

Celiac Disease Who to Test & How to Test

Ivor D. Hill, MB, ChB, MD.
Wake Forest University
School of Medicine.

Disclosure Statement

I have the following financial relationship to disclose:

Astra-Zeneca - Consultant

No products or services produced by this company is relevant to my presentation.




Celiac Disease

- Case # 1 - 10 year old girl
- Excess gas x 6-7 weeks
 - Frequent burping and malodorous flatulence
- Preceding viral gastroenteritis - resolved
- Abdominal cramping +/- improved off dairy
- Examination
 - WDWN
 - Abdominal distension - tympanic ++
- KUB - gas +++ throughout
- Diagnosis - lactose intolerance



Celiac Disease

- Case #2 – 7 year old boy
 - Parental concern for short stature
 - Grew well until 4 years (25-50% tile)
 - Progressive fall in height to below 5% tile
 - Weight maintained on 25% tile
 - Initial endocrine work up negative
 - Examination
 - Short but healthy (wt 25% and height < 5%)
 - Provisional diagnosis – “constitutional”



Celiac Disease



- Case #3 – 19 month old girl
 - Progressive misery since a year of age
 - Per mother – “clingy, irritable, low energy”
 - Poor appetite and weight gain
 - No vomiting or diarrhea
 - Problems began with starting regular milk
 - Examination
 - Fretful, thin appearing – height 25 % tile, weight <5% tile
 - Poor muscle bulk, abdominal distension
 - Provisional diagnosis CMPI



Celiac Disease

Celiac disease!

- Celiac disease factoids!
 - Affects ~ 1% of the USA population
 - 2-3 million cases in the USA
 - 5-20 affected children in average practice
 - 90% undiagnosed



Celiac Disease

The 3 Steps to Diagnosis

Clinical suspicion
Screening Test
Confirmation

WAKE FOREST UNIVERSITY
School of Medicine

Celiac Disease

- Aims
 - Identify children in need of testing
 - Symptomatic
 - Asymptomatic - but at risk
 - Choose the best test for screening
 - Limitations of testing
 - Pitfalls in testing
 - Confirmation of the diagnosis

WAKE FOREST UNIVERSITY
School of Medicine

Celiac Disease



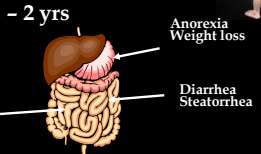
Manifestations

- Early Gastrointestinal →
- Late Gastrointestinal →
- Non Gastrointestinal →
- Associated conditions →
- Asymptomatic →

WAKE FOREST UNIVERSITY
School of Medicine

Celiac Disease

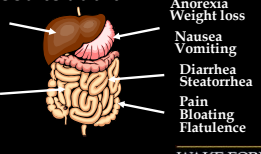
- Symptomatic group
 - Gastrointestinal - early onset
 - Age - 6 mths - 2 yrs



WAKE FOREST UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease




- Symptomatic group
 - Gastrointestinal - late onset
 - Age - childhood to adult



WAKE FOREST UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease

- Symptomatic group
 - Non-Gastrointestinal




WAKE FOREST UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease


At Risk Groups

Autoimmune	Non-autoimmune
Type 1 DM	Relatives
Thyroiditis	Down syndrome
A.I. Hepatitis	Turner syndrome
Sjogren's	Williams syndrome
Arthritis	IgA deficiency



Celiac Disease




■ **Who to test?**



Celiac Disease


■ **Screening recommendations**

- **Symptomatic – consensus!**
 - Typical GI symptoms – first line test
 - “Atypical” – second line test
- **Asymptomatic – schizophrenia!**




Celiac Disease Screening - asymptomatic

- Recommendations
 - NIH Consensus Development Program **Some**
 - NASPGHAN **All**
 - American Gastroenterological Association **None**



Celiac Disease Screening

- Asymptomatic screening problems
 - Natural history unknown
 - Benefits uncertain
 - Compliance unlikely
 - QOL issues
- Concerns
 - Mortality - malignancies
 - Morbidity - osteoporosis, autoimmune diseases, growth stunting




Celiac Disease Screening

- Static vs. dynamic disorder?

Fate of Five Celiac Disease-Associated Antibodies During Normal Diet in Genetically At-Risk Children Observed from Birth in a Natural History Study
Sattu Simell, M.D., J.2 Sanna Hoppu, M.D., Ph.D., I.4 Anne Hekkala, M.D., et al.
Am J Gastroenterol 2007;102:2026-2035.
- Malignancy myth?


Malignancies in cases with screening-identified evidence of coeliac disease: a long-term population-based cohort study.
Lohi S, Maki M, Montonen J, et al.
Gut 2009;58:643-647.



Celiac Disease

- How to test?

Consensus!




Logos for NASPGHAN, NIH Consensus Development Program, American Gastroenterological Association, and Wake Forest University School of Medicine.

Celiac Disease

- Commercial serological tests.

- Antigliadin - IgG & IgA
- Endomysial - IgA
- Transglutaminase – IgA & (IgG)
- Deamidated gliadin – IgA & IgG




Wake Forest University School of Medicine logo.

Celiac Disease

Serological tests

- AGA (IgG & IgA)
 - Advantages – cheap & easy to perform
 - Disadvantage – variable sens/spec.
- EMA (IgA)
 - Advantages – high sens/spec.
 - Disadvantages – expensive, time consuming, operator dependent, no use in IgA deficiency



Wake Forest University School of Medicine logo.

