

What is anti-tissue transglutaminase (atTG) and What does it mean?

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Celiac Disease: Definition

- Permanent sensitivity to gluten in wheat and related proteins found in barley and rye
- Occurs in genetically susceptible individuals
- Manifests as an immune mediated enteropathy
- Defined by characteristic changes on small bowel histology
- Resolution of symptoms and prevention of complications by LIFE LONG Gluten Free Diet

NASPGHAN Guidelines Hill et al JPGN 2005; 40 (1): 1-19

Who should be screened for Celiac Disease?

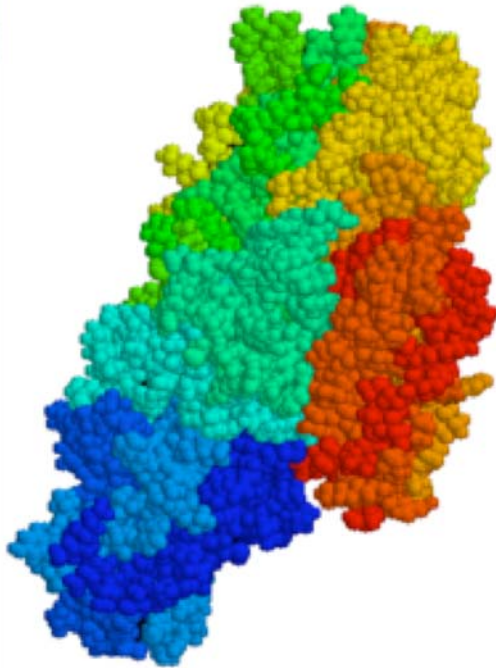
- Pts with symptoms
- 1st, 2nd relatives of pts with Celiac
- PHx Autoimmune diseases such as thyroid; liver; IDDM
- IBS
- Anemia
- Fibromyalgia
- Chronic diarrhea
- Chronic fatigue syndrome
- Unexplained weight loss
- Short stature
- Unexplained osteoporosis
- Epilepsy
- Infertility
- Unexplained abn LFT's

Learning Objectives

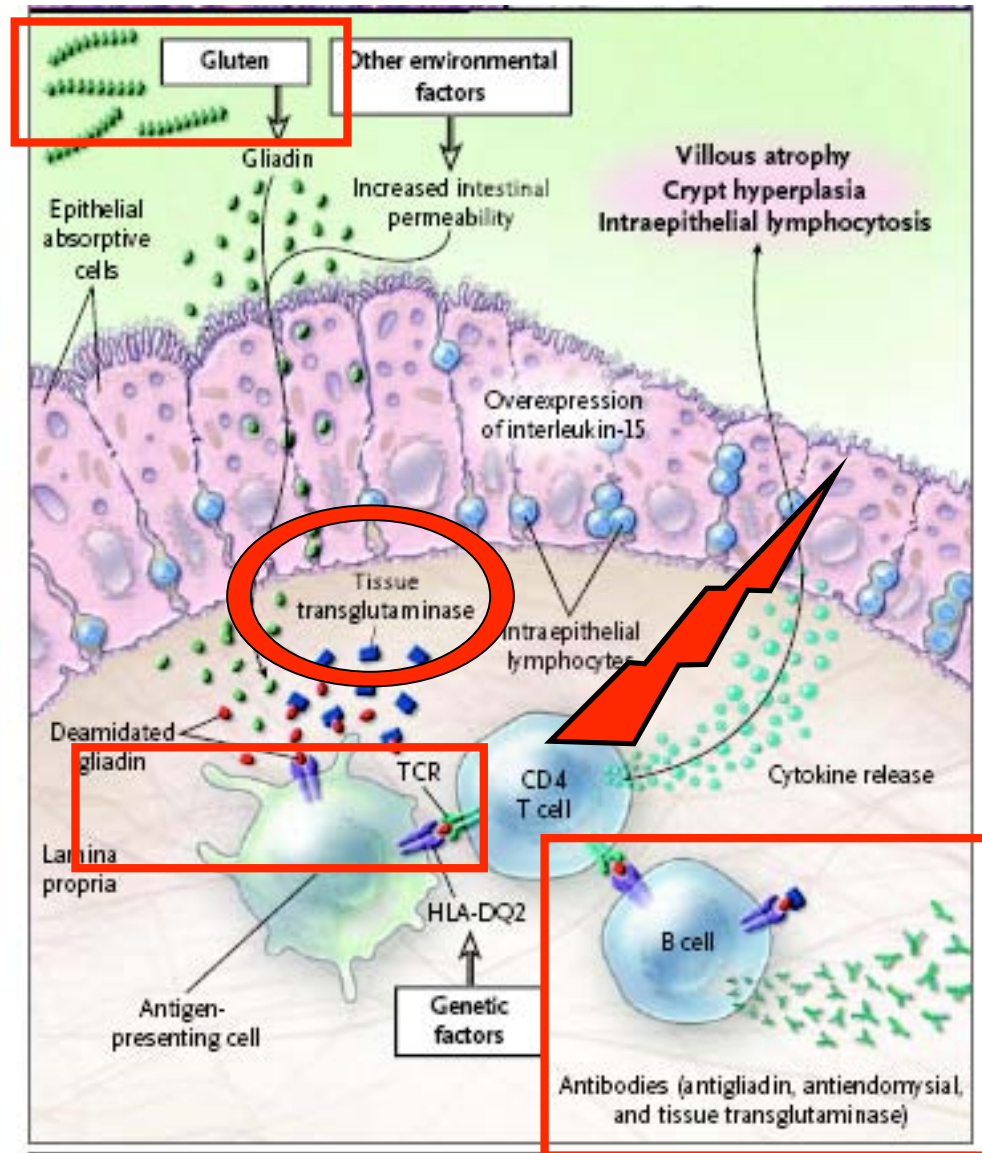
At the end of this presentation participants should understand that:

