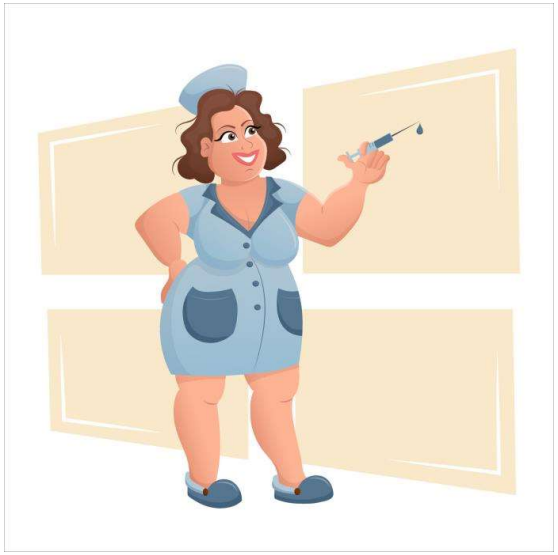

Coeliac Cases
GLMS CME 13th March 2024

Case one: Marissa



50 year old nurse

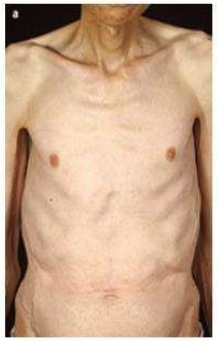
- Abdominal pain, constipation and bloating for 3 years
- No rectal bleeding, diarrhoea or weight loss
- **Background:**
  - Type 1 diabetes
  - Normal colonoscopy 2023
- **Examination:**
  - BMI 36kg/m^2, looks well.
  - Centrally obese, otherwise abdominal examination unremarkable

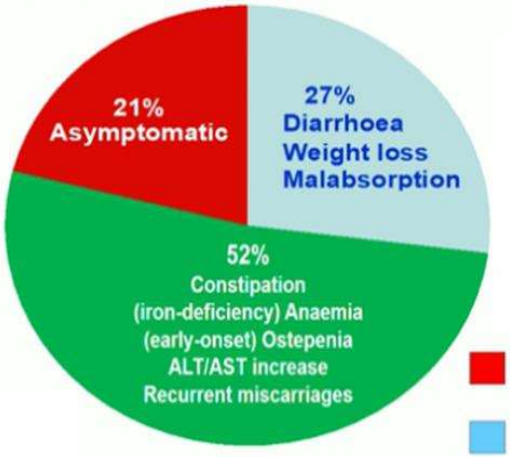
Started a gluten free diet after being recommended by friends

- Perhaps a slight improvement
- “Do I have IBS?”

Mistake #1: Clinical features of CD changed over time...

n= 770 CD pts diagnosed and followed at the Center for Coeliac Disease, St. Orsola Hospital, Bologna (1998-2012)





Volta U., et al., BMC Gastroenterology 2014; 14:194

In adults, **gluten challenge** should be proposed in patients with uncertain CD diagnosis who have been started on a gluten free diet

No universal protocol: 3g of gluten per day 2 weeks sufficient for most patients but some protocols up to 10g of gluten per day 6-8 weeks

4x slices of wheat based bread or equivalent 4-8 weeks – *Coeliac NZ*

- Full blood c
rate, and co
- Faecal calp

HLA-DQ2/DQ8 is a good **rule out** test
~99% NPV *i.e. only useful if negative*

Used in the setting of discordant serology and histopathology, or if unable to undergo gluten challenge

Positive does not mean CD
Some studies positivity in up to 47.7% DQ2 and/or DQ8

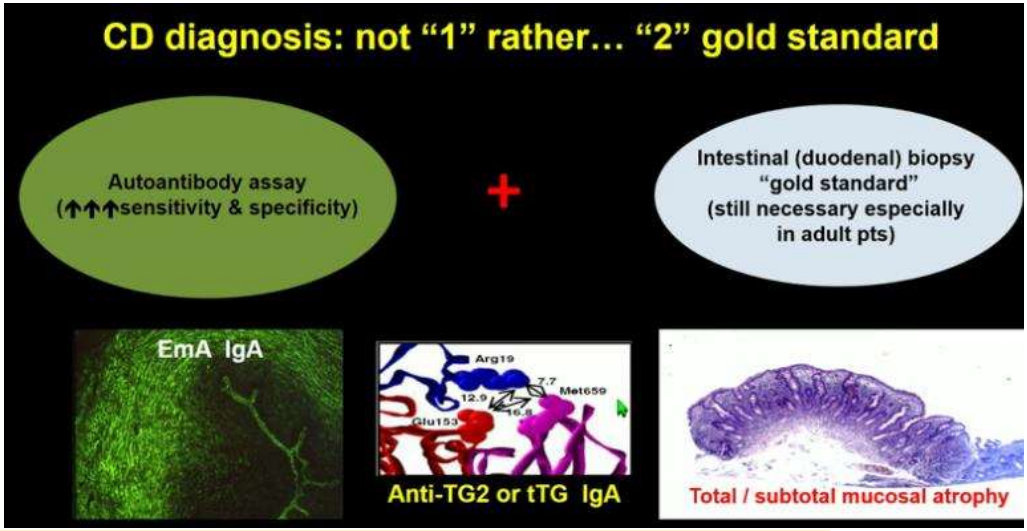
Q: What would you do next?

