Use of POCT in celiac disease

Jernej Dolinšek, MD, PhD

Department of Pediatrics

Gastroenterology unit

University Medical Centre Maribor, Slovenia

Dubrovnik, 19. 10. 2013

Overview

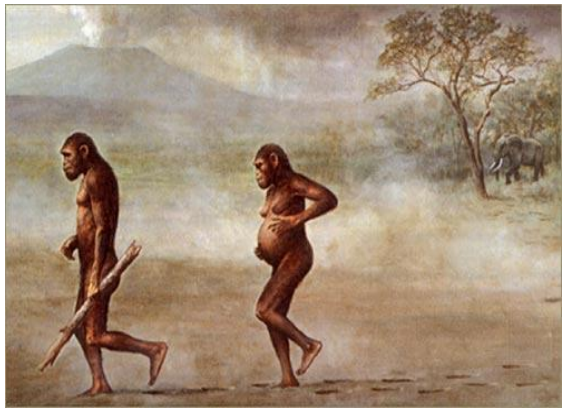
- definition
- background
- diagnostic algorythms
- diagnostic tools
- use of POCT
- conclusions

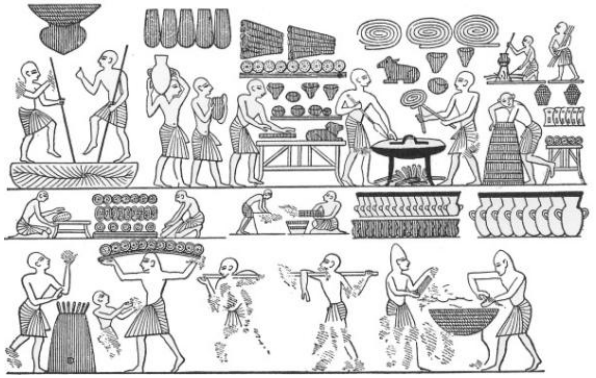
Celiac disease – definition

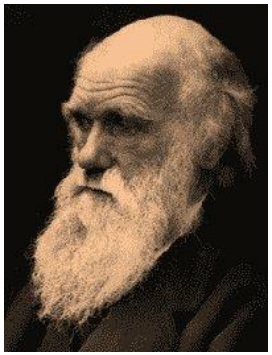
Celiac disease is an **autoimmune** systemic disease (disorder) triggered by the ingestion of **gluten** in **genetically** predisposed subjects.

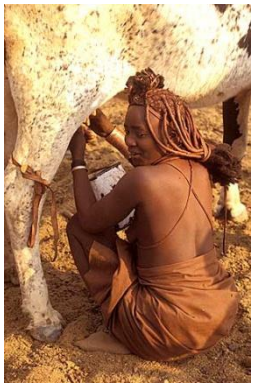
The disease is characterized by the production of disease **specific antibodies,** which disappear after introduction of a gluten-free diet (GFD).

All patients must comply with **life-long** strict GFD.





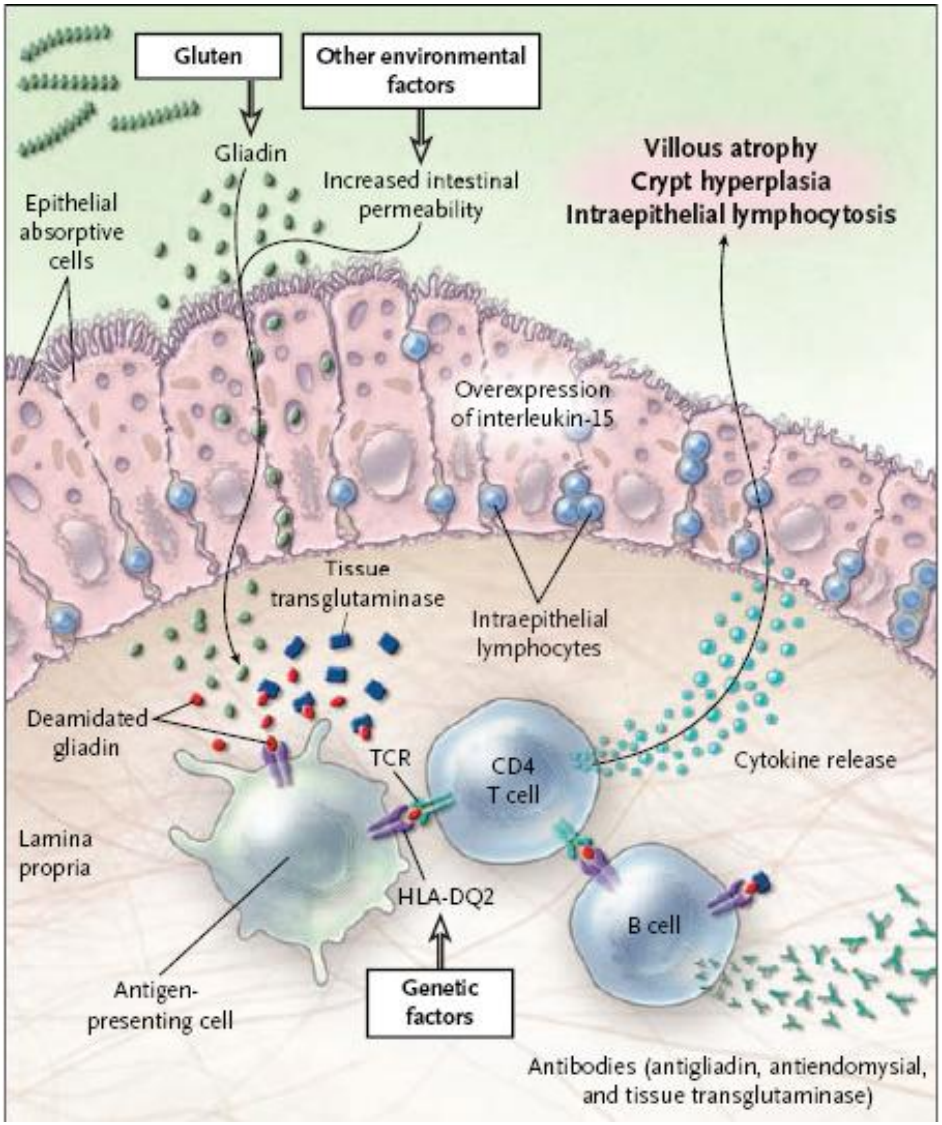




"nature does nothing uselessly "

Aristotle

Celiac disease – immunology



Green P and Cellier C. N Engl J Med 2007.