- Tissue Transglutaminase is an essential enzyme for tissue maintenance and repair
- Anti-tTG is an IgA auto-antibody
- +ve atTG antibody is PREDICTIVE but NOT diagnostic of celiac disease
- A definitive diagnosis of celiac can ONLY be made by duodenal biopsy on a normal diet

What is tTG?



- Essential enzyme
- Crosslinks ϵ -amino group of lysine and γ carboxamide of glutamine
- Creates intra- or inter-molecular bond resistant to proteolysis
- Role in apoptosis, cellular differentiation and matrix stabilization
- Deamidates gliadin
- It is the auto-antigen for EMA
- Allows for interaction with HLA-DQ2 or HLA-DQ8 on antigen presenting CD4+T cells
- Leads to antibody production & mucosal damage



Green P NEJM 357: 1731-43, 2007

Serology screening for Celiac

- All screening and diagnostic tests need to be done with the patient on a gluten-containing diet *
- Old serology – high false +ve/-ve rates
 - IgG/IgA anti-gliadin antibodies
 - antireticulin antibodies
- IgA EMA – qualitative immunofluorescence technique
 - monkey esophagus or human umbilical cord
- **IgA anti-tTG** – quantitative immunosorbant assay
 - guinea pig (GP) or human recombinant (HU)

*NIH Consensus Document 2004;

AGA technical review: Gastroenterology 2006;131:1977-1980



What are the Celiac screening tests good for?

- Screening individuals with symptoms
- Screening individuals at risk
- Screening individuals with family history
- Screening, Screening, Screening
- ?Role in follow-up after small bowel biopsy to assess response to strict gluten free diet

Celiac Case Finding in 1ry Care

- Prospective multicenter study to improve detection of Celiac Disease in 1ry Care
- atTG & IGA levels ordered in all pts >18 with ANY symptom or risk factor for celiac disease – detailed list
- All +ves had small bowel biopsy
- 2.3% of 720 pts +ve: highest prevalence
 - Thyroid disease 6.2%; FHx CD 5%; chronic diarrhea 4.9%; infertility 3.7%; weight loss 2.9%; anemia 2.8%
- ↑'d detection rate of Celiac disease by **32 to 43 fold**

Catassi & Fassano et al; Detection of Celiac in Primary Care;
Am J Gastro; 2007; 102: 1454-1460

Are these Screening Tests really that good?