1) Refer for colonoscopy and gastroscopy
2) Repeat Coeliac serology after gluten challenge
3) Reassure her without further investigations
4) Refer for HLA DQ2 DQ8 testing
5) Start a low FODMAP diet for IBS

Case one: Marissa

Mistake #2: Do not establish a CD diagnosis based on GFD-induced symptom improvement / resolution

- **Mainly seen in primary care**
- **Physicians should not advise patients to start GFD before testing them thoroughly**
- **If a diagnosis of CD has been ruled out (by appropriate investigations), the persistence of intestinal / extraintestinal symptoms induced by gluten might suggest NCG/WS**



Q: Which statement is most correct regarding diagnosis of Coeliac disease?

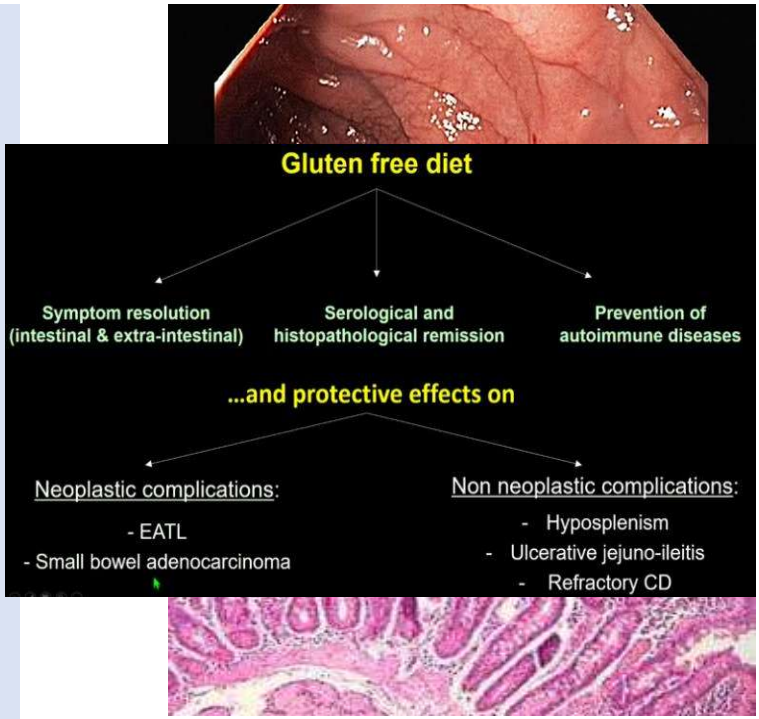
1) Duodenal biopsies is the gold standard and always required
2) Biopsies alone is sufficient for the diagnosis of coeliac disease
3) **In adults, a combination of serology and duodenal biopsies is required**
4) Biopsies are useful to exclude Non-coeliac gluten/wheat sensitivity
5) Biopsies are not required if symptoms improve with a GFD

Symptoms typically resolve within a month but **serology is unlikely to be normal by 6 months and can take up to 2-3 years to normalize**. **Mucosal healing can lag serological response** *in one study, the median time to achieve a normal villous height was 3.8 years*.

Repeating antibodies routinely at 12 months is recommended regardless of symptoms. If levels fall and symptoms resolve → reassurance

Follow up biopsies are not universally recommended but may be **reasonable after 2 years** of GFD in high risk patients

But…**elevation of antibodies after normalization** may suggest gluten **re-exposure**. Persistently stable positive serology suggest **inadvertent gluten exposure,** and dietican input may be helpful



Q: Which statement is INCORRECT regarding Coeliac disease?

1) First degree relatives of affected individuals should be tested
2) **Serology and histology always return to normal within 1 year of GFD**
3) Complications of Coeliac disease can be avoided with a GFD
4) A life-long gluten free diet is the only effective treatment
5) Inadvertent exposure to gluten is very common

Case two: Eliza

Marissa's asymptomatic 21 year old daught

Eliza comes to see you for testing.

