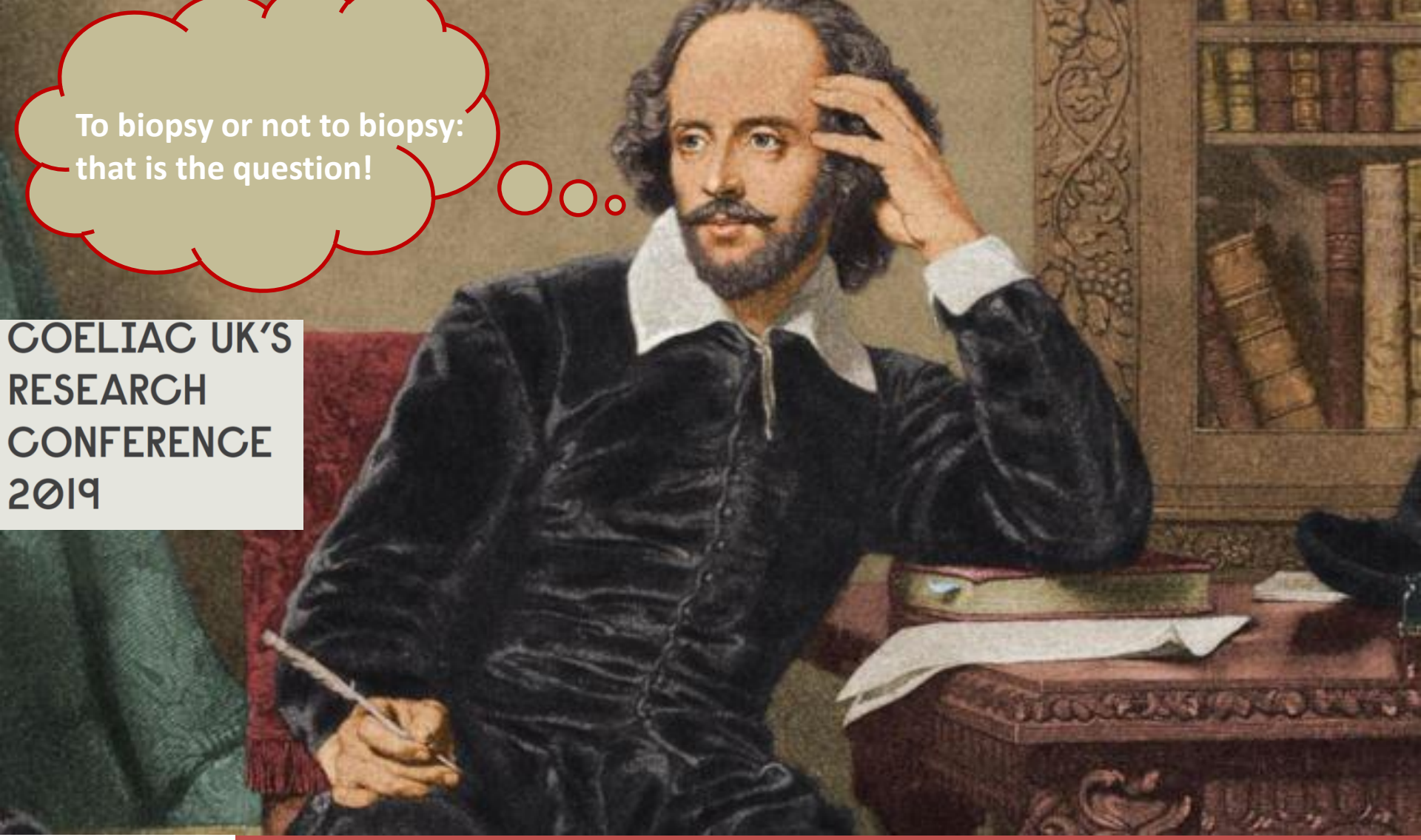


COELIAC UK'S RESEARCH CONFERENCE 2019

Carolina Ciacci

Celiac Centre at University of Salerno

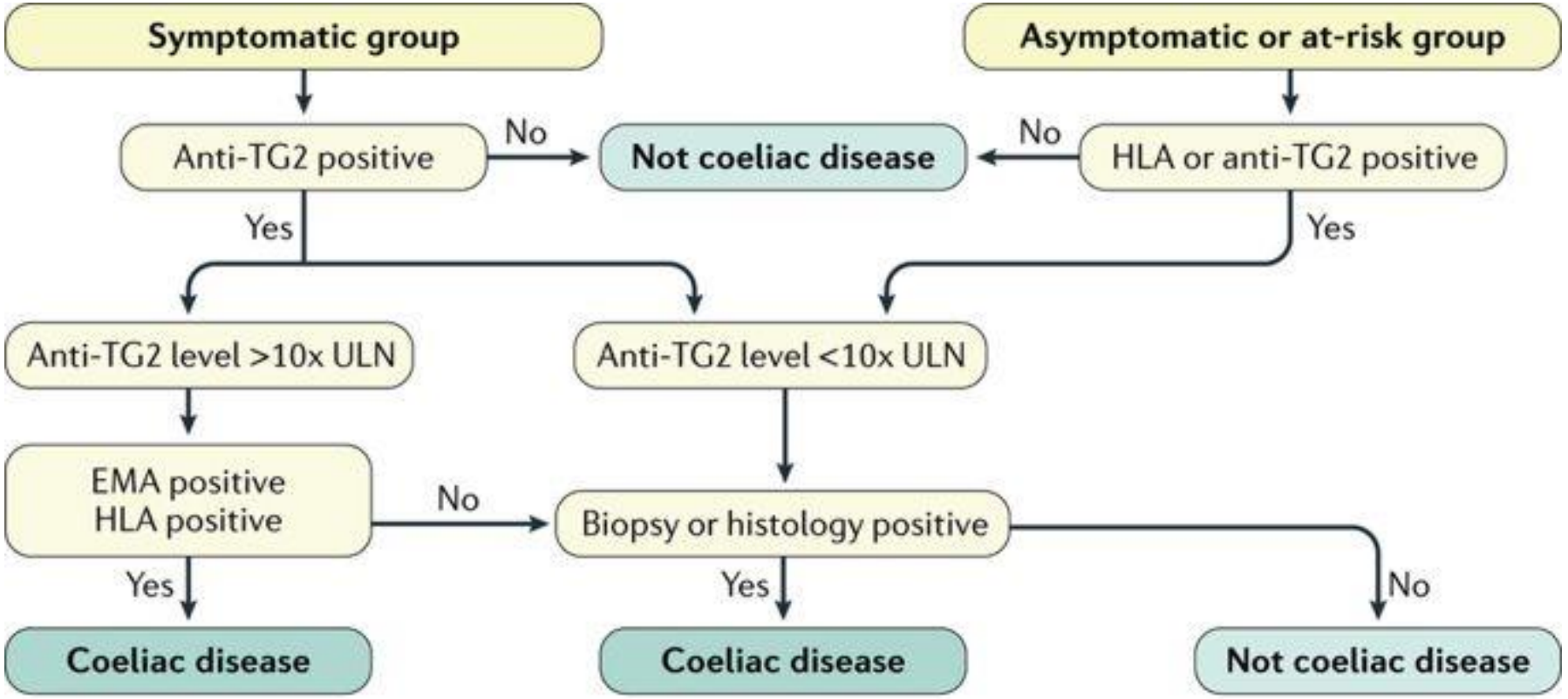
To biopsy or not to biopsy: that is the question!

And if yes, when?

- ❖ At diagnosis
- ❖ At follow-up

Biopsy-avoiding diagnostic pathway for coeliac disease

European Society for the Study of Paediatric Gastroenterology, Hepatology and Nutrition criteria



Reilly et al. 2018 **Nature Reviews** | Gastroenterology & Hepatology

Adults at diagnosis

- **Guidelines:** Adults always undergo biopsy

- **It that always necessary?**

A subgroup of adults with CeD might not need a biopsy, previous evidences:

- Tortora et Al, APT 2014
- Fuchs V et Al, l APT Feb 2019
- Marks L et Al , UEGW 2018

Main issues *pro* biopsy

- **Endoscopy is a safe** procedure
- We may miss **another diagnosis**
- **Precision** in diagnosis - **some diagnoses with low titre/contrasting abs anti-TG2 level could represent a false positive**
- **Potentials** would go right away on GFD
- We may miss **complications**: Avoiding biopsy is claimed to delay the diagnosis of RCD:

30% persistent symptoms following GFD , then endoscopy to rule out complications, overlapping diseases, and RCD

BIOPSY AVOIDANCE STRATEGY IN ADULT CeD

Marks L.J. Lau M., Kurien M., Cross S., Egner W., Hadjivassiliou M., Rees M., Rostami K., Sargur R., Swallow K., Wild G., Sanders D.S.