Celiac disease – epidemiology

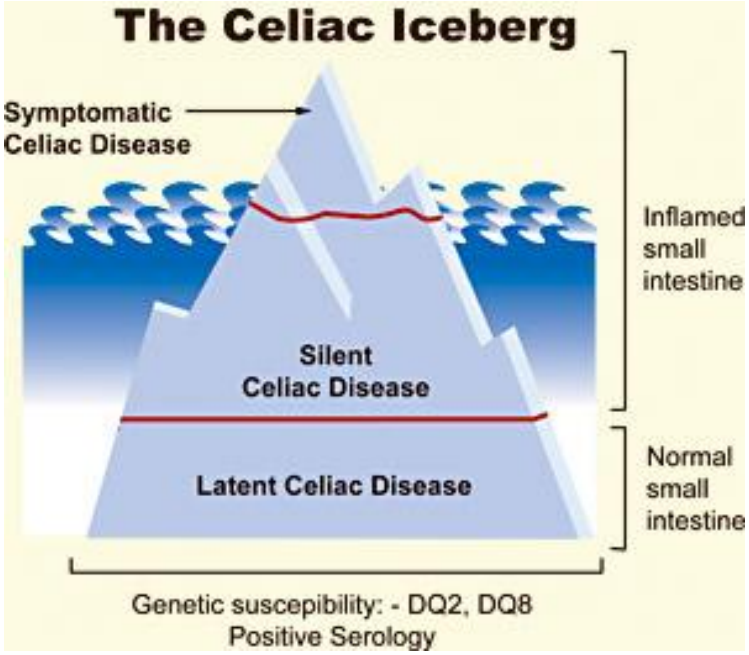
Incidence of symptomatic disease in NE Slovenia in 2009 1/452

undiagnosed vs. diagnosed CD (5-13):1

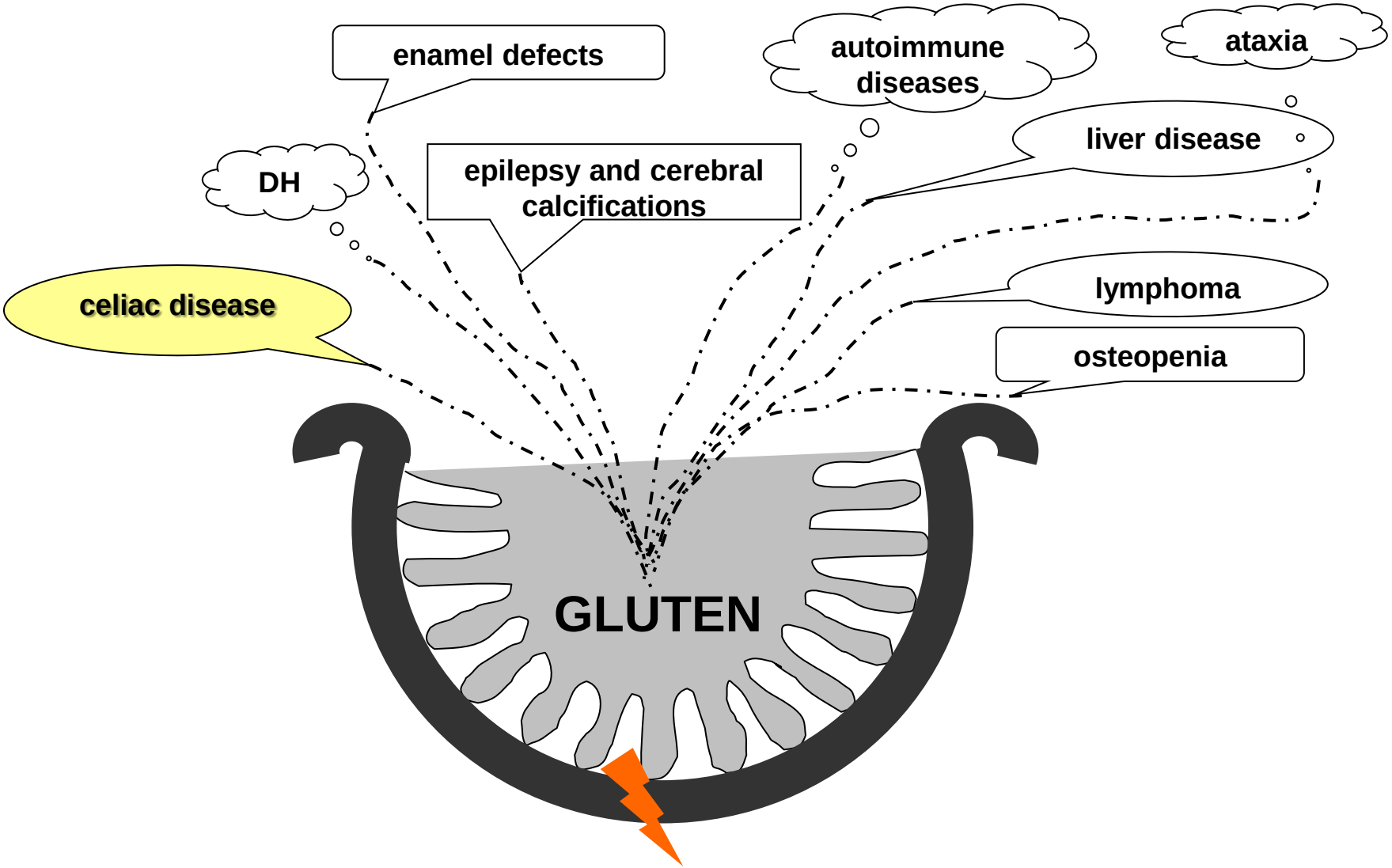
Prevalence of coeliac disease increases by age

