

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



# Celiac Disease

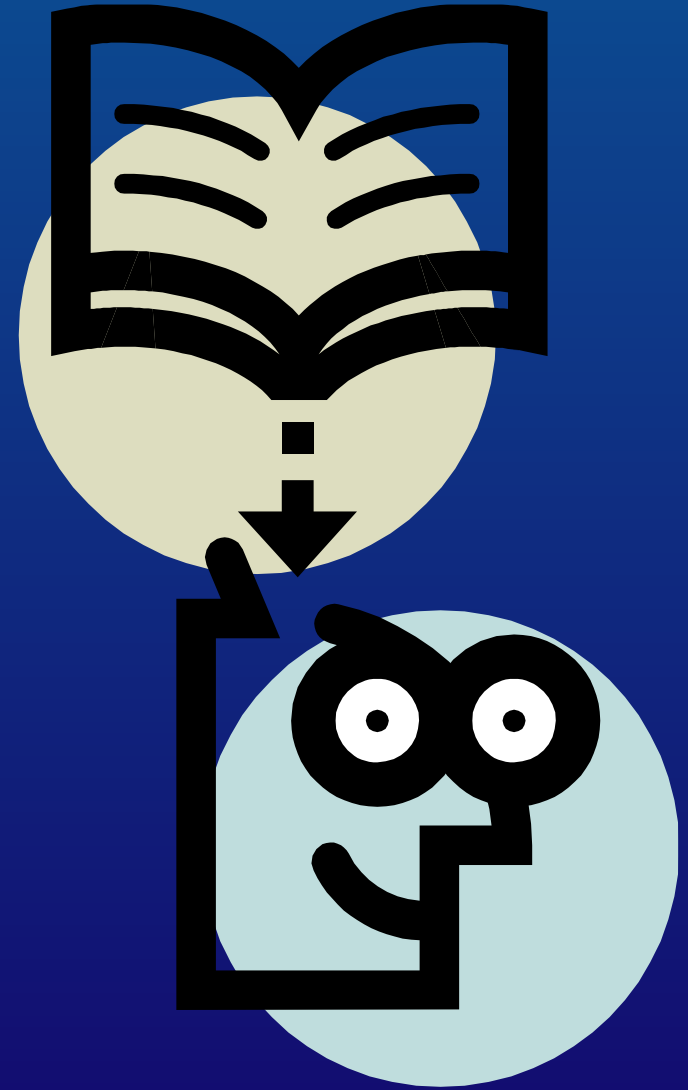
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MD. Gastroenterologist  
PhD. Gastroenterology

# حالة سريرية 1

- راجعتني الأنسة ر. خ 23 سنة من دمشق بقصة ألم بطني كولوني الصفات مع امسك متناوب مع اسهال كاذب ونقص وزن حديث وقلاعات فموية مع طفح جلدي حاك + دورة منتظمة غزيرة
- الفحص السريري: طفح جلدي حطاطي حاك
- مخبرياً:

WBC	6.8	CRP	1.29
Hb	11	Ferritin	8.3
MCV	78.4	Stool analysisi	Neg
MCH	26.7	Anti tTG IgA	Neg (4.98)
Plet	306		

- تنظير معدة طبيعي أخذت خزعات معدة وعفج
- خزعات المعدة التهاب معدة مزمن فعال بالHP
- خزعات العفج : Marsh 3a
- Anti DGP IgG سلبي



