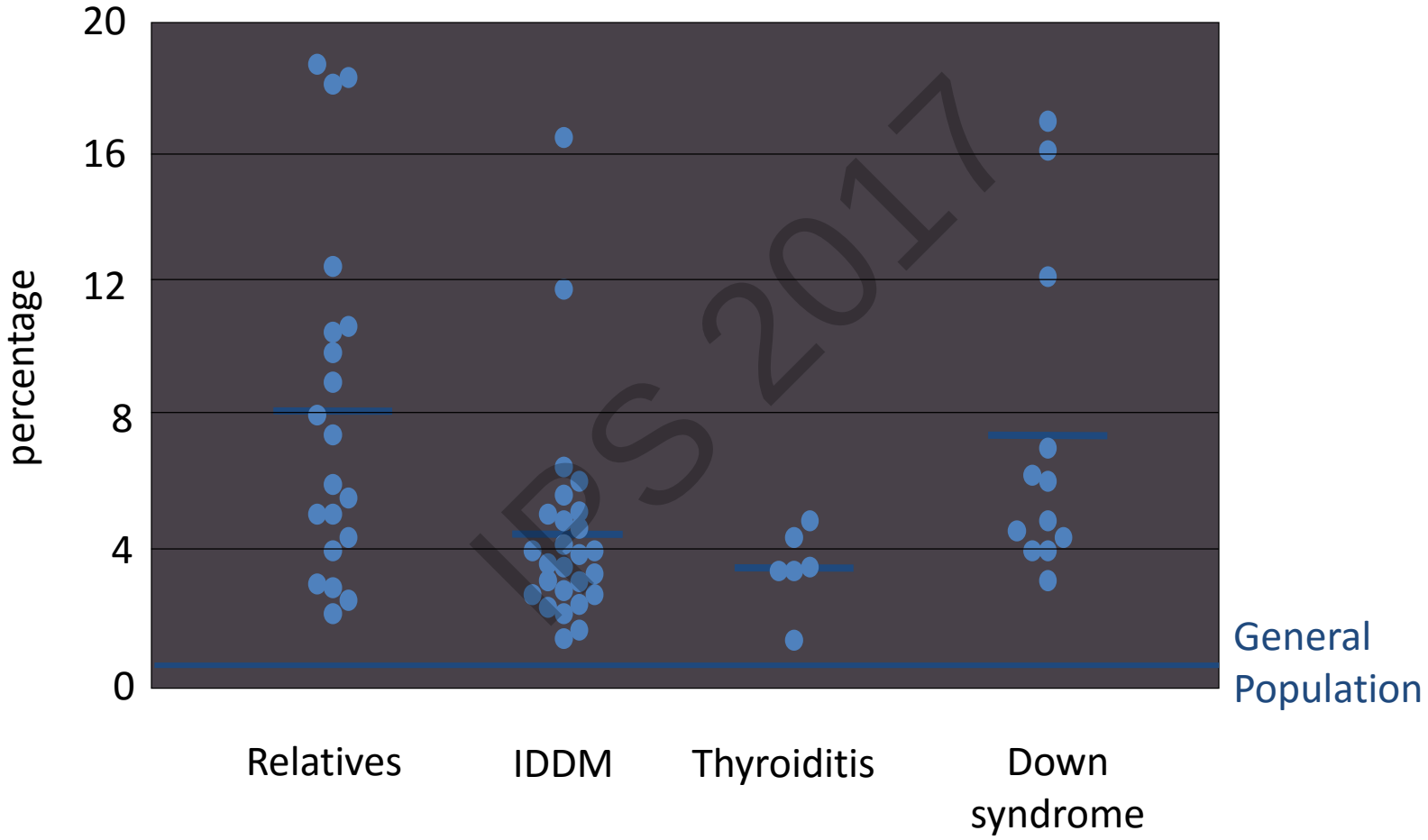
Associated Conditions



Genetic Disorders

- Down Syndrome: 4-19%
- Turner Syndrome: 4-8%
- Williams Syndrome: 8.2%
- IgA Deficiency: 7%
  - Can complicate serologic screening

Prevalence of Celiac Disease is Higher in Other Autoimmune Conditions

Type 1 Diabetes Mellitus:	3.5 - 10%
Thyroiditis:	4 - 8%
Arthritis:	1.5 - 7.5%
Autoimmune liver diseases:	6 - 8%
Sjögren's syndrome:	2 - 15%
Idiopathic dilated cardiomyopathy:	5.7%
IgA nephropathy:	3.6%

Relatives

- Healthy population: 1:133
- 1st degree relatives: 1:18 to 1:22
- 2nd degree relatives: 1:24 to 1:39

Fasano, et al, *Arch of Intern Med*, Volume 163: 286-292, 2003

Polling Question

Patients with potential for Celiac Disease have:

A- a normal biopsy but positive serology
B- a damaged mucosa but have no symptoms
C- a damaged mucosa, positive serology but do not possess neither DQ2 nor DQ8
D- a normal biopsy, negative serology but are first degree relatives of celiac

Polling Question

- Answer: A

-A normal biopsy but positive serology

Current Classification of Celiac Disease Presentations

Type	Serology (tTG and/or EMA)	Age affected	Symptoms	Pathology
"Typical"	Positive	Toddler, Young Child	Abdominal Pain, Distention Diarrhea Vomiting Anorexia Constipation	Marsh 2-3
"Atypical"	Positive	Older Child Adult	Mostly extra-intestinal	Marsh 1-3
Silent	Positive	All Ages	None	Marsh 2-3
Potential	Positive	Any age	None Gastrointestinal Extra-intestinal	Marsh 0-1 (may or may not develop enteropathy if left on gluten)
Latent	Positive or Negative	Mostly Adults	None Gastrointestinal Extra-intestinal	Marsh 0-1 (previously had gluten-dependent enteropathy)

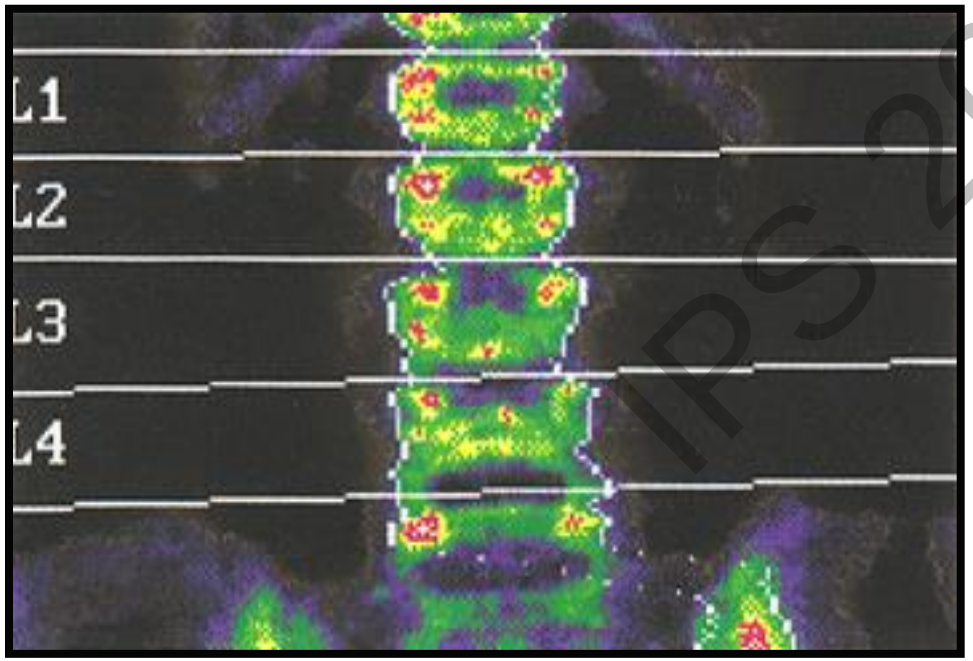
Who Should Be Screened?