	Clinical prevalence	Total (clin+screen) prevalence
Children	0.03%	1.5 %
Adults	0.5%	2.0%
Elderly	0.9%	2.5%

Mäki et al NEJM 2003;348:2517, Collin et al J Clin Gastroenterol 2007;41:152
Lohi et al APT 2007;26:1217, Vilppula et al Dig Liver Dis 2008;40:809



Clinical presentation of “celiac disease”

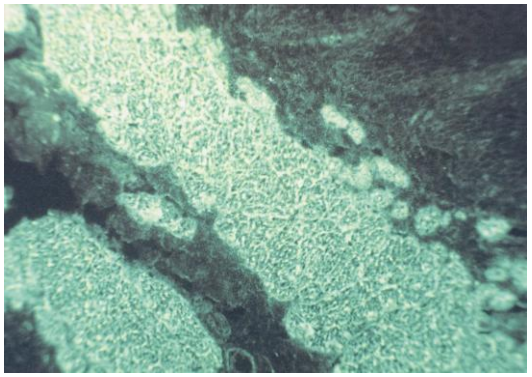


Celiac disease – diagnostic approach

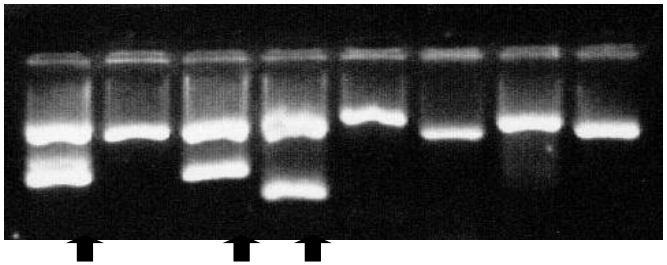
- **History and physical exam**
  - Symptomatic CD
    - Gastrointestinal disease
      - Prolonged diarrhea
      - Abdominal distension
      - Failure to thrive, weight loss
    - Extra-gastrointestinal disease
  - Asymptomatic CD

