



Microscopic Enteritis

Kamran Rostami

Clinical Lecturer
School of Medicine,
University of Birmingham, UK



Outline

- Coeliac disease
- Microscopic Enteritis
 - Definition
 - Epidemiology
 - Differential diagnosis
 - Pathogenesis
 - Diagnostic and Pitfalls



Long ago when celiac disease was recognized

Celiac disease: changing dogma on historical diagnosis

V. Villanacci, C. Catassi, K. Rostami and U. Volta, 13 January 2010



GastroHep.com

By Founder Peter Cottan PhD/Peter van Gool MD

The Global Online Resource for Gastroenterology, Hepatology and Endoscopy



Coeliac Disease



Prevalence of celiac disease in Egyptian children disputes the east-west agriculture-dependent spread of the disease.

Abu-Zekry M, Kryszak D, Diab M, Catassi C, Fasano A. *J Pediatr Gastroenterol Nutr.* 2008 Aug;47(2):136-40.



Epidemiology

Prevalence of autoantibodies or prevalence of coeliac disease?

Non-coeliac GLUTEN SENSITIVITY ARE YOU 1 IN 10?

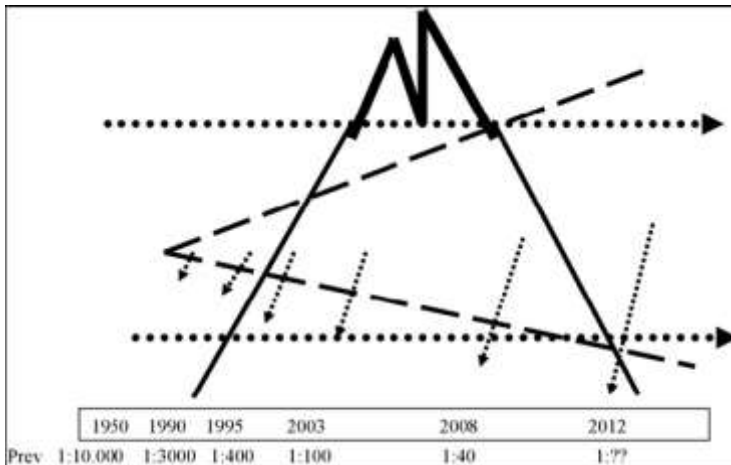
Polly J Bingley et al.
Undiagnosed coeliac disease at age seven: population based prospective birth cohort study
BMJ 2004; 328: 322 - 323



West et al. Seroprevalence, correlates, and characteristics of undetected coeliac disease in England. Gut. 2003 ;52:960-5.



The prevalence of CD is increasing directly proportional with identifying non-classic or atypical gluten-sensitive cases



Rostami K, Villanacci V. Dig Liver Dis. 2008 Jul 24.

Undetected coeliac disease in the elderly: a biopsy-proven population-based study. Viippula A, Collin P, et al Dig Liver Dis. 2008 Oct;40(10):809-13. Epub 2008 May 7.



Clinical presentation

- Historically no relationship between the degree of mucosal damages and malabsorption syndrome
- Recent studies;
 - Malabsorption in cases with microenteropathy
- Atypical predominant
- *Brar P, Green PH et al. Lack of correlation of degree of villous atrophy with severity of clinical presentation of coeliac disease. Dig Liver Dis 2007;39:26-9*



