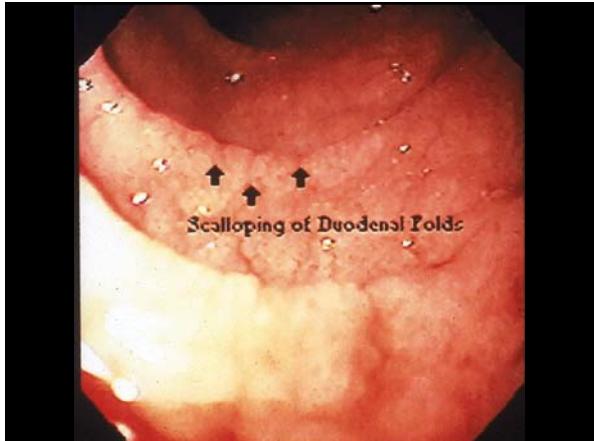


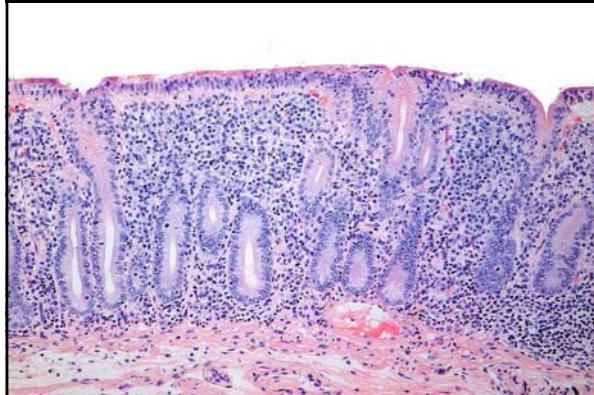


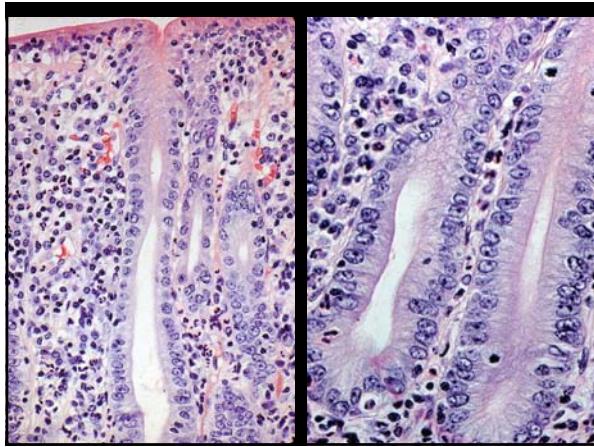
## **Small Bowel Malabsorptive Disorders: celiac disease and other entities**

**John Hart, M.D.**  
**Chief of GI and Hepatic Pathology**  
**University of Chicago Medical Center**



## **Classic Old School Celiac Disease**





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### Clinical Correlation is Mandatory

- HLA testing: absence of HLA DQ2 and DQ8 essentially excludes celiac disease
- Serologic tests:
  - Anti-tissue transglutaminase IgA (gold standard)
  - Anti-endomysium IgA antibody
  - Anti-deamidated gliadin peptide IgA
  - [Anti-gliadin IgA – no longer recommended]
- IgA deficient individuals (quant IgA level):
  - Anti-TTG IgG (gold standard)
  - Anti-DGP IgG

Rubio-Tapia A et al. ACG Clinical Guidelines: diagnosis and management of celiac disease.  
Am J Gastroenterol 2013; 108:656-76.

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### Complete Villous Flattening with Crypt Hyperplasia

- CELIAC DISEASE
- Autoimmune enterocolitis
- Viral enteritis (rare cases)
- Tropical sprue (rare cases)
- Common variable immunodeficiency (rare cases)
- Medication (sartan) induced enteropathy

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11-26029

## Clinical History

- 32 year old male with abdominal distress and diarrhea
- Endoscopic findings:
  - Esophagus & stomach normal
  - Flattening and decreased folds in the 2<sup>nd</sup> and 3<sup>rd</sup> parts of the duodenum
  - Scalloped folds in the 2<sup>nd</sup> part of the duodenum

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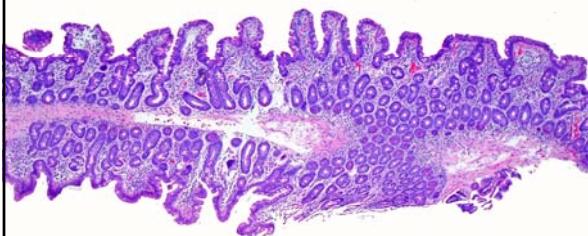
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Moderate villous blunting and crypt hyperplasia



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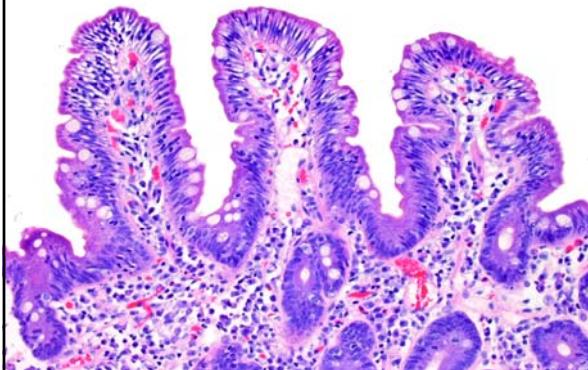
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Increased intra-epithelial lymphocytes



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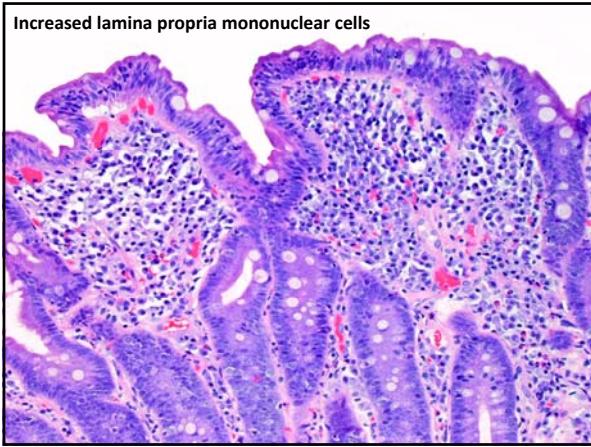
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#### No Knowledge of Celiac Panel Results

Upper GI endoscopic biopsies, duodenum:  
- Duodenal mucosa with moderate villous blunting and increased intraepithelial lymphocytes. See comment

Comment: Celiac disease is a diagnostic consideration. Correlation with serologic tests results is necessary.

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#### Pathologist is Aware Celiac Panel is Positive

Upper GI endoscopic biopsies, duodenum:  
- Duodenal mucosa with moderate villous blunting and increased intraepithelial lymphocytes, consistent with celiac disease.

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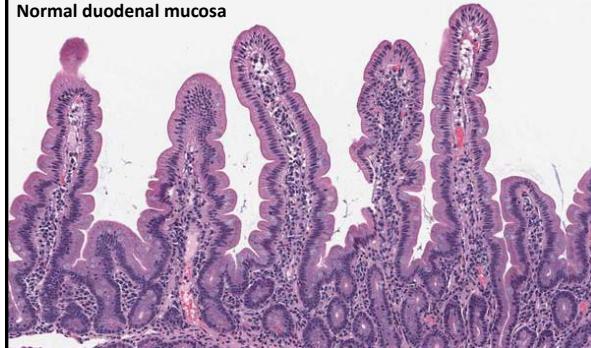
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**Provided Clinical History:**  
**Rule out celiac disease**

Normal duodenal mucosa



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**Whether the celiac panel is:**

- not known
- negative
- positive

**Upper GI endoscopic biopsies, duodenum:**

- Duodenal mucosa without diagnostic abnormality.  
See comment.

**Comment:** Sections of these large and well oriented biopsies reveal that the duodenal villi are long and slender and there is no increase in intraepithelial lymphocytes.

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**Malabsorptive Disorders**  
**Morphologic Patterns**

1. Complete villous blunting with crypt hyperplasia
2. Lesser degree of villous blunting with crypt hyperplasia (focal or diffuse)
3. Villous and crypt shortening (mucosal atrophy)
4. Normal mucosal architecture  
+ / - “distinctive features”

Intraepithelial lymphocytosis

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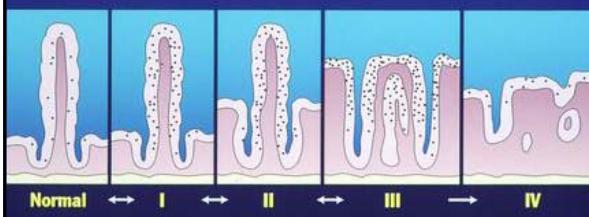
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### Marsh Classification

Gastroenterology 1992; 102:330-54.

- Type 0 – Normal architecture; no increase in IELs
- Type 1 – Normal architecture; > 40 IEL
- Type 2 – Crypt hyperplasia, normal villi; > 40 IELs
- Type 3 – Crypt hyperplasia & villous blunting; > 40 IELs
- Type 4 – Crypt & villous atrophy



### Modified Marsh Classification

- Type 0 Normal architecture; no increase in IELs  
Type 1 Normal architecture; > 25 IELs  
Type 2 Crypt hyperplasia, normal villi; > 25 IELs  
Type 3 Crypt hyperplasia, villous blunting; > 25 IELs  
    3a – mild villous blunting  
    3b – subtotal villous blunting  
    3c – total villous blunting  
Type 4 Crypt & villous atrophy

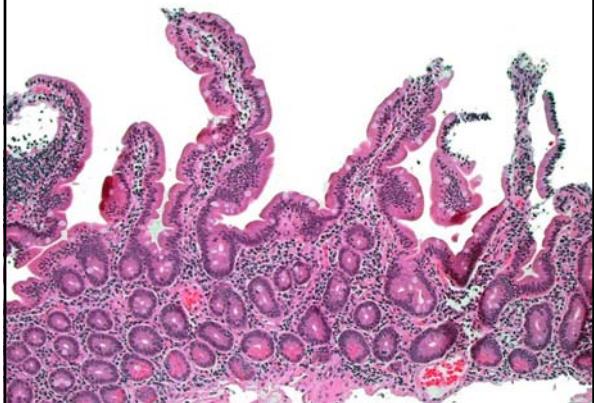
Oberhuber G et al. Eur J Gastroenterol Hepatol 1999; 11:1185-94.

### Current Treatment of Celiac Disease by Marsh/Oberhuber subtype

- Type 0 - Gluten free diet for symptomatic patients?  
Type 1 - Gluten free diet  
Type 2 - Gluten free diet  
Type 3  
    3a - Gluten free diet  
    3b - Gluten free diet  
    3c - Gluten free diet  
Type 4 - Gluten free diet (? and immunosuppression)

You don't have to give a MARSH score  
(unless it will make your clinician love you)

**Celiac Disease Type 1 (celiac serology panel positive)**



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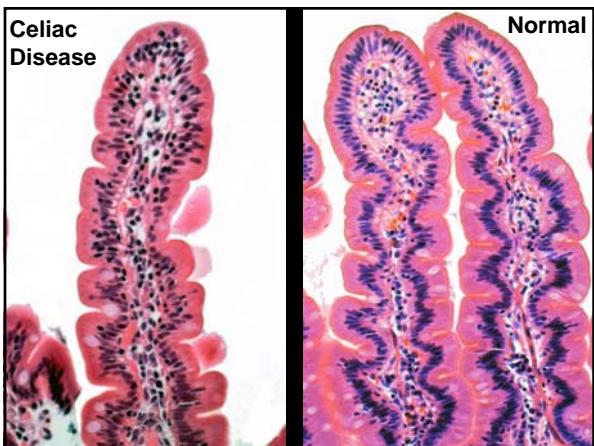
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A side-by-side comparison of two histological sections of intestinal tissue. The left section, labeled 'Celiac Disease', shows a significant reduction in the height of the villi and an increase in the number of lymphocytes and plasma cells within the lamina propria. The right section, labeled 'Normal', shows healthy, tall villi with a normal distribution of immune cells.



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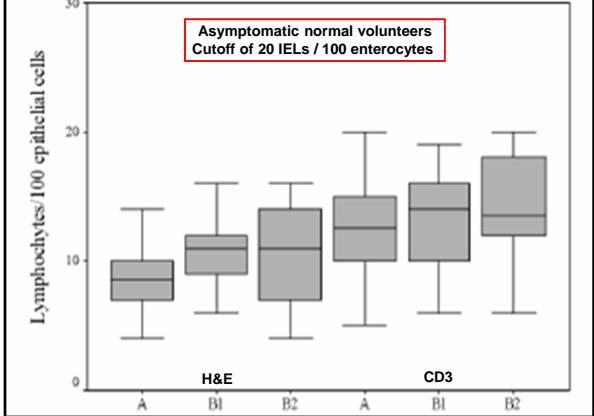
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Veress B et al. Scand J Gastroenterol 2004; 39:138-44.



