

# A 45-Year-Old Man With Recurrent Abdominal Pain, Bloating, Flatulence, and Intermittent Loose Stools

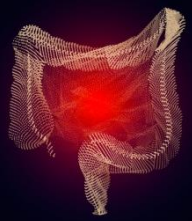
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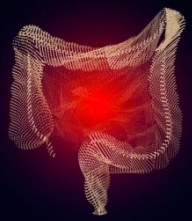
# Case Study: Alan

**Alan is a 45-year-old man with a 3-year history of recurrent, right lower-quadrant abdominal cramping, bloating, flatulence, and intermittent loose stools.**

- His symptoms began after an acute gastrointestinal illness he developed while vacationing. His stools are loose and non-bloody, without mucous.
- His weight has been stable. Alan has no fecal incontinence but has had several “close calls.”
- He limits his social engagements, and when he does go out, he always looks for the nearest bathroom.
- Alan has tried loperamide and bismuth intermittently, with only limited success.



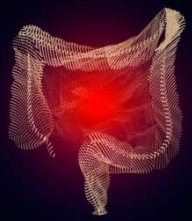
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# History and Physical Exam

- **Family history is negative**
- **Affect is normal**
- **Physical exam is unremarkable except for mild LLQ tenderness with deep palpation**
  - Rectal exam reveals soft brown guaiac negative stool in the vault
  - Tone and squeeze pressures as well as relaxation of the anal sphincter appear normal

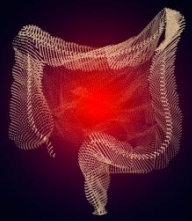
LLQ = left lower quadrant.



# IBS: Epidemiology, High Burden

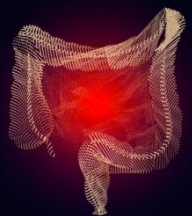
- **Estimated prevalence: 11% worldwide,<sup>1</sup> 12% in US<sup>2</sup>**
- **Most common between ~30–50 years of age; affects women > men<sup>1,3</sup>**
- **IBS is common following an enteric infection**
- **Decreased work productivity<sup>3</sup>**
- **IBS patients have HRQoL similar to patients with chronic depression and renal failure**
- **IBS is second only to GERD for burden of GI illness<sup>4</sup>**
  - \$1.6 billion – direct costs<sup>5</sup>
  - \$19.2 billion – indirect costs<sup>5</sup>

IBS = irritable bowel syndrome; HRQoL = health-related quality of life; GERD = gastroesophageal reflux disease; GI = gastrointestinal.