Presented at UEGW 2018

- ESPGHAN criteria in adults, a prospective analysis
- 443 pts 2008-2016 GI symptoms 60-70% TTG IgA 10x
- TTG +EMA predicting VA in 98,6%

IgA tTG level 10x the ULN had a PPV of 100% for VA

Risk of complications in coeliac patients depends on age at diagnosis and type of clinical presentation Biagi et al DLD 2018

- 1999 -- 2015, **2225 adult CeD patients**
- 17 of them developed a complication and 29 died

>60 years at diagnosis the risk increased of 18x vs 18–40 ys and 9x than vs 40–60 years

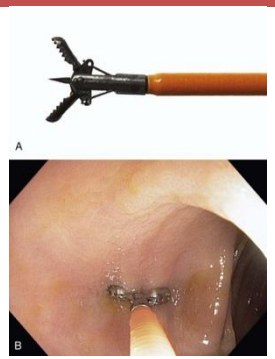
Classical presentation increases the risk of complications 7x compared to non-classical presentation

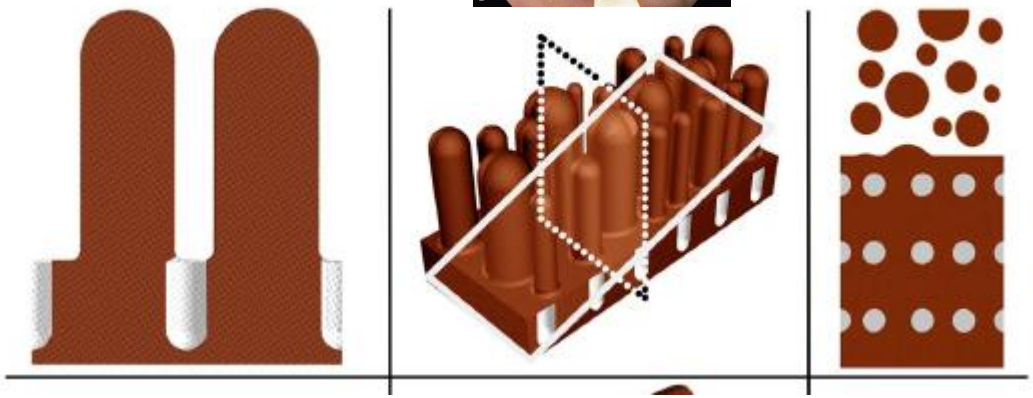
In **asymptomatic** patients the risk of complication is virtually absent

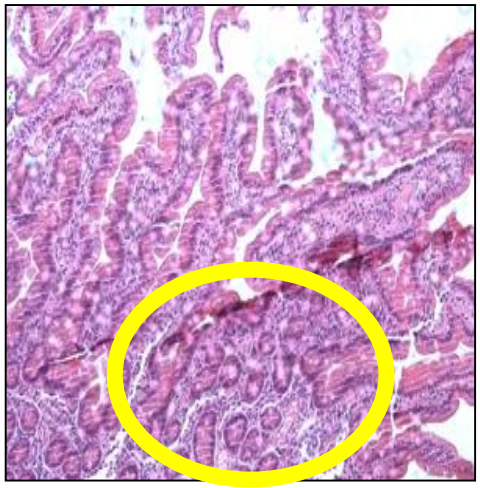
Main issues *contra* biopsy

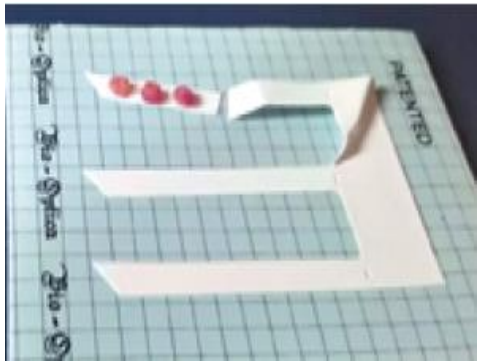
- **Serology has a high ppv (no other test has such a ppv!)**
- Patients with positive TTG may **refuse the** endoscopy
- Endoscopy and histology are expensive and invasive
- **In the vast majority of cases, histology confirms the diagnosis of CeD suggested by serology**
- Sometimes (or often) the biopsies are few, non-oriented, and pathologists will not appropriately describe the mucosa

Orientation is the key of success









Computerized 3D-model demonstrates the effects of correct and incorrect planes of cutting on readout results.

