



## Accuracy of IgA tTG for Predicting Mucosal Healing In Children with Celiac Disease On A Gluten Free Diet

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**CELIAC RESEARCH PROGRAM**  
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## NASPGHAN ★★ 2015

Maureen Leonard  
**Has documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.**



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## Celiac Disease is Changing

- More patients present with atypical symptoms or asymptotically from high risk groups
- Celiac disease (CD) can develop at any age
- Average age at diagnosis has increased
- Mucosal disease may be less severe at diagnosis

Fasano, A. Arch Intern Med 2003  
Catassi, C. Ann Med 2010  
Maki, M. Acta Ped Scand 1988  
McGowan, KE. Pediatrics. 2009  
Roma, E. Digestion. 2009  
Kivela, L. J of Pediatrics. 2015

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### Current Management

- The gluten free diet (GFD) is the only therapeutic option for the treatment of CD
  - Dietary counseling
- Serology tests(IgA tTG) in order to assess dietary compliance and for use as a surrogate marker of mucosal healing
- These tests have not been validated for follow up or to monitor for compliance

Rostrum, Gastro, 2006  
Rubio-Tapia, A. Am J. of Gastro 2013  
Hill, J. JPGN, 2005

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### Adult Patients with Celiac Disease Have Slow Mucosal Recovery

- 33%-66% of adults with CD have persistent mucosal damage after 2 years on a GFD
- Early pediatric data suggested a faster and more complete mucosal recovery
- Anecdotally this is explained by a decreased regenerative capacity of the adult intestine

Ciacci, C. Digestion, 2002  
Rubio-Tapia, Am J. of Gastro, 2010

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### Does IgA tTG Predict Mucosal Healing?

- Objective:
  - Assess mucosal healing in pediatric patients with CD on a GFD
- Aim:
  - Assess whether IgA tTG correlates with intestinal disease activity at time of follow-up endoscopy

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## Methods

- Retrospective Chart Review
  - Subjects: 129 subjects
    - Identified by Research Database
      - 71 pts ages 1-21 @ MGH/C 1/2012-3/2015.
      - 58 pts ages 1-21 @ CHB 1/2008-12/2013.
- Inclusion Criteria:
  - Diagnosis of CD, defined as Marsh 3 histologically
  - 2<sup>nd</sup> endoscopy w/ duodenal biopsy at least 4 months after initiation of the GFD
- Descriptive Statistics were used to analyze results

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## Results: Subject Characteristics At Diagnosis

Age at diagnosis (y) (Mean ± SD)	10.8±5.1
Gender	58% Female
IgA tTG positive at diagnosis	87.4%
Co-morbid autoimmune disease	9.4%

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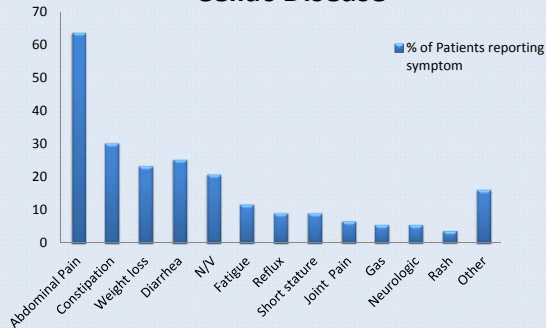
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## Presenting Symptoms at Diagnosis of Celiac Disease




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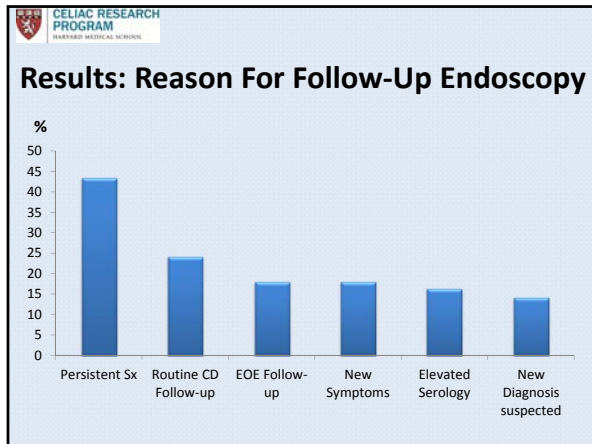
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### Results: Subject Characteristics at Repeat Endoscopy