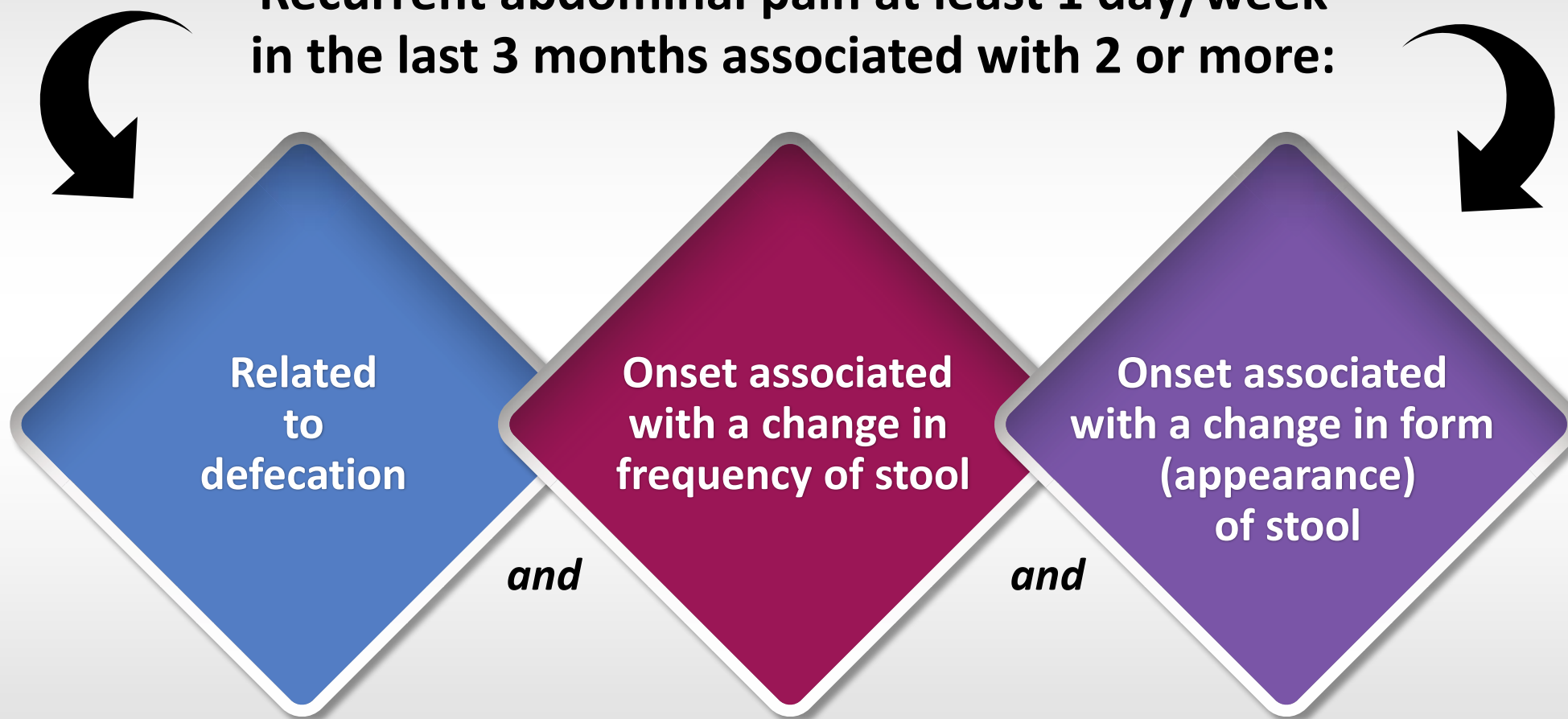
# Overview of IBS Pathophysiology

Host Factors	Environmental Factors	Luminal Factors
GI motility	Psychosocial distress	Dysbiosis
Visceral hypersensitivity	Food	Neuroendocrine mediators
Intestinal permeability	Antibiotics	Bile acids
Brain-gut interactions	Enteric infection	
Immune activation		

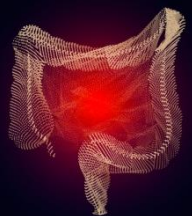


# Rome IV Criteria\*: Irritable Bowel Syndrome

Recurrent abdominal pain at least 1 day/week  
in the last 3 months associated with 2 or more:










\*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis



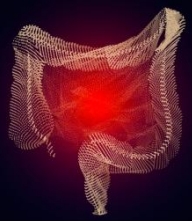
# IBS Subtypes (Rome IV) Are Based on Stool Consistency During Days With Abnormal BMs

## Bristol Stool Form Scale<sup>1,2</sup>

Type 1		Separate hard lumps, like nuts (hard to pass)	} <b>IBS-C<sup>2</sup></b> Hard/lumpy stools $\geq 25\%$ Loose/watery stools $< 25\%$
Type 2		Sausage-shaped but lumpy	
Type 3		Like a sausage but with cracks on its surface	
Type 4		Like a sausage or snake, smooth and soft	} <b>IBS-M<sup>2</sup></b> Hard/lumpy stools $\geq 25\%$ Loose/watery stools $\geq 25\%$
Type 5		Soft blobs with clear-cut edges (passed easily)	
Type 6		Fluffy pieces with ragged edges; a mushy stool	} <b>IBS-D<sup>2</sup></b> Hard/lumpy stools $< 25\%$ Loose/watery stools $\geq 25\%$
Type 7		Watery, no solid pieces; entirely liquid	

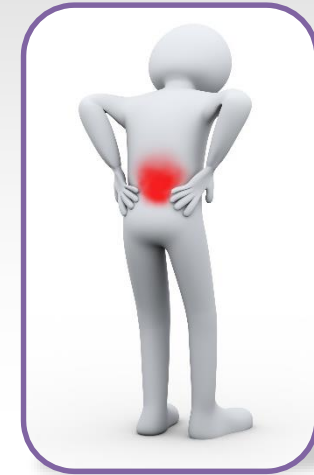
BM = bowel movement; IBS-C = IBS with constipation; IBS-M = IBS mixed; IBS-D = IBS with diarrhea.

1. O'Donnell LJ. BMJ. 1990;300:439-440; 2. Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.  
Adapted from ), Lacy BE, et al. *Gastroenterology*. 2016;150(6):1393-1407.



# Other Associated Conditions

- **GI motility disorders**
  - Dyspepsia, GERD, cyclic vomiting, gastroparesis, etc.
- **Psychiatric disorders**
  - Anxiety, depression, somatoform disorders, PTSD
- **Chronic back pain**
- **Fibromyalgia, chronic fatigue syndrome**
- **Chronic headaches, “migraines”**
- **Chronic pelvic pain – men and women**
- **Functional urinary symptoms (e.g., interstitial cystitis)**
- **Dysmenorrhea**



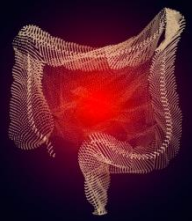
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GERD = gastroesophageal reflux disease; PTSD = post-traumatic stress disorder.