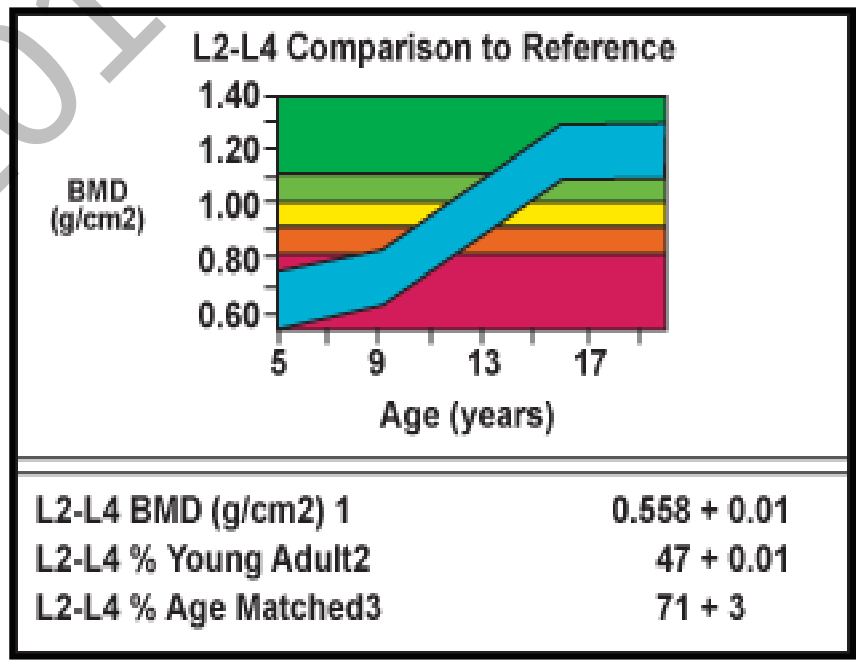
- **Subjects with suggestive GI complaints**
  - Diarrhea (±FTT)
  - Vomiting
  - Anorexia
  - Abdominal distention
  - Recurrent abdominal pain
  - Constipation
- **Subjects with extra-intestinal manifestations**
  - Dental enamel dysplasia
  - Short stature
  - High Transaminases
  - Fe-deficient anemia (unexplained)
  - Fatigue
  - Arthritis….

Major Complications of Celiac Disease

- Short stature
- Dermatitis herpetiformis
- Dental enamel hypoplasia
- Recurrent stomatitis
- Fertility problems
- Osteoporosis
- Gluten ataxia and other neurological disturbances
- Refractory celiac disease and related disorders
- Intestinal lymphoma

Low Bone Mineral Density (DXA) in a Child With Untreated Celiac Disease





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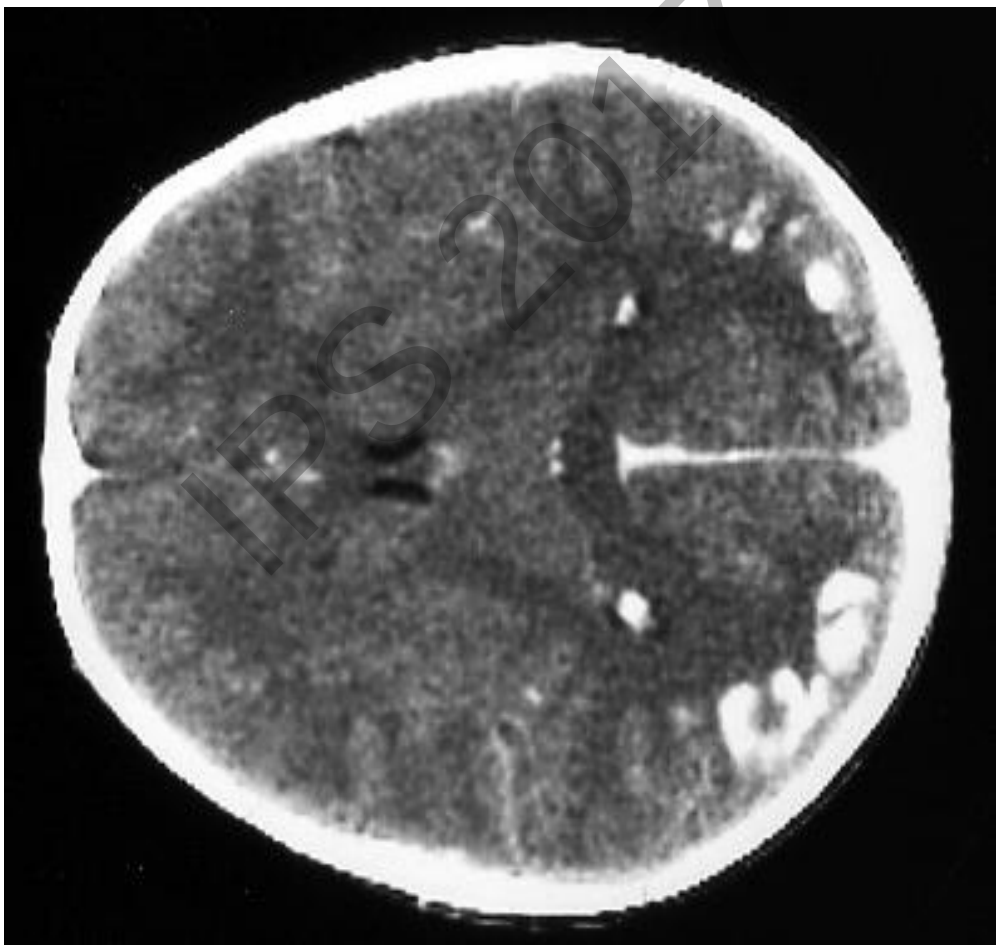
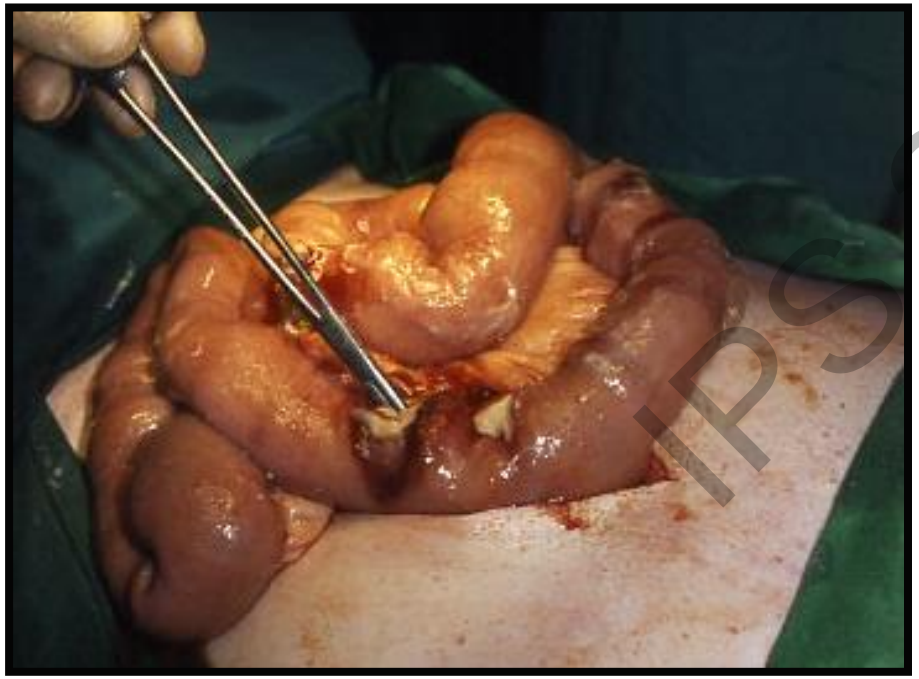
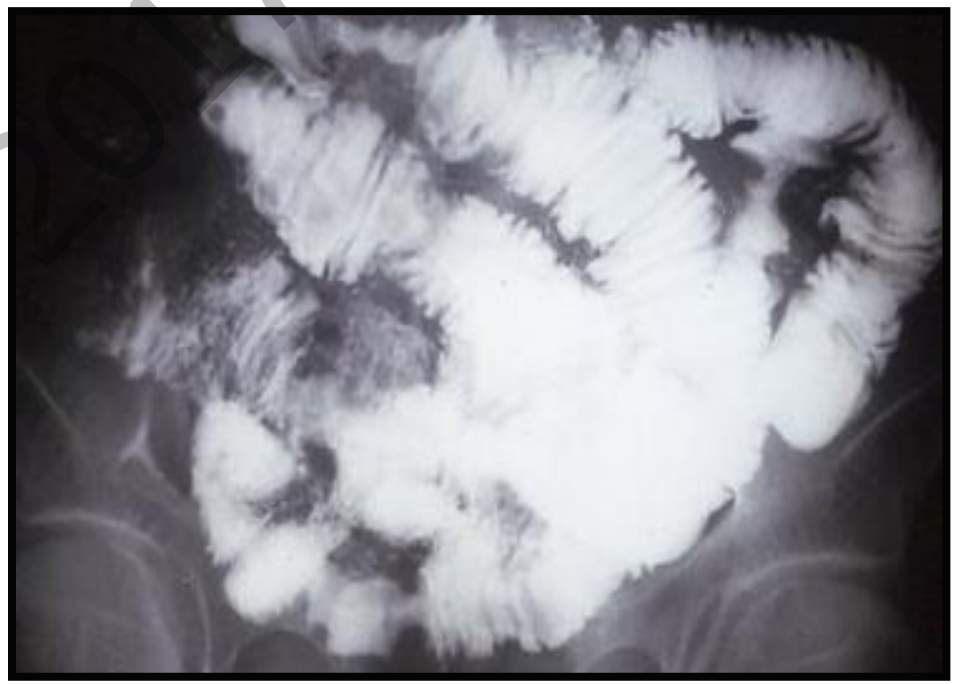
CT Scan Showing Occipital Calcifications in a Boy with Celiac Disease and Epilepsy