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**CD3 Immunostain  
(don't do this)**



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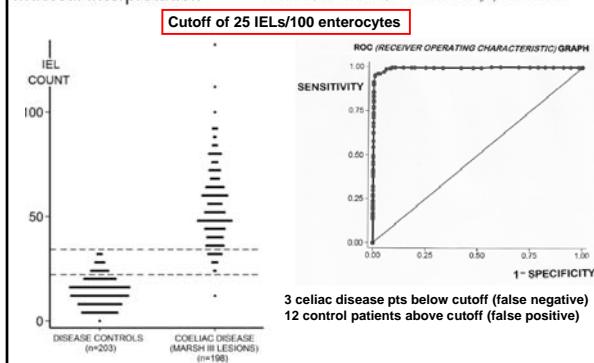
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**ROC-king onwards: intraepithelial lymphocyte counts, distribution & role in coeliac disease mucosal interpretation**

Rostami K, et al. Gut 2017;0:1–7, doi:10.1136/gutjnl-2017-314297



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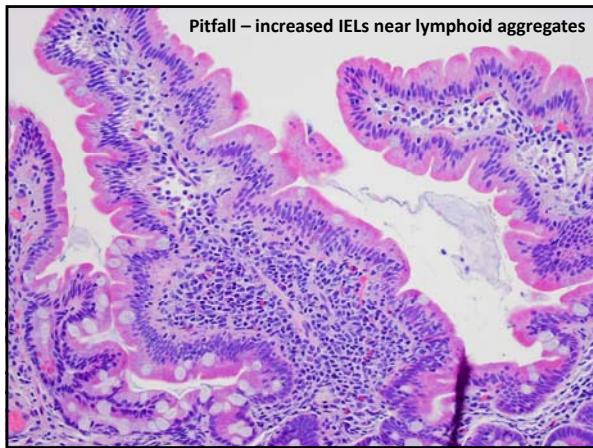
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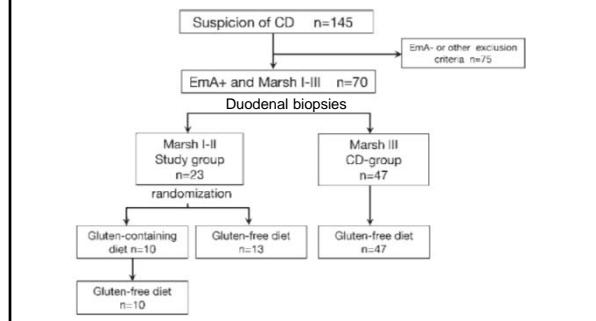
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**Diagnosing Mild Enteropathy Celiac Disease: A Randomized, Controlled Clinical Study**  
GASTROENTEROLOGY 2009;136:816–823

KALLE KURPPA,\* PEKKA COLLIN,<sup>†,§</sup> MERVI VILJAMAA,\* KATRI HAIMILA,<sup>¶</sup> PÄMI SAAVALAINEN,\* JUKKA PARTANEN,\* KAUJA LAURILA,<sup>\*\*</sup> HEINI HUHTALA,<sup>\*\*</sup> KAUJA PAASIKIVI,<sup>¶</sup> MARI-OU MÄKI,<sup>\*</sup> and KATRI KAUKNEN<sup>‡,§</sup>




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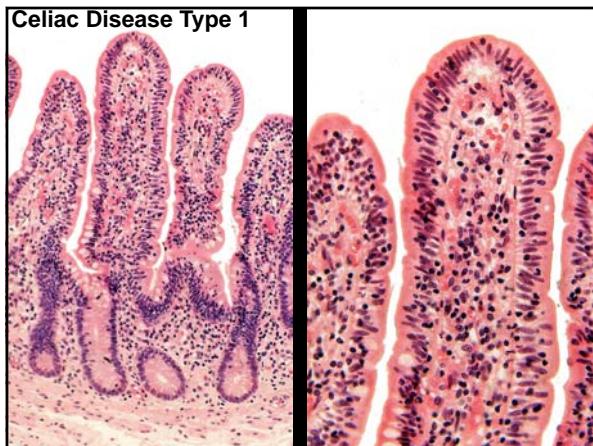
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**Celiac Disease Type 1**




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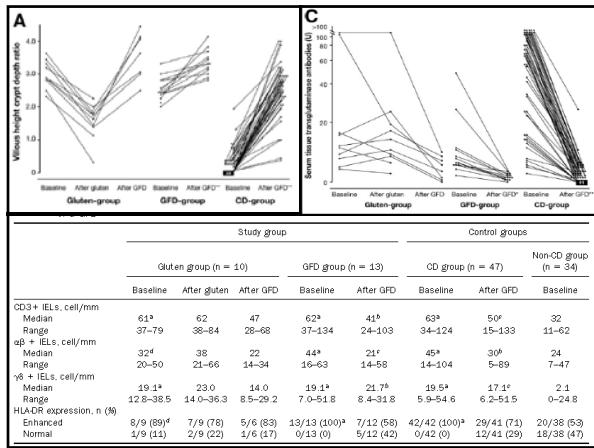
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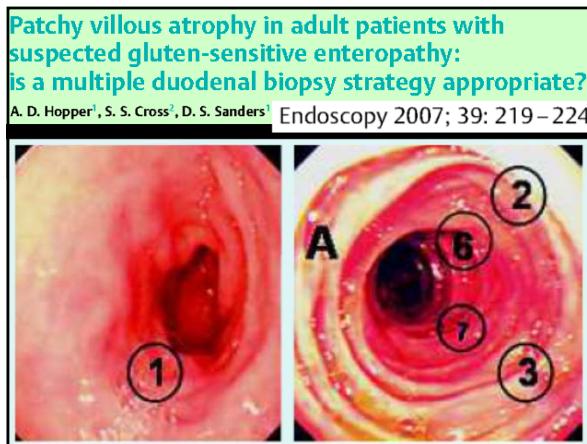


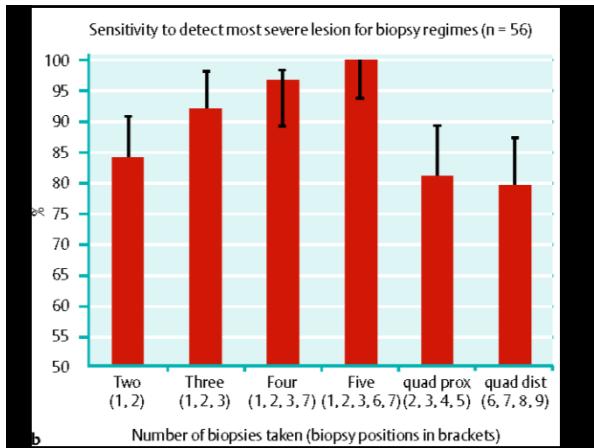
**Celiac Disease without Villous Atrophy in Children: A Prospective Study**

Kalle Kurppa, MD, Merja Ashorn, MD, PhD, Sari Itanen, MD, PhD, Lotta L. E. Koskinen, PhD, Päivi Saavalainen, PhD, Outi Koskinen, MD, Markku Mäki, MD, PhD, and Katri Kaukinen, MD, PhD  
(J Pediatr 2010;157:373-80).

**Table II.** Baseline and follow-up data on the 17 children who were endomysial antibody positive with normal small-bowel mucosal villous morphology at baseline

Sex	Age, years	Main symptoms	Baseline			Follow-up			Intervention	Symptoms	EmA	Tg2-ab U	Marsh grade
			EmA titr	Tg2-ab U	Marsh grade	EmA titr	Tg2-ab U	Marsh grade					
1 F	6	Abdominal pain	1:1000	33.2	1	Gluten	Remained	1:1000	40.6	3			
2 M	10	Asymptomatic <sup>a</sup>	1:500	28.2	1	Gluten	None	1:500	>120.0	3			
3 F	11	Abdominal pain	1:200	>120.0	1	Gluten	Remained	ND <sup>b</sup>	ND	3			
4 M	11	Abdominal pain	1:200	36.4	1	Gluten	Remained	1:200	19.5	3			
5 F	10	Diarrea	1:50	5.0	1	Gluten	Remained	1:500	13.9	3			
6 F	17	Abdominal pain	1.5	47.0	1	Gluten	Remained	1:500	3				
7 F	6	Flatulence	1.5	9.4	1	Gluten	Remained	1:50	15.2	0			
8 F	13	Abdominal pain	1.5	5.0	0	Gluten	Remained	1:50	1.5	3			
9 F	11	Diaraea	1:1000	52.5	1	GFD	None	1:<5	<5.0	ND <sup>b</sup>			
10 M	4	Weight loss	1:200	13.6	1	GFD	Alleviated	1:<5	<5.0	ND <sup>b</sup>			
11 M	5	Abdominal pain	1:100	10.3	1	GFD	None	1:<5	<5.0	ND <sup>b</sup>			
12 F	13	Diaraea	1:100	5.2	1	GFD	None	1:<5	<5.0	ND <sup>b</sup>			
13 F	5	Abdominal pain	1.5	7.4	0	GFD	None	1:<5	<5.0	ND <sup>b</sup>			
14 F	15	Abdominal pain	1:100	16.3	0	ND <sup>b</sup>	ND	ND	ND	ND			
15 M	10	Abdominal pain	1:50	6.4	1	ND <sup>b</sup>	ND	ND	ND	ND			
16 F	16	Poor growth	1:50	5.5	1	ND <sup>b</sup>	ND	ND	ND	ND			
17 M	11	Weight loss	1.5	<5.0	1	ND <sup>b</sup>	ND	ND	ND	ND			





**Duodenal Bulb Biopsies in Celiac Disease: A Multicenter Study**  
*J Pediatr Gastroenterol Nutr. Vol. 47, No. 5, November 2008*

\*Margherita Bonamico, \*Enina Thanasi, \*Paolo Mariani, \*Raffaella Nenna,  
 †Rita Pia Lara Luparini, †Cristiana Barbera, †Isabella Morni, †Pietro Letro,  
 ‡Graziella Guariso, ‡Costantino De Giacomo, §Serenella Scotta, †Stefano Pontone,  
 \*\*Francesco Carpino, \*\*Fabio Massimo Magliocca, and the Società Italiana di Gastroenterologica,  
 Epatoologia, e Nutrizione Pediatrica

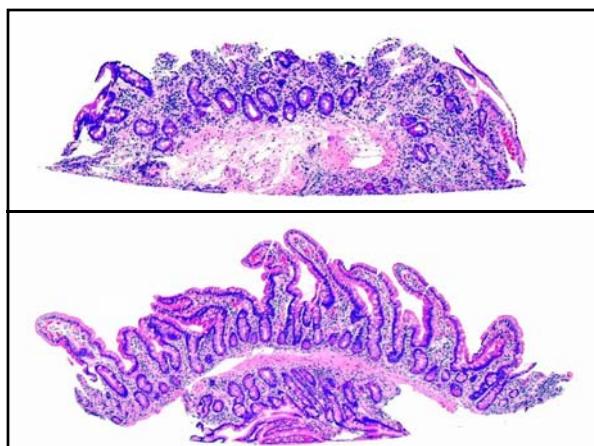
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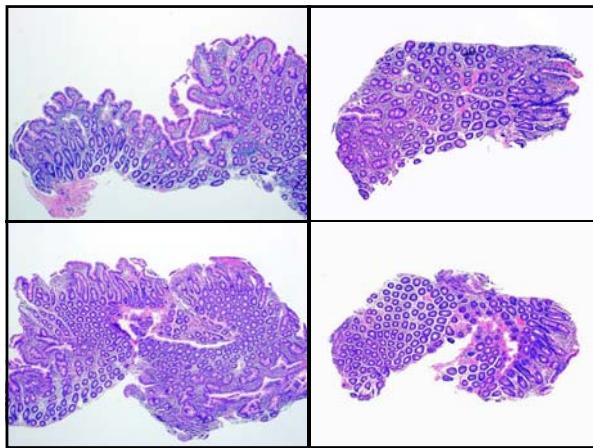
**One biopsy of duodenal bulb and four of the distal duodenum**

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Patients (no.)	Group 1A (16)	Group 1B (20)	Group 1C (629)
Type 1 (%)	1 (6.25)	1 (5)	23 (3.67)
Type 2 (%)	1 (6.25)	0	19 (3.02)
Type 3a (%)	1 (6.25)	1 (5)	76 (12.08)
Type 3b (%)	4 (25)	5 (25)	240 (38.15)
Type 3c (%)	9 (56.25)	13 (65)	271 (43.08)

CD = celiac disease; group 1A: only bulbar lesions; group 1B: lesions patchily distributed; group 1C: diffuse lesions.