Taavela et al.
Plos One 2013

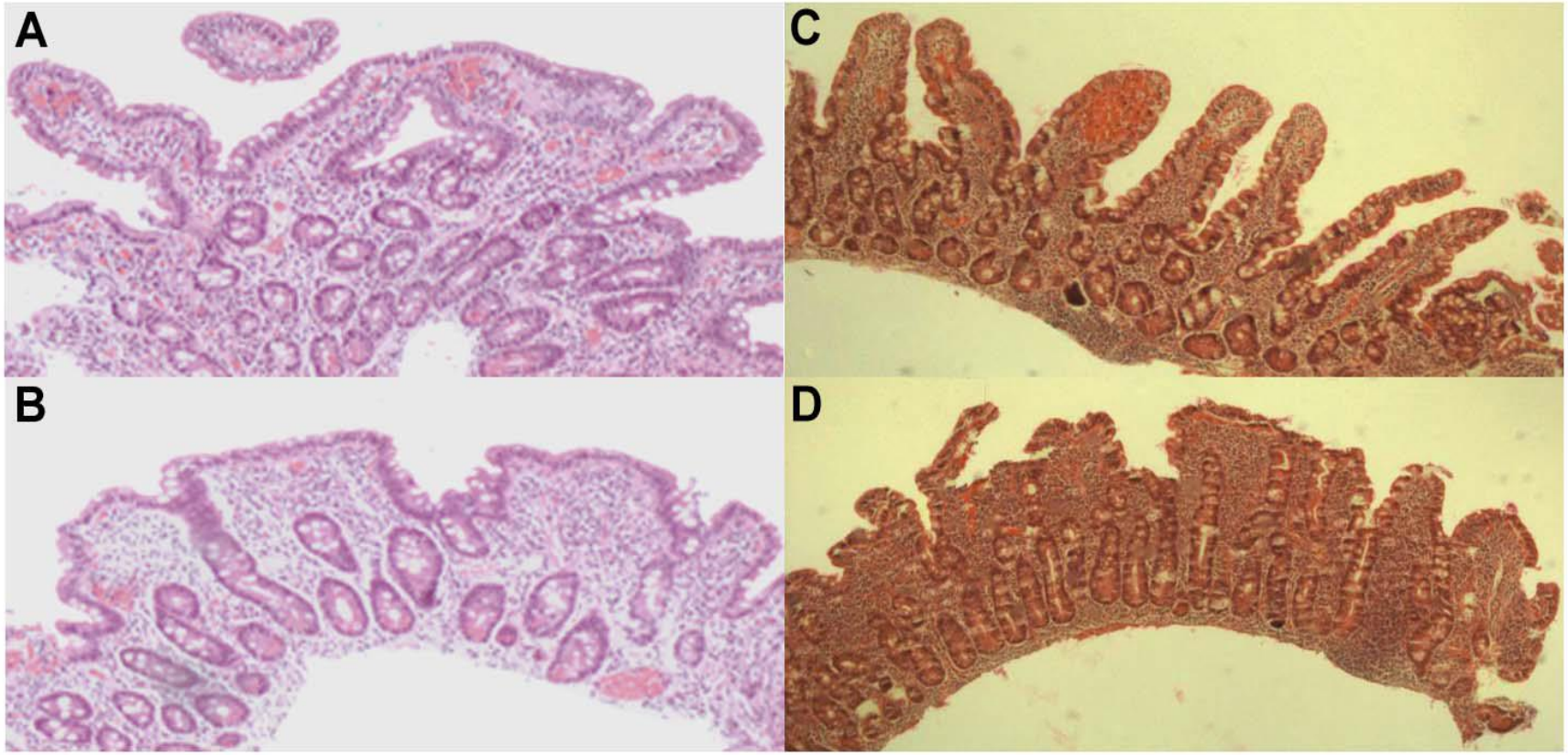
Specimens: 4 + 2 in bulb

Tilting the blocks…

5 independent pathologists

Normal mucosa

Marsh 0-1



villous atrophy -crypt hyperplasia

Marsh 3b-3c

From Taavela PONE 2013

Tricks of the trade: How to avoid histological Pitfalls in celiac disease

Alberto Ravelli[a,*], Vincenzo Villanacci[b]