Celiac Disease Complicated by Enteropathy-Associated T-cell Lymphoma (EATL)





By permission of G. Holmes, Derby (UK)

Miley Cyrus: Gluten-Free Diet Is Responsible For Weight Loss

Posted: 04/10/2012 11:01 am Updated: 04/10/2012 1:51 pm

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Miley Cyrus took to Twitter yesterday to refute claims that she's suffering from an eating disorder. Instead, she says, her weight loss is due to a shift toward gluten-free and lactose-free eating for health reasons.

"For everyone calling me anorexic I have a gluten and lactose allergy," she wrote. "It's not about weight it's about health. Gluten is crapppp anyway!"

While her fans are most certainly aware that Cyrus is not a medical professional, it's valuable to fact-check her statement anyway. First of all, it is impossible to be allergic to gluten. Those who have difficulty digesting gluten have either a condition called celiac disease or non-celiac gluten sensitivity. About 1 percent of the population suffers from celiac and about 10 percent have a less specific sensitivity, according to the Mayo Clinic.

Celiac sufferers have an immune response to gliadin, a gluten protein found in wheat, rye and barley. Symptoms range from chronic fatigue, diarrhea, bloating and headaches to "failure to thrive" in young children. Weight gain is not a symptom of

The Gluten Free Diet: Not Only Celiac Disease

Wheat Allergy

IgE-Mediated Wheat Allergy

- Food allergy, by definition, depends on an underlying immune-mediated process for its occurrence
- Food allergy is most common in the first year of life, decreasing in adolescence and adulthood
- Wheat is among the 10 most common allergens responsible for food allergy

Wang et al. *J Clin Invest.* 2011;121(3):827-35.
Venter et al. *Allergy.* 2008;63(3):354-9.
Inomata et al. *Curr Opin Allergy Clin Immunol.* 2009;9:238-243.

Wheat-dependent, Exercise-induced Anaphylaxis

- High index of suspicion needed for diagnosis
- Ingestion of wheat is a pre-condition, but clinical picture does not manifest unless subject engages in exercise
- Intensity of exercise can be as mild as game of ping-pong or walking up hill
- Exercising within 2 hours carries high risk of unchaining immune reactions leading to anaphylaxis

Morita et al. *J Dermatol Sci.* 2007; 47(2):109-17.
Shadick et al. *J Allergy Clin Immunol.* 1999;104(1):123-7.

Non-Celiac Gluten Sensitivity

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)