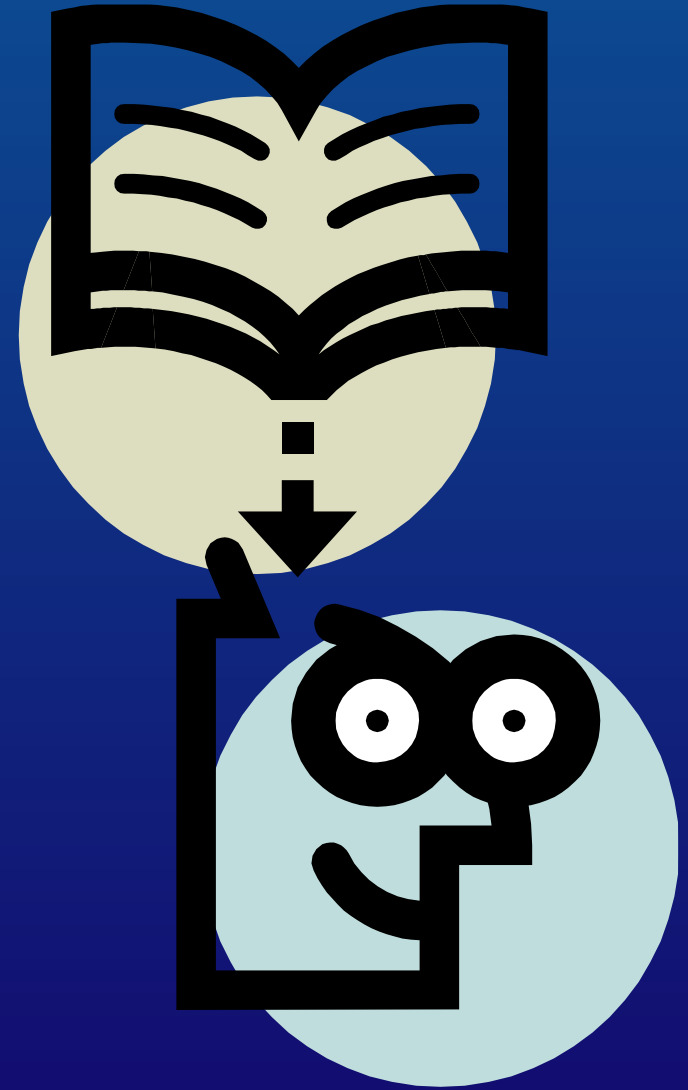
## حالة سريرية 2

- راجعتني الطبيبة ر. ص 24 سنة بشكوى عدم كسب للوزن حيث عانت المريضة من نقص وزن حوالي 8 كغ خلال 4 سنوات تذكر وجود شدة نفسية خلال هذه الفترة لم تستعد الوزن السابق بعدها رافقت الشكاية عسرة هضم واسهال مزمن متردد وألم كولوني الصفات بدون علامات حمراء .
- الفحص: لا شيء مميز سوى النحول

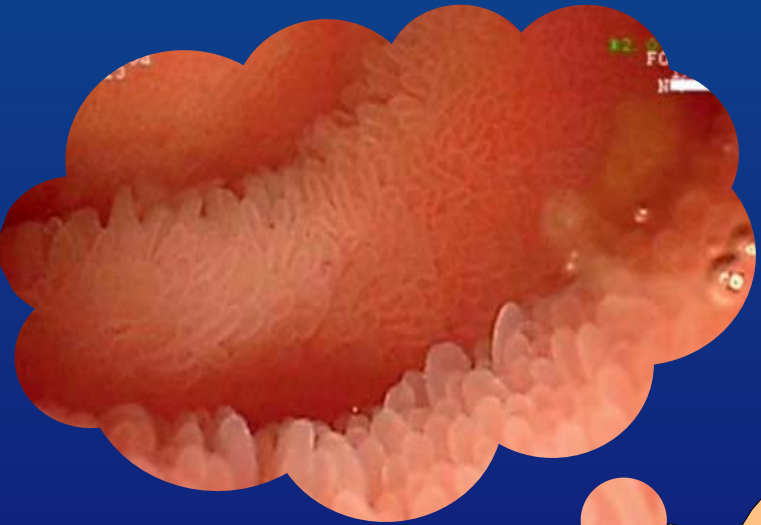
• مخبرياً:

WBC	8.5	CRP	1.3
Hb	13.2	ESR	6
MCV	88.89	Ferritin	27.5
MCH	29.3	Stool analysisi	كيسات زحارية
Plet	205	Anti tTG IgA	Neg (5.1)
B12	276	TSH	3.63

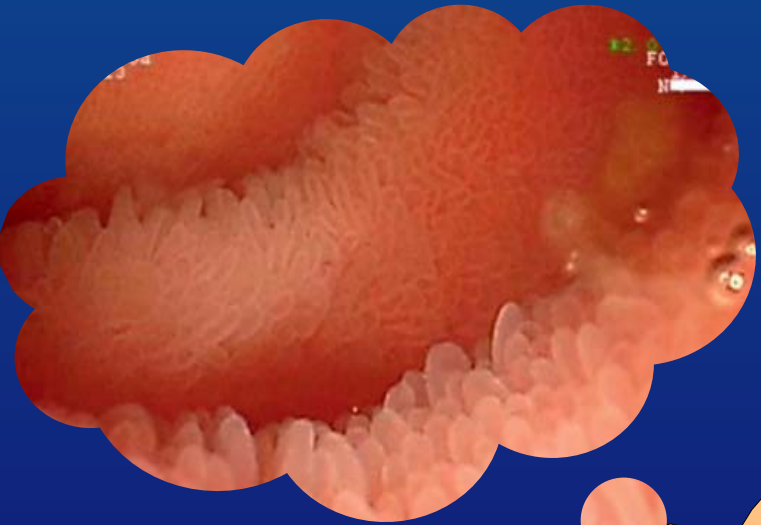
- تنظير معدة : التهاب أسفل المري درجة A ، حمamy بالغار ( خزعات التهاب معدة مزمن فعال بال HP )، نقص ارتفاع بثنيات العفج ( الخزعات العفج : Marsh 2 )
- تنظير كولون : طبيعي حتى 15 سم من الدقاق النهائي ( خزعات كولون: WNL ) ( خزعات دقاق: Marsh2 )
- Anti DGP IgG سلبى



“Think of CD and you will find it”