Celiac disease – diagnostic approach

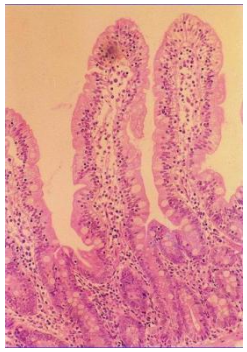
- **Serology**

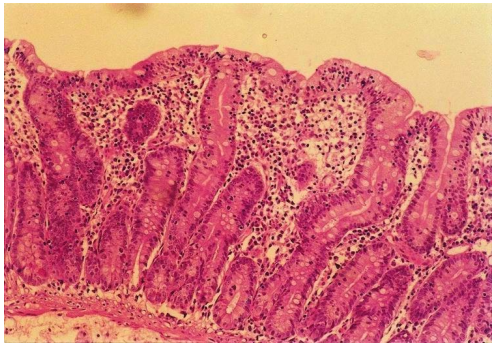


- **Genetics**

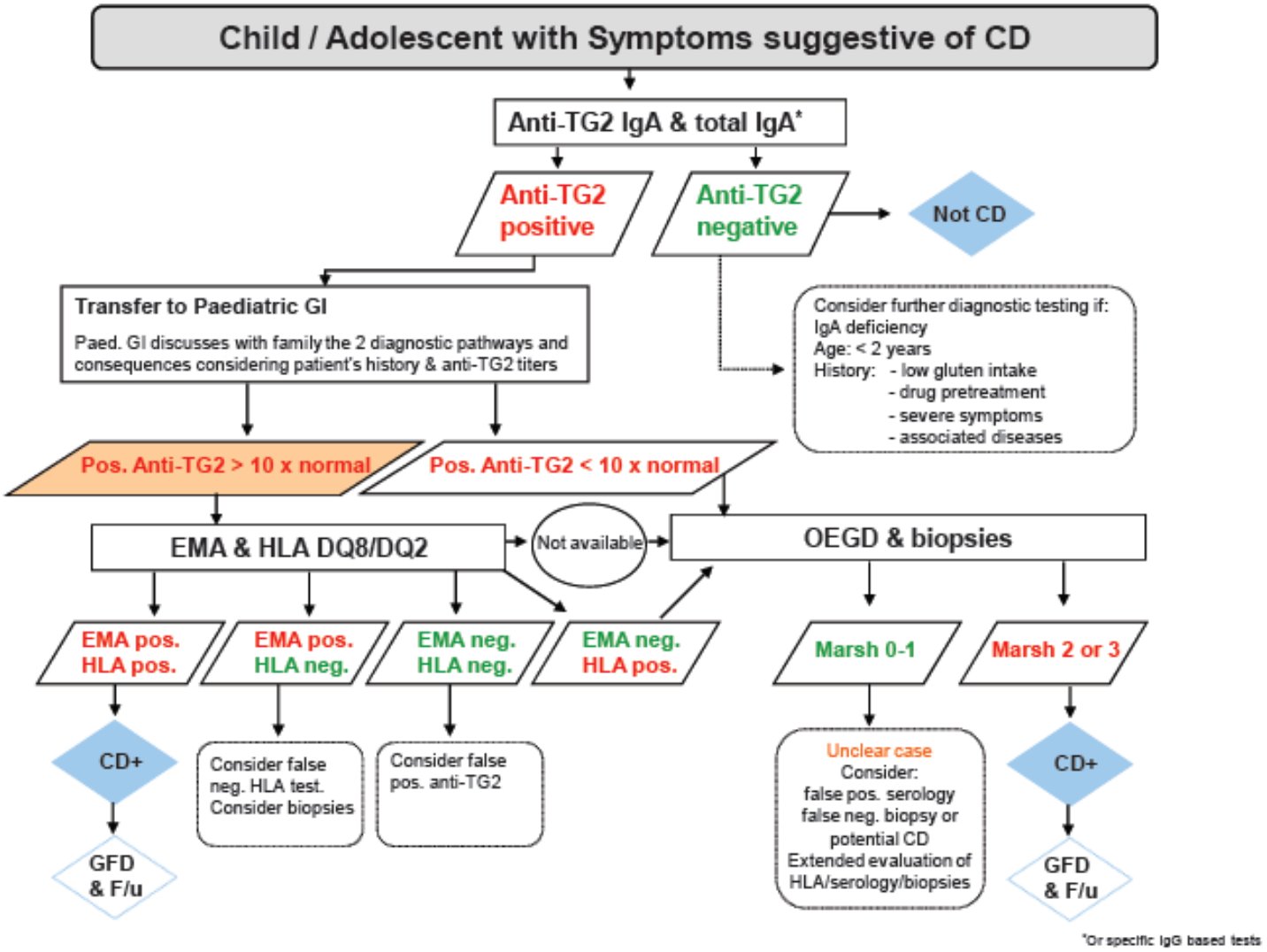


- **Intestinal biopsy**





Celiac disease – new diagnostic criteria



Celiac disease – reality

Diagnostic delays

duration of symptoms before dg

- adults 11 years
- children1.3 years
- large regional differences

Celiac disease – diagnostic tools

Celiac disease – diagnostic tools

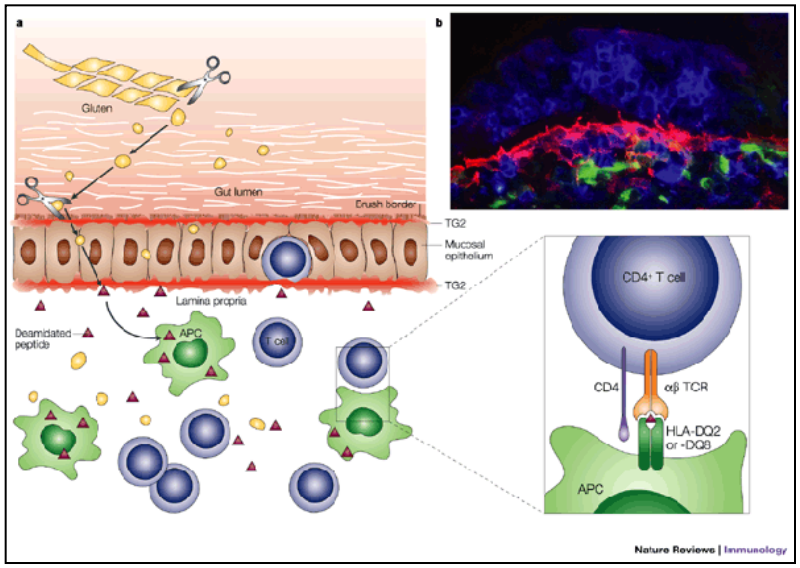
- disease specific tools
  - serological tests
  - genetic tests
  - biopsy/histology

- nonspecific tools
  - clinical picture
  - tests of malabsorption
  - ...

Celiac disease – serology

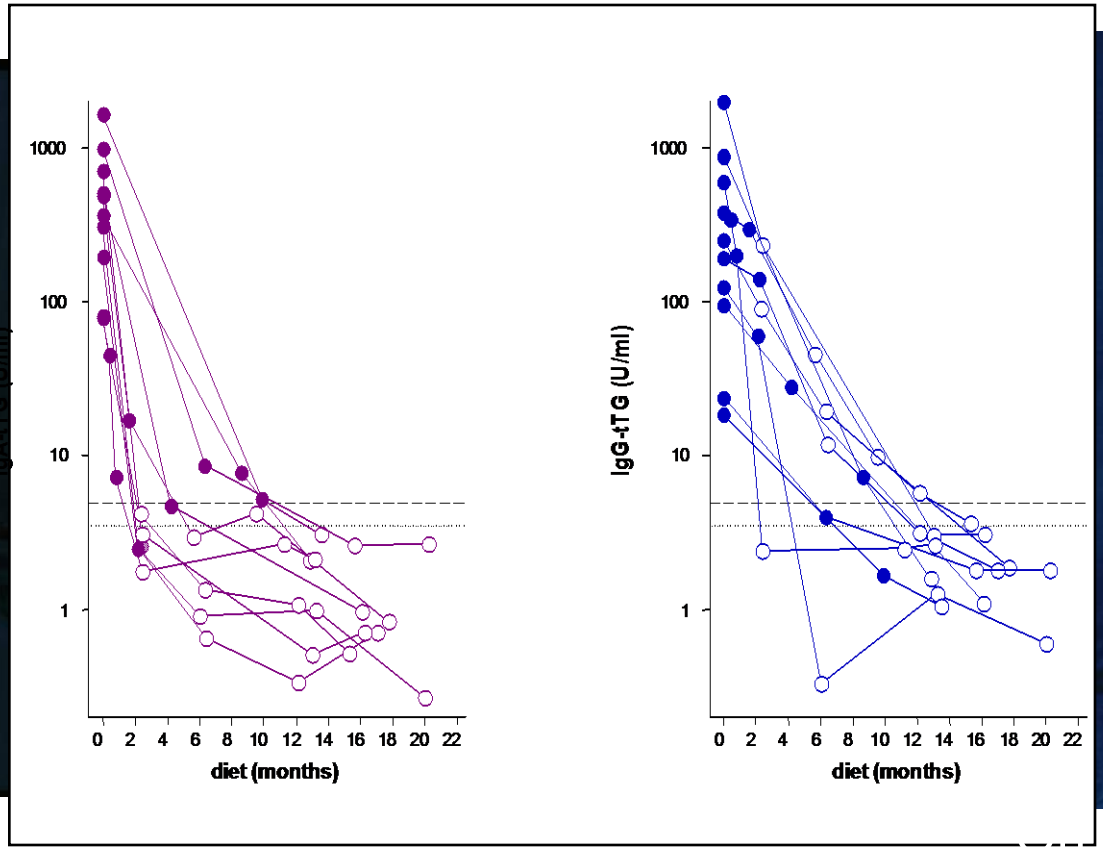
Celiac disease – serology

- Serological markers
  - AGA IgA and IgG
  - markers of autoimmunity
    - EMA IgA (IgG)
    - t-TG IgA (IgG)
    - DGP IgA (IgG)
    - other Ab (ARA, JAB, antiglutenin)
  - importance of total IgA determination
    - IgA deficiency – IgG Ab determination