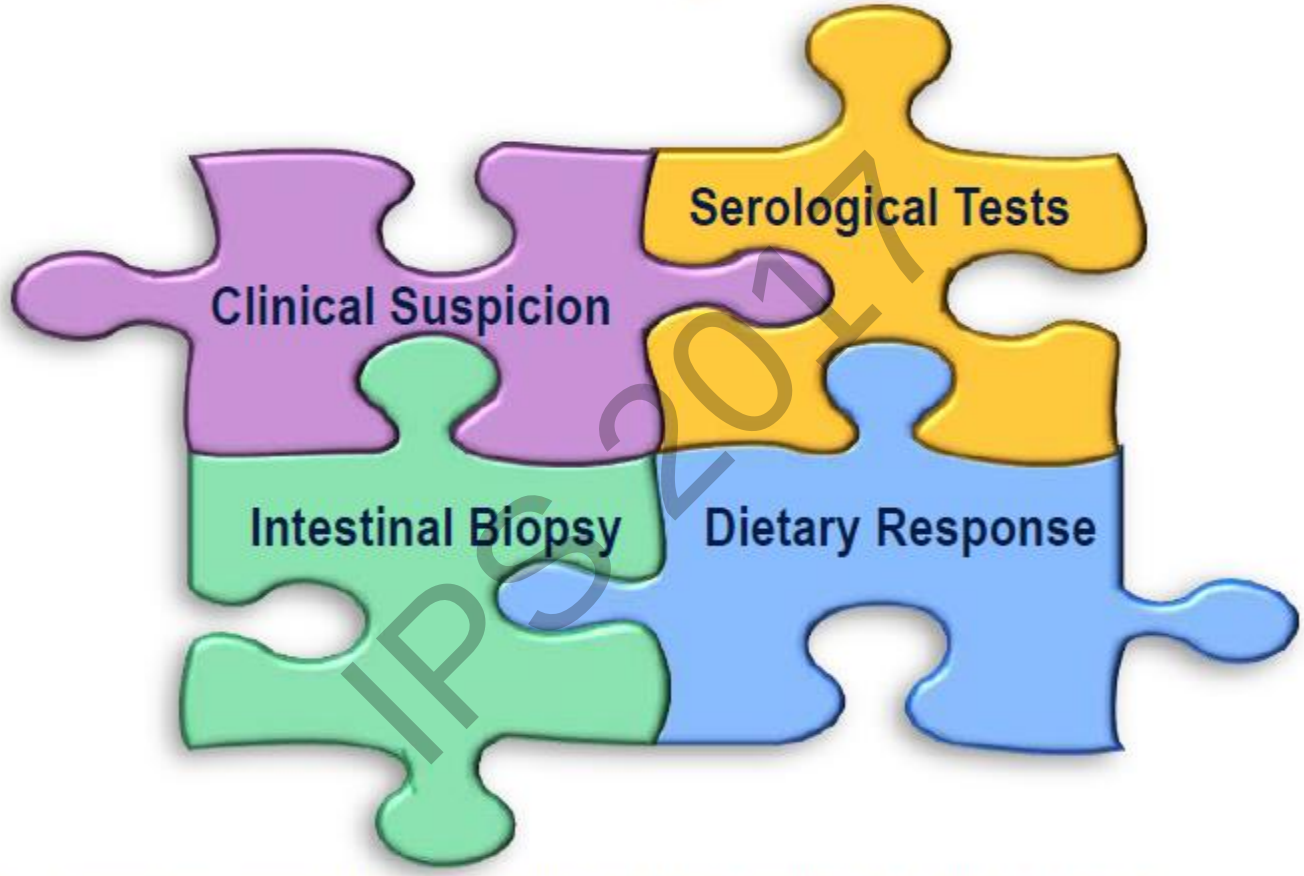
Gluten Sensitivity: What Kind Of Symptoms?

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%

Diagnosis of Celiac Disease vs. Wheat Allergy vs. Non Celiac Gluten Sensitivity

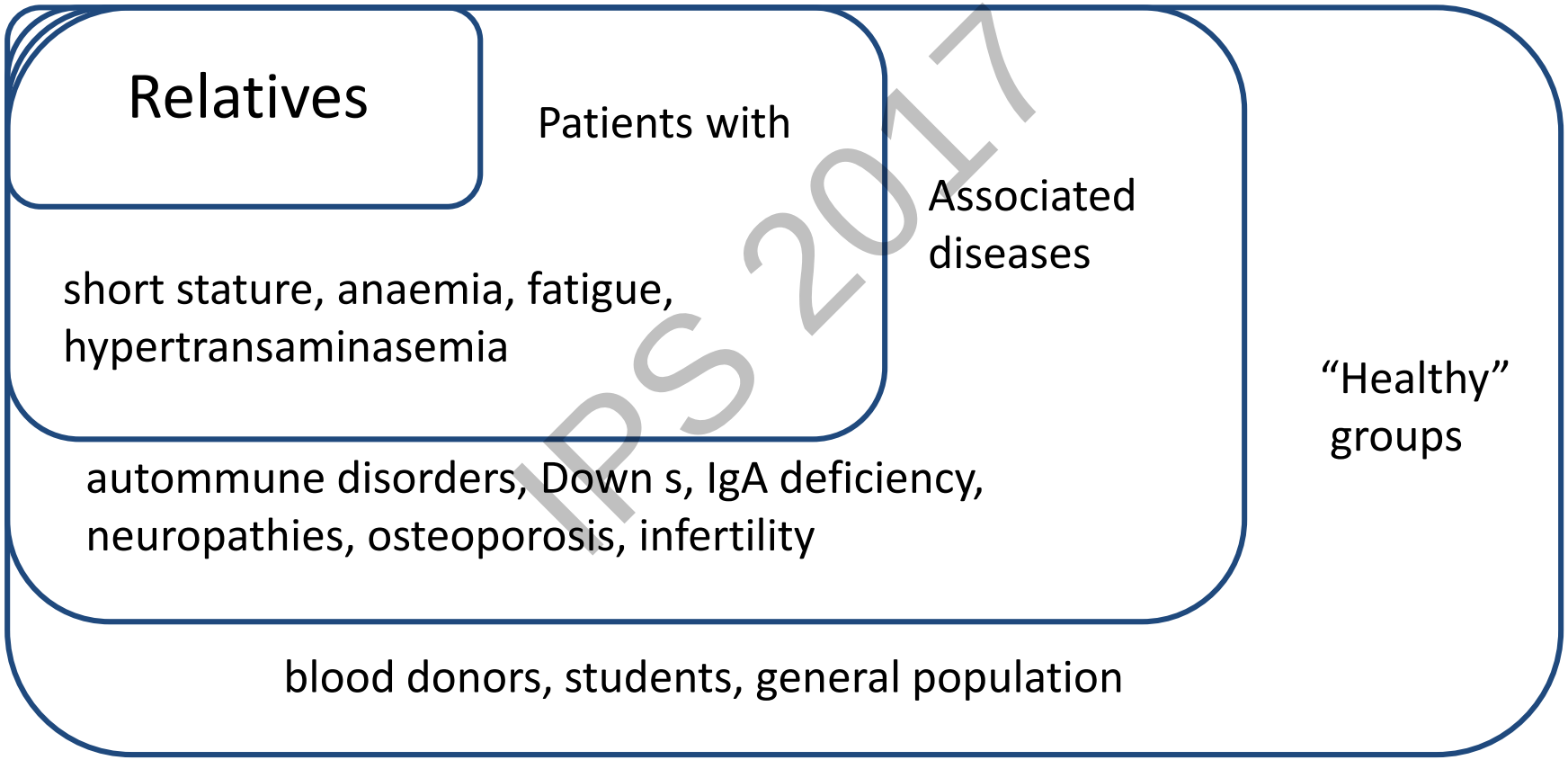
Celiac Diagnosis



Rubio-Tapia et al. *J Gastroenterol.* 2013; 108:656–676; doi:10.1038/ajg.2013.79; published online 23 April 2013. Hill et al. *J Pediatr Gastroenterol Nutr.* 2005;40:1-19. Husby et al. *J Pediatr Gastroenterol Nutr.* 2012;54:136-160.AGA Institute. *Gastroenterology.* 2006;131:1977-1980.

NASPGHAN FOUNDATION
For Children's Digestive Health & Nutrition

Mines of Celiac Disease Were Found Among:



The Changing Celiac Epidemiology

The availability of sensitive serological markers made it possible to discover Celiac Disease even when the clinical suspicion was low.