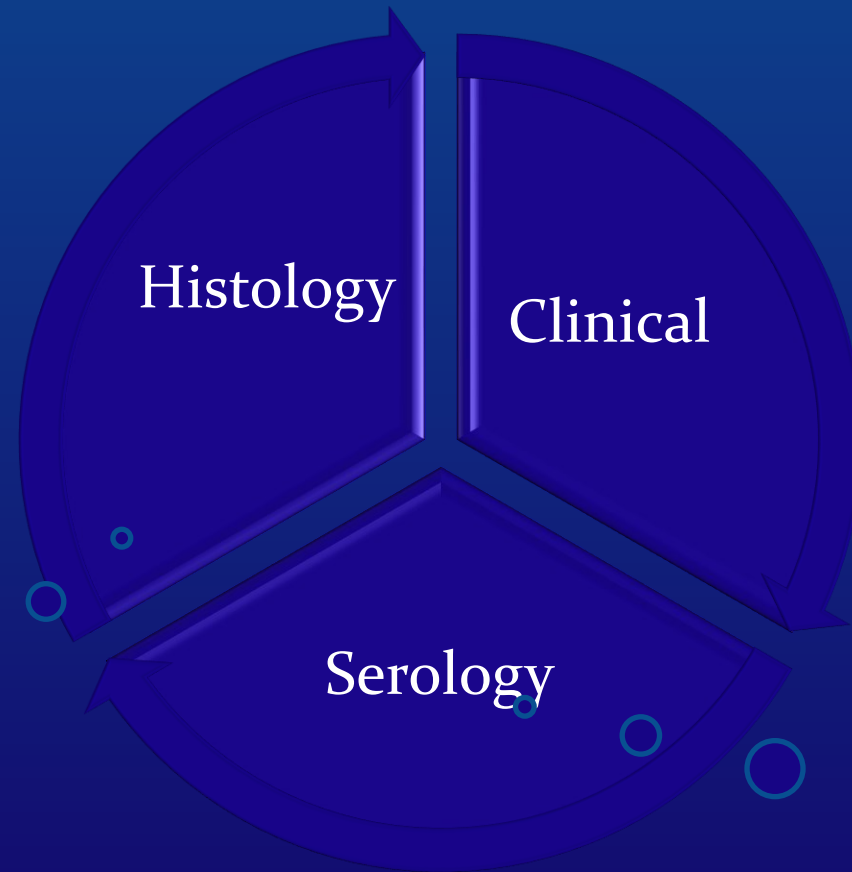


If you think a lot ?? Over diagnosis??





# HOW CAN WE CONFIRM DIAGNOSIS OF CD?



Marsh  $\geq 2$

Anti-tTG IgA  
Anti DGP IgG

(ESsCD) guideline for coeliac disease  
and other gluten-related disorders.2019

The image features a solid dark blue background. At the top, there are several overlapping, wavy lines in shades of cyan and light blue, creating a sense of motion or a decorative header. The word "Clinical" is centered in the lower half of the image.

**Clinical**

القرن 21

القرن 20

مرض مناعي ذاتي  
تظاهرات جهازية  
جميع الأعمار

مرض هضمي  
تظاهرات هضمية  
يصيب الأطفال

الداء الزلاقي بين قرنين

# Celiac disease is a 'multi-system' disorder

## General

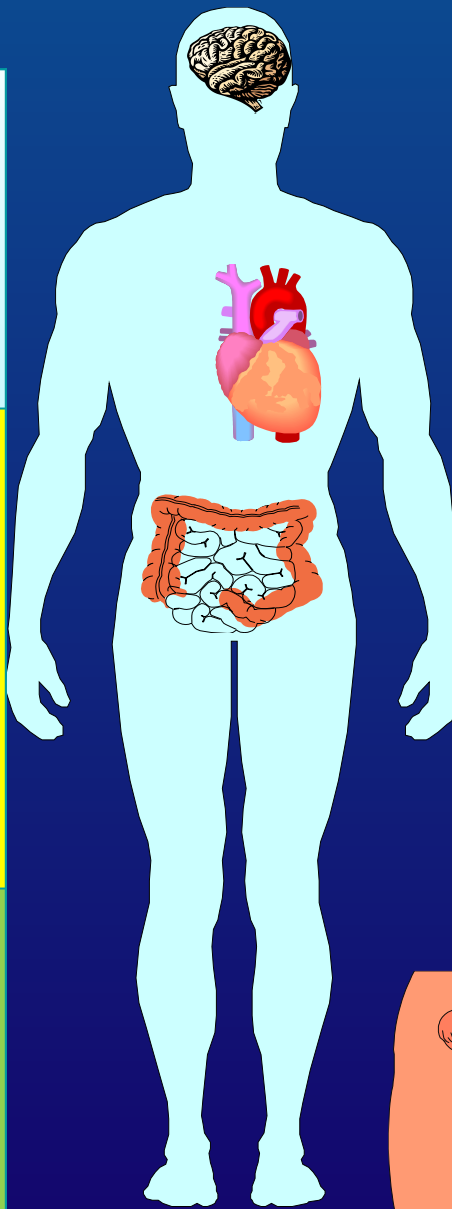
- Pubertal & Growth delay
- Malignancies
- Anemia

## GI System

- Diarrhea, vomiting
- Distention, abdominal Pain
- Malnutrition, weight loss
- Hepatitis, Cholangitis