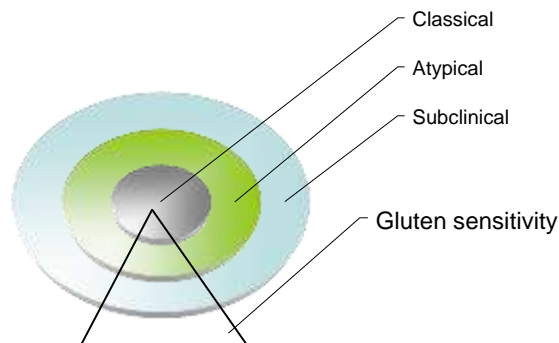
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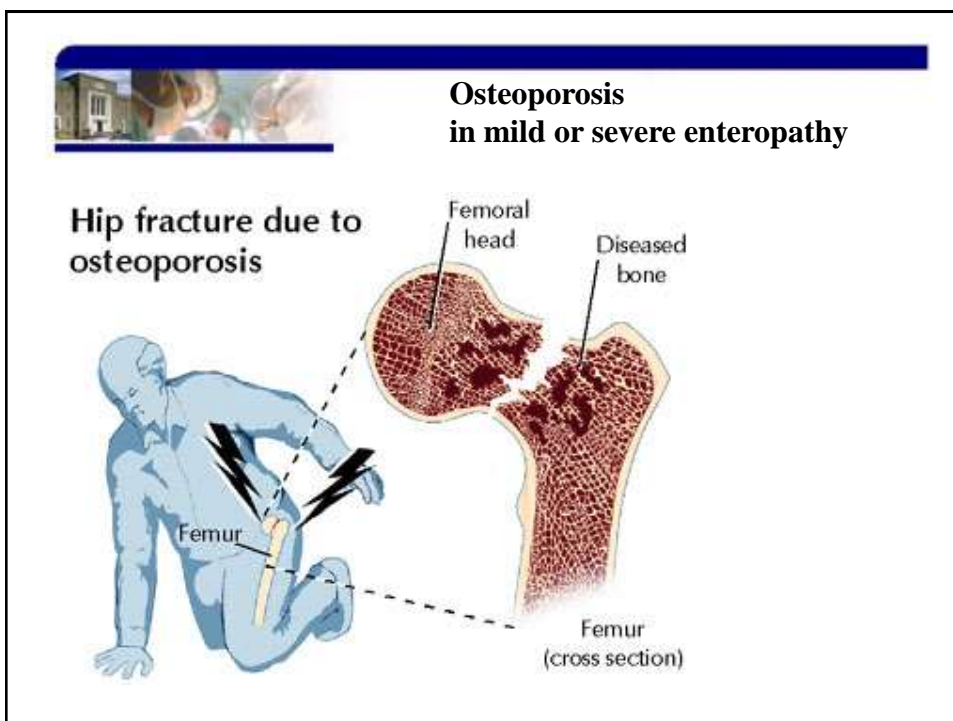
Subclinical celiac disease

Confusing terminologies:

Latent
Potential
Silent

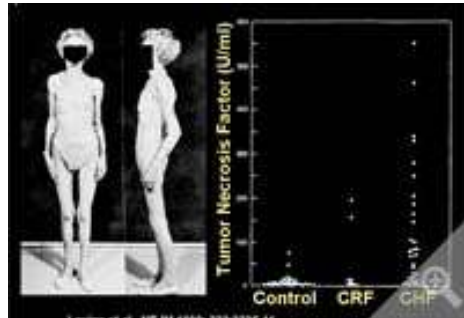


*Rostami Nejad et al, Subclinical celiac disease and gluten sensitivity
Gastroenterol Hepatol From Bed to Bench. 2011;4(3): 102-108*





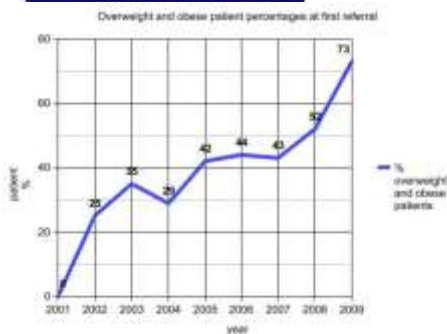
Severe enteropathy and classical CD is still rare



R M Furse and A S Mee. Atypical presentation of Coeliac Disease *BMJ* 2005; 330: 773 - 774