Endomysial Antibody - EMA

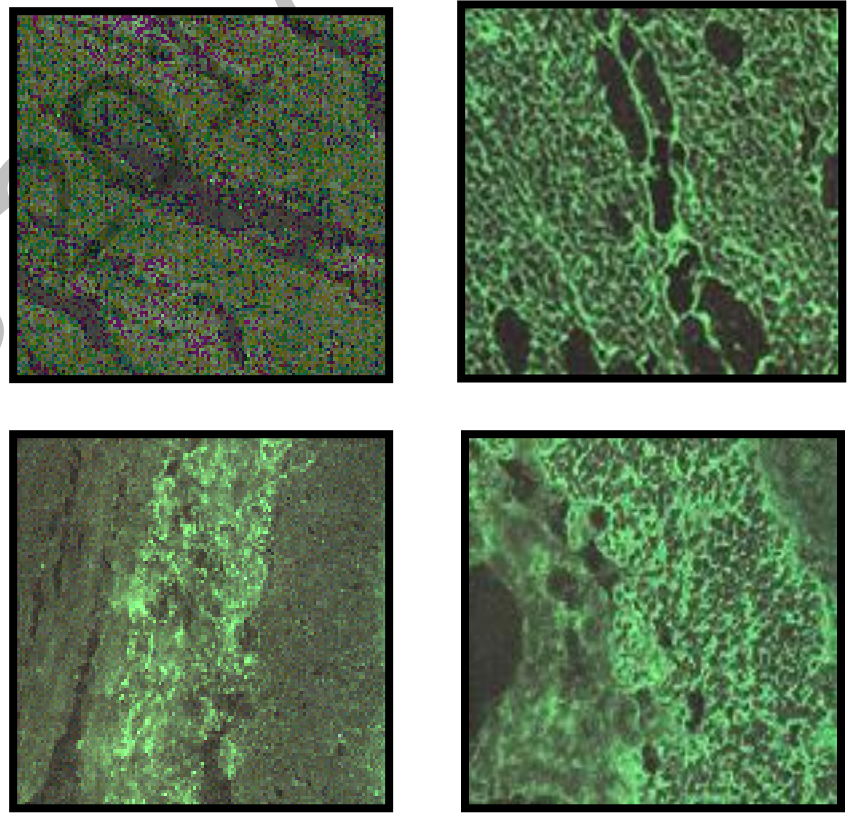
- IgA based antibody against reticulin connective tissue around smooth muscle fibers
- Advantages
  - high sensitivity and specificity
- Disadvantages
  - false negative in young children
  - operator dependent
  - expensive & time consuming
  - false negative in IgA deficiency

Endomysial Antibody - EMA

Antibodies against the outer layer of the smooth muscle of monkey esophagus

NEGATIVE

POSITIVE



Tissue Transglutaminase - TTG

- IgA based antibody against tissue transglutaminase (Celiac Disease autoantigen)
- Advantages
  - high sensitivity and specificity (human TTG)
  - non operator dependent (ELISA/RIA)
  - relatively cheap
- Disadvantages
  - false negative in young children
  - false negative in IgA deficiency
  - possibly less specific than EMA

Serological Tests

Antigliadin –IgA & IgG

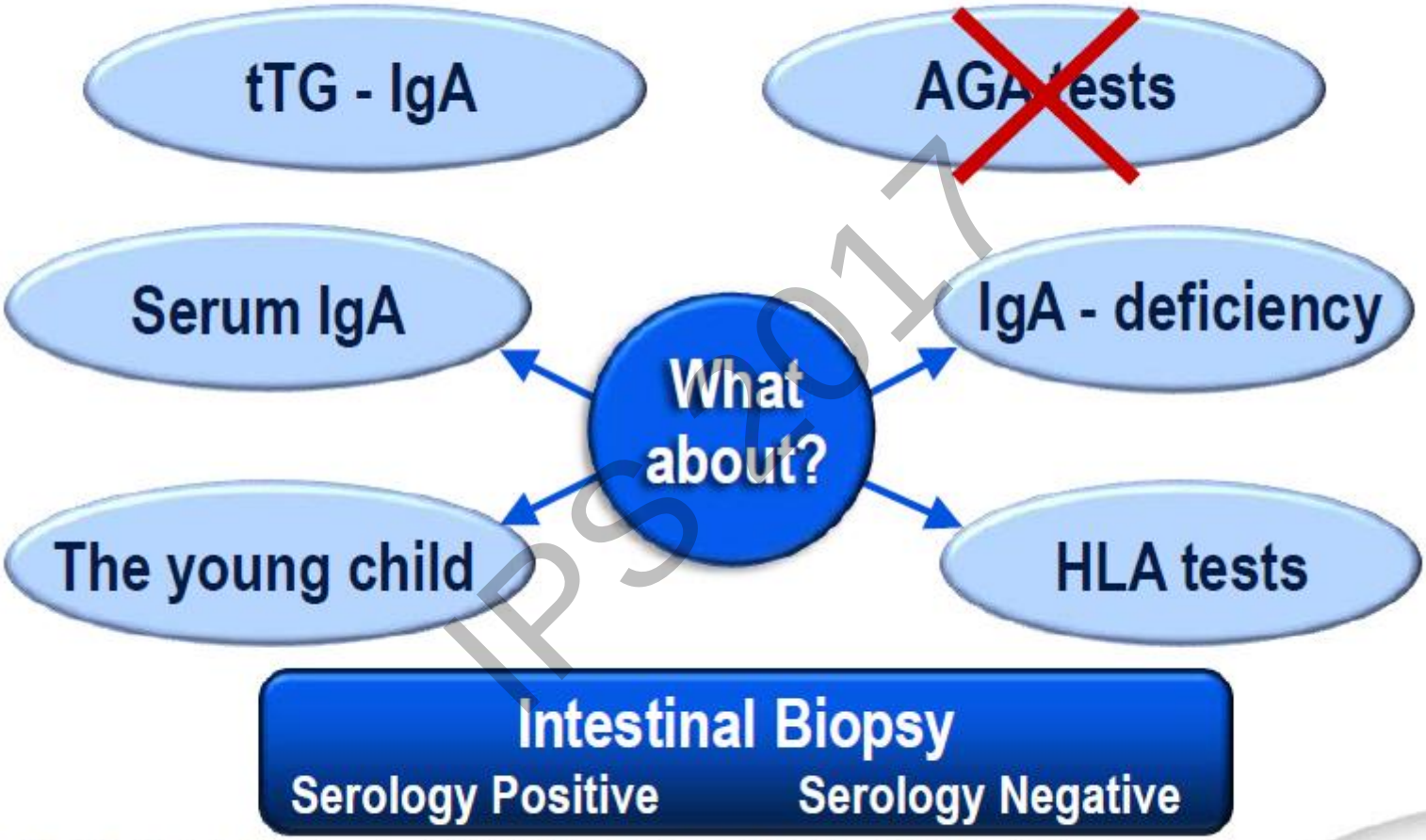
Endomysium – IgA (IgG)

Tissue Transglutaminase – IgA (IgG)

Deamidated Gliadin Peptides –IgA & IgG

Rubio-Tapia et al. *J Gastroenterol*. 2013; 108:656–676; doi:10.1038/ajg.2013.79; published online 23 April 2013. Hill et al. J *Pediatr Gastroenterol Nutr*. 2005;40:1-19. Husby et al. *J Pediatr Gastroenterol Nutr*. 2012;54:136-160.AGA Institute. *Gastroenterology*. 2006;131:1977-1980.