## Bones

- Osteoporosis, fractures
- Arthritis
- Dental anomalies



## Central Nervous System

- Ataxia, seizures
- Depression

## Heart

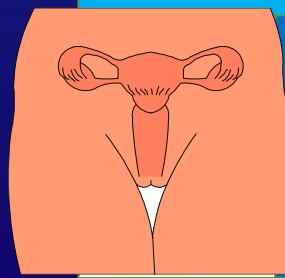
- Carditis

## Skin & Mucosa

- Dermatitis herpetiformis
- Aphthous Stomatitis
- Hair loss

## Reproductive

- Miscarriage
- Infertility

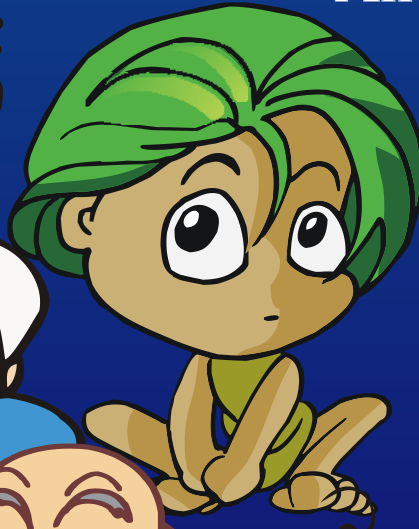


# The Many Faces of Celiac Disease

IBS



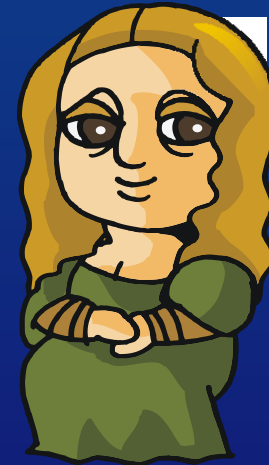
Gas



Anemia



Constipation



Bloating

Fatigue



Diarrhea

Weight loss

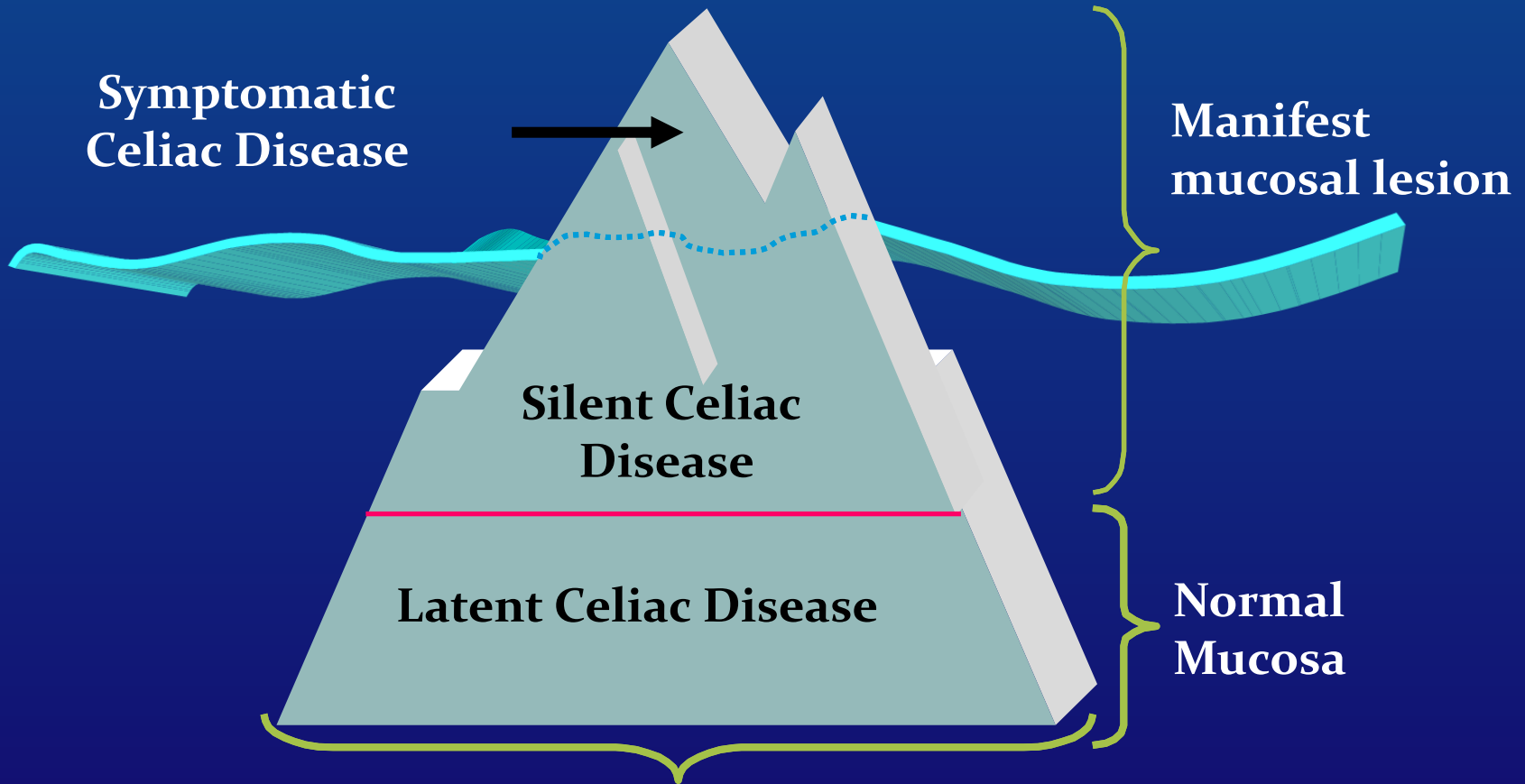


Osteoporosis



Vitamin deficiency

# The Celiac Iceberg



Genetic susceptibility: - DQ<sub>2</sub>, DQ<sub>8</sub>  
Positive serology

# SEROLOGY

# The role of serology

Antigen	Antibody type		
Gliadin	IgA		
	IgG		4-50, 80
Endomysium	IgA	(100-86) 95	(100-97) 99
	IgG	(90-70) 80	(100-95) 97
Tissue transglutaminase	IgA		(100-90) 98
			(100-94) 95
	IgG		(95-80) 90
			(100-95) 98

AGA NOT recommended

First screening test  
= Anti- TTG IgA  
At any age



**Ab -IgA**

• **Ab+Total IgA**

2-3% of CD

**IgA-  
deficiency**

• **IgG-DGP**

• **IgG-TG2**

# Histology

If positive histology is this  
CD?

Marsh classification = CD??

# Normal villous architecture and increased IELs

- Food hypersensitivity (cow's milk, soy, fish, eggs, etc.)
- Peptic ulcer disease
- **Helicobacter pylori-associated gastroduodenitis**
- Drugs (NSAIDs, proton pump inhibitors)
- Infections (e.g., viral enteritis, Giardia, Cryptosporidium)