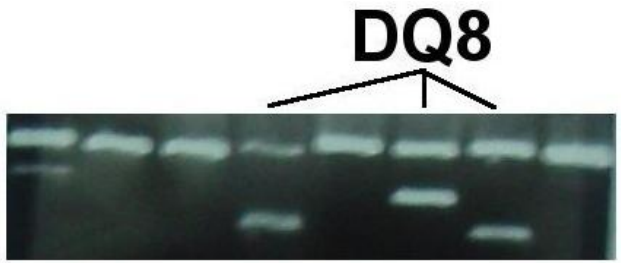


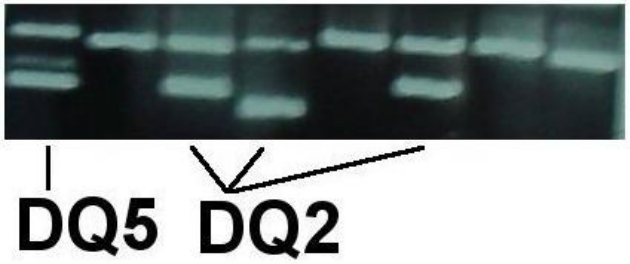
Celiac disease – serology

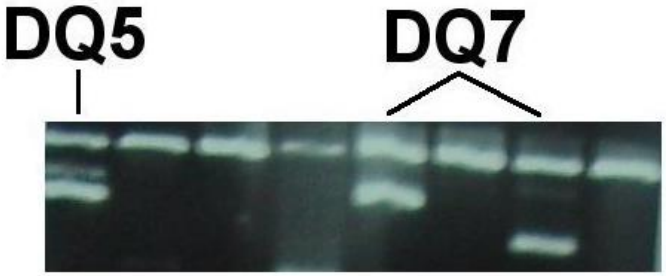
- tissue transglutaminase Ab



Celiac disease – genetic testing







Celiac disease – histology

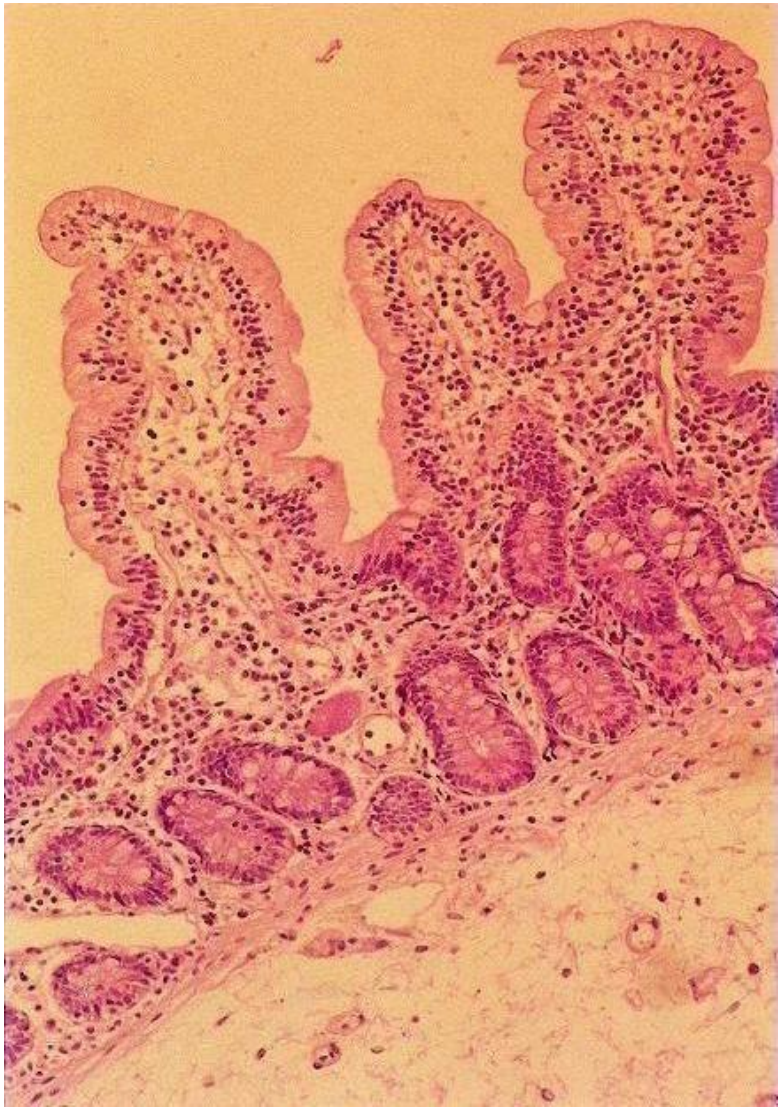
- histological changes – intestinal biopsy
  - aspiration capsule
  - endoscopic biopsy

