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Current Management of Celiac Disease and Identifying an Appropriate Patient Population(s) for Pharmacologic Therapies in Pediatric Patients

Alessio Fasano, M.D.

Mucosal Immunology and Biology Research Center

And Center for Celiac Research

Massachusetts General Hospital, Boston MA – U.S.A.



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DISCLOSURE

- **Alba Therapeutics: Co-founder and stock holder;**
- **Mead Johnson Nutrition: Sponsored research;**
- **Inova Diagnostics: Sponsored research;**
- **Regeneron: Sponsored research;**
- **Pfizer: Consultant**



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CeD IN PEDIATRICS: THE PAST AND THE PRESENT

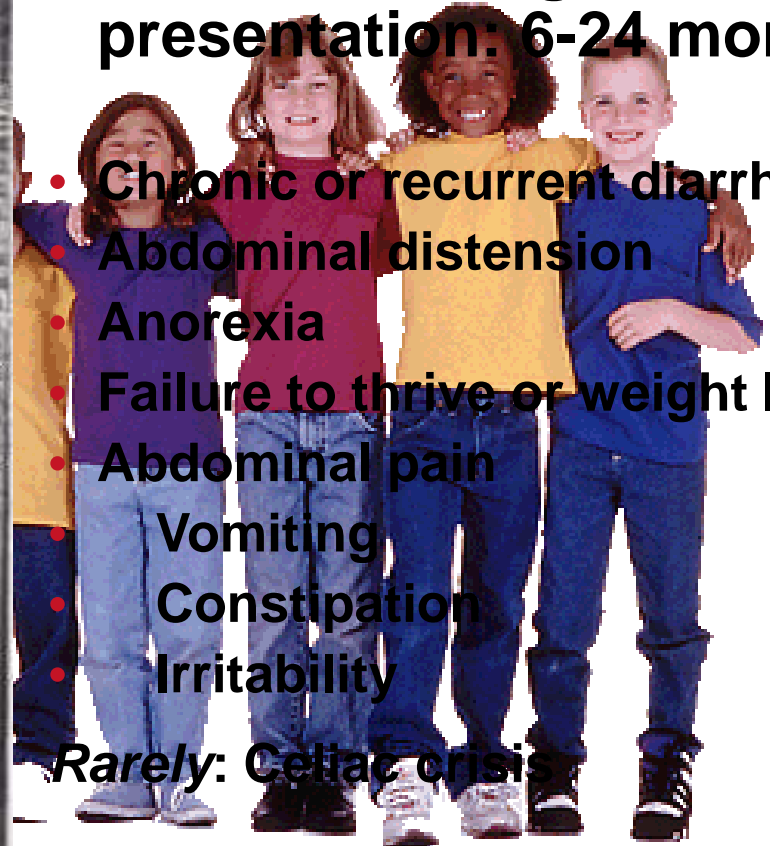


Fig. 2.—Photograph of five cases of coeliac disease showing the general clinical features.

Most common age of presentation: 6-24 months

- Chronic or recurrent diarrhea
- Abdominal distension
- Anorexia
- Failure to thrive or weight loss
- Abdominal pain
- Vomiting
- Constipation
- Irritability

Rarely: Celiac crisis



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Non Gastrointestinal Manifestations

Most common age of presentation: older child and teenager

- **Arthritis and/or joint pain**
- **Behavioral changes**
- **Delayed puberty**
- **Dental enamel hypoplasia of permanent teeth**
- **Dermatitis Herpetiformis**
- **Eczema**
- **Epilepsy with occipital calcifications**
- **Headache/Migraine**
- **Hepatitis**
- **Iron-deficient anemia resistant to oral Fe**
- **Osteopenia/Osteoporosis**
- **Short Stature**