Path res and practice 2011

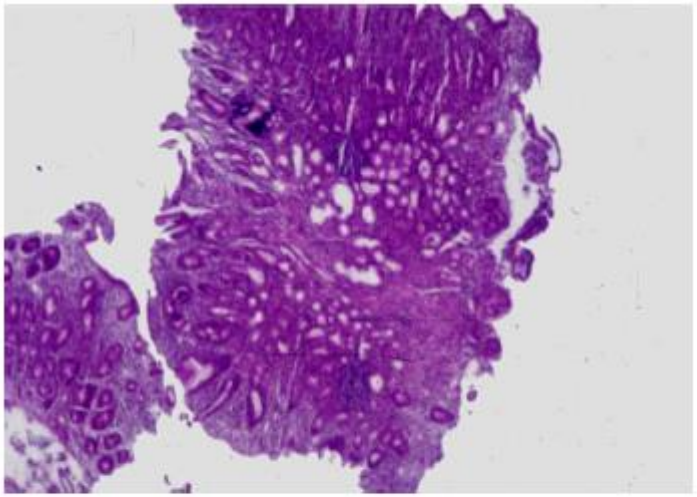


Fig. 4. Duodenal biopsy not correctly oriented, where it is impossible to define the degree of histological lesion (H&E, 20×).

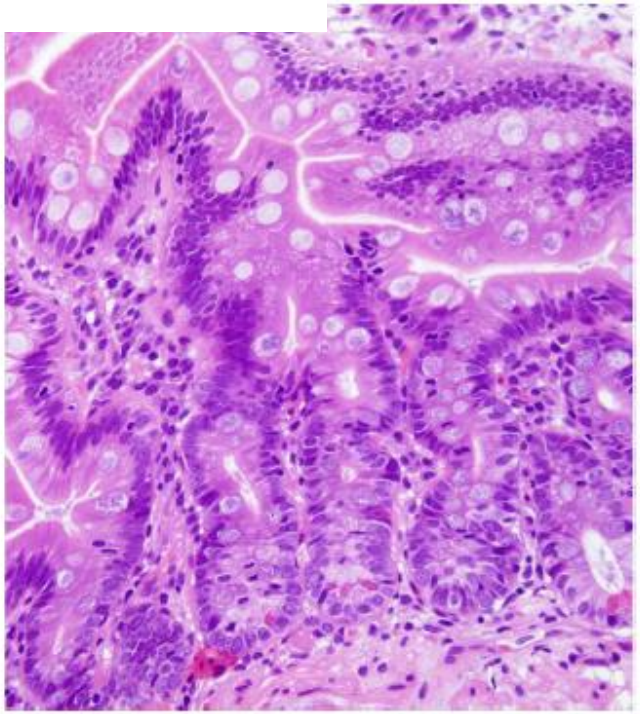


Fig. 5. A biopsy that has been cut tangentially due to bad orientation makes it extremely difficult if not impossible to correctly define the villous:crypt ratio (H&E,