How to Test?



Rubio-Tapia et al. *J Gastroenterol.* 2013; 108:656–676; doi:10.1038/ajg.2013.79; published online 23 April 2013. Hill et al. J *Pediatr Gastroenterol Nutr.* 2005;40:1-19. Husby et al. *J Pediatr Gastroenterol Nutr.* 2012;54:136-160.AGA Institute. *Gastroenterology.* 2006;131:1977-1980.

Serological Test Comparison

	Sensitivity %	Specificity %
AGA-IgG	69 – 85	73 – 90
AGA-IgA	75 – 90	82 – 95
EMA (IgA)	85 – 98	97 – 100
TTG (IgA)	90 – 98	94 – 97

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Farrell RJ, and Kelly CP. Am J Gastroenterol 2001;96:3237-46.

Serum IgA Level

- Individuals with IgA deficiency are at increased risk for Celiac Disease
- IgA deficient individuals will have negative EMA-IgA & TTG-IgA
- Check IgA levels with Celiac Disease serology in all symptomatic individuals
- Consider IgG based tests (EMA-IgG & TTG-IgG) in IgA deficiency

Biopsy: recommendations

Histological assessment may be omitted in:

- Symptomatic cases
- With high IgA anti-TG2 levels, (10 x upper normal limits)
- Verified by EMA positivity
- HLA DQ2 and/or DQ8 heterodimer positive

Follow up should include significant symptomatic improvement as well as normalization of coeliac antibody tests.

HLA Test

HLA alleles associated with Celiac Disease

- DQ2 found in 95% of celiac patients
- DQ8 found in remaining patients
- DQ2 found in ~30% of general population

Value of HLA testing

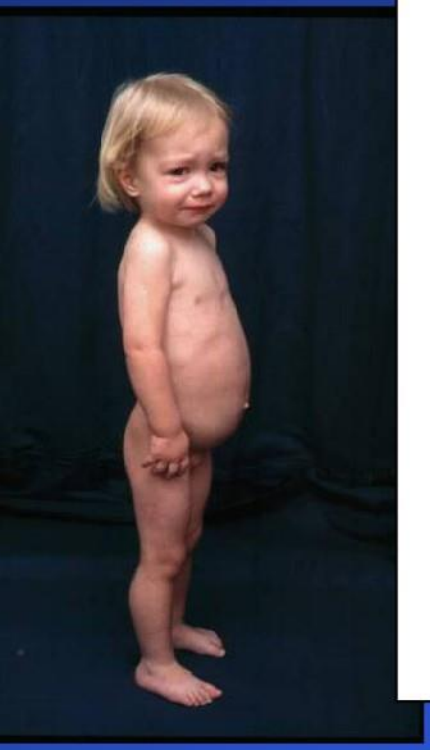
- High negative predictive value
  - Negativity for DQ2/DQ8 excludes diagnosis of Celiac Disease with 99% confidence

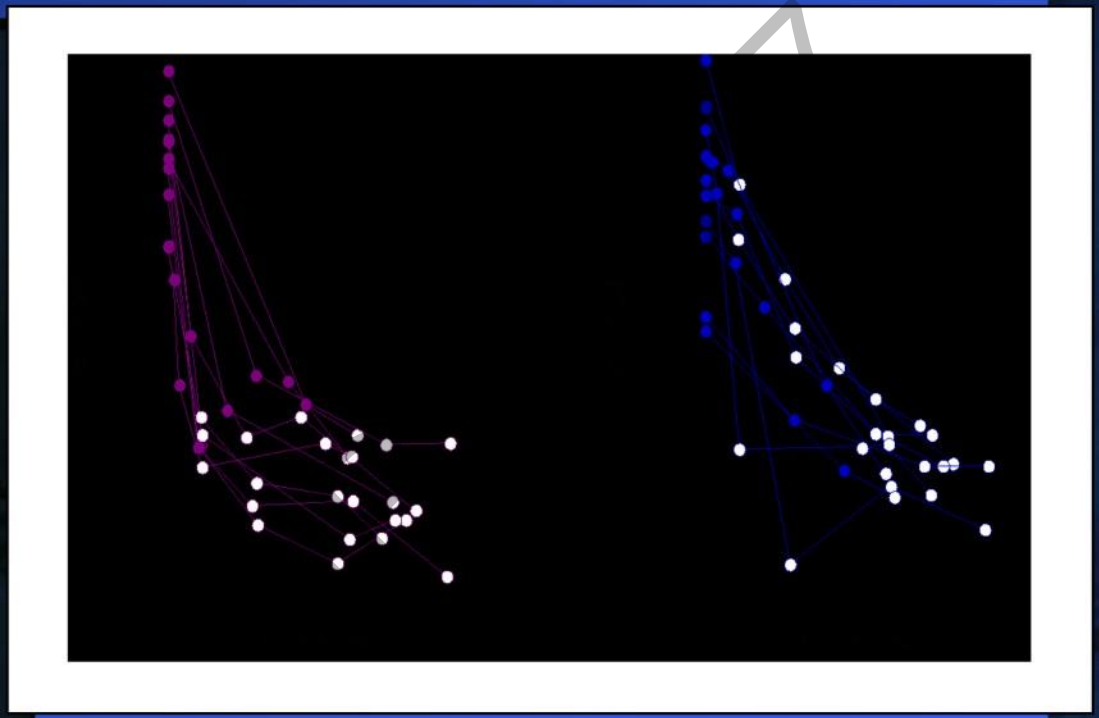
Schuppan. Gastroenterology 2000;119:234
Kaukinen. Am J Gastroenterol 2002;97:695

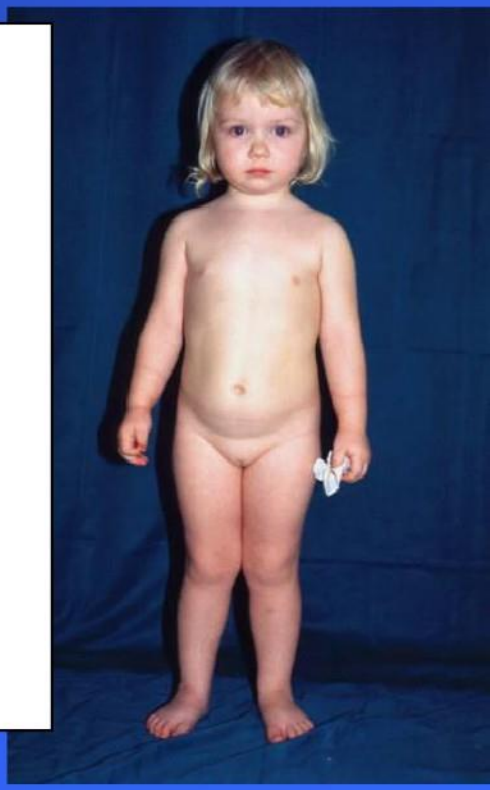
HLA Tests

- Potential role for DQ2/DQ8
  - asymptomatic relatives
  - Down, Turner & Williams syndrome
  - type 1 diabetes
  - diagnostic dilemmas