- Immune dysregulation (rheumatoid arthritis, Hashimoto's thyroiditis, SLE, multiple sclerosis, autoimmune enteropathy)
- CVID
- Graft-versus-host disease (GVHD)
- Inflammatory bowel disease (IBD)
- **Bacterial overgrowth**
- **Blind loop syndrome**
- Microscopic colitis (lymphocytic and collagenous)
- IBS
- NCGS

# VA +/- increased IELs

- **Infections** (tropical sprue, Giardia, Whipple disease, Mycobacterium avium complex, AIDS enteropathy)
- Collagenous sprue
- Autoimmune enteropathy
- CVID
- GVHD
- **IBD (Crohn disease)**
- Drugs (mycophenolate mofetil, colchicine, olmesartan, losartan)
- Chemoradiation therapy
- Immunomodulatory therapy (anti-CTLA4 antibody)
- Eosinophilic gastroenteritis
- **Bacterial overgrowth**
- Enteropathy-associated T cell lymphoma (EATL)
- **Nutritional deficiency**
- Amyloidosis

# Etiologies of Seronegative Villous Atrophy

## Immune-mediated

Seronegative CeD

CVID

Autoimmune enteropathy

Intestinal lymphoma

Sarcoidosis

## Infectious

Parasitic infections  
(*Giardia lamblia*)

Tropical sprue/environmental enteropathy

Whipple disease

Small intestinal bacterial overgrowth

Tuberculosis

HIV enteropathy

## Iatrogenic

### Medications

- Olmesartan
- Azathioprine
- Mefenamic acid
- Methotrexate
- Mycophenolate mofetil
- Chemotherapy

Graft vs host disease

Radiation enteritis

Transplanted small intestine

## Inflammatory

Crohn's disease

Collagenous sprue

Eosinophilic enteritis

# SERONEGATIVE CD

2–15% CD patients are seronegative

All of

VA

response to a GFD

negative coeliac serology

- (IgA/IgG-EMA, IgA/IgG-TG2 and IgG-DGP)