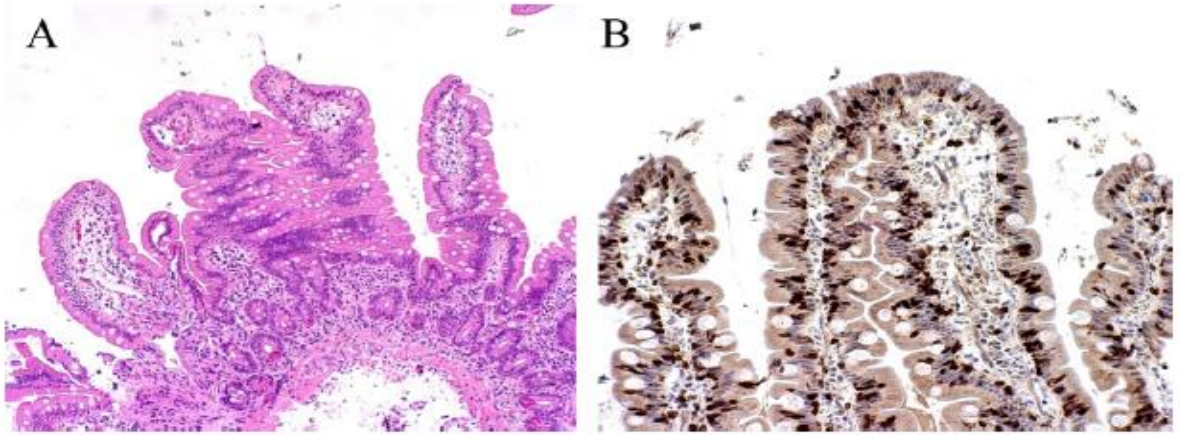
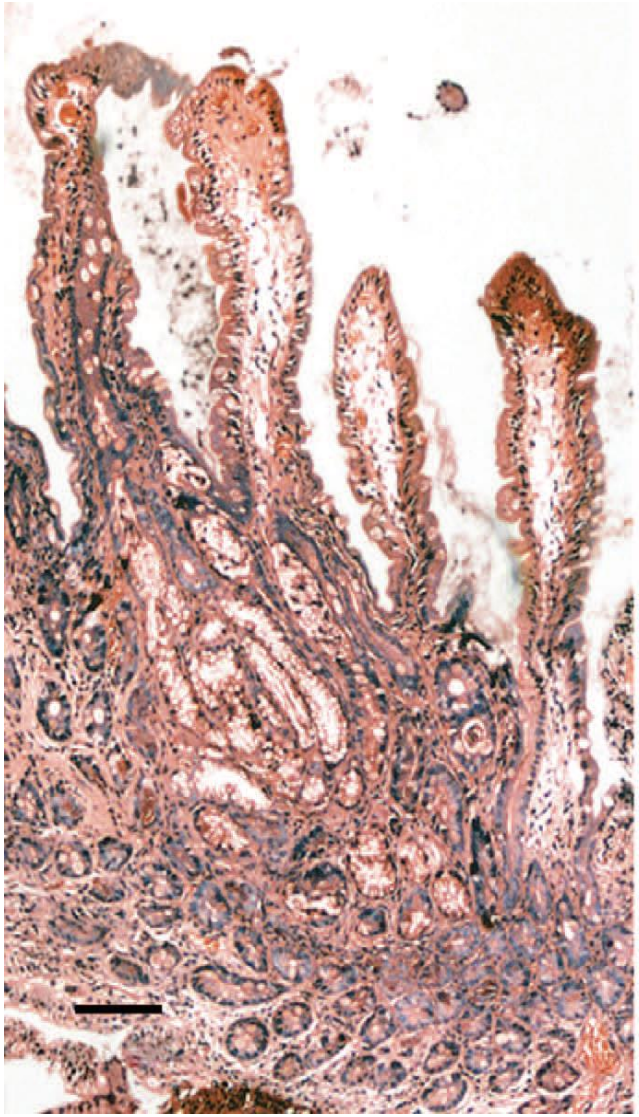
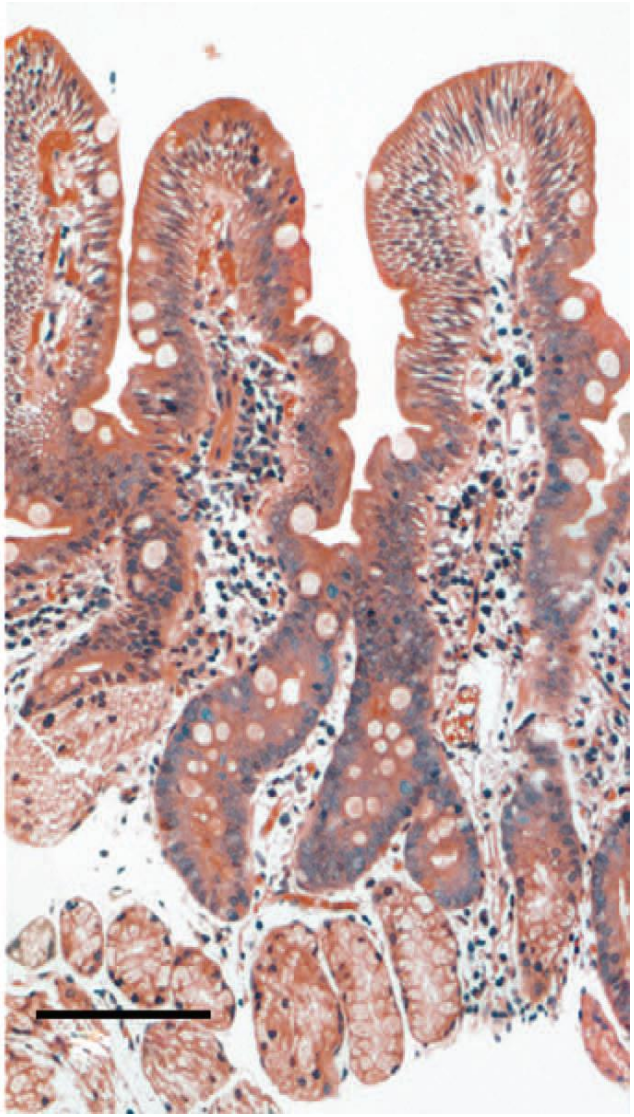


Fig. 6. (A) The crushing of villi may resemble partial villous atrophy (H&E, 10×), whereas (B) partial fusion of villi may prevent a correct count of intraepithelial lymphocytes despite CD3 immunostaining (CD3 immunostain, 20×).