Increased percentage of Overweight and obese CD patients from 2001 – 2009

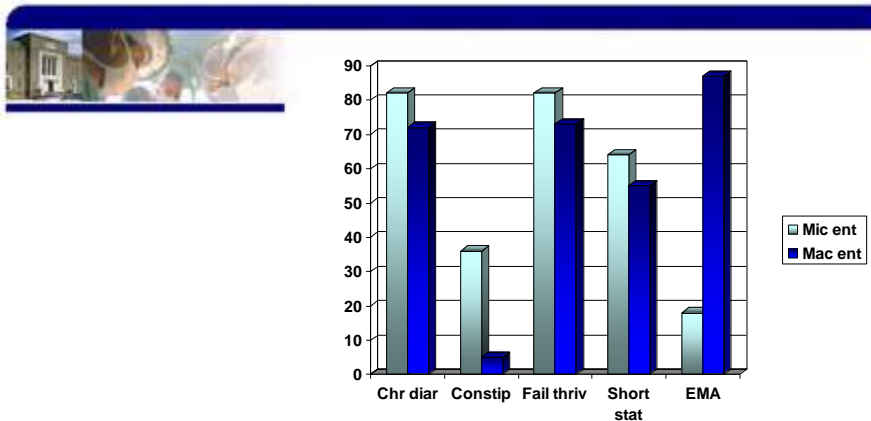


44% had a BMI of 25 or above
13% had a BMI of 30 or above

E. Tucker¹, K. Rostami, S. Prabhakaran, D. M. Aldulaimi THE INCIDENCE OF OBESITY AMONG PATIENTS WITH COELIAC DISEASE *UEGW* 2009

Neurological Disorders and microscopic enteritis

- MS
- Epilepsy with cranial calcifications
- Gluten ataxia
 - Anti-tissue transglutaminase IgA antibodies are present in the gut and brain of patients with gluten ataxia with or without an enteropathy
 - The deposition most pronounced in the
 - » cerebellum,
 - » pons, and
 - » medulla
 - *Hadjivassiliou M et al. Autoantibody targeting of brain and intestinal transglutaminase in gluten ataxia. Neurology. 2006 Feb 14;66(3):373-7.*



Clinical presentation in microscopic enteritis (Mic ent, Marsh I) compared to macroscopic enteritis (Mac ent, Marsh IIIa-c) in percentage.

Chronic diarrhea,
constipation,
failure to thrive,
short stature

Shahraki T, Rostami K et al, UEGW 2009



Histopathology of coeliac disease

History

Original Classification Marsh MN, 1990-92

Modified Marsh Classification 1998-9, Rostami et al

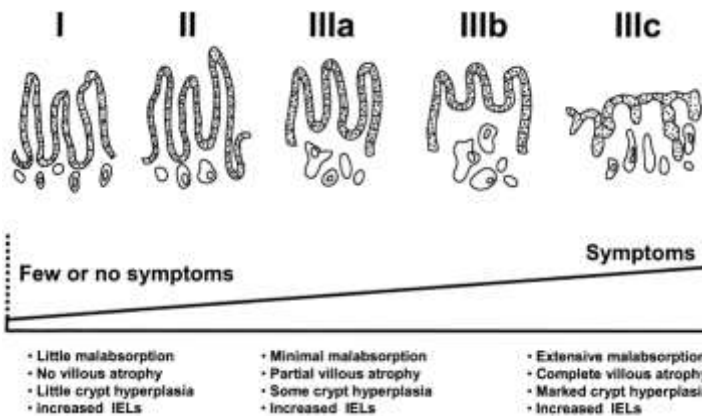
Modified Marsh Classification 1999, Oberhuber et al

Corraza-Villanacci

Rostami -Villanacci



Marsh MN.
Grains of truth: evolutionary changes in small intestinal mucosa in response to environmental antigen challenge.
Gut. 1990 Jan;31(1):111-4





Oberhuber

- Oberhuber G, Granditsch G, Vogelsang H. The histopathology of coeliac disease: time for a standardized report scheme for pathologists. *Eur J Gastroenterol Hepatol*. 1999 Oct;11(10):1185-94.
- 40 IEL/100EC



Microscopic Enteritis

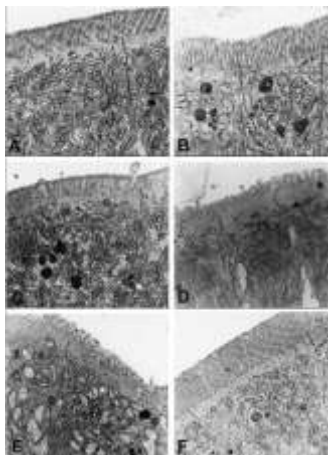
- **Definition:**
 - Sub-microscopic (Marsh 0)
 - Microscopic presentation (Marsh I-II)
- **Characteristics:**
 - Sub-microscopic
 - Alteration of enterocytes,
 - Microvilli atrophy
 - Increased γ/δ TCR



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History



(A) alterations of the enterocyte, significant reduction of the microvillous height

(B) normal enterocyte and microvillous ultrastructure at TEM.