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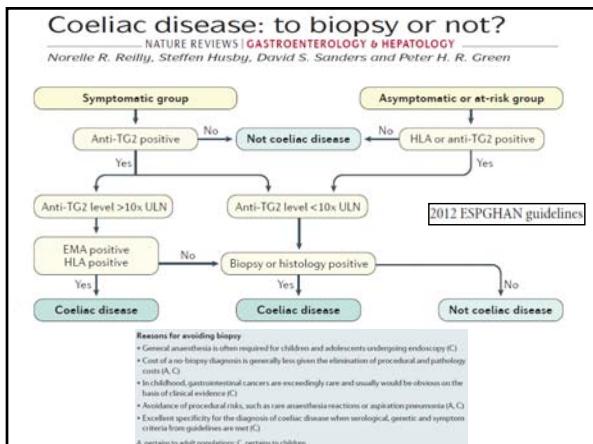
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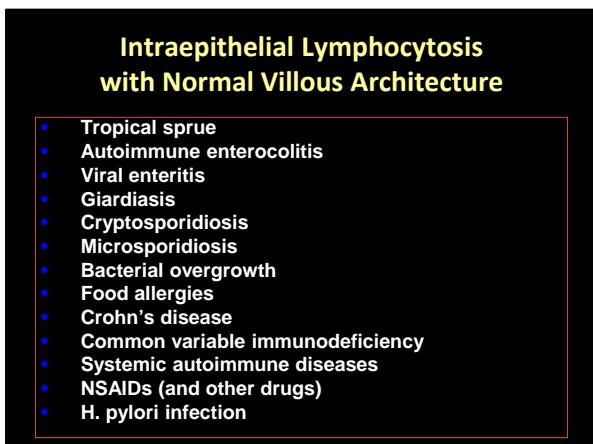
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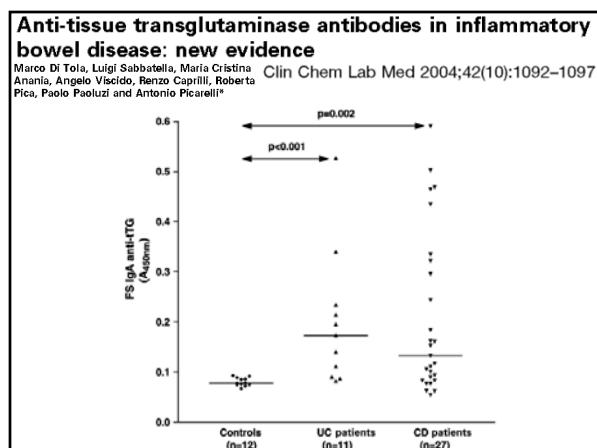
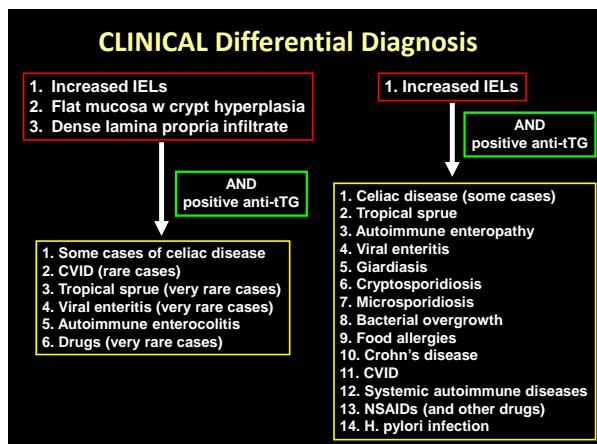
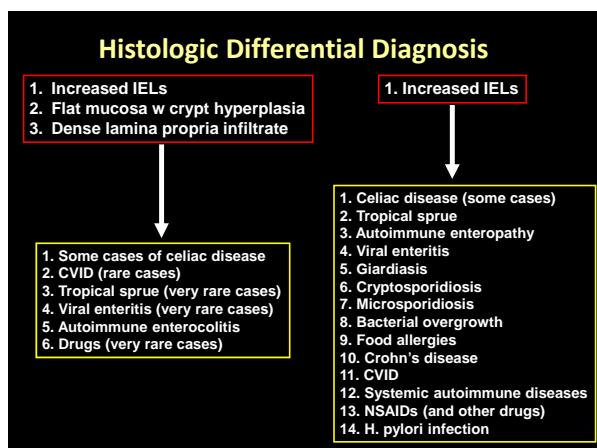
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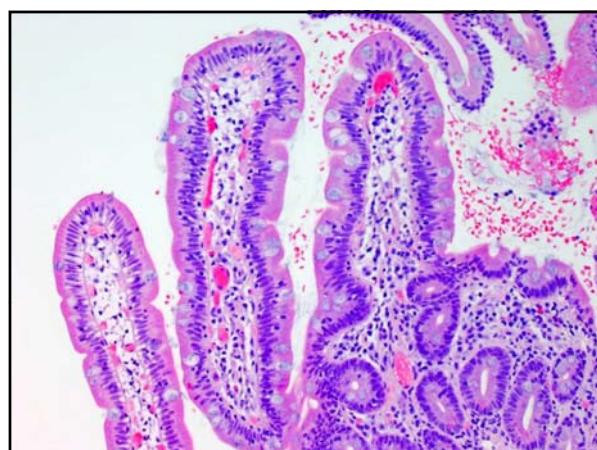
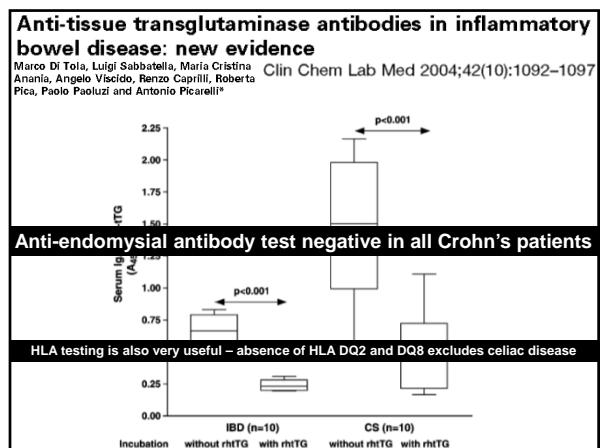
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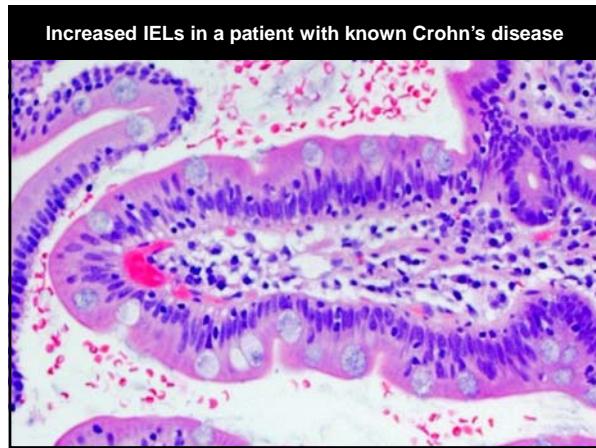
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### Refractory Sprue Clinical Features

- Redefine diarrhea while on a GFD
- Usually elderly and with weight loss
- There should be a well established Dx of CD

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### Refractory Sprue Causes

- Inadvertent gluten ingestion
- Lymphocytic or collagenous colitis
- Ulcerative jejuno-ileitis (lymphoma)
- Enteropathy associated T-cell lymphoma
- Collagenous sprue
- Pancreatic insufficiency
- Food allergy
- Nutrient deficiency (zinc, folic acid)

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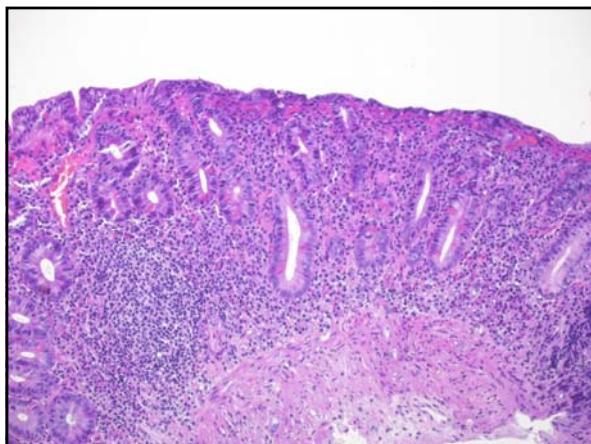
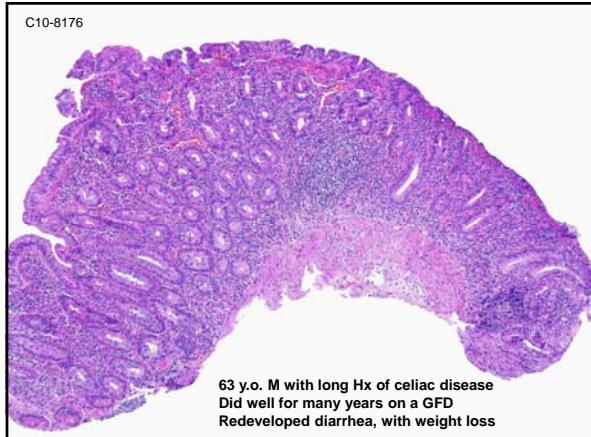
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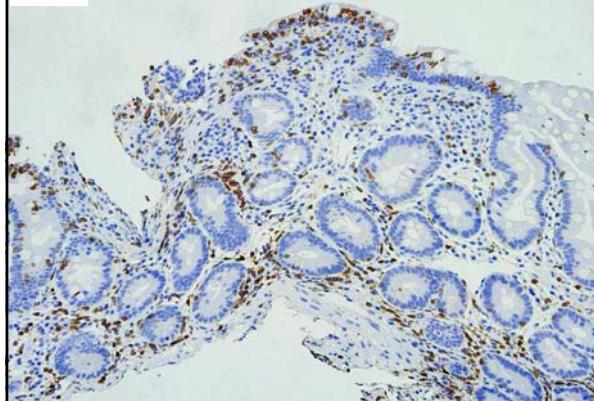
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## Refractory Sprue Pathologic Features

- Persistent abnormal histology while on a GFD:
  - Usually there is severe villous blunting
  - Usually there is a marked increase in IELs
- Type 1:
  - IELs normally express CD3 with CD4 or CD8
  - Polyclonal by T-cell receptor gene rearrangement studies
- Type 2:
  - IELs CD3+ but CD8- and CD4- (and TCR-beta -)
  - Clonal T-cell receptor gene population

Patey-Mariaud De Serre N. et al. Histopathology 2000; 37:70-7.



**CD3**

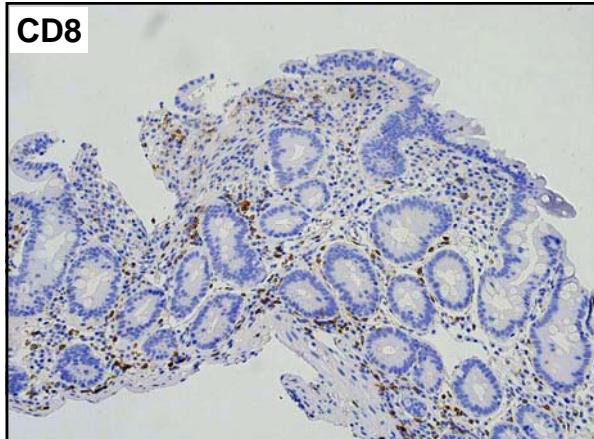
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**CD8**

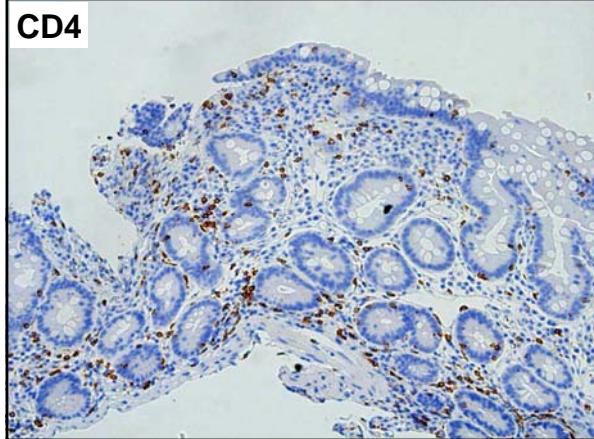
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**CD4**

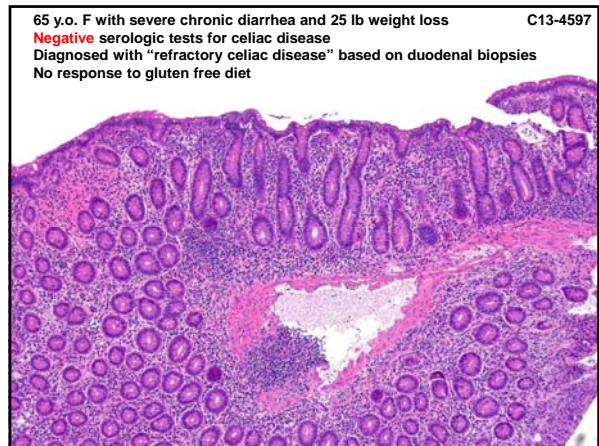
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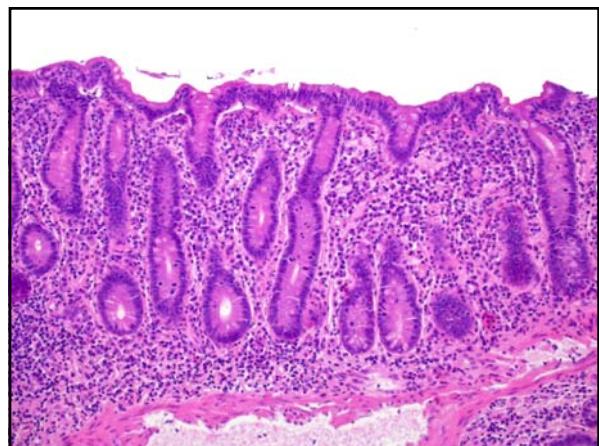
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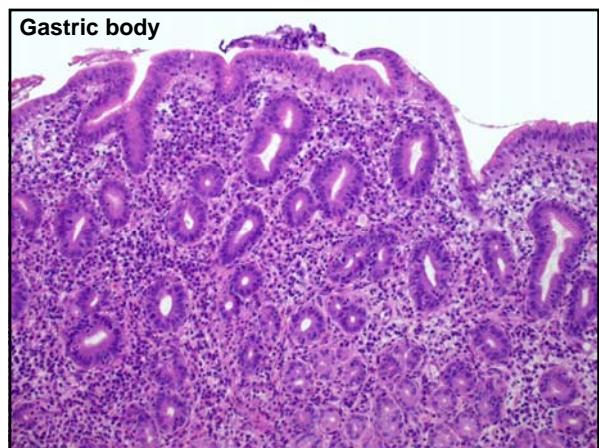
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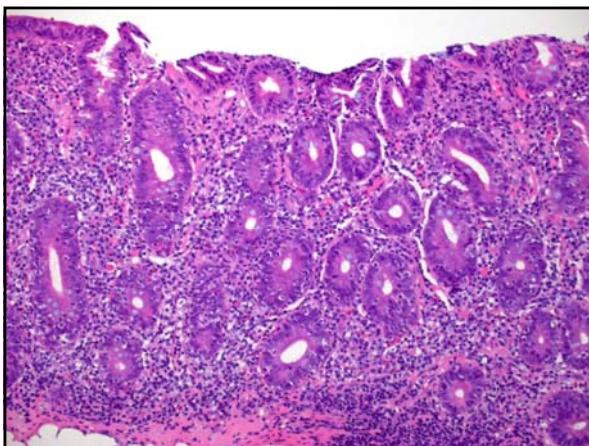
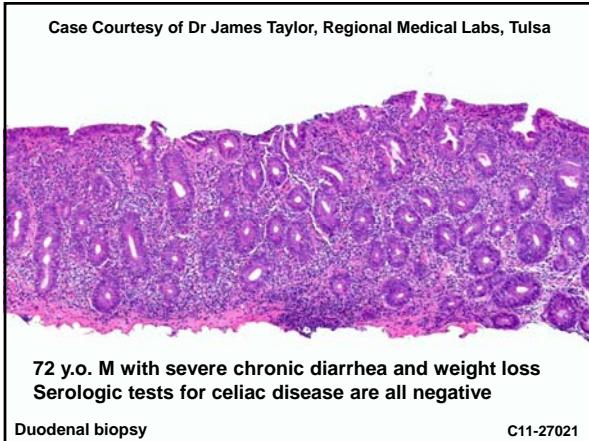
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## Severe Spruelike Enteropathy Associated With Olmesartan