Non-oriented



reoriented

Bulb biopsies

Taavela et al.
Am J Gastro 2015

To biopsy or not to biopsy: we need experts' opinion and a few studies…

Gastroenterology and Hepatology from Bed to Bench
Journal | Aim & Scope | Author Guideline | Submit a Manuscript

Gastroenterol Hepatol Bed Bench. 2018 Summer; 11(3): 209–215.

PMCID: PMC6040038
PMID: 30013744

The serological diagnosis of coeliac disease - a step forward

Geoffrey Holmes[1] and Carolina Ciacci[2]

Future considerations

Go to:

In recent years there has been a movement away from morphological to serological criteria, to establish the diagnosis of CD and as serological tests are refined and more information accumulates, this is likely to accelerate. A multicentre study using a standardised approach is now required to further explore the serological cut-off that predicts CD in a large number of patients. Such an investigation will also allow the role of endomysial antibodies in a serological diagnosis strategy to be determined. Serological tests for CD are among some of the best performing tests in medicine and gastroenterologists are fortunate to have them available. These have transformed knowledge regarding the prevalence of CD and have aided the diagnosis immeasurably but still have to be used intelligently.

Gastroenterology and Hepatology from Bed to Bench
Journal | Aim & Scope | Author Guideline | Submit a Manuscript

Gastroenterol Hepatol Bed Bench. 2018 Summer; 11(3): 175–177.

PMCID: PMC6040029
PMID: 30013738

The serological diagnosis of adult coeliac disease – a cautious step forward?

Lauren JS Marks, Matthew Kurien, and David S Sanders

To advance our practice and cement a **no biopsy policy** into adult practice **we require a multi-centre prospective study** which will provide: 1) high quality data on the percentage of adult patients that do not require a biopsy; 2) The PPV and validity of numerous serological titres; 3) The role of HLA in the pathway for adults with suspected coeliac disease. Finally and crucially we require a clear message to all clinicians that positive serology equates to immediate referral to a Gastroenterology Consultant and not a presumptive diagnosis of CD and trial of a GFD in primary care!

AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease Gastroenterology 2018
Husby S, Murray JA, Katzka DA

- **Best Practice Advice 2a**:
- strongly positive TG2-IgA + EMA in a second blood sample: the ppv for CeD is virtually 100%.

- In adults, esophagogastroduodenoscopy (EGD) and duodenal biopsies may then be performed for purposes of differential diagnosis

The Bi.A.CeD study

- prospective, multicenter, international study, aimed **to evaluate the possibility to avoid duodenal biopsy** in a subgroup of patients with suspected CeD

- Collect blood sample and histology of consecutive CeD at diagnosis
- Send the sera to central labs
- Send the histology to central Pathologist
- Follow-up

19 Centres

ITALY Univ. Salerno, Univ Padua, Univ. Palermo, Univ. Verona, Univ. Pavia, Hospital Santorso. (6 different centers)

7. Hospital de Gastroenterología Dr. C. Bonorino Udaondo Buenos Aires , Argentina

8. Univ. Tampere Finland

9. Dpt of Gastroenterology and Human Nutrition All India institute of Medical Science Ansari Nagar, New Delhi

10. Shahid Beheshti University of Medical Sciences, Tehran-Iran

11. Gastroenterologie si Hepatologie Fundeni – Centru de Excelenţă acreditat de Ministerul Educaţiei si Cercetării Bucharest, Romania