Serologic markers - t-TG



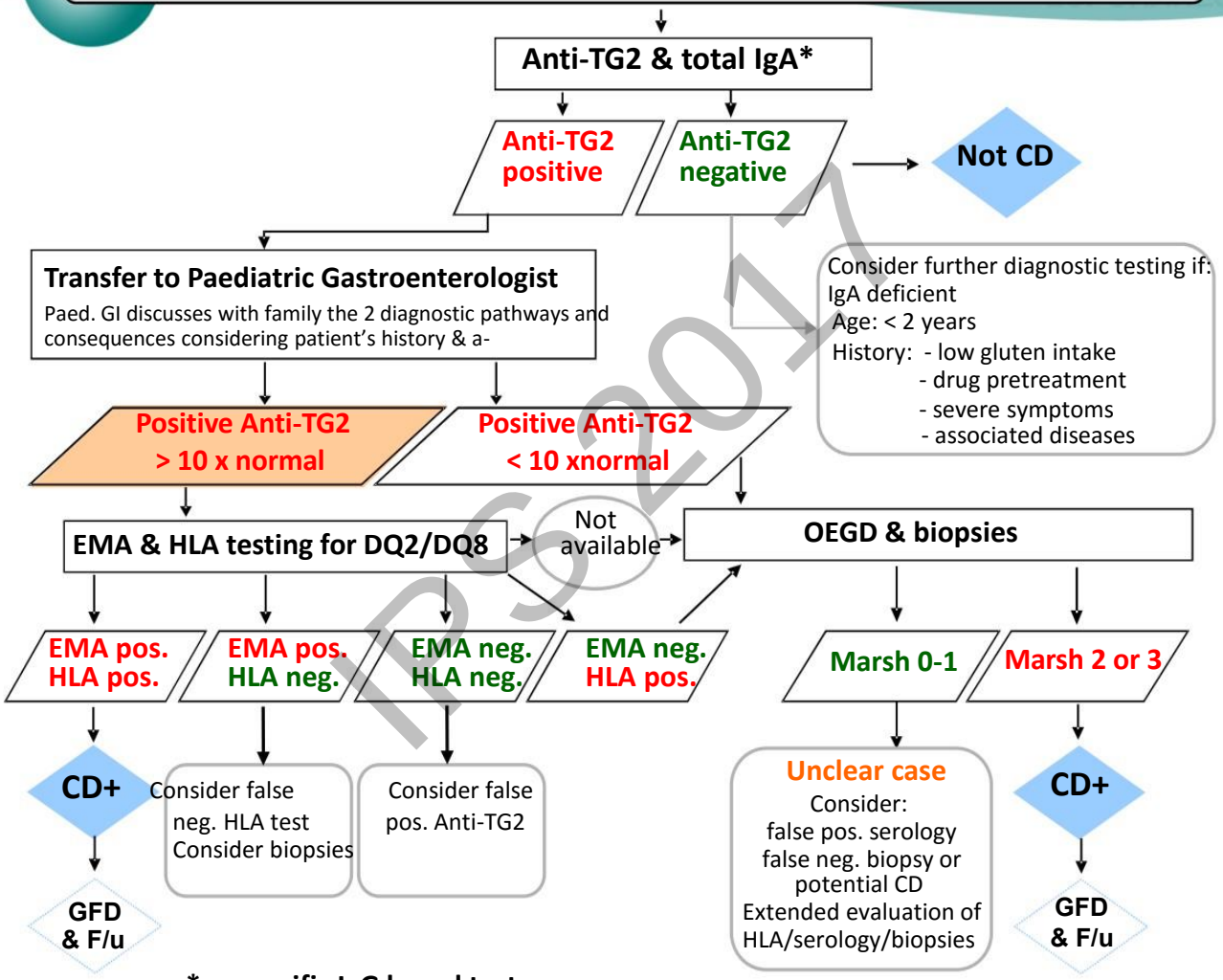




Untreated

On diet for 6 months

Child / Adolescent with Symptoms Suggestive of CD



*or specific IgG based tests

Treatment

- Only treatment for celiac disease is a gluten-free diet (GFD)
  - Strict, lifelong diet
  - Avoid:
    - Wheat
    - Rye
    - Barley

Sources of Gluten

- OBVIOUS SOURCES
  - Bread
  - Bagels
  - Cakes
  - Cereal
  - Cookies
  - Pasta / noodles
  - Pastries / pies
  - Rolls

Other Items to Consider

- Lipstick/Gloss/Balms
- Mouthwash/Toothpaste
- Play Dough
- Stamp and Envelope Glues
- Vitamin, Herbal, and Mineral preparations
- Prescription or OTC Medications

Potential Nutritional Complications in Untreated Celiac Disease

- Low Iron
- Low Folate
- Low Vitamin B-12
- Low Vitamins ADEK
- Low Thiamine
- Low Niacin
- Low B6 (rare)
- Low Beta-carotene
- Low Zinc
- Essential Fatty Acid Deficiency

Lactose Intolerance & Celiac Disease: Incidence

- Secondary lactase deficiency is estimated to be 20-40%
- Increasing lactose Intolerance with delayed diagnosis
- Increased incidence in patients with GI symptoms in Celiac Disease
- Decrease calcium and vitamin D intake in lactose intolerance

Lactose Intolerance & Celiac Disease: Treatment

- Gluten free diet
- Temporary lactose-reduction
- Lactase enzymes
- Lactose-free milk
- Gluten-free milk substitute
- Supplement with calcium & vitamin D where appropriate

Possible Causes of GI Symptoms on a Gluten-Free Diet

- Acidic foods
- Sorbitol
- Olestra
- Guar gums
- Antibiotics
- Lactose

- Alternate flours made from beans or nuts
- Food Allergens such as Milk Protein, Soy, Nuts, Egg, Corn
- Food Intolerance to fructose Foods high in salicylates and amines

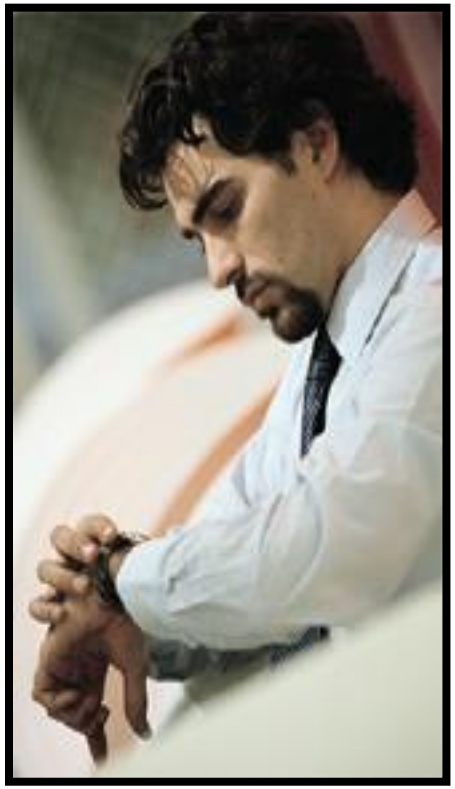
Dietary Adherence: A Common Problem

- Only 50% of Americans with a chronic illness adhere to their treatment regimen including:
  - diet
  - exercise
  - medication
- Dietary compliance can be the most difficult aspect of treatment