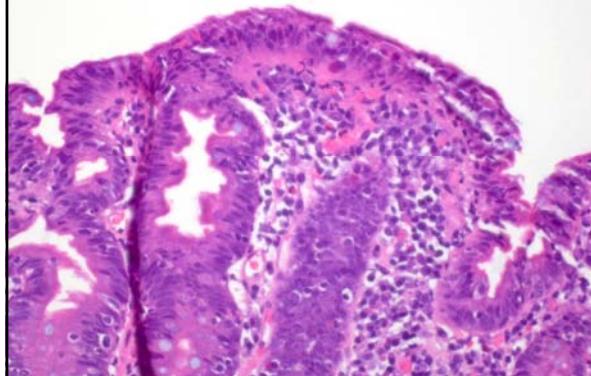
Mayo Clin Proc. 2012;87(8):732-738

TABLE 2. Histologic Findings in 22 Patients With Spruelike Enteropathy Associated With Olmesartan\*

Patient No.	Villous atrophy	Ela (1/100)	Audiactive inflammation	Thickened collagen band (refraction)	Absent villus	Outcome following discontinuation of olmesartan	Baseline duodenal biopsy results		Time (d) <sup>a</sup>	Other GI findings <sup>b</sup>	
							Normal	No		Gastric	Colorectal
1 Total	Normal	Yes	No	No/NA	Normal	404	Lymphocytic gastritis (H&P negative, immunostain)	NA	54	Collagenous gastritis	Normal
2 Total	80-100	Yes	Yes	No/NA	Improvement, focal partial villous atrophy	NA	Chronic gastritis (H&P negative, immunostain)	NA	NA	Collagenous gastritis	Normal
3 Total	Normal	Yes	No	No/NA	Normal	231	NA	NA	NA	Collagenous gastritis	NA
4 Total	40	Yes	Yes	No/NA	Normal	263	Collagenous gastritis	NA	NA	NA	Normal
5 Total	>100	Yes	No	NA/NA	Normal	54	NA	NA	NA	NA	Normal
6 Partial	40	Yes	No	NA/NA	NA	NA	NA	NA	NA	NA	Normal
7 Partial	30-50	Yes	No	NA/NA	Normal	129	NA	NA	NA	NA	Normal
8 Total	40-60	Yes	No	NA/NA	Normal	143	Lymphocytic gastritis (H&P negative, immunostain)	NA	NA	NA	Normal
9 Total	60-80	Yes	No	No/NA	Normal	188	NA	NA	NA	NA	Normal
10 Partial	Normal	No	No	No/NA	Normal	404	NA	NA	NA	NA	Normal
11 Partial	50	Yes	No	No/NA	NA	NA	Mild lymphocytic gastritis (H&P negative, immunostain)	NA	NA	NA	Normal
12 Partial	Normal	Yes	No	No/NA	Normal, focal active enteritis	116	Mild active chronic gastritis (H&P negative, immunostain)	Mild active chronic gastritis	NA	NA	Normal
13 Total	40	Yes	Yes	NA/NA	Normal	171	Active chronic gastritis (H&P negative, immunostain)	NA	NA	NA	Normal
14 Partial	60-80	No	No	NA/NA	Normal	240	Mild active chronic gastritis (H&P negative, immunostain)	NA	NA	NA	Normal
15 Total	Normal	No	Yes	NA/NA	Normal	181	Mild chronic gastritis (H&P negative, no immunostain)	Normal	NA	NA	Normal
16 Total	Normal	No	Yes	No/NA	Normal	407	Collagenous gastritis	NA	NA	NA	Normal
17 Total	40-40	Yes	Yes	No/NA	NA	NA	Mild chronic gastritis (H&P negative, no immunostain)	Focal acute colitis	NA	NA	Normal
18 Partial	Normal	No (marked eosinophilia)	No	NA/NA	NA	NA	NA	NA	NA	NA	Normal
19 Total	30	Yes	No	NA/NA	Normal	76	Severe active chronic gastritis and ulceration (H&P negative, immunostain)	NA	NA	NA	Normal
20 Total	Normal	No	Yes	No/NA	Normal	207	Lymphocytic gastritis (H&P positive)	NA	NA	NA	Normal
21 Total	80-100	Yes	No	NA/NA	Normal	179	NA	NA	NA	NA	Normal
22 Total	80	Yes	No	NA/NA	Normal	184	Lymphocytic gastritis (H&P negative, immunostain)	NA	NA	NA	Normal



"collagenous sprue"



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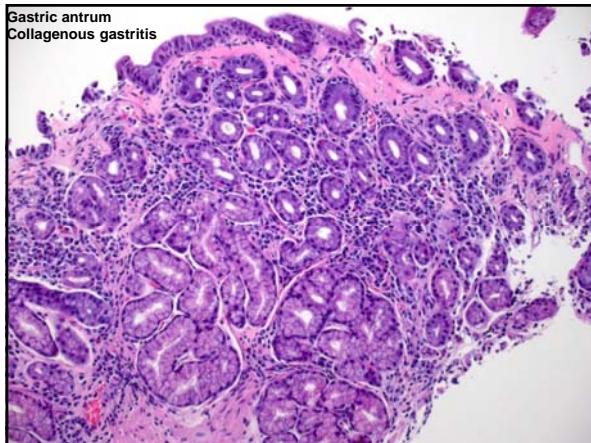
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Gastric antrum  
Collagenous gastritis



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### Olmesartan Induced Enteropathy

- Angiotensin II receptor antagonist
- Commonly used to treat hypertension
- Clinical presentation:
  - Diarrhea begins 2-10 years after drug is started
  - Chronic watery diarrhea and weight loss
  - Celiac-like histology (+/- collagen thickening)
  - +/- coexistent lymphocytic or collagenous gastritis
  - +/- coexistent lymphocytic or collagenous colitis
  - Negative serologic tests for celiac disease
  - Diagnosis of "refractory sprue"
  - No response to a gluten free diet
  - Responds slowly to withdrawal of medication

Scialom S et al. PLoSOne 2015; 10:e0125024.

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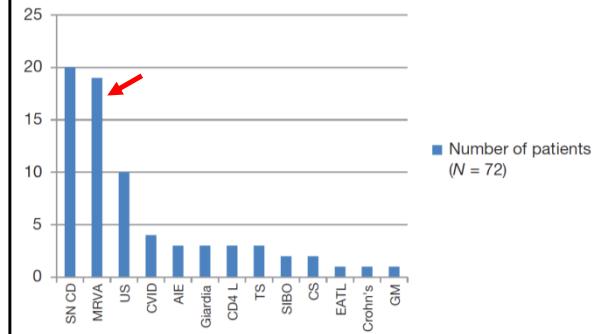
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## Villous Atrophy and Negative Celiac Serology: A Diagnostic and Therapeutic Dilemma

*Am J Gastroenterol* 2013;108:647–653

Marisa DeGaetani, MD<sup>1,2</sup>; Christina A. Temnyson, MD<sup>2</sup>; Benjamin Lebowitz, MD, MS<sup>1,2</sup>; Suzanne K. Lewis, MD<sup>1,2</sup>; Hussein Abu Daya, MD<sup>2</sup>; Carolina Arguelles-Grande, MD<sup>3</sup>; Govind Bhagat, MBBS<sup>3</sup> and Peter H.R. Green, MD<sup>1,2</sup>



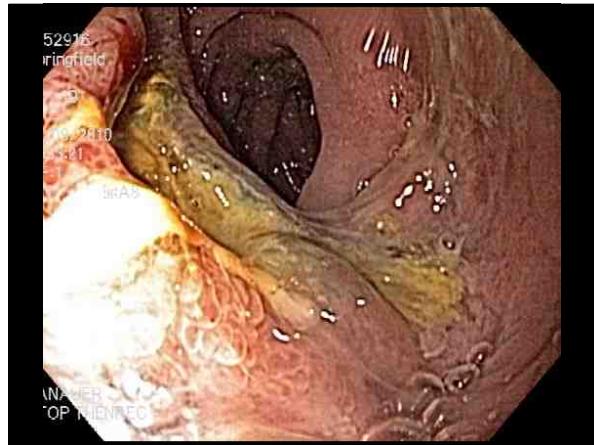
## Villous Atrophy and Negative Celiac Serology: A Diagnostic and Therapeutic Dilemma

*Am J Gastroenterol* 2013;108:647–653

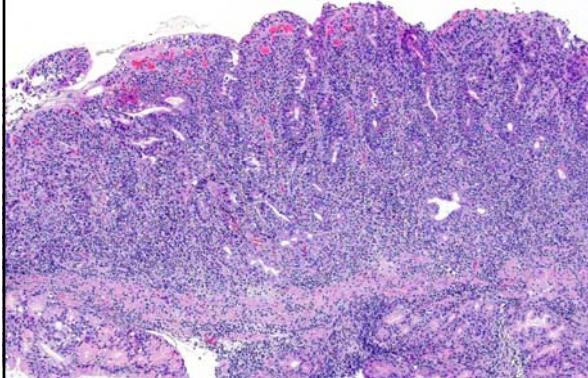
oxcarbazepine

Table 3. Medication-related villous atrophy

No.	Age (yrs/ex)	HLA DQ2/8	Culprit med?	Degre of initial bx	Increase in epithelial collagen	Increase in IEL on bx	GFD	Clinical improv./Abx	Clinical improv./Abx	Clinical improv./IS	Relapse off IS?	Clinical improv. after stopping med
1	61M	+	Olmesartan	TVA	+	+	—	+	?	+	+	+
2	73F	+	Olmesartan	TVA	+	+	+	—	NA	+	+	+
3	82M	NT	Olmesartan	PVA	+	+	—	+	?	+	+	+
4	63M	+	Olmesartan	STVA	+	+	—	—	NA	+	+	+
5	69F	—	Olmesartan	TVA	+	+	—	—	NA	+	+	+
6	66M	+	Olmesartan	TVA	+	+	—	+	+	+	+	+
7	75F	+	Olmesartan	DNS	+	+	—	+	+	+	+	?
8	63F	+	Olmesartan	TVA	+	+	—	—	NA	+	+	+
9	52M	NT	Olmesartan	STVA	—	—	—	+	—	+	+	+
10	58F	+	Olmesartan	PVA	+	—	—	—	NA	+	+	+
11	83M	+	Olmesartan	DNS	—	+	—	+	—	+	+	+
12	67F	+	Olmesartan	PVA	+	—	+	+	—	+	+	+
13	75M	+	Olmesartan	TVA	—	—	+	—	NA	+	+	+
14	68F	+	Olmesartan	TVA	—	+	—	+	—	+	+	+
15	62M	+	Olmesartan	TVA	+	+	—	+	—	+	+	+
16	64F	NT	Olmesartan	DNS	—	—	—	—	NA	+	+	+
17	74F	+	MMF	PVA	+	—	+	—	—	NA	NA	NA
18	57F	NT	MMF	PVA	—	—	—	NA	—	NA	NA	NA
19	67F	NT	Methotrexate	PVA	—	—	+	—	NA	NA	NA*	NA



**Enteropathy Associated T-cell Lymphoma (EATL)**



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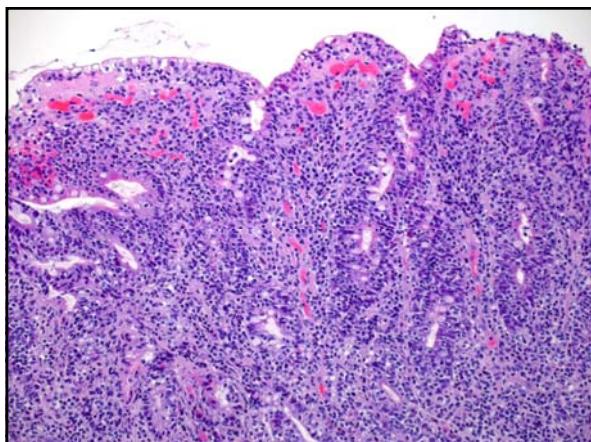
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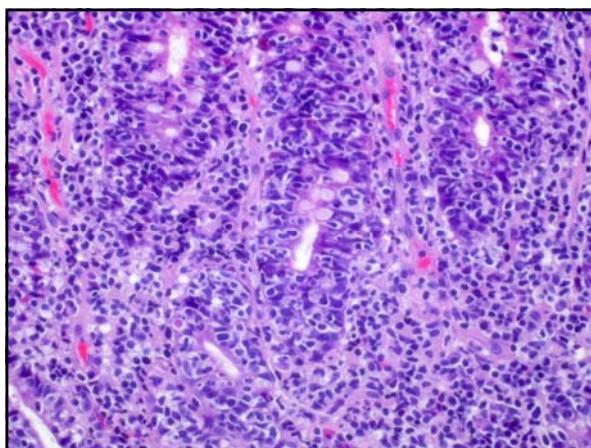
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### Ulcerative Jejuno-ileitis