Subject met with dietician	96.9%	
Months on a gluten free diet: Median (Range)	18.7 (4-144)	
Serology positive	36.3%	
Symptomatic when repeat scope recommended	Yes	65.1%
	No	34.9%
Excellent or good dietary adherence*	95.3%	

\*Self reported

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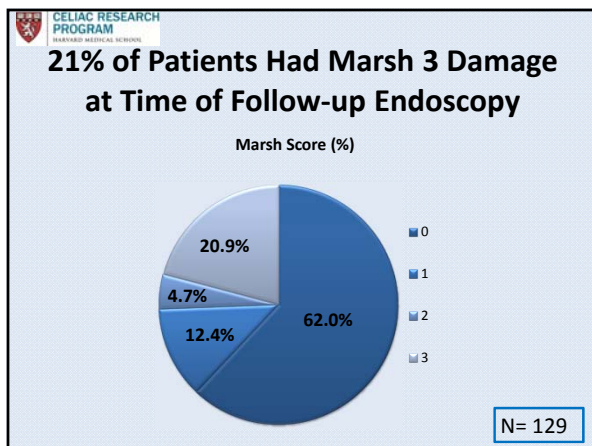
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### IgA tTG is Not Predictive of Mucosal Disease in Patients with Celiac Disease on a Gluten Free Diet

- Sensitivity: 40%
- Specificity: 65%
- Positive Predictive Value: 24%
- Negative Predictive Value: 79%
- Accuracy: 59%

N= 113

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### There Were No Predictors of Mucosal Healing

Characteristic	Marsh 0-2 (n=102)	Marsh 3 (n=27)	P
Female sex	59 (57.8%)	16 (59.3%)	0.89
Age at diagnosis (y)	10.6±5.0	11.9±5.3	0.23
Months from start of GFD to repeat scope	29.0±24.9	32.9±38.4	0.62
Excellent adherence to GFD	94 (92.2%)	21 (80.8%)	0.14
Symptomatic at clinic visit when 1 <sup>st</sup> repeat scope recommended			0.47
Yes	68 (66.7%)	16 (59.3%)	
No	34 (33.3%)	11 (40.7%)	
Repeat serology positive or equivocal	31 (35.2%)	10 (40.0%)	0.66

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### Summary Of Results

- 1 in 5 pediatric patients with CD on a GFD had persistent mucosal injury described as a Marsh 3 lesion
- We were unable to identify any variables helpful in predicting which patients had mucosal healing vs. persistent mucosal damage
- In our population, IgA tTG was not an accurate measure of intestinal mucosal activity for patients with CD on a GFD

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## Limitations

- tTG assays run at different sites
  - tTG dichotomized according to various cut off levels
- MGHfC and CHB as referral celiac centers may be less generalizable
- Retrospective
  - 80% serology sent <4 months of procedure
  - Villous height: crypt depth ratio
  - Standardized blinded pathologists
- Sample size similar to recent study

Barnister, E. Am J Gastro 2014  
de Chasse Martin, L. PLoS one. 2015

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## Conclusions

- IgA tTG is an accurate and cost-effective screening test for patients at risk for or suspected to have CD
- Despite current recommendations to use serology tests as a biomarker of compliance with a GFD or as a measure of mucosal healing, available serological tests have not been validated for this use
- In our population the accuracy of IgA tTG when used as a surrogate measure of mucosal healing in patients with confirmed CD on a GFD is poor
- Consider a low threshold to repeat the endoscopy in patients with CD on a GFD

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## Acknowledgments

- Dascha Weir, MD
- Paul Mitchell, MS
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- Maya DeGroote, BA
- Alan Leichtner, MD
- Alessio Fasano, MD

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## Future Directions

- Medications for patients with CD are under development
- FDA has prioritized the need to develop accurate endpoints to assess mucosal healing for patients with CD.
- Prospective studies identifying and validating endpoints are needed
  - Adequate dietary adherence scales
  - Employing a biomarker for dietary adherence (IgA AGA)
  - Exploring tTG vs. DGP as a marker of mucosal healing
  - Evaluating cut-off values for serology tests at follow-up
  - Investigating the mechanism by which the mucosal healing process takes place in children and adults

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