Celiac Disease

Serological tests

- **TTG (IgA)**
 - Human recombinant protein
 - Advantages – cheaper than EMA, easier to perform, non operator dependent
 - Disadvantages – ? less specific than EMA, no use in IgA deficiency

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease

- **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

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

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease

- **The new kid on the block?**
 - **Deamidated Gliadin antibodies**

Usefulness of Antibodies to Deamidated Gliadin Peptides in Celiac Disease Diagnosis and Follow-up
 Umberto Volta, Alessandro Granito, Erica Fiorini, et al.
 Dig Dis Sci 2008;53:1582-1588

	Celiac subjects – 128	Controls – 134
	IgA	IgG
Sensitivity	83.6%	84.4%
Specificity	90.3%	98.5%

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease

- **The new kid on the block?**
 - **Deamidated Gliadin antibodies**

Comparative Usefulness of Deamidated Gliadin Antibodies in the
Diagnosis of Celiac Disease

Shadi Rashtak, Michael W. Ettore, Henry A. Homberger, Joseph A Murray
Clin Gastroenterol Hepatol 2008;6:426-432.

	Controls – 124		
	IgA	IgG	IgA + IgG
Celiac subjects – 92			
Sensitivity	74%	65%	75%
Specificity	95%	98%	94%

WAKE FOREST
UNIVERSITY
School of Medicine

Celiac Disease

- **Recommendations**
 - Transglutaminase
 - Serum IgA?
 - Single test vs. panel?
 - Serial testing - TTG → EMA?

WAKE FOREST
UNIVERSITY
School of Medicine

Celiac Disease

- **Pitfalls in serological testing!**
 - Research setting vs. the real world
 - Diabetics?
 - Young children (< 2 years)

Antigliadin and antiendomysium antibody determination for celiac
disease.

Burgin-Wolff A, Gaze H, Hadziselimovic F, et al.
Arch Dis Child 1991;66:941-7

WAKE FOREST
UNIVERSITY
School of Medicine

Celiac Disease

- Pitfalls in serological testing!
 - Young children (< 2 years)

Antigliadin immunoglobulin A best in finding celiac disease in children younger than 18 months of age
Lagerqvist C, Dahlbom I, Hansson T, et al.
J Pediatr Gastroenterol Nutr 2008;47:428-35.

Subjects – 428 (7.5 mth to 14 yr) Controls – 216 (8.5 mth to 14.6 yr)

	AGA-IgA	tTG-IgA & EMA-IgA
Under 18 mth	97%	83%
Over 18 mth	94%	99%

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE

Celiac Disease

- Pitfalls in serological testing!
 - Young children - consider
 - Transglutaminase
 - Serum IgA
 - Antigliadin
 - Deamidated gliadin ???

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE


Celiac Disease

- Definitive diagnosis
- Always confirm before treating
- Confirmation mandates GFD for life
 - Following a strict GFD is not easy
 - Diet has potential QOL implications
- Failure to treat has potential long term adverse health consequences
 - increased morbidity and mortality

WAKE FOREST
UNIVERSITY
SCHOOL OF MEDICINE



Celiac Disease

- **Definitive diagnosis**
 - **Revised ESPGHAN criteria**
 - Characteristic histology
 - Symptom resolution
 - +/- serological tests
 - **Biopsy**
 - Serology positive
 - Serology negative




Celiac Disease






- **Biopsy technique**


	vs.	
Capsule Jejunum	vs.	Endoscope Duodenal

Small intestinal biopsies in celiac disease: duodenal or jejunal?
Meijer JWR, Wahab PF, Mulder CJJ.
Virchows Arch 2003;442:124-8.



Celiac Disease

- **Biopsies**
 - **Endoscopic appearance**
 -  Normal
 -  Scalloping
 -  Nodularity
 - **Magnification**
 -  Normal
 -  Villous blunting



Celiac Disease

- Biopsy recommendations



Consensus!




Celiac Disease


- Biopsy recommendations
 - Number - minimum of 4
 - Site - D2 and beyond - duodenal bulb?

Patchy villous atrophy of the duodenum in childhood celiac disease.
Bonamico M, Mariani P, Thanasi E, et al.
J Pediatr Gastroenterol Nutr 2004;38:204-207.


Duodenal bulb biopsies in celiac disease - a multi-center study.
Bonamico M, Thanasi E, Mariani P, et al.
J Pediatr Gastroenterol Nutr 2008;47:618-622




Celiac Disease




Normal 0




Infiltrative 1




Hyperplastic 2




Partial atrophy 3a



Subtotal atrophy 3b




Total atrophy 3c



Celiac Disease


- **Diagnostic confidence**
 - Marsh grade 3 – strong
 - Marsh grade 2 – moderate/weak (need additional evidence)
 - Marsh grade 1 – highly suspect (need alternative strategies)

Diagnosing mild enteropathy celiac disease: A randomized, controlled clinical study.
Kurppa K, Collin P, Viljamaa M, et al.
Gastroenterology 2009;136:816-23.



Celiac Disease

- **Conclusions**
 - Diagnosis depends on:
 - High index of clinical suspicion
 - Use of appropriate serological tests
 - Multiple intestinal biopsies
 - Therapeutic response



Celiac Disease

- **Suggestions for change**
 - Consider celiac disease more often
 - Use “cost effective” screening protocol
 - A final plea!!!

Always confirm before you treat!



© Original Artist Reprinted with permission from www.CoverlyCartoon.com

DAVE COVERLY

SCHOOL OF MEDICINE

Celiac Disease

- **Resources**
 - www.cdhnf.org or (www.celiachealth.org)
 - Guidelines for evaluation and management
 - Patient information brochures
 - Start up diet
 - Gluten free drug list
 - NASPGHAN guidelines - JPGN 2005;40:1-19.
 - NIH Consensus Conference - Gastroenterology 2005;S1-S9.
 - AGA guidelines - Gastroenterology 2006;131:1977-1980.
 - Technical Review - Gastroenterology 2006;131:1981-2002.

WAKE FOREST
UNIVERSITY
School of Medicine