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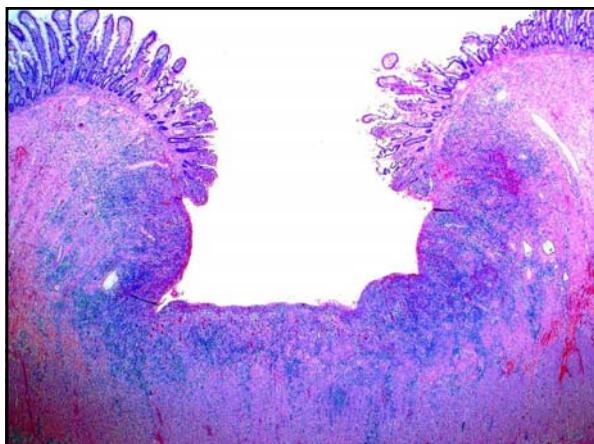
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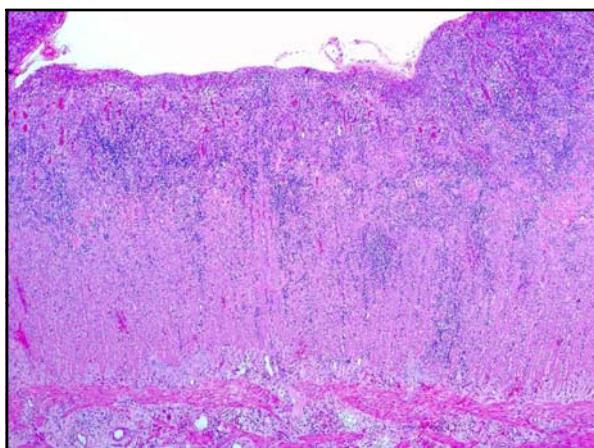
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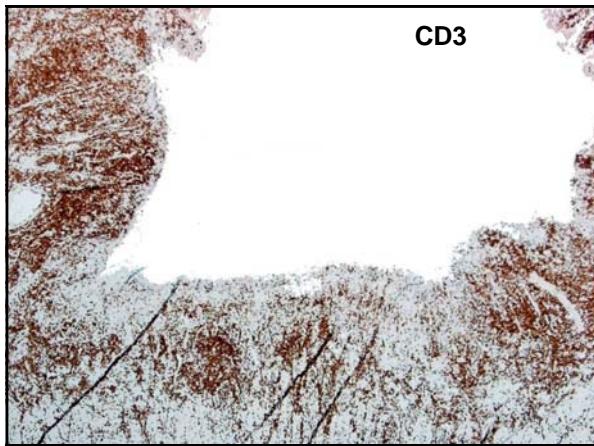
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C11-25813

### Clinical History

- 31 y.o. M with a long history of non-bloody diarrhea
- 25 lb weight loss over the past two years (118 lbs.)
- Diagnosed with diabetes, but no weight gain with oral hypoglycemic agents
- Upper endoscopy:
  - Scalloped duodenal folds
  - Biopsies reveal features consistent with celiac disease
- Celiac HLA and serology panel:
  - DQ2 positive
  - IgA deficient (IgA less than 5)
  - Anti-gliadin IgG positive
- Placed on GFD – continued diarrhea; no weight gain
- Repeat upper endoscopy with duodenal biopsies

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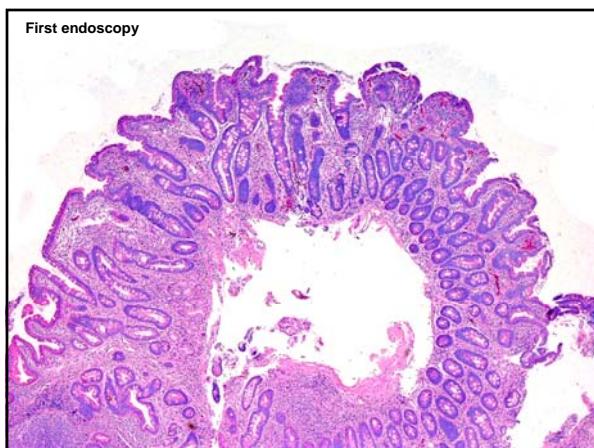
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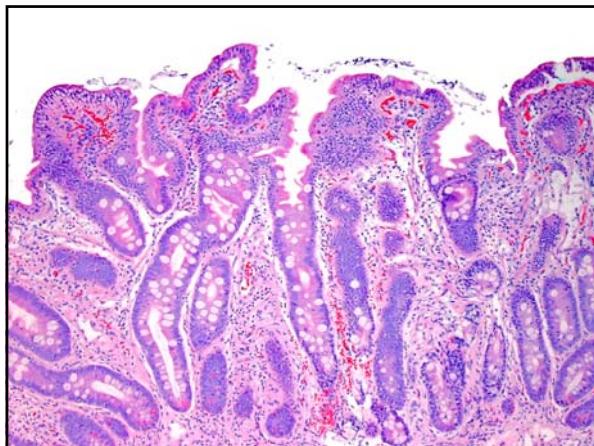
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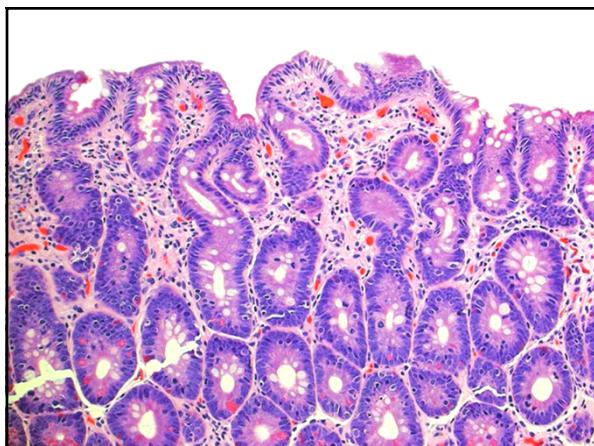
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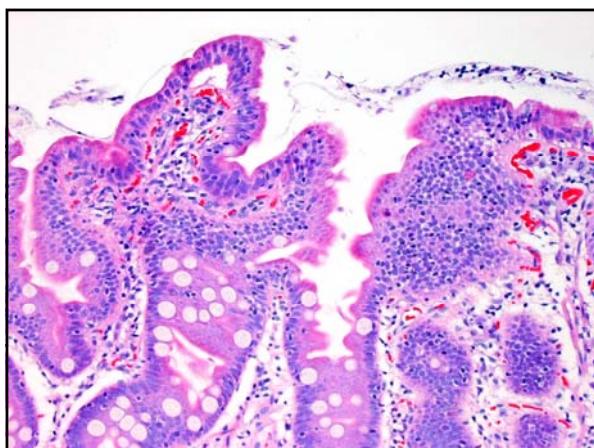
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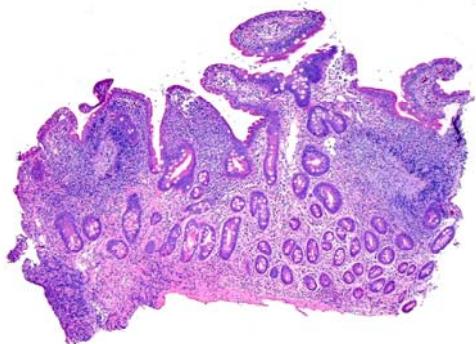
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Repeat endoscopy



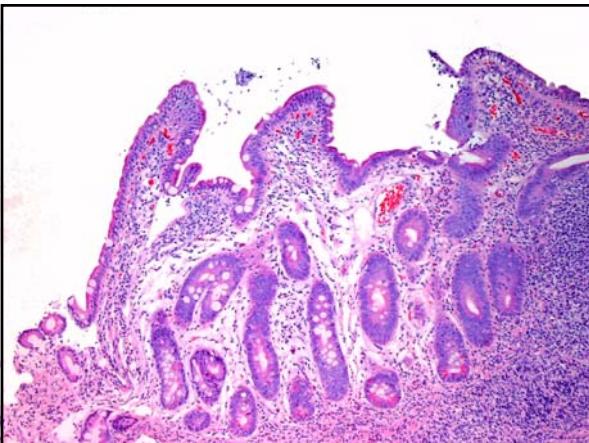
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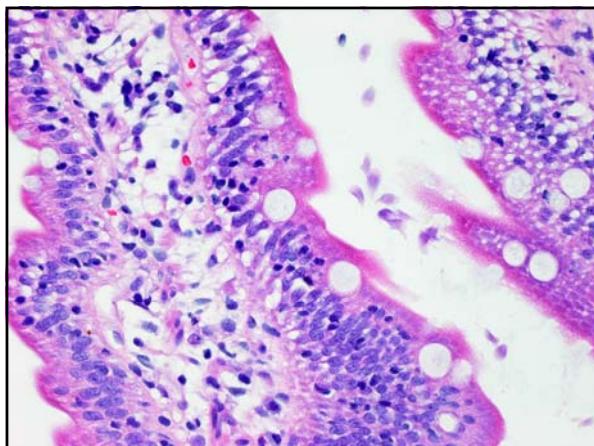
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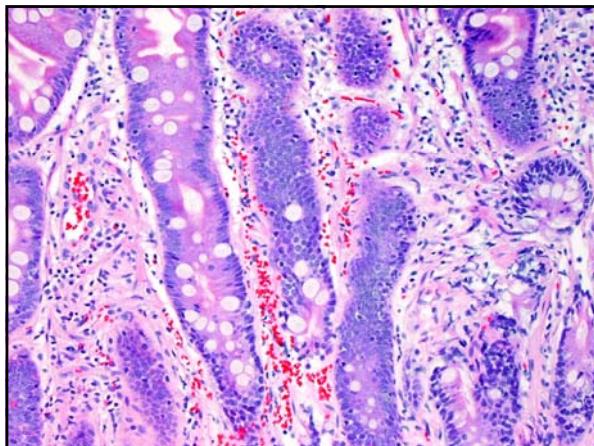
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#### Additional Laboratory Evaluation

- DGP IgG negative
- Iron, vitamin D, zinc & folate deficient
- Quantitative immunoglobulin levels:
  - IgA = < 5 (110-490 mg/dL)
  - IgG = 410 (800-1700 mg/dL)
  - IgM = 6 (50-320 mg/dL)

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Dx: Common variable immunodeficiency with Giardia infection

#### Histologic Features distinct to CVID

- *Absent or greatly decreased* plasma cells
- Crypt cell apoptosis
- Significant neutrophilic infiltrates
- Mucosal lymphoid follicles
- Giardia lamblia infection

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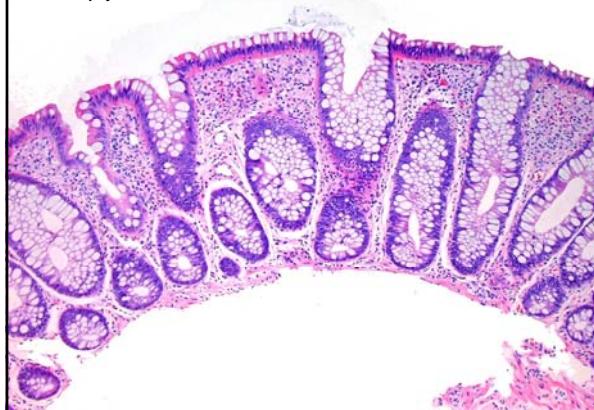
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Colon biopsy



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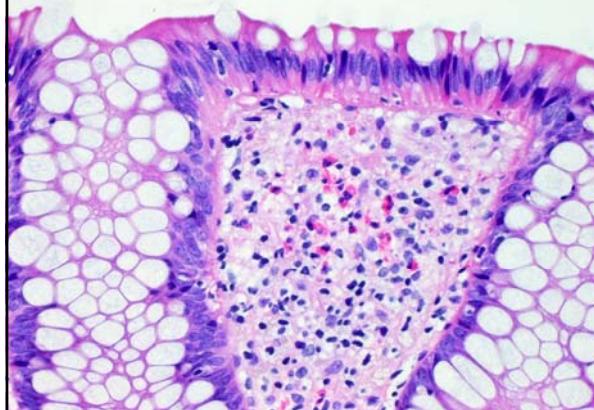
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Colon biopsy – no plasma cells!