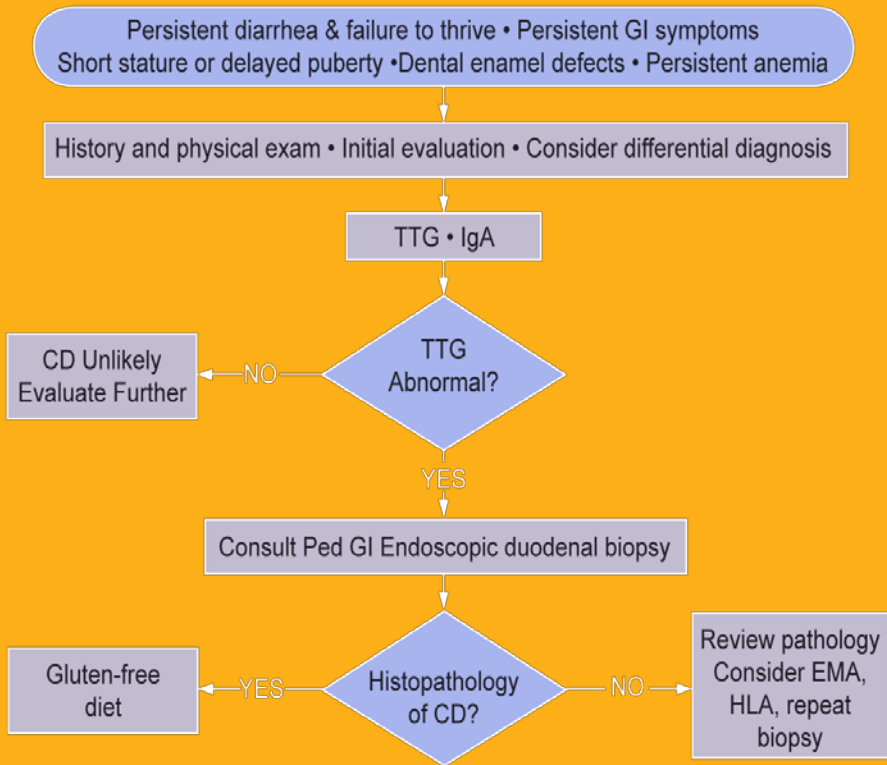


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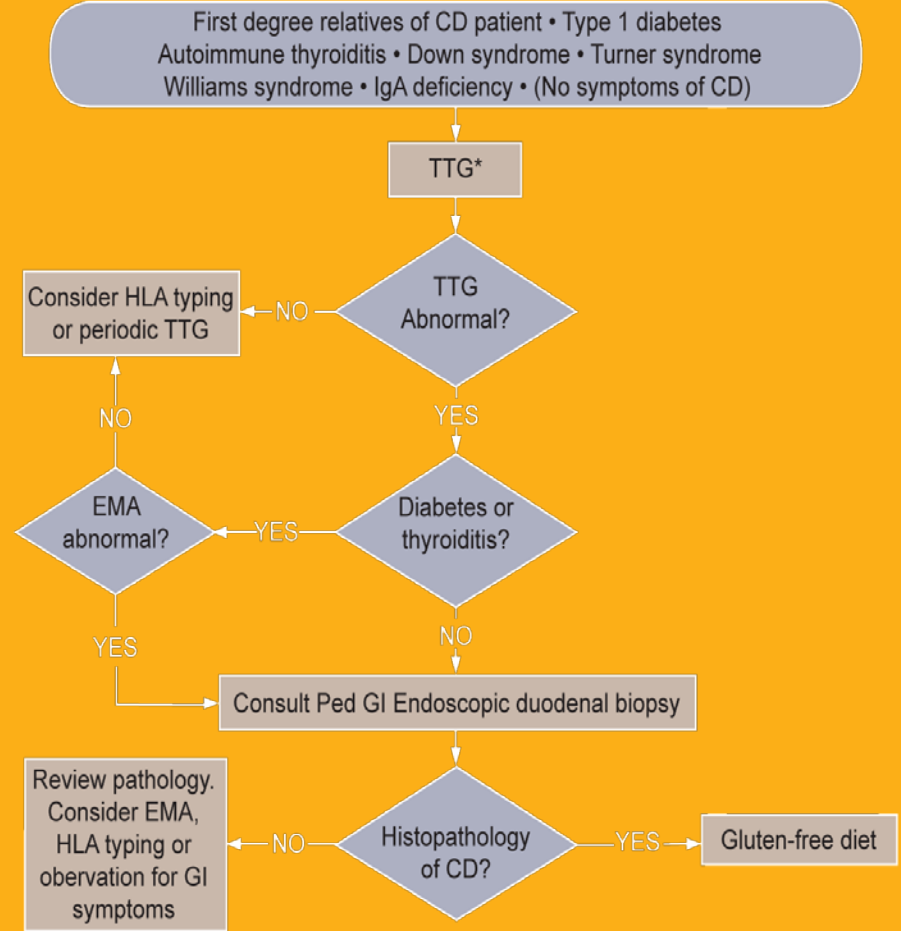
Listed in descending order of strength of evidence

Current Management: Diagnostic Criteria

Symptomatic Cases



Screening-Identified Cases



Current Management: Revised Diagnostic Criteria

European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Working Group on Coeliac Disease Diagnosis has recently issued revised guidelines.

These are the revised criteria:

Endoscopy and intestinal biopsy can be avoided in cases satisfying the following four criteria:

- 1. Presence of signs or symptoms compatible with CeD;**
- 2. Positive serology (TTG X10 N.V. eventually confirmed by EMA);**
- 3. Compatible HLA (DQ2 e/o DQ8 positive);**
- 4. Resolution of symptoms and normalization of CeD serology following implementation of a gluten free diet**

WHILE SEVERAL PEDIATRIC GASTROENTEROLOGISTS IN THE U.S. ARE FOLLOWING THESE REVISED CRITERIA, THEY DO NOT REPRESENT STANDARD OF CARE IN OUR COUNTRY



Current Management: Follow Up

- **Follow up 6 months after diagnosis to check:**
 - Symptoms;
 - Serology (not validated for monitoring but recommended by current guidelines);
 - Compliance/difficulties with the implementation of the GFD
 - If problems, follow up in 3 months, otherwise:
- **Follow up 12 months after diagnosis to check:**
 - Symptoms;
 - Serology(not validated for monitoring but recommended by current guidelines);
 - Compliance/difficulties with the implementation of the GFD

Currently a repeated endoscopy is not routinely recommended in Pediatrics unless patients still experience CeD-associated symptoms despite good compliance to the GFD

CURRENT MANAGEMENT: COMPLIANCE TO THE GFD

One of the most challenging issues related to the treatment of CeD is proper compliance of strict gluten free diet for life.