12. Carol Davila University of Medicine and Pharmacy · Dpt of Internal Medicine and Gastroenterology, Romania

13 *University of Oslo · Institute of Clinical Medicine*

14. VUmc Amsterdam , Holland

15. *Sheffield University UK*

16. Servicio de Medicina Interna del Hospital de León, Spain

17. Madrid 1

18. Madrid 2

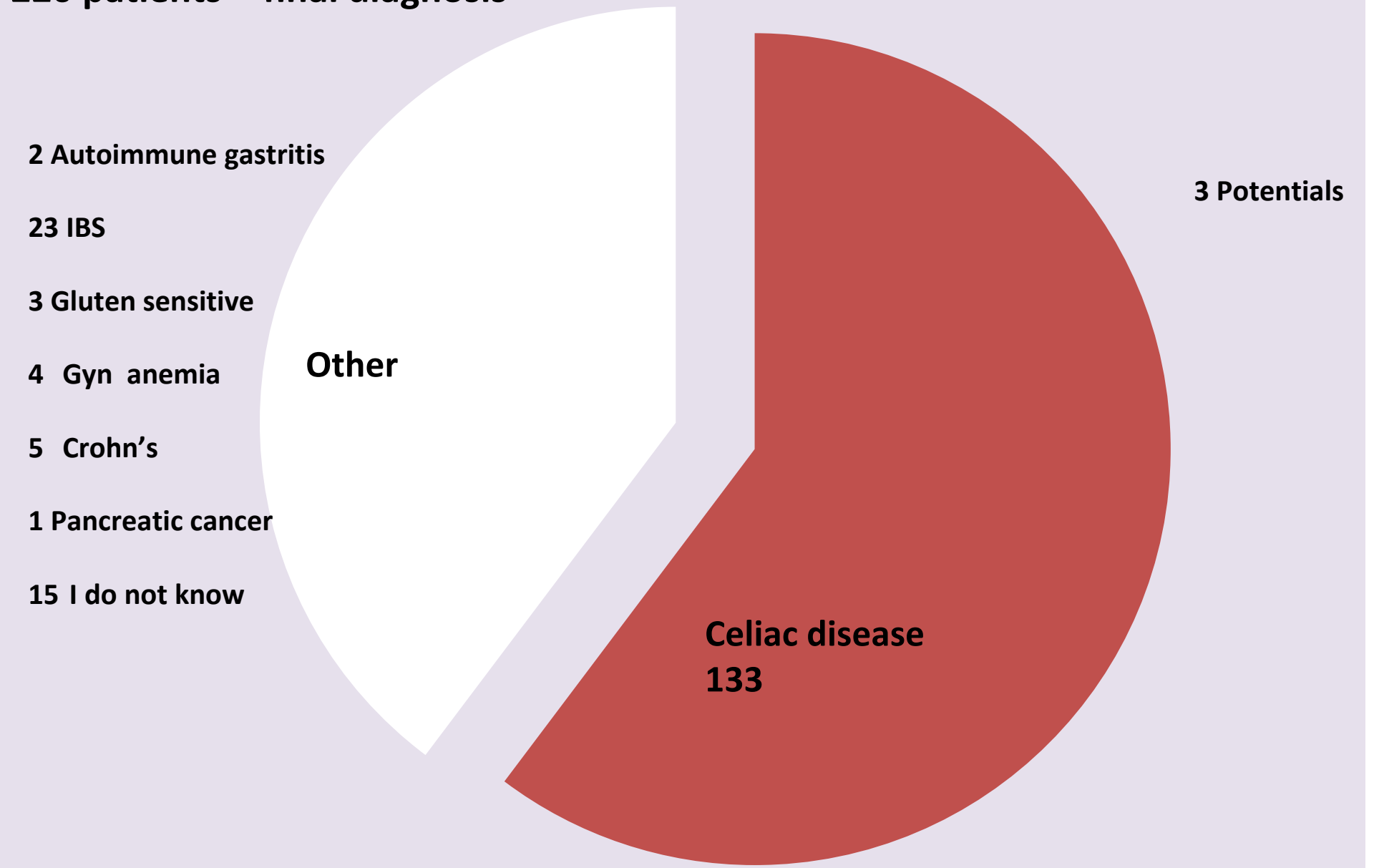
19. New Zealand

220 patients : symptoms/signs

• Iron deficiency	88/220	40%
• GI symptoms	78/220	
• Fatigue	73/220	
• Osteoporosis	18/220	
• Infertility	10/220	
• Asymptomatic	9/220	~4%

serology	Histology , Marsh classification	
• EMA n 30		
• Ttg IgA n 75	Marsh 0*	49
	Marsh 1*	37
• Ttg + EMA n. 115	Marsh 2*	3
	Marsh 3 a	26
	Marsh 3 b	36
	Marsh 3 c	69

220 patients - final diagnosis



Take home message

- in our days, histology is may be the pitfall of CeD diagnosis
- experts and studies suggest that there is the possibility to avoid the biopsy in a subgroup of adults with the suspicion of CeD
- It may be possible that the ESPGHAN criteria may be adopted also in adults (age limitation?)
- A prospective, multicenter, controlled trial is needed (ongoing)

The difficulty lies not so much in developing new ideas as in escaping from old ones

JM Keynes

GASTRO.UNISA

UNIVERSITÀ DEGLI STUDI DI SALERNO