(C) brush border in a group A patient;

(D) brush border in a group B patient;

(E) severe enterocytic lesion in a patient with Pierre–Robin syndrome;

(F) normal brush border from a control patient.

7 +Ve EMA, 4/7 abnormal TEM of intestinal absorptive surface. 10.000

Sbarbati et al. Gluten sensitivity and 'normal' histology: Is the intestinal mucosa really normal? Digestive and Liver Disease 35 (2003) 768–773




Inspiration



*Rostami K, Villanacci V.
Microscopic Enteritis
Dig Liver Dis. 2009
Apr;41(4):245-52*

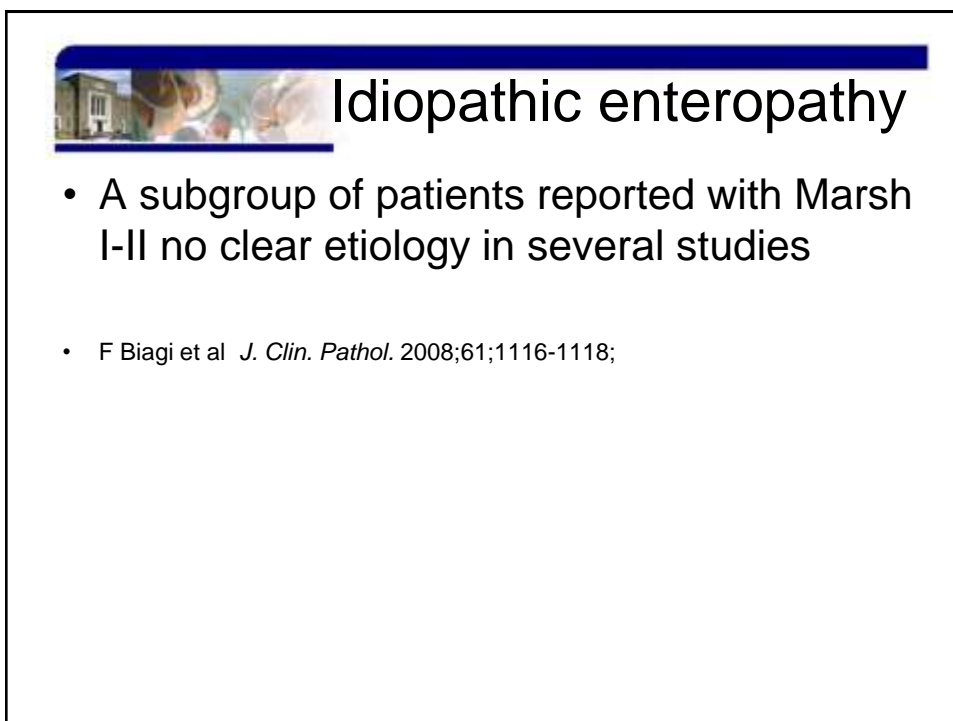
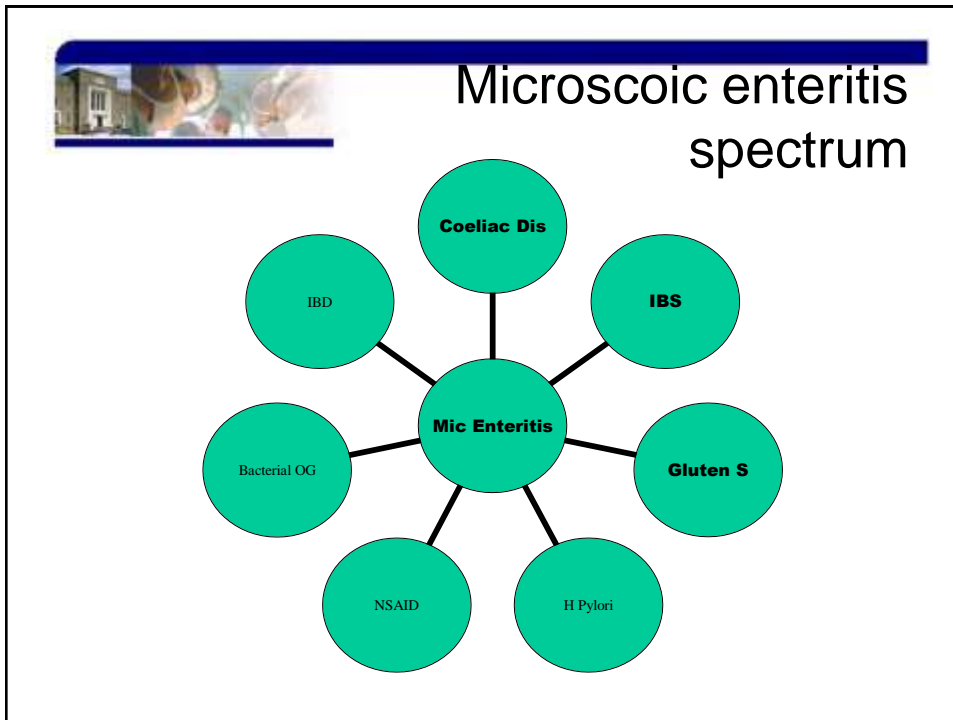
Società Italiana Endoscopia Digestiva