Celiac disease – histology

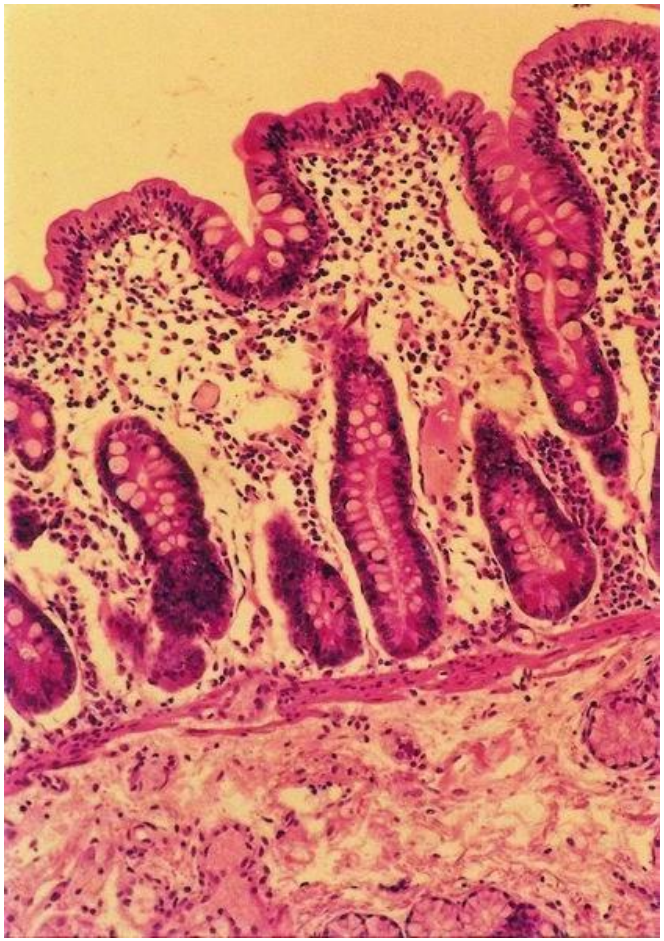
- Histological changes
  - mucosal atrophy
    - Marsh classification
      - type 0: preinfiltrative phase
      - type 1: infiltrative phase
      - type 2: infiltrative-hyperplastic phase
      - type 3 (a, b, c): destructive phase
      - type 4: atrophic-hypoplastc phase
    - villous atrophy, crypt hyperplasia, IEL count

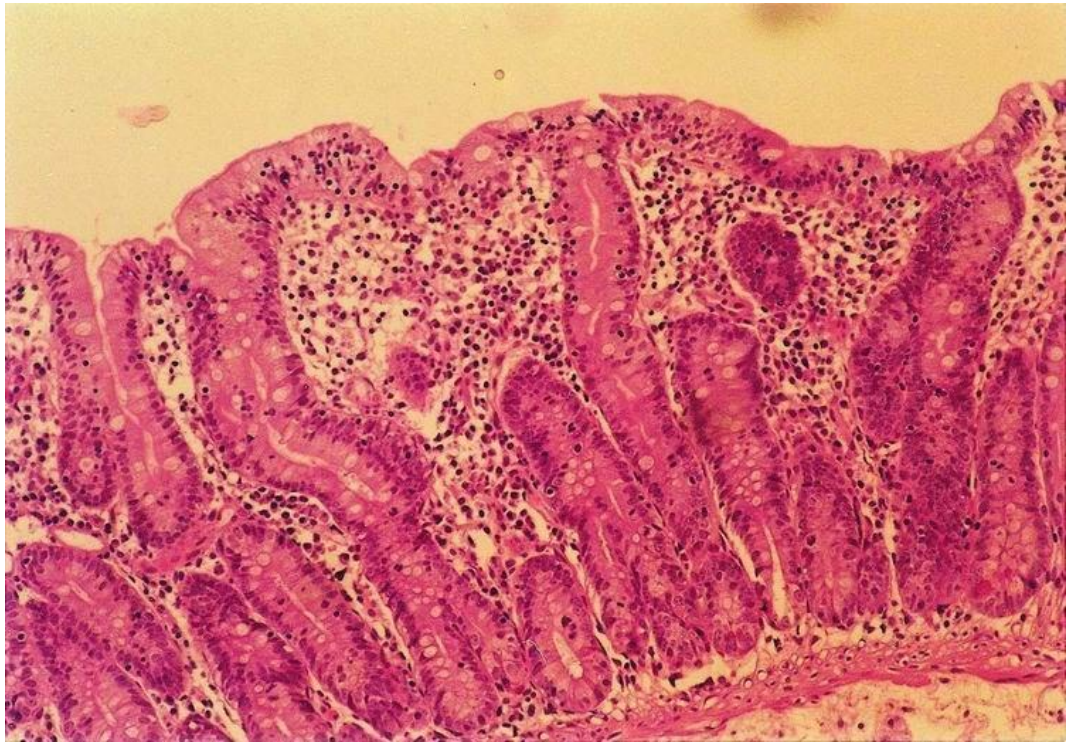
Marsh MN. Gastroenterology 1992.
Oberhuber G et al. Eur J Gastroenterol Hepatol 1999.