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### The Enteropathy Associated With Common Variable Immunodeficiency: The Delineated Frontiers With Celiac Disease

*Am J Gastroenterol* 2010; 105:2262–2275;

Georgia Malamut, MD, PhD<sup>1-3</sup>, Virginie Verkarre, MD, PhD<sup>1,4</sup>, Felipe Suarez, MD<sup>1,5</sup>, Jean-François Viallard, MD, PhD<sup>6</sup>, Anne-Sophie Lascaux, MD<sup>7</sup>, Jacques Cosnes, MD, PhD<sup>8</sup>, Yoram Bouhnik, MD, PhD<sup>9</sup>, Olivier Lambotte, MD, PhD<sup>10</sup>, Dominique Béchade, MD, PhD<sup>11</sup>, Marianne Ziol, MD, PhD<sup>12</sup>, Anne Lavergne, MD, PhD<sup>13</sup>, Olivier Hermine, MD, PhD<sup>1,5</sup>, Nadine Cerf-Bensussan, MD, PhD<sup>1,3</sup> and Christophe Cellier, MD, PhD<sup>1-3</sup>

#### 50 patients with CVID and duodenal biopsies

- Mean age at diagnosis of CVID was 36.8 +/- 15.6 yrs
- Mean onset of GI symptoms was 34.5 +/- 14.3 yrs
- Anemia in 56% and malabsorption in 54%
- DQ2 or DQ8 in 77% of tested patients
- 31 of 50 (62%) with increased duodenal IELs
- 21 of 31 (67%) with inc. IELs had villous atrophy
- 3 of 38 patients tested positive celiac serologic tests
- No response to gluten free diet in 10 treated patients

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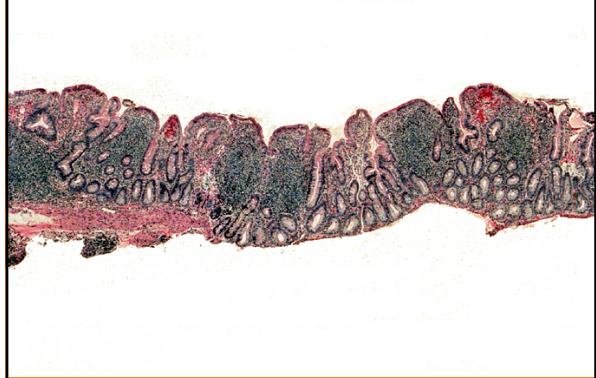
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### Nodular Lymphoid Hyperplasia



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### Clinical History

- 23-month-old M with failure to thrive and a 1 mo Hx of severe watery diarrhea.
- Diarrhea persisted despite discontinuation of oral feeding and administration of TPN.
- Serologic tests for celiac disease were all negative.
- HIV antibody test negative
- Duodenal biopsies obtained

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### Autoimmune Enterocolitis



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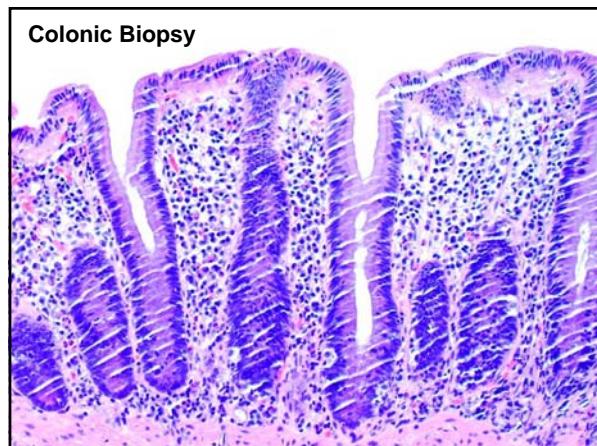
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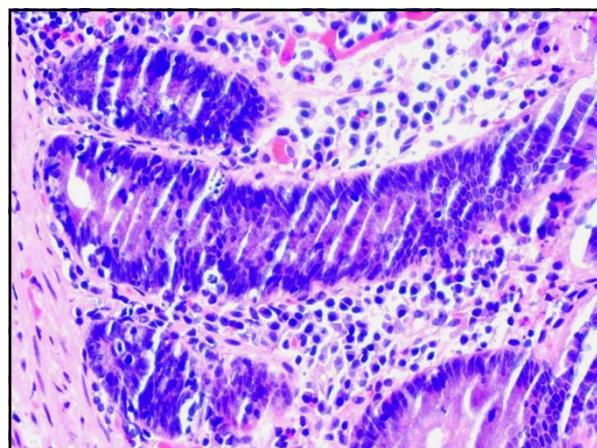
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## Autoimmune Enterocolitis

- Presentation in first year of life, or as adult
- Severe diarrhea, even when NPO on TPN
- Do not respond to gluten free diet
- Serologic tests for celiac disease negative
- Anti-enterocyte/goblet cell antibodies (non-specific)
- **Usually affects both small and large bowel**
- Duodenal morphology similar to celiac disease in some cases
- Treated with immunosuppressive drugs

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## Other Rare Neonatal Enteropathies

- Congenital transport protein defects:
  - Chloride-bicarbonate exchanger
  - Sodium-hydrogen exchanger
  - Ileal bile acid receptor
- Enterokinase deficiency
- Tufting enteropathy
- Microvillous inclusion disease
- IPEX syndrome

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## Crypt and Villous Atrophy Pattern

- Collagenous sprue
- Microvillous inclusion disease
- Drug toxicity:
  - cis-platinum
  - Vincristine
- Cow's milk protein intolerance

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## Clinical History

- 4-week-old F with poor weight gain and watery diarrhea and severe metabolic acidosis
- Diarrhea continued despite TPN and discontinuation of oral feedings
- Family history significant for a parental consanguineous marriage of cousins
- Older sibling died at 4 weeks of age of uncontrollable diarrhea

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Microvillous Inclusion Disease



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Microvillous Inclusion Disease



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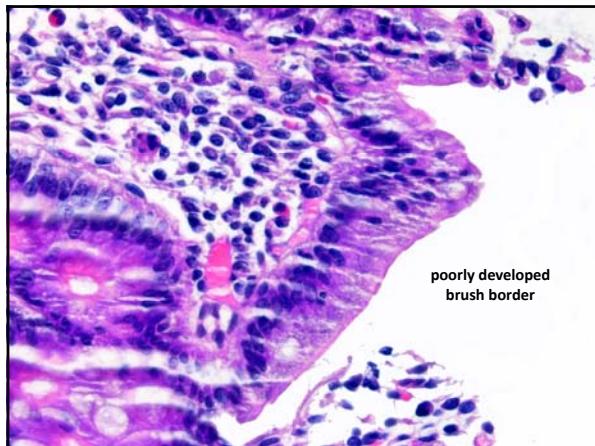
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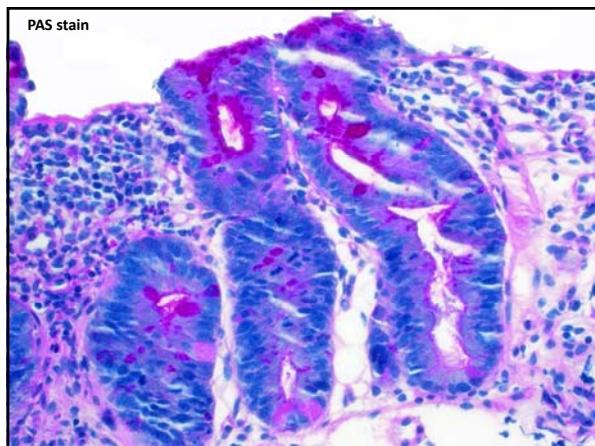
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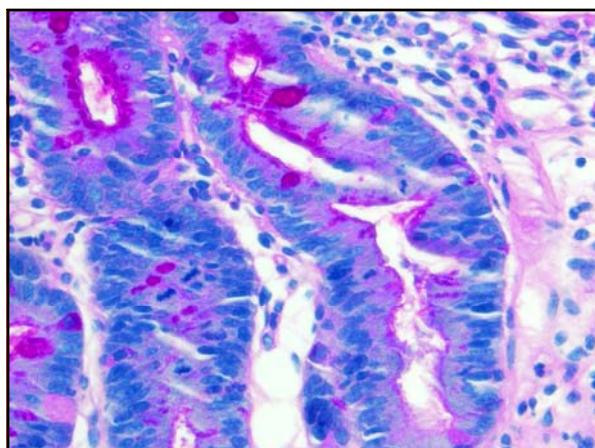
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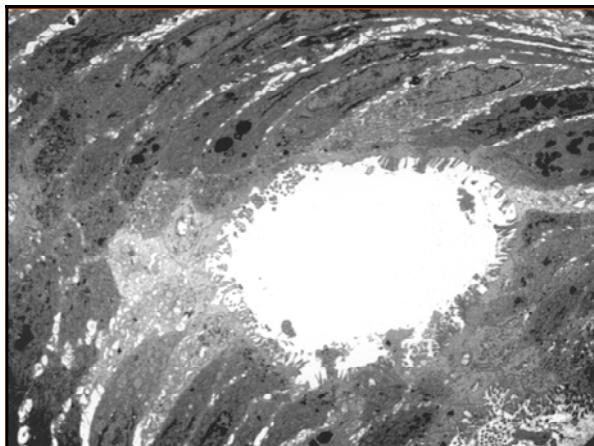
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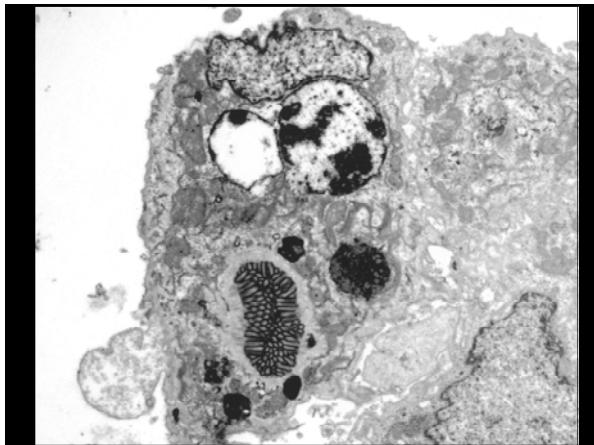
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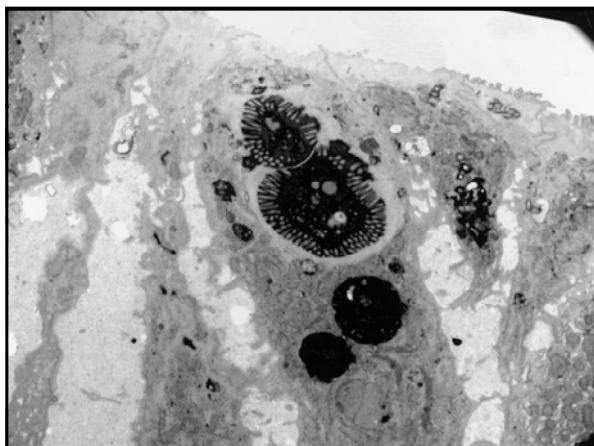
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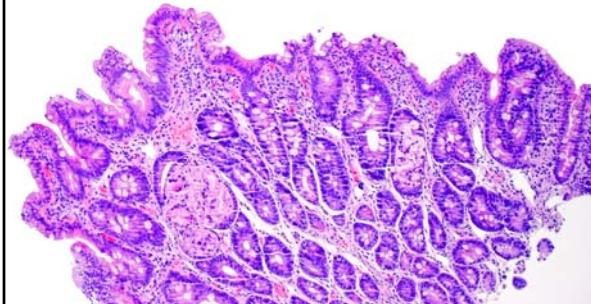
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**Tufting enteropathy**



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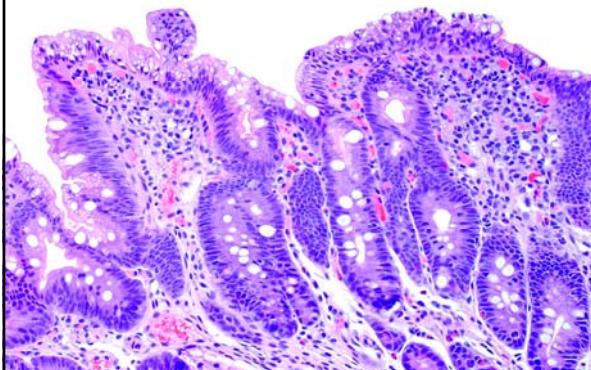
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**Tufting enteropathy**



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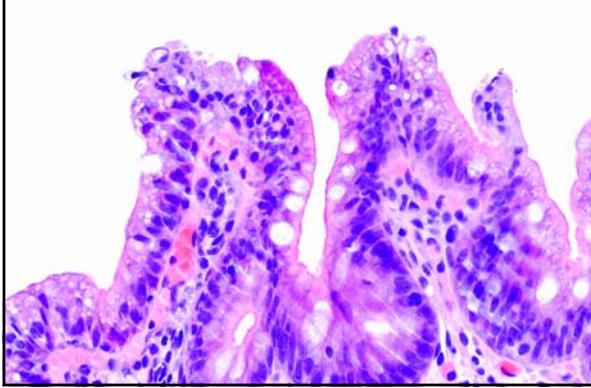
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**Tufting enteropathy**



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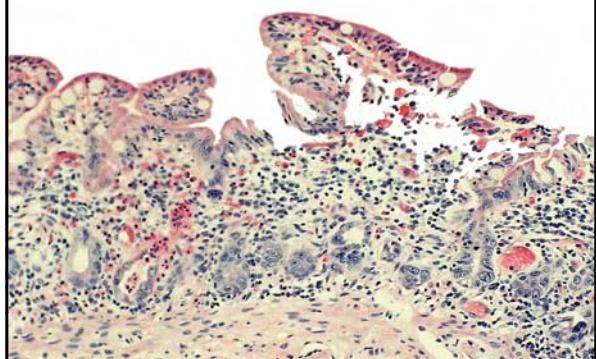
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8 y.o. F treated with procarbazine, CCNU, and vincristine  
for recurrent medulloblastoma



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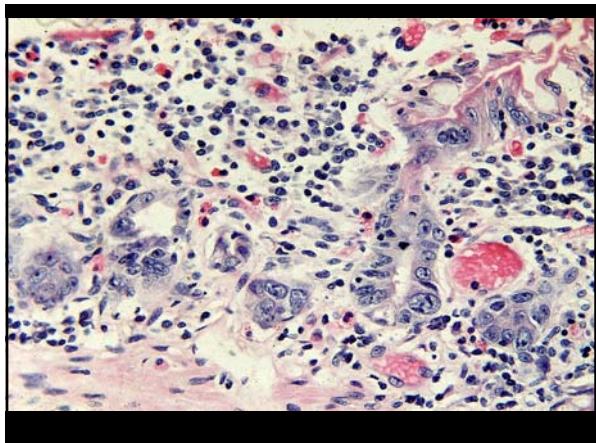
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5-week-old F with failure to thrive  
and a 3-week history of watery diarrhea



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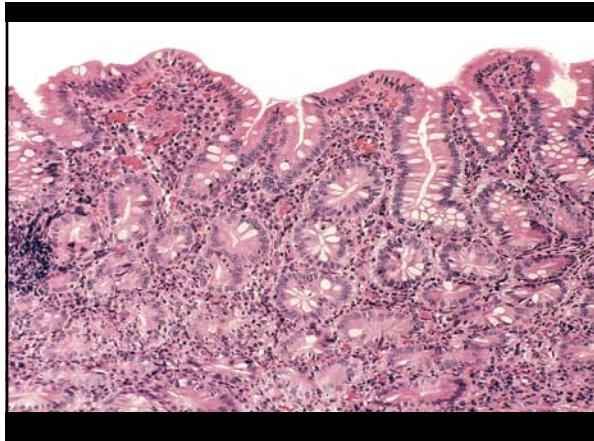
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### Cow's Milk Protein Intolerance