Coeliac serology after a gluten diet reveals:

- IgA tTG 11U/ml (<15) Normal
- IgA 0.3g/L (0.8-4.0) LOW
- Endomysial antibodies negative

IgA tTG and IgA EmA are **highly sensitive and specific tests for Coeliac disease**

	Sensitivity %	Specificity %	PPV %	NPV %
IgA tTG	98	90	91	98
IgA EmA	95	100	100	95

However, around **7% of Coeliac patients have IgA deficiency**, and will be negative. **DGP (deamidated gliadin peptides) IgG** would be the next step

True seronegative Coeliac disease is rare 2-8%

IgA AGA are no longer useful in diagnosis and follow up

Q: Which statement is most correct?

1) Coeliac disease cannot be excluded

2) IgA tTG and IgA EmA are not very sensitive for Coeliac dis

3) IgA deficiency is uncommon in Coeliac disease

4) Anti-gliadin antibodies are useful in diagnosis of Coeliac

5) Seronegative Coeliac disease is common

1) **Anti-Gliadin (AGA)** Berger E, et al. Klin Wschr. 42: 788-90, 1964

2) **Anti-Reticulin (ARA)** Seah PP, et al. Lancet. 25 (7726): 681-2, 1971

3) **Anti-Endomisial (EMA)** Chorzelski TP, et al. Br J Dermatol. 111: 395-402, 1984

4) **Anti-Translutaminase (a-tTG)** Dieterich W, et al. Nat Med. 3: 797, 1997

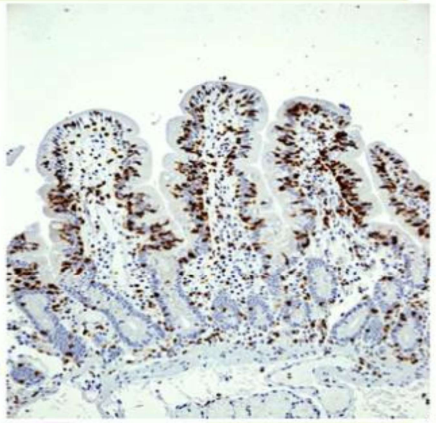
5) **Anti- Deamidated gliadin peptides (a-DGP)** Sugai E, et al. Clin Gastroenterol Heptol 4: 1112–7, 2006

6) **Point-of Care tests (tTG or DGP)** Mooney PD. Clin Gastroenterol Heptol 2015

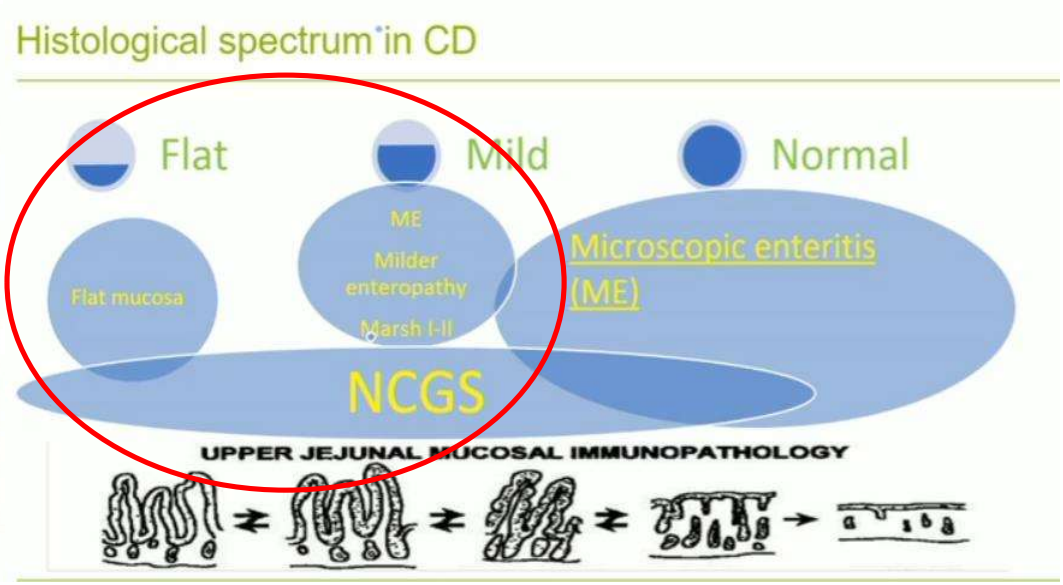
Case two: Eliza

Mistake #4: Make CD diagnosis based on minimal lesion (Marsh 1) at histopathology

- Marsh 1, i.e. IEL >25%, does not indicate CD
- A wide array of conditions may show Marsh 1:
  - HP infection / Giardiasis
  - Autoimmune diseases
  - Drugs (NSAIDs)
  - Lactose intolerance
  - NCG / WS
  - ...
- Pts with Marsh 1 with +ve serology, +ve HLA-DQ2 /DQ8 are potential CD (about 10% of all Marsh 1)



Same biopsy after appropriate orientation shows normal villi architecture



Q: Which statement is incorrect regarding Coeliac disease?