Celiac disease – histology



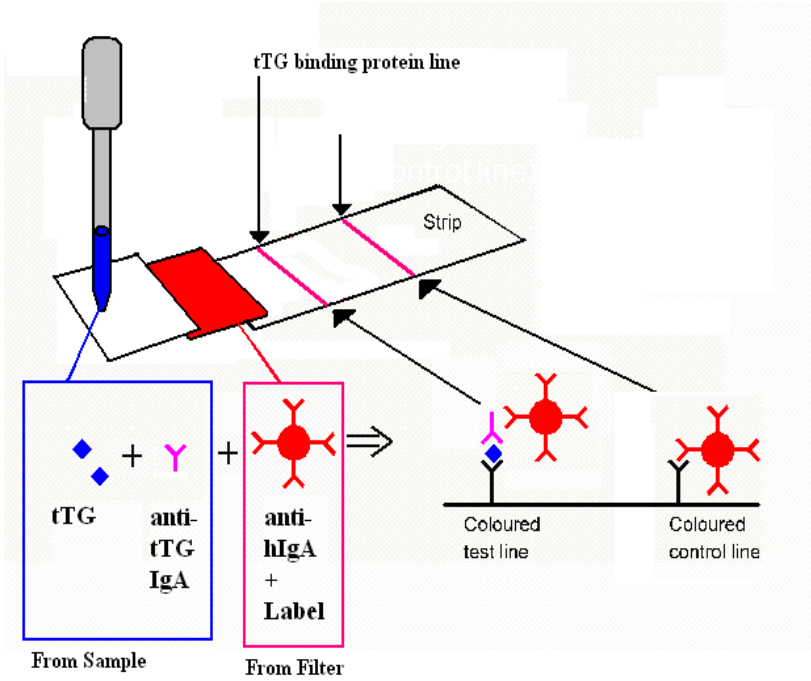
Celiac disease – histology

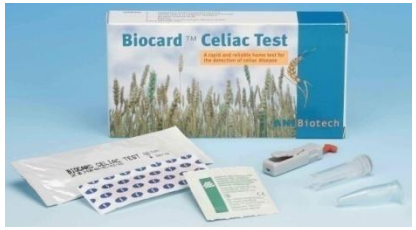


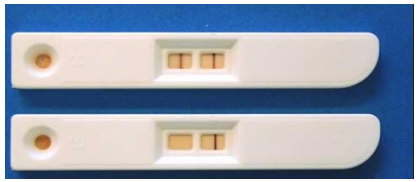


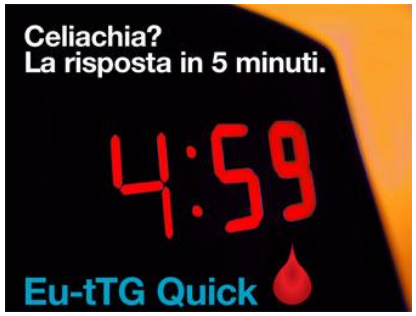
Celiac disease – serology - POCT

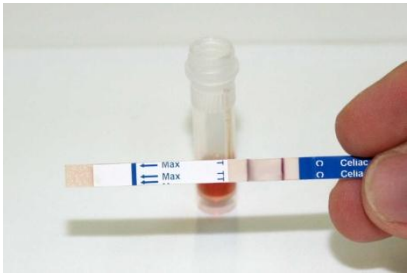
- PoC tests
  - rapid finger prick test
  - immunochromatography
    - antigen: self t-TG
  - many commercial kits
    - inexpensive
  - intermediate sensitivity and specificity











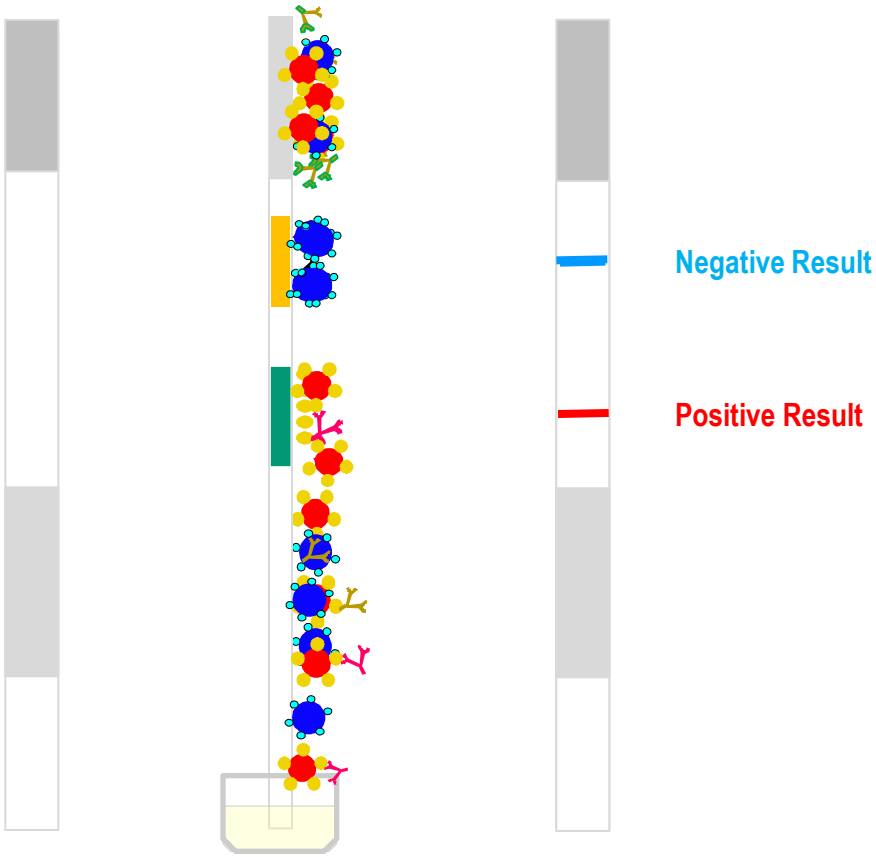
Korponay-Szabo I et al. BMJ 2007; Dolinsek J et al. ICDS 2011.