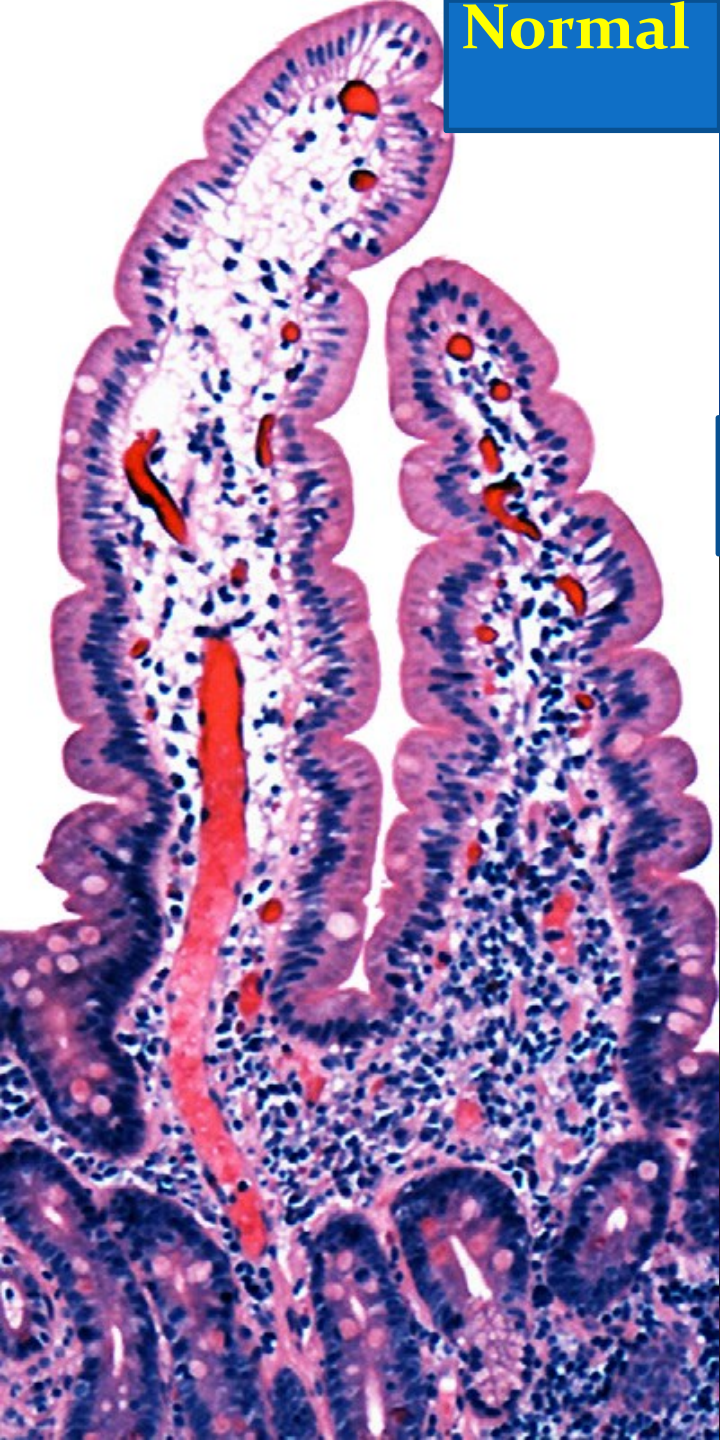
presence of HLA-DQ2/or-DQ8

Excluding other causes of seronegative VA

# **HISTOPATHOLOGIC EVALUATION OF CD**

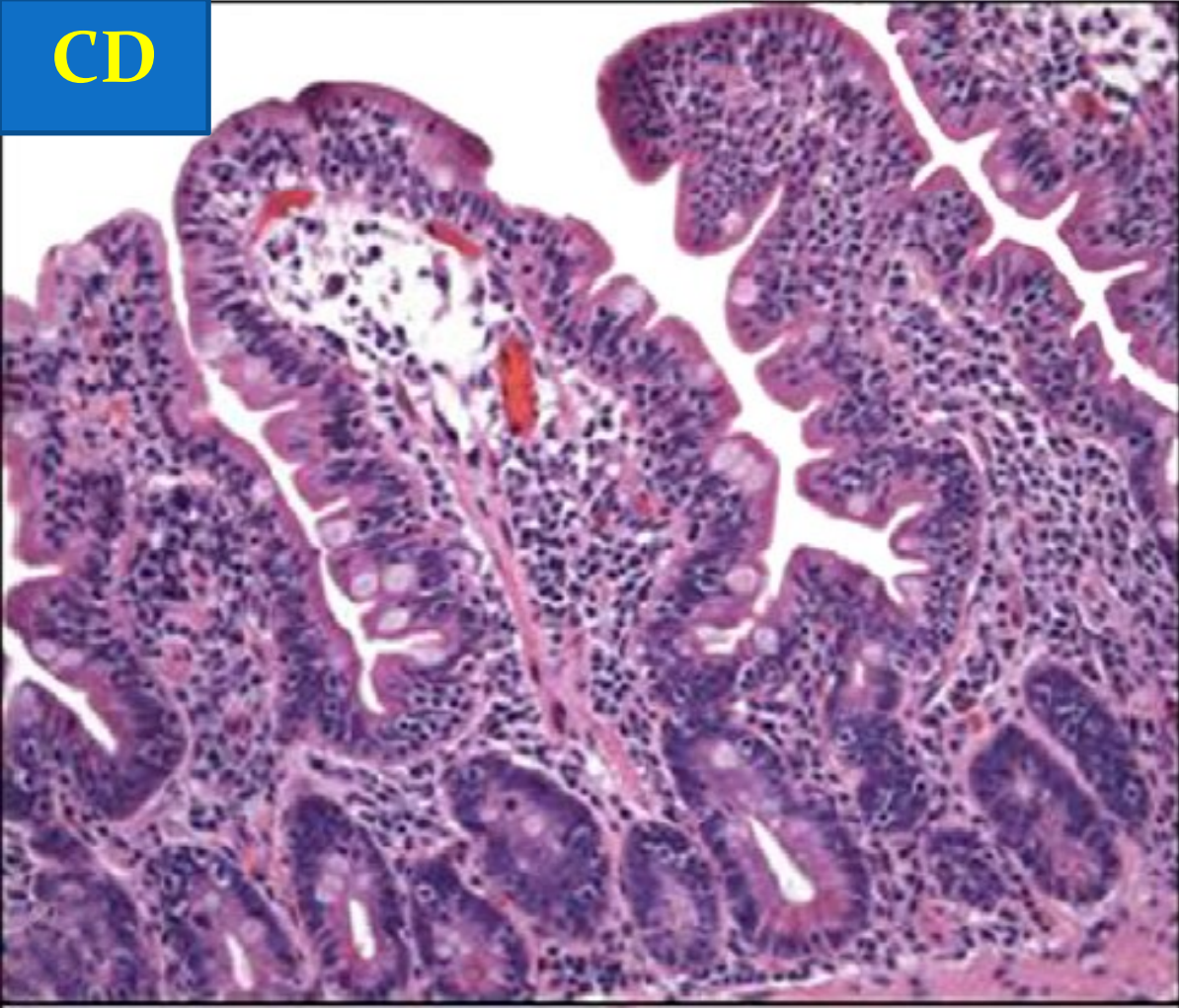