- Immune reaction to a variety of peptides within cow's milk
- Metabolic acidosis and blood in stool in severe cases
- Peripheral blood eosinophilia uncommon
- Tissue eosinophilia uncommon
- Can affect small or large bowel or both
- No specific test – RAST testing often performed
- Re-challenge necessary for definite diagnosis

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### Variable Villous Blunting with Crypt Hyperplasia

- Viral enteritis
- Tropical sprue
- Bacterial overgrowth
- Zollinger-Ellison syndrome
- Whipple disease
- *Mycobacterium avium intracellulare*
- CMV infection
- Cryptosporidium
- Isospora
- Microsporidium

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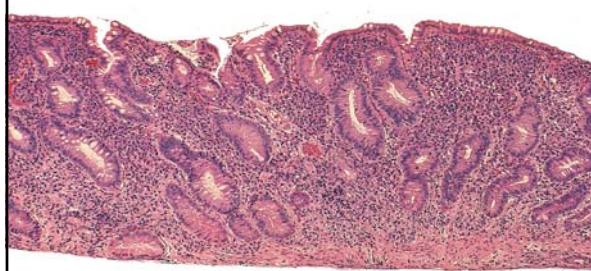
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### Viral Enteritis



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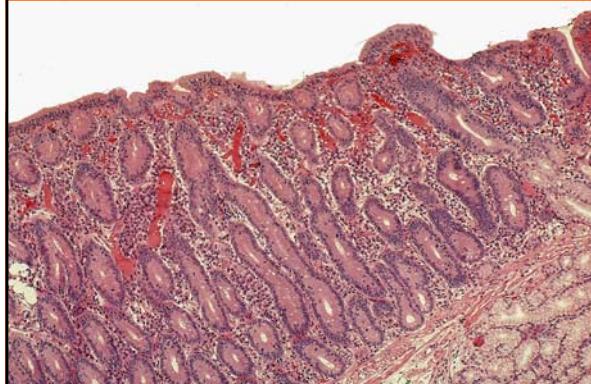
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### Tropical Sprue



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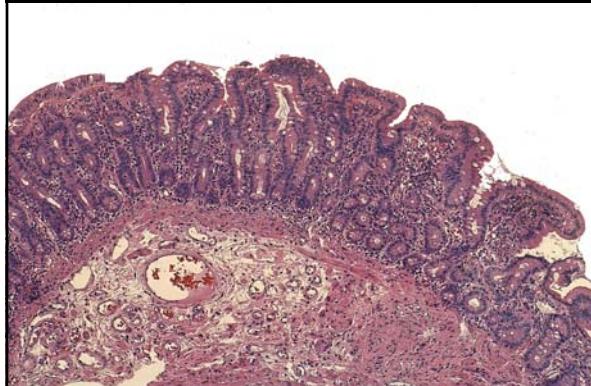
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### Bacterial Overgrowth



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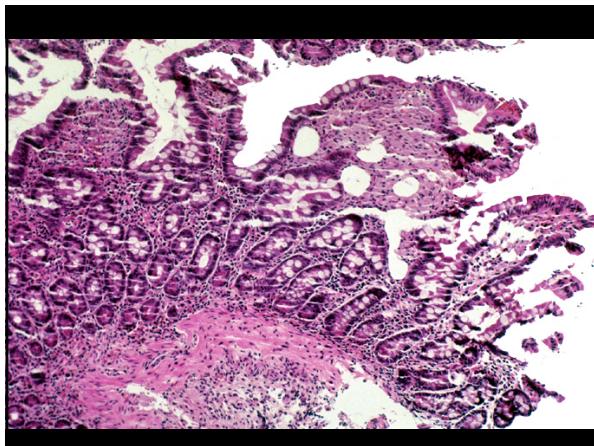
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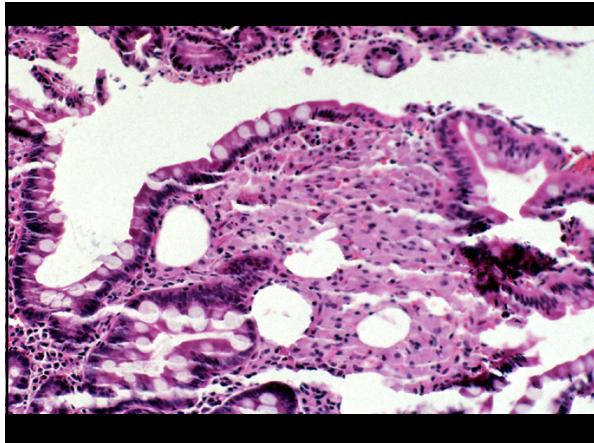
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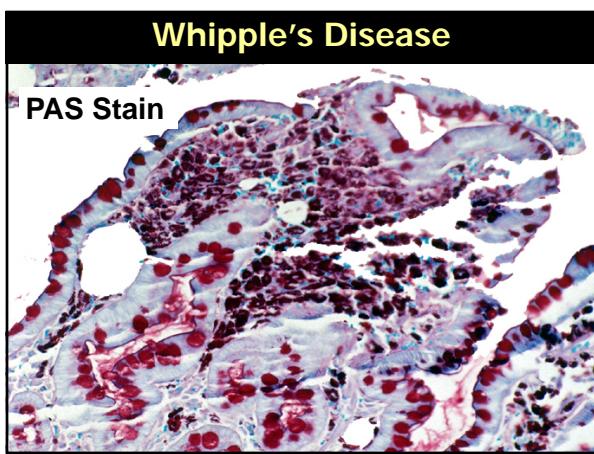
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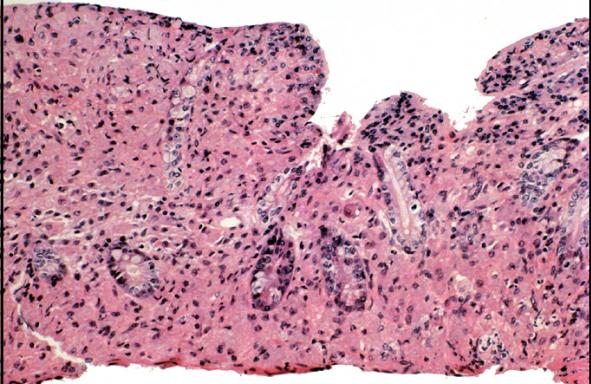
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**23 y.o. Male with AIDS**



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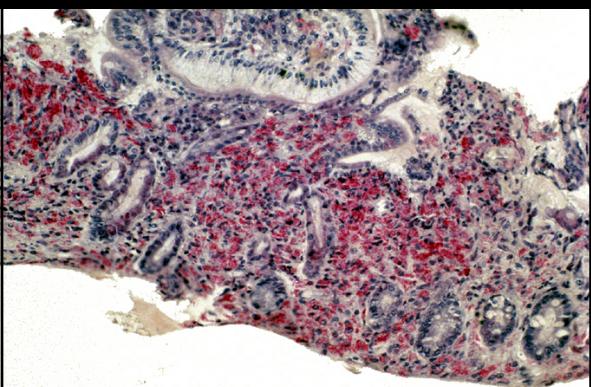
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**Fite Stain**



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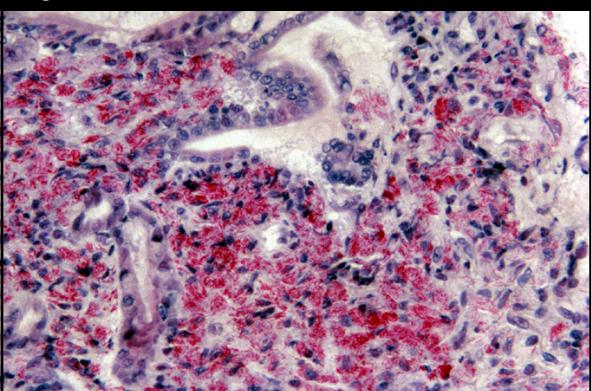
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**Mycobacteria Avium Intracellulare**



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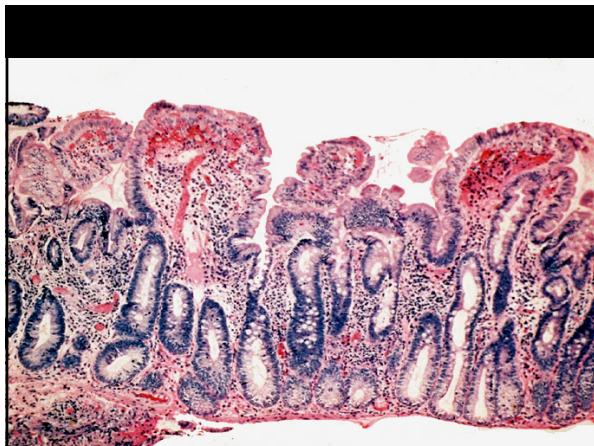
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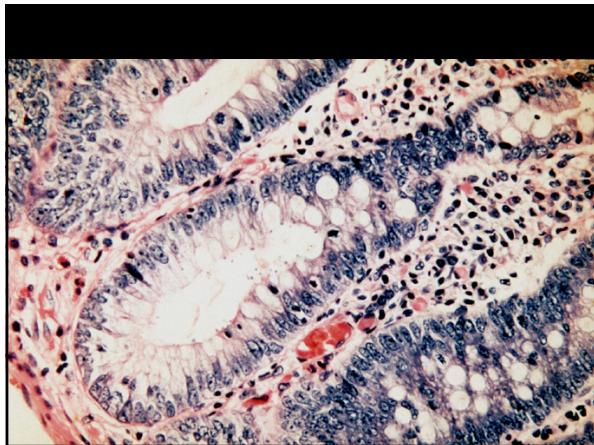
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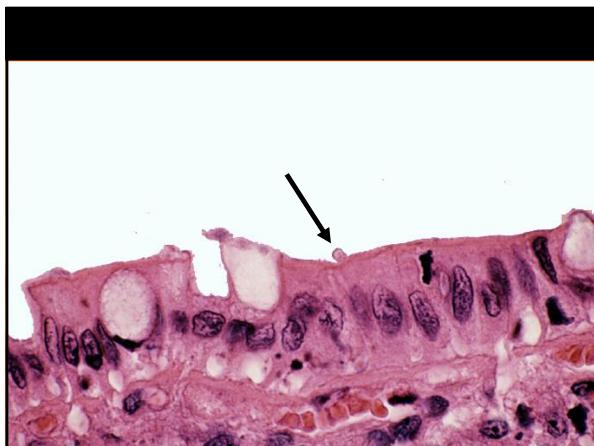
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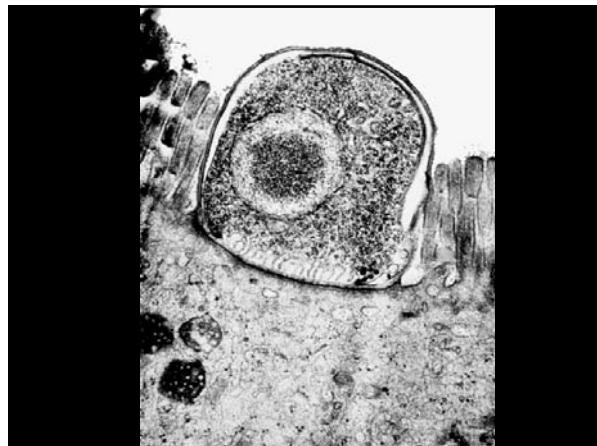
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### Normal Mucosal Architecture

- Celiac disease
- Cryptosporidium
- Giardia
- Eosinophilic gastroenteritis
- Lymphangiectasia
- Abetalipoproteinemia
- Systemic mastocytosis
- Amyloidosis

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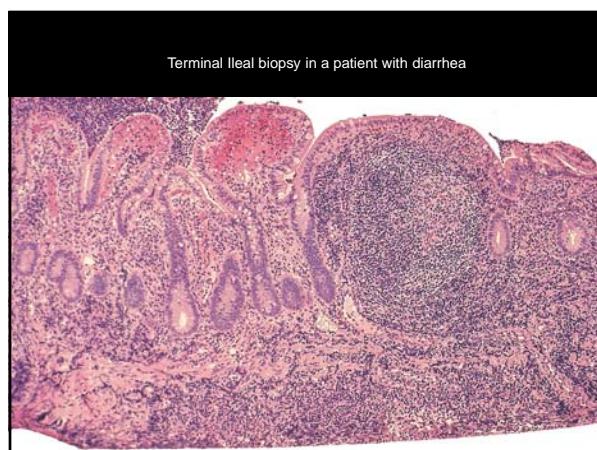
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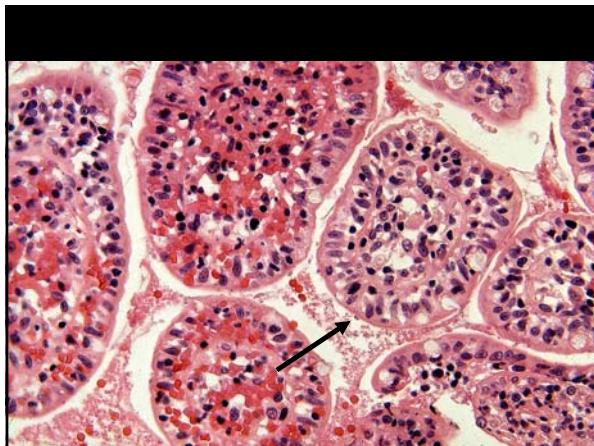
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## Clinical History

- 40 y.o. F with sudden onset of abdominal pain
- She also reports mild intermittent diarrhea
- Similar episodes in the past but extensive work-up has been negative
- Colonoscopy and upper endoscopy with biopsies two years ago were reportedly normal
- No medications except for Tylenol during the painful episodes