Beside facing the same issues that adult CeD patients experience, including risk of cross-contamination while traveling, vacationing, eating out, etc, pediatric patients have unique challenges that make the compliance to the GFD extremely difficult



UNIQUE CHALLENGES FOR COMPLIANCE TO THE GFD IN PEDIATRICS

- **Birthday parties**
- **School lunch**
- **Sleepovers**
- **Peer pressure**
- **Lack of appreciation for long term consequences for specific behavior;**
- **Transitioning to college lifestyle**



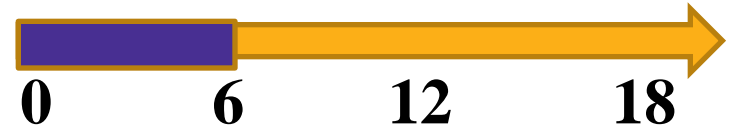
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Case Presentation



Description of the Case

JJA 17 y old M



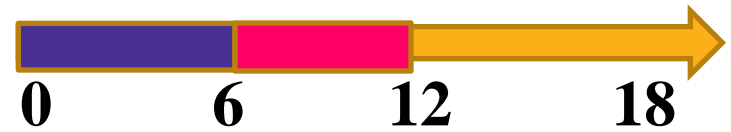
- Diagnosed with CeD (tTG: 49 (N.V.<7)
EGD+Histology: Marsh IIIb) at age 15 with following symptoms:
- Recurrent abdominal pain
- Anemia
- Constipation
- tTG: 49 (N.V.<7)
- EGD+Histology: Marsh IIIb

At the 6 months FY symptoms resolved, but tTG still slightly positive (15)



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Description of the Case



The 12 months FY visit revealed a 10 pounds weight loss, chronic diarrhea, and RAP. tTG positive (78)

Discussing the situation privately with JJ he admitted that he cheated with the diet soon after the previous visit he started dating a young girl and, when they went to dinner, he felt uncomfortable to share that he had to be on a special diet. Eating gluten did not cause any symptoms and, therefore, at the following date he continued to eat an unrestricted diet. After 3 months that he abandoned the GFD he started experiencing the symptoms listed above.

The dietician and psychologist of the center were involved and JJ agreed to return to a GFD and discuss his disease with the girlfriend.



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Description of the Case

The subsequent follow up 18 months after the diagnosis revealed resolution of his symptoms, tTG within normal values (3) and weight gain.

The availability of a treatment integrative of the GFD would have given to this patient a concrete alternative to the abandonment of the GFD, so avoiding relapse of symptoms and possible long term consequences.

Efficacy Readout From Patient Prospective

Adults:

**Improvement of
quality of life**



Pediatrics:

**Blend with peers,
being not different
from others**



Pediatric Patients Most Likely To Benefit From Pharmacological Therapies For The Treatment of Celiac Disease

- 1. Children in which the GFD does not control clinically (resolution of symptoms) and/or serologically the disease. The goal is to achieve control of CeD not treated by good compliance to GFD;**
- 2. CeD children affected by neuro-developmental/behavioral diseases (i.e. Down's syndrome) in which judgment of consequences to lack of compliance to GFD can be impaired. The goal is to provide a “safety net” for those children in which compliance to the GFD is challenging;**
- 3. CeD children affected by type 1 diabetes (T1D). The goal is minimize the burden of very restrictive diets, particularly considering that the GFD is rich in sugars;**

Pediatric Patients Most Likely To Benefit From Pharmacological Therapies For The Treatment of Celiac Disease

- 1. CeD children during specific social events: sleepovers, birthday parties, summer camps, etc. These are activities with increased risk of cross-contamination. In this case the goal is to temporarily protect children from inadvertent exposure to gluten in situations in which control of GFD can be complicated;**
- 2. Young adults attending college. College lifestyle present unique challenges in terms of compliance to GFD. The goal in this case is to give the opportunity to protect against exposure to gluten in a setting where cross-contamination in dining halls are frequent;**
- 3. Refractory sprue: rare in pediatrics, but pharmacological therapies will be the only valuable option in these cases.**

CONCLUSIONS

- **The CeD pediatric population would have an even stronger need for pharmacological therapies alternative/integrative to the gluten free diet compared to the adult population.**
- **Metric to establish efficacy of a pharmacological treatment of CeD includes resolution of symptoms, normalization of CeD serology (with the caveat that current tests have not been validated for monitoring) and resolution of CeD enteropathy;**
- **Since a repeated endoscopy after implementation of a GFD that successfully resolve the presenting symptoms is not recommended and in consideration that some children will not have a baseline endoscopy if managed with the revised ESPGHAN diagnostic criteria, other metrics to establish efficacy of pharmacological therapies are even more imperative than in adult patients**