Barriers to Compliance

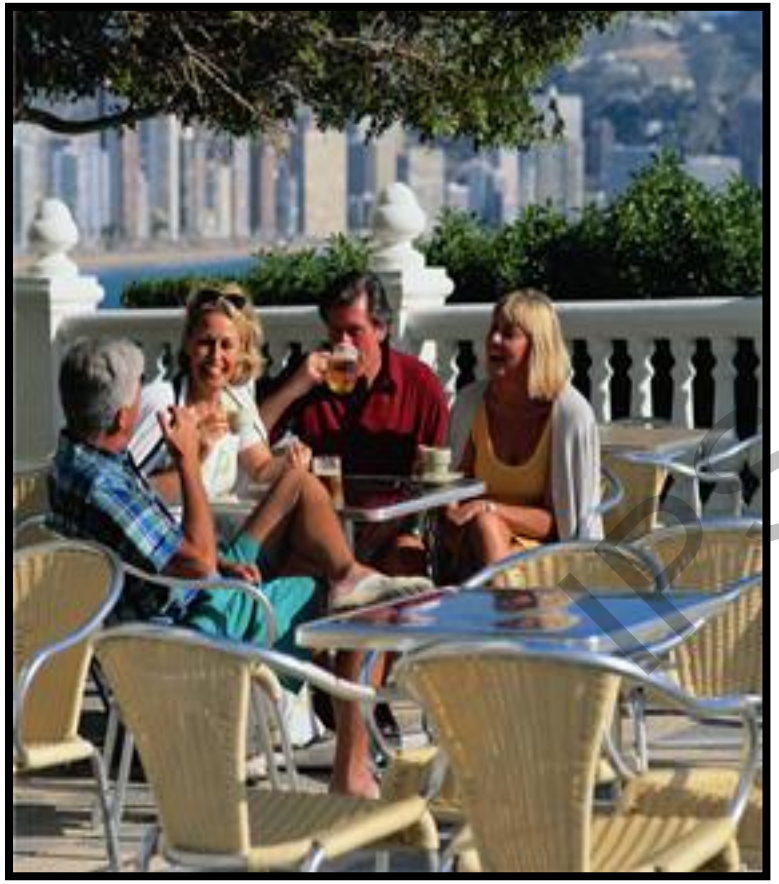
- Ability to manage emotions – depression, anxiety
- Ability to resist temptation – exercising restraint
- Feelings of deprivation
- Fear generated by inaccurate information

Barriers to Compliance



- Time pressure – time to plan, prepare food is longer
- Planning – work required to plan meals
- Competing priorities – family, job, etc.
- Assessing gluten content in foods/label reading
- Eating out – avoidance, fear, difficult to ensure food is safe

Barriers to Compliance



- Social Events – Not wanting to look/be different
- Support of Family and Friends – “Just a little bit – it won’t hurt you”

The Key to Dietary Compliance is Follow Up Care

- NASPGHAN Guidelines apply to adults and children
- The health effects are motivation
  - When one believes they are real
  - Testing measures the health effects of eating gluten
- Follow up testing provides important feedback

Resources

- Reputable websites
  - Celiac.Com (www.celiac.com)
  - National Institutes of Health (www.niddk.nih.gov)
  - American Dietetic Association (www.eatright.org)
- Local Support Groups
  - Celiac.Com (www.celiac.com)
- National Support Groups
  - The Gluten Intolerance Group – GIG (www.gluten.net)
  - Celiac Disease Foundation – CDF (www.celiac.org)
- Research and Information
  - Center for Celiac Research (www.celiaccenter.org)

Celiac Disease-Diagnosis: The Future

- Diagnosis Strategies
  - Mass population screening
    - Not cost effective (research tool)
    - Benefits uncertain
- Active case finding
  - Selective serological testing
  - Biopsy confirmation

Celiac Disease-Diagnosis: The Future

- Non biopsy diagnosis
  - Characteristic clinical subgroups
  - Refined (standardized) serological tests
  - Use of HLA typing
  - Discovery of biomarkers
  - Specific gene identification

Celiac Disease-Management: The Future

- Gluten free diet remains best treatment
- Refined understanding of “gluten free”
- FDA mandates better food labeling
- Commercial recognition of the “value” of gluten free products

Gluten Related Disorders

- Wheat Allergy
  - skin prick tests
  - allergen specific IgE antibodies
  - oral wheat challenge
- Non Celiac Gluten sensitivity
  - negative tests for celiac disease
  - negative tests for wheat allergy
  - DBPCFC

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Differential Diagnosis Between CD, GS, & 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)

Fasano et al. *N Engl J Med*. 2012;367:2419-26.

Diagnosis - Summary

Celiac Disease
- Clinical indication
- Serological test
- Intestinal biopsy
- Response to GFD

Wheat Allergy
- Clinical indication
- Skin prick tests
- Allergen specific IgE
- Oral food challenge

Non CD Gluten Sensitivity
- Clinical indication
- Negative CD serology
- Negative allergy testing
- DBPCFC

Summary

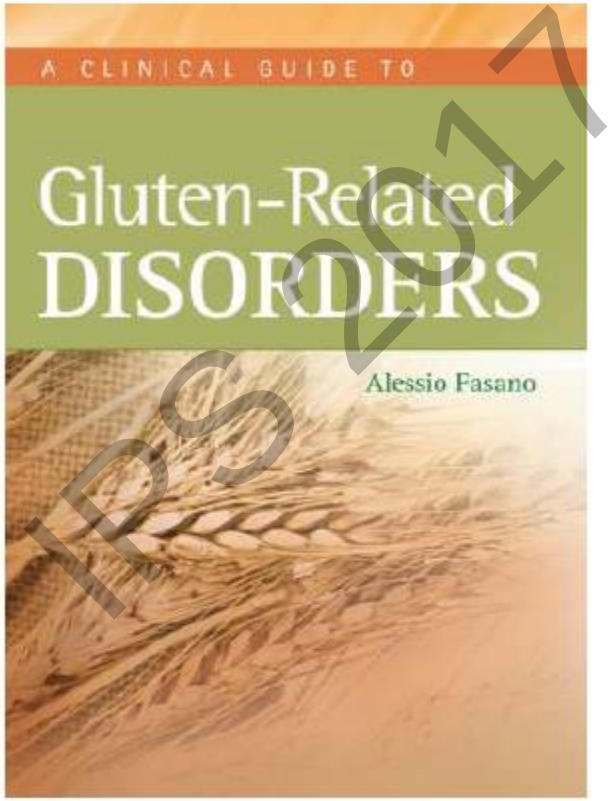
- Gluten can trigger celiac and other immune-mediated disorders (wheat allergy and non-celiac gluten sensitivity)
- The three forms of gluten related disorders can clinically overlap and cannot be distinguished on the basis of their clinical presentation;
- The prevalence of wheat allergy/celiac disease is well established, but the magnitude of non-celiac gluten sensitivity remains un-established. (lack of validated biomarkers)

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!!!

Clinical Guide to Gluten Related Disorders
published by Wolters Kluwer



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Thanks
Questions!