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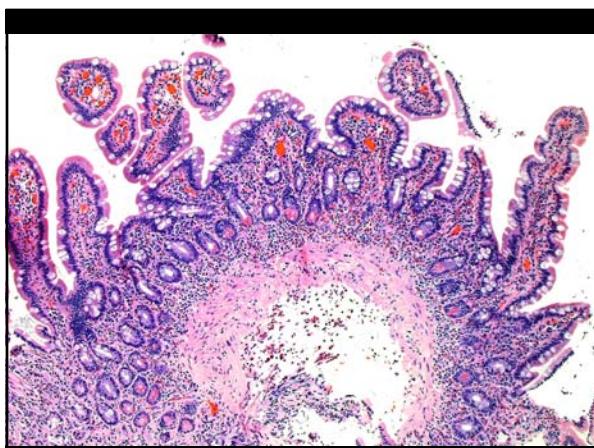
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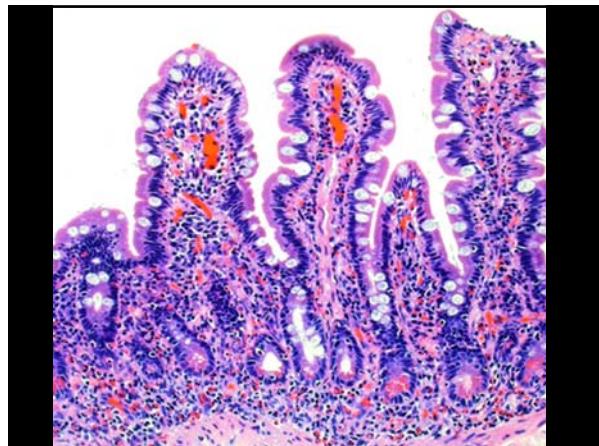
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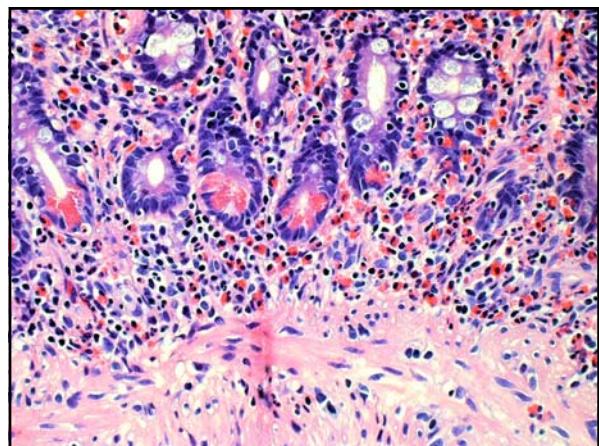
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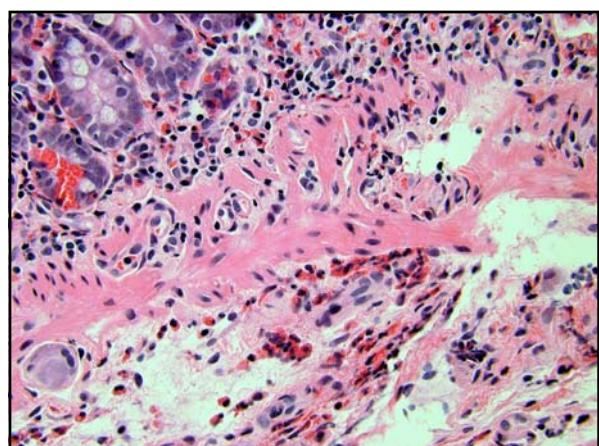
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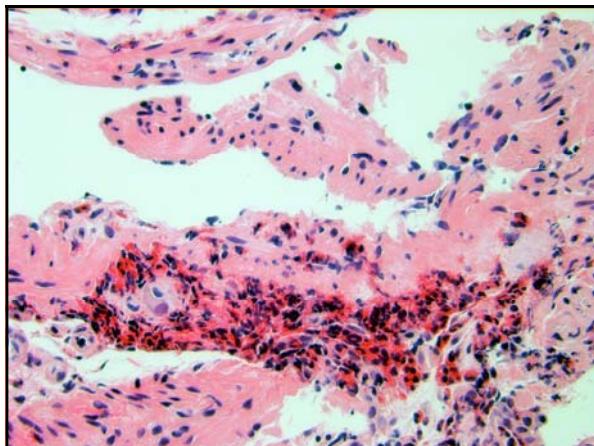
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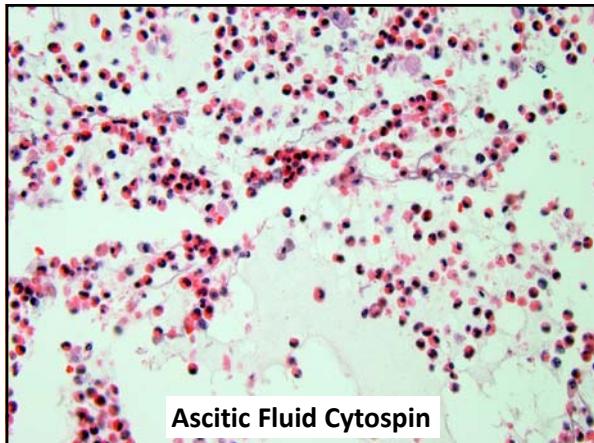
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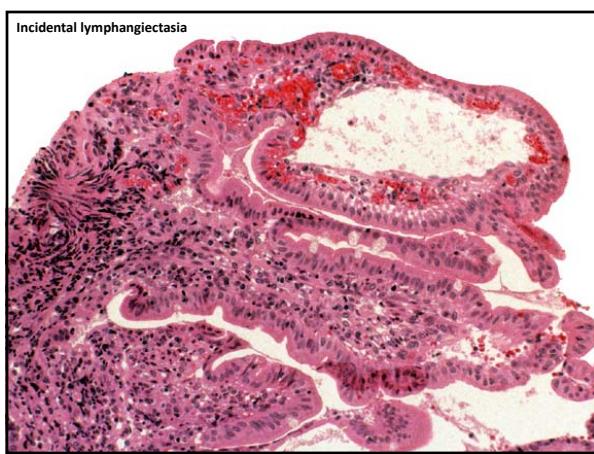
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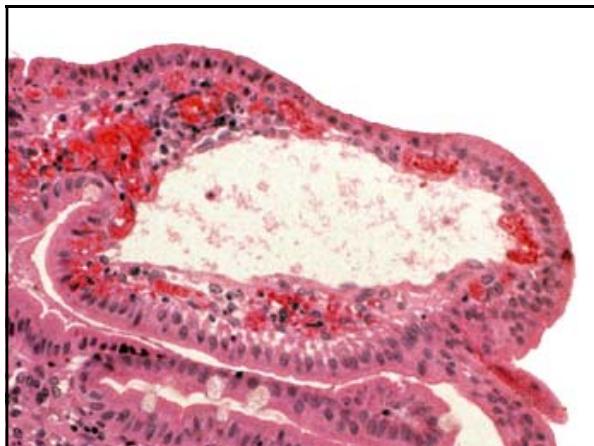
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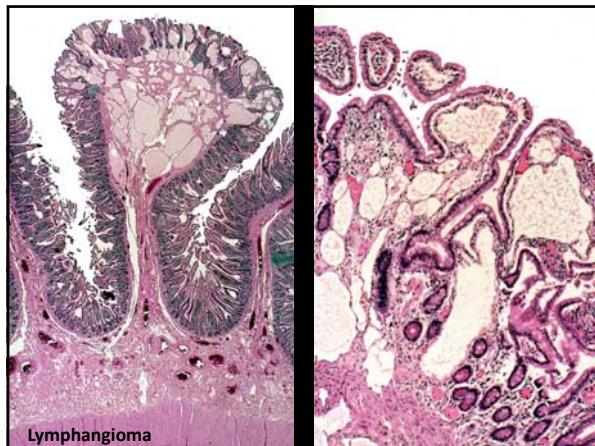
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Lymphangioma

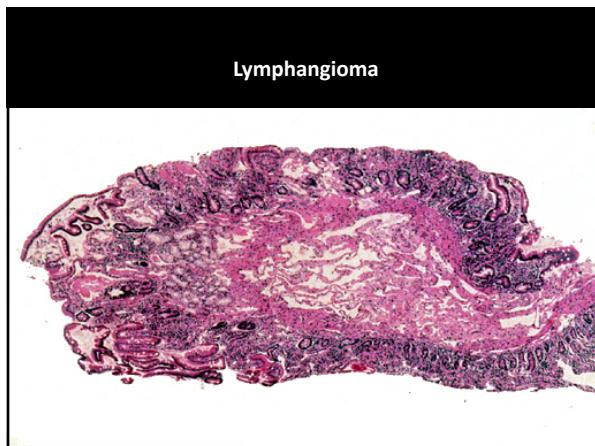
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Lymphangioma

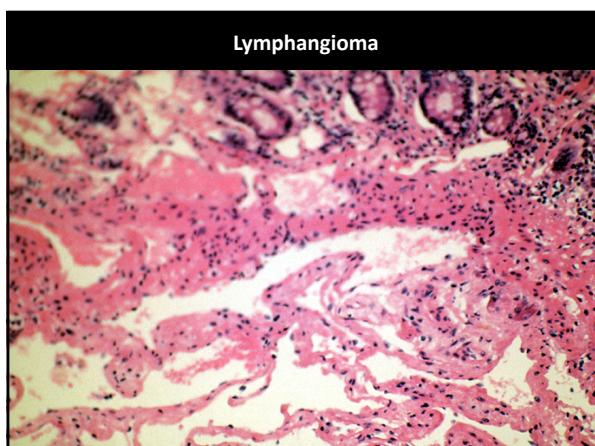
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Lymphangioma

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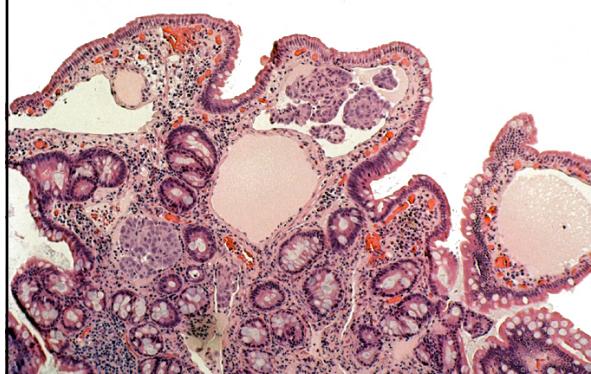
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Lymphangiectasia due to pancreatic cancer infiltrating the root of the mesentery



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### Clinical History

- 8-month-old F with diarrhea and failure to thrive
- Physical exam: listless & generalized mild hypotonia
- 72-hour stool collection reveals severe steatorrhea
- Liver chemistry tests mildly elevated

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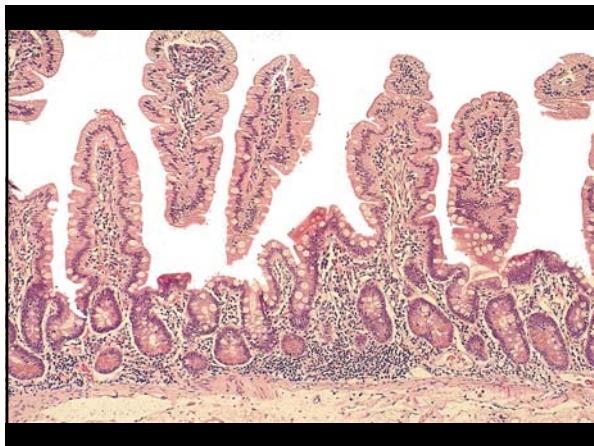
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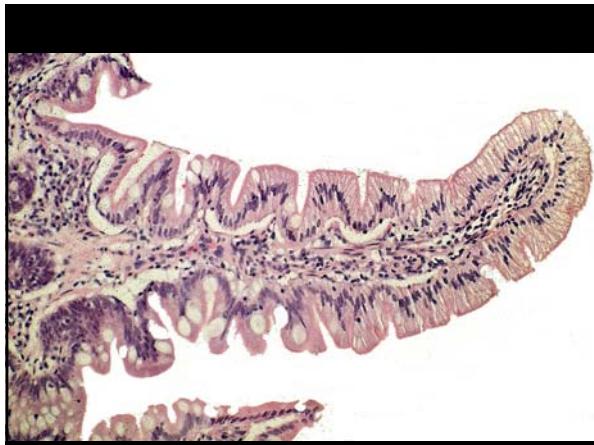
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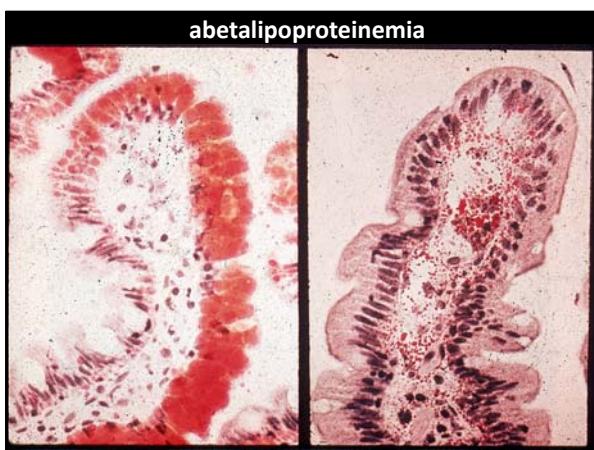
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Normal physiologic change due to not being NPO before endoscopy



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## Summary

- As much clinical history as possible
- As many biopsies as possible
- Some conditions have distinctive features, but many do not
- Many conditions produce an increase in IELs
- Cooperation between endoscopist and surgical pathologist is essential

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