Microscopic Enteritis Differential diagnosis

Non-specific

- Coeliac disease with milder enteropathy Marsh 0-II
- Non-coeliac Gluten sensitivity
- Gluten allergy
- IBS
- Idiopathic enteropathy
- NSAIDs related
- Parasitic Bacterial/viral enteritis
 - H Pylori
 - Bacterial overgrowth
- Inflammatory bowel disease



Idiopathic enteropathy

- A subgroup of patients reported with Marsh I-II no clear etiology in several studies
- F Biagi et al *J. Clin. Pathol.* 2008;61;1116-1118;

A small inset image in the top left corner shows a person's face and hands.



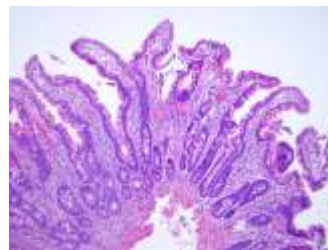
Severe enteropathy

- Severe enteropathy like Marsh IIIb-c
 - Mainly Coeliac disease
 - Tropical sprue
 - Enteropathy Associated With Olmesartan



Alberto Rubio-Tapia, Joseph A. Murray et al.
Severe Spruelike Enteropathy Associated With Olmesartan

FIGURE. Photomicrographs showing reversible spruelike enteropathy associated with olmesartan. (hematoxylin-eosin, original magnification 100). A, Duodenal biopsy specimen obtained while the patient was taking olmesartan shows total villous atrophy and intraepithelial lymphocytosis. B, Biopsy specimen obtained 6 months after withdrawal of olmesartan and initiation of a gluten-containing diet shows recovery of villi on duodenal mucosa.





Malabsorption in ME!!!