**Normal**



well oriented biopsy pieces that contain 3 to 4 consecutive villous-crypt units visualized in their entirety and arranged parallel to each other

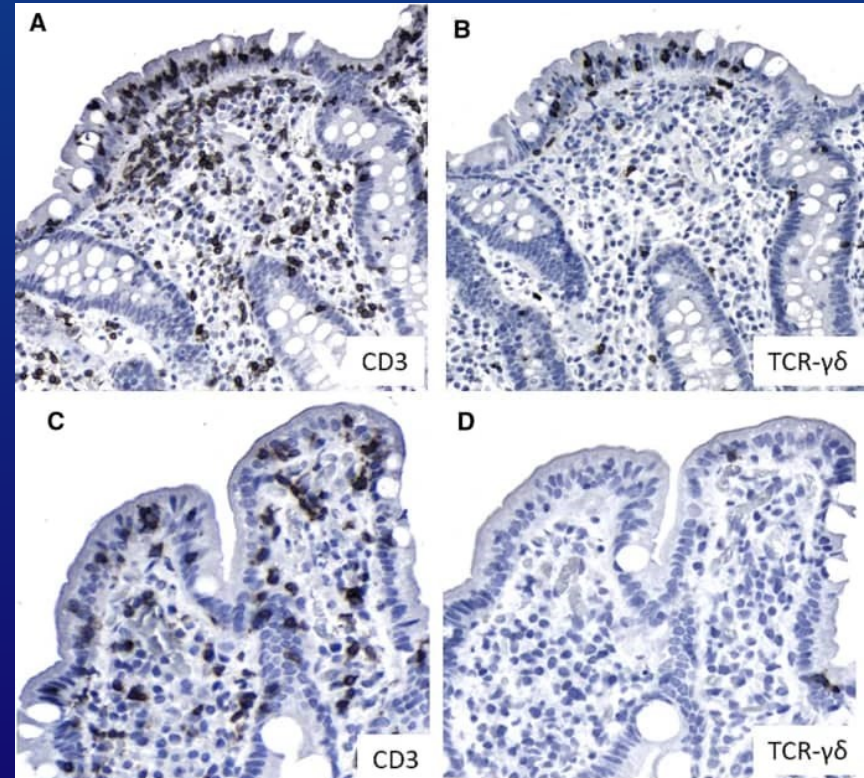
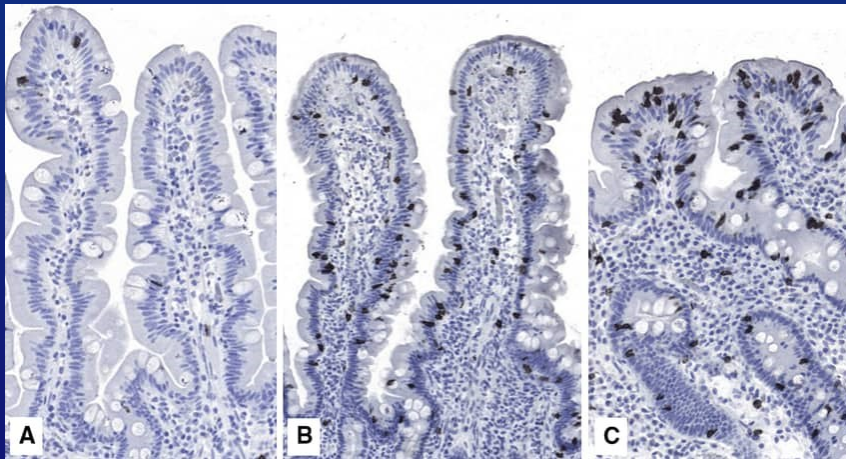
**CD**