- Well....**YES**
- Good in populations at high-risk for Celiac as defined by 'at-risk' groups
- May be useful to follow adherence to GFD*
 - Expect ↓ by 50% at 4 wks and to 'N' by 12wks
- **BUT....NO**
- PPV is lower in groups where the prevalence of CD is < 25%
- There are false +ves and false -ves

*Moor et al Celiac Symposium 2004: P11

Celiac Disease - Diagnosis

- Serologic studies:
- Highly sensitive/specific in screening for CD but:
 - Laboratory variations in operating properties
 - Regional variations in tests & availability
 - Impact of concomitant immune deficiency
 - Accuracy of serology is impacted by patient's diet
- Both atTG and EMA are IGA antibodies
- When –ve is CD ruled out?
- When +ve is CD always present?

*NIH Consensus Document 2004;

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Review of Serology tests

	Sensitivity	Specificity	PPV	NPV
IgA tTG (GP)	81-100	92-98	60-97.9	74-100
IgA EMA (ME)	74-100	97-100	93-100	88-100

NIH Consensus document 2004

Causes of 'False +ve' Serology

Patient with +ve serology but normal biopsy

- ?Latent Celiac
- ?Early enteropathy - with only ↑'d IEL's
- ?Patient already on low gluten diet
- ?Patchy enteropathy – like DH
- ?Biopsy techniques/sampling/handling
- Underlying auto-immune disease
- Unknown ???

Causes of False –ve Serology

Patient with –ve serology but +ve biopsy

- **IgA deficiency** up to 5% of celiac pts
- Self imposed GF or low Gluten diet
- In early or minimal enteropathy
- Patients on immunosuppressants
- Down's syndrome & other genetic syndromes
- Smokers especially women
- Laboratory issues

BIOPSY ALL SYMPTOMATIC PTS




Do you need a small bowel biopsy
to diagnose Celiac disease??

- **YES!!!**



What should the Doctor do for a patient with +ve Celiac Serology?

- DO NOT START GFD based on serology alone
- Expedite a referral to specialist for Duodenal BIOPSY
- Advise consultant re: abnormal tests & review of symptoms
- Explain to the patient NOT to start a GFD until after a biopsy is done




Challenges for individuals **ALREADY** on a GFD before biopsy

- Confirming a diagnosis of celiac disease is **VERY** difficult as the mucosa will be healing
- Consultant may want the individual to undergo a “gluten challenge” before biopsy
- In young children it is particularly important **NOT** to start GFD before biopsy as the serology tests are not as reliable

What does the Specialist do for the patient with +ve Celiac Serology

- Advise the GP that the patient should be on a NORMAL diet until biopsy is completed
- Establish a positive diagnosis of Celiac Disease with the patient on a NORMAL diet
 - This reduces the chances of having an uncertain diagnosis with many questions down the road
- Excellent recovery expected with adherence to a strict gluten free diet
- Encourage serology screening of 1st and 2nd degree relatives
- Encourage a yearly medical check-up



Things to remember if you take a Celiac – “home test”

- This is a atTg IgA based blood test
- If it is positive – **SEE YOUR DOCTOR**
 - Remember that false positives may occur
 - Have a biopsy **BEFORE** going Gluten Free
- If it is negative – **SEE YOUR DOCTOR**
 - False negatives do occur
 - If you have symptoms you may need a biopsy to rule out celiac disease

What should you do if you have a +ve Celiac Serology?

- If you have done a “home test” see your own Doctor and ask for referral to a specialist*
- DO NOT START A GLUTEN FREE DIET UNTIL THE DIAGNOSIS IS CONFIRMED
- DO NOT START GFD based on serology alone
- Expect that your Doctor will repeat the testing at an accredited and “regulated” laboratory

*Celiac News; 2008: 22(1):9

Learning Objectives

Participants now understand that:

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