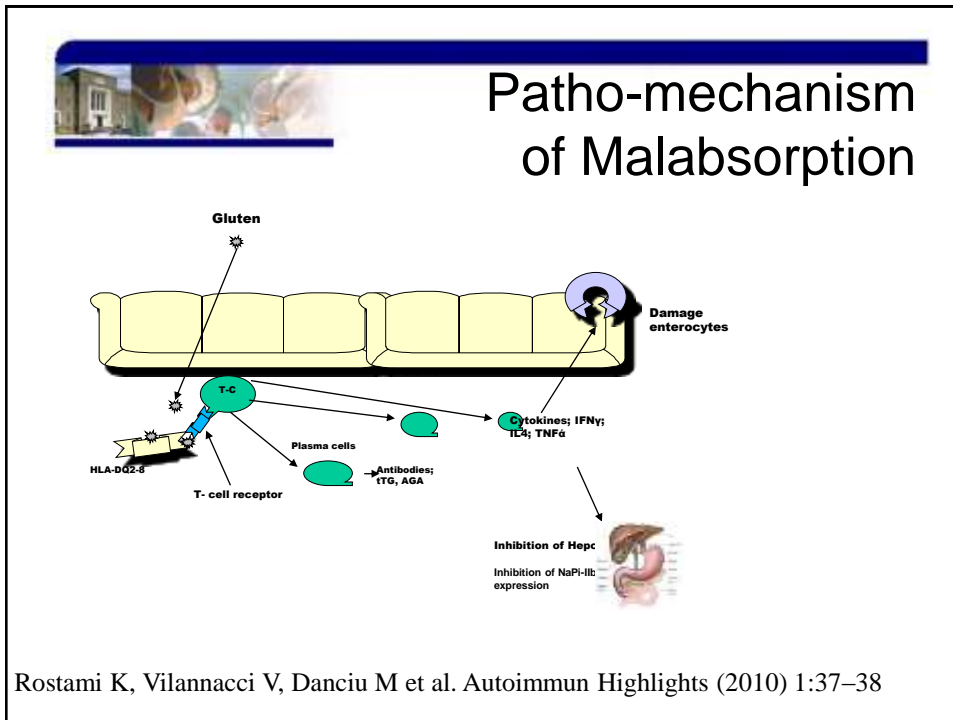
- Question;
 - What is the patho-mechanism of Malabsorption in ME?



Anaemia

- **4-40% Microcytic anemia CD**
 - Caused by inflammation
- **Megaloblastic/Macrocytic anemia –folate is absorbed primarily in the proximal third of the small intestine (location of folate hydrolases)**
- **Vitamin B-12 deficiency occurs**
- **Cytokines involvement**

Most common non-GI manifestation in adults and elderly



Malabsorption caused by inflammation

- Intestinal phosphate absorption mediated by NaPi-IIb protein is reduced in colitis.
- This inhibition is mediated by the proinflammatory cytokine TNF- α

Chen H et al *Tumor necrosis factor-alpha impairs intestinal phosphate absorption in colitis. Am J Physiol Gastrointest Liver Physiol.* 2009 Apr;296(4):G775-81.



Diagnostic pitfalls

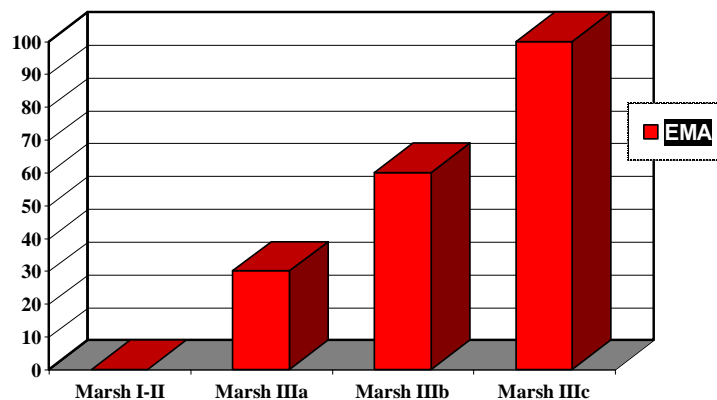
- Clinical
- Serological
- Endoscopy
- Histological




Green PH, Rostami K, Marsh MN. Diagnosis of coeliac disease. Best Pract Res Clin Gastroenterol. 2005;19:389-400



Serology sensitivity

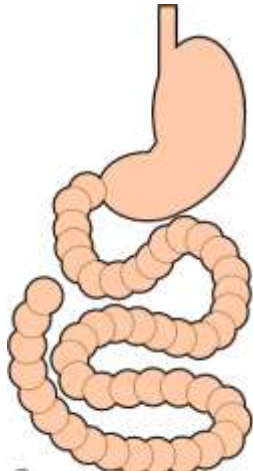


Rostami, Mulder et al. American J Gastroenterol 1999;94:888-894



Endoscopy

- Looking normal in most cases
- Abnormal in severe mucosal changes
- Segmental biopsy would be required Including Bulb