# Immunohistochemistry

$\gamma\delta$  T cell Lymphocytes

CD3 T lymphocytes





# **SOME DIFFERENTIAL DIAGNOSIS**

# Tropical sprue (TS)

Visitor to tropic country

Histology = CD

Terminal ileum



# Autoimmune enteropathy (AE)

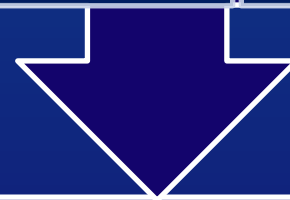
Children & young adults

Histology = CD

IELs = more often seen in the crypts

dense lymphoplasmacytic in the lamina propria

Hallmark = presence of antienterocyte antibodies



# Common variable immunodeficiency (CVID)

↓serum Ig levels

absence or rarity of plasma cells in the lamina propria

immunohistochemical stain for CD138

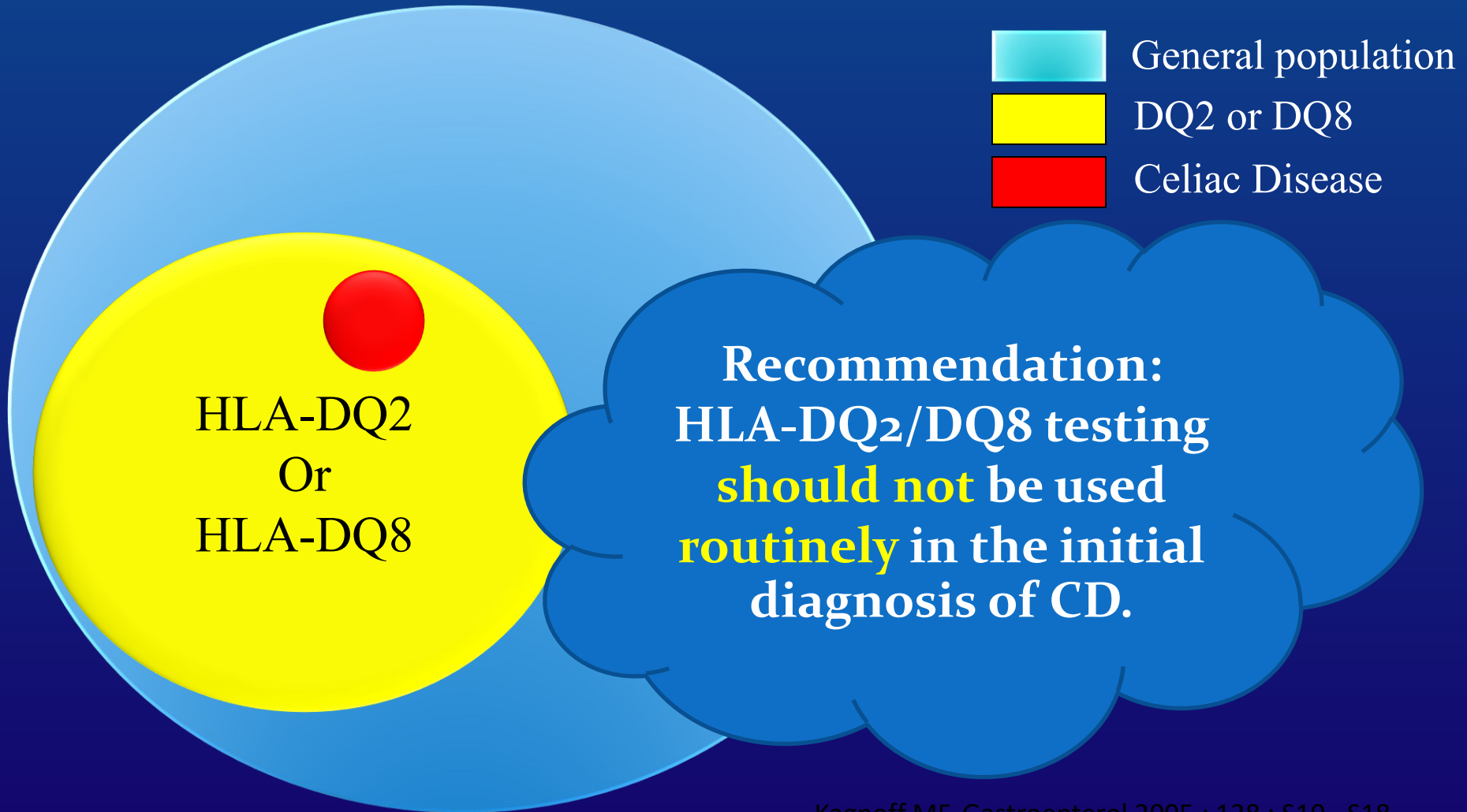


# Collagenous sprue (CS)

thick subepithelial collagen band (usually >10 μm)

**HLA Pos = NECESSARY CD?**

# Distribution of DQ2 & DQ8



# When should we use HLA-DQ2/DQ8 testing

## Rule out CD

Evaluation of patients who started GFD

When the results of serology and histology are discrepant

VA

tTG IgA+ Total IgA

tTG (Neg) + Normal IgA

IgA DGP + IgA EMA

+

CD

-

Review histological with pathologist

Review medical, travel and medication history

Clinical and histological review suggest etiology other than CD

Yes

Test for CVID, SIBO, Giardia, AE

Etiology identified

Yes

Treat

No

Unspecific enteropathy

Treat empirically budesonide

IgA deficient

tTG (Pos)

tTG IgG OR DGP IgG

CD

-

+

CD

No

HLA

-

+

Treat empirically with GFD

Reassess symptoms and repeat biopsy



شكراً لحسن اصغائكم