Celiac disease – POCT market

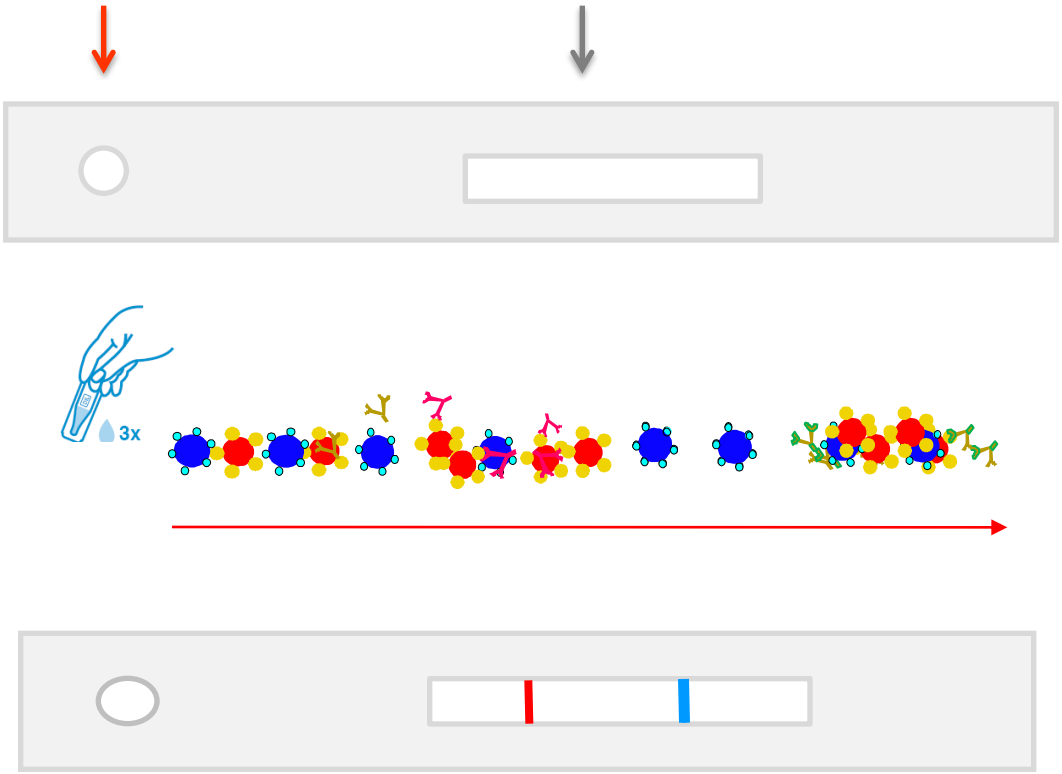
Celiac disease – POCT market

Company	Brand	Sample	Parameters
Ani Biotech	BioCard	Whole blood	Anti-tTG (IgA), Total IgA
Augurix	Sintomax	Whole blood	Anti-DGP (IgA &IgG), Total IgA
Eurospital	XeliacTest	Whole blood	Anti-tTG (IgA & IgG)
	Eu-tTG Screen CD Screen	Serum	Anti-tTG (IgA & IgG) Anti-tTG / Gliad IgA
Operon	Simple CD1WB Stick CD1	Whole blood Serum	Anti-tTG (IgA & IgG)
	Simple CD2WB Stick CD2	Whole blood Serum	Anti-tTG / Gliad IgA

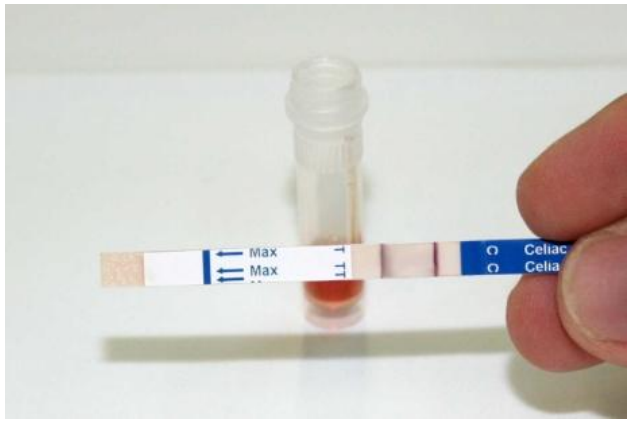
Celiac disease – stick assay - serum



Celiac disease – cassete – whole blood



Celiac disease – POCT interpretation



Celiac disease – POCT in IgA deficiency

- A negative result with an IgA-based assay may occur due to total serum IgA deficiency and lead to a doubtful interpretation of the result.
- Two options to offset total serum IgA deficiency:
  - Simultaneous detection of both class IgA and IgG antibodies
  - Detection of total serum IgA
    - In same cases, total serum IgA deficiency is indicated by the absence of both Test and Control lines.
    - The same may occur when a test is not performed properly.

Celiac disease – POCT performance

		Sens.	Spec.	PPV	NPV
Diagnosis	5 min	82.9%	93.6%	78.0%	97.7%
	10 min	96.9%	89.5%	54.3%	99.1%

Dolinsek et al. 2012

Anti-tTG		**CD**	**Healthy**	
		Pos	Neg	
Whole blood	Pos	117	7	124
	Neg	4	100	104
	Total	121	107	228
	Sens.	96.7%	PPV	94.4%
	Spec.	93.5%	NPV	96.2%

Raivio et al. 2006

Anti-tTG		**CD**	**Healthy**	
		Pos	Neg	
Whole blood	Pos	110	7	117
	Neg	4	208	212
	Total	114	215	329
	Sens.	96.5%	PPV	94.0%
	Spec.	96.7%	NPV	98.1%

Nemec et al. 2006

Celiac disease – POCT performance in GFD

- Use of POC tests for GFD follow-up is still under evaluation.
  - Some studies confirm their use for monitoring the compliance with the diet.
  - On the other hand, a qualitative response does not provide an indication of the antibody level, which is important to check a diet adherence.

Future perspectives

- New microsystems
  - finger prick blood, 30 minutes
  - simultaneous
    - multiple Ab test
      - t-TG, DGP (IgA, IgG)
    - total IgA determination
    - HLA-DQ2/DQ8 status


1. End user: General practitioner, nurse...


2. Single drop of blood.


6. User-friendly Feedback.


3. Biomedical interface.


5. Communication with hospital information systems.


4. Disposable fluidic cartridge.

SEVENTH FRAMEWORK PROGRAMME

CD medics

Coeliac Disease Management Monitoring and Diagnosis using Biosensors and an Integrated Chip System

http://www.etseq.urv.es/cdmedics/index.php

UKC MARIBOR Univerzitetni klinični center Maribor

Conclusions

- Celiac disease is important health problem
- diagnostic tools are reliable, but invasive
- POCT tests available
  - high NPV, satisfactory PPV
  - possibilty of use in developing regions
  - limitations
    - qualitative
    - not diagnostic (not included in recommendations)
    - possibilty of false negative results in IgA deficiency
    - GFD monitoring
- new promising tools appearing

Conclusions