© Tomonori Yano, JGIM Medical School

*Kate E Evans, David S Sanders et al.
 A Prospective Study of Duodenal Bulb Biopsy in Newly Diagnosed and Established Adult Celiac Disease The American Journal of Gastroenterology 2011;106, 1837-1742*


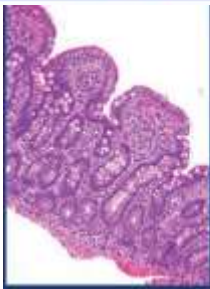




Fig. 1. Most celiac patients present with atypical form with milder enteropathy. Serology and endoscopy both have a poor sensitivity in patients with milder enteropathy (Marsh 0-IIIa).



100% sensitivity for serology and endoscopy in Total villous atrophy Marsh IIIc



Poor sensitivity for serology (<40%) and endoscopy in Partial villous atrophy Marsh IIIa

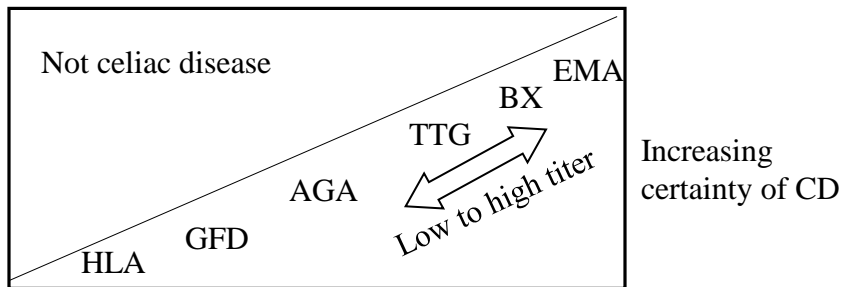


Ishaq S, Mahmood R, Vilannacci V, Bassotti G and Rostami K. REV ESP ENFERM DIG 2012; 104 (6): 334



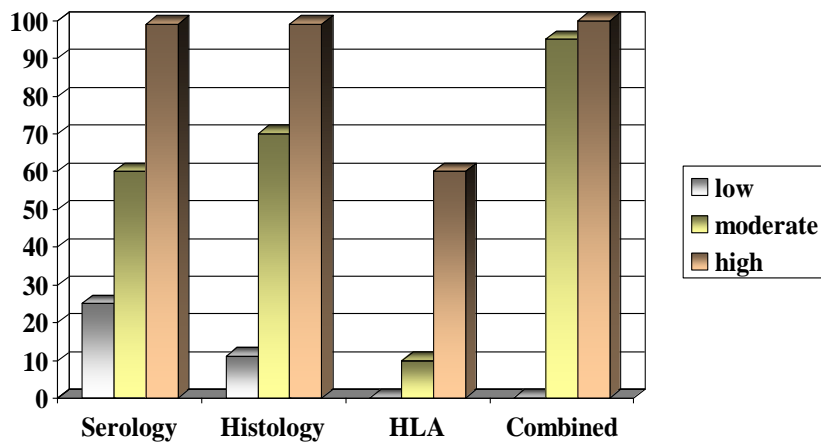
Relative discriminative ability of tests for celiac disease

- BSG_OSLO



Diagnostic accuracy measures at different thresholds:

A) Serology defined as low: negative/low positive, moderate(3x above normal value), high >10x above normal value B) Histology defined as low: (Marsh 0-II), moderate (Marsh IIIa), high (Marsh IIb-c), C) HLA defined as low (negative) moderate (positive DQ8) and high (positive DQ2) D) Combination:





Summary

- Presentation with milder enteropathy like Microscopic Enteritis is very common and non-specific
- Often this might be the presentation of coeliac disease
- Pathologists don't ignore milder enteropathy ;)



Any Question?