1) It can affect the small bowel in a patchy manner
2) Inadequate biopsies may lead to a false negative diagnosis
3) Partially treated disease may lead to milder changes on histology
4) **Increased IEL (Marsh 1) is diagnostic of coeliac disease**
5) Other conditions which can mimic Marsh 1 histology

Current diagnostic strategy and tools

Is duodenal histology the "gold standard"?

	Year	% error	Commentaries
Scandinavia *	2000	13	Over-diagnosis (1)
Netherlands *	2011	7.4	Over-diagnosis (4)
Sweden *	2011	7.3	Sub-diagnosis (5)
Argentina	2009	46	Over-diagnosis (2)
Italy	2009	20	Over-diagnosis(3)
USA	2012	25	Sub-diagnosis (6)

* Among experts of academics institutions

1- Weile et al. APMIS 2000; 2- Pinto-Sanchez et al. AGLA 2009; 3- Biaggi et al. CJG 2009; 4- Mubarack et al. SJG 2011; 5- Webb et al. JPGN 2011; 6- Arguelles-Grande et al. JCP 2012;

Mistake #5: Overestimation of refractory coeliac disease in patients whose symptoms persist on GFD

- Refractory CD (RCD) (~1% of all CD) is characterized by the lack of clinical response and persistence of villous atrophy after at least 1 year of strict GFD
- RCD diagnosis is of paramount importance because it evolves to EATL and ulcerative jejuno-ileitis

Refractory coeliac disease 1-5% of Coeliac disease patients, rare <30 years old.

- Can lead to **Ulcerative jejunitis** and **intestinal lymphoma**

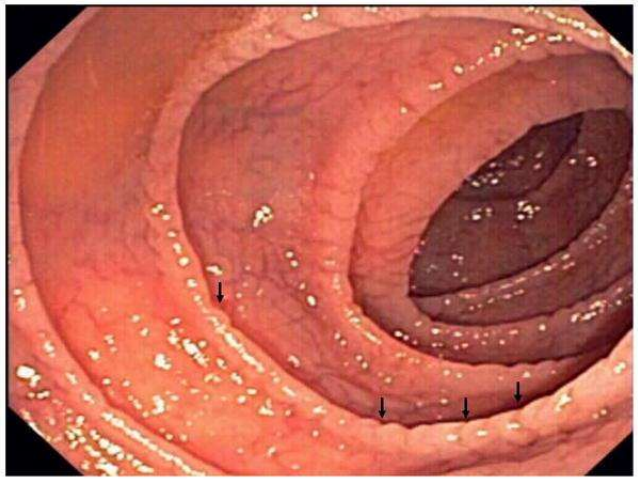
Q: Which of these statements are correct?

1) GFD compliance should be reassessed
2) Repeat Coeliac serology and duodenal biopsies should be considered
3) Other enteropathies and gastrointestinal pathologies should be considered
4) Refractory coeliac disease is rare but can be associated with poor outcomes
5) All the above

Case three: Thomas

Foods and products that may contain gluten

Frequently overlooked foods that may contain gluten and need to be verified:
Brown rice syrup
Breading and coating mixes
Croutons
Energy bars
Flour or cereal products
Imitation bacon
Imitation seafood
Marinades
Panko (Japanese bread crumbs)
Pastas
Processed luncheon meats
Sauces, gravies
Self-basting poultry
Soy sauce or soy sauce solids
Soup bases
Stuffings, dressing
Thickeners (roux)
Communion wafers
Herbal supplements
Probiotic products*
Drugs and over-the-counter medications
Nutritional supplements
Vitamins and mineral supplements
Play-Doh, crayons, paint, glue, paper mache – A potential problem if the child puts their hands on or in the mouth while playing; wash hands after using these products



* In 2015, a study of 22 commonly used probiotics revealed that 12 (55%) contained gluten, including 2 that were labeled gluten-free despite containing gluten levels higher than the 20 parts per million required for gluten-free labeling.[1]

NOT ALLOWED in any form:
Wheat (einkorn, durum, faro, graham, kamut, semolina, spelt)
Rye
Barley
Triticale
Malt, malt flavoring, malt vinegar (are generally made from barley; verify the source)

Careful dietician assessment completed

Gluten free diet – no improvement

Coeliac serology - *negative*

Gastroscopy - *persistent villous atrophy*

HLA DQ2 DQ8 *presence*

Colonoscopy *normal random colon biopsies*

Others: *Faecal elastase, stool parasite screen, H. pylori serology, HIV, Immunoglobulins*