# Diagnosis of IBS-D: Detailed History and Physical Examination

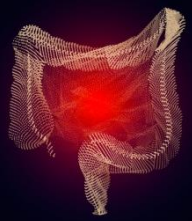
## History

- Presenting symptoms
- Establish history timeline
- Presence of alarm features
- Family history: IBS, organic GI disorder
- Prior tests and treatments
- Review current medications

## Examination

- Signs of systemic and local diseases
- Carnett's test: somatic vs visceral pain
- Assess the anorectum and pelvic floor muscles
- Other relevant abnormalities

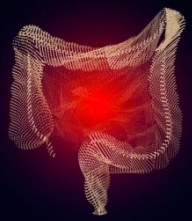
GI = gastrointestinal.



# Patients With Alarm Features Require More Detailed Investigation

- **Common Alarm Features (i.e., red flags)**
  - Onset of symptoms after age 50 years
  - GI bleeding or iron-deficiency anemia
  - Nocturnal diarrhea
  - Weight loss
  - Family history of organic GI disease (colorectal cancer, IBD, celiac disease)

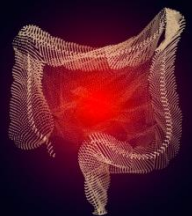




# Which of the following is a consideration in the diagnosis of IBS-D?

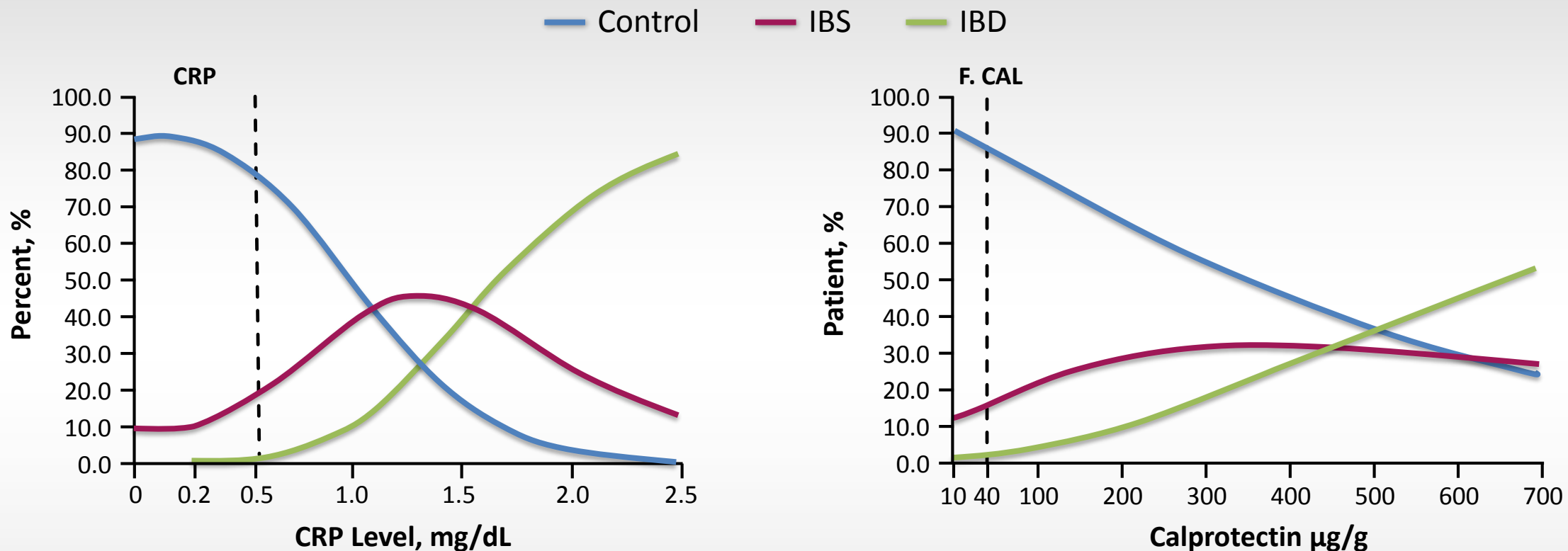


- 1. C-reactive protein (CRP) and fecal calprotectin can aid in excluding IBD in patients with IBS symptoms**
- 2. It is not recommended that a tissue transglutaminase (tTg) IgA antibody be checked in patients with IBS-D**
- 3. Colonoscopy has a high yield in detecting IBD in patients with IBS symptoms who do not have alarm features**



# Differential Diagnosis: Excluding IBD

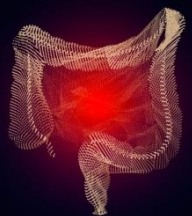
## Role of CRP and Fecal Calprotectin in Excluding IBD in Patients With IBS Symptoms



CRP = C-reactive protein;  
ESR = erythrocyte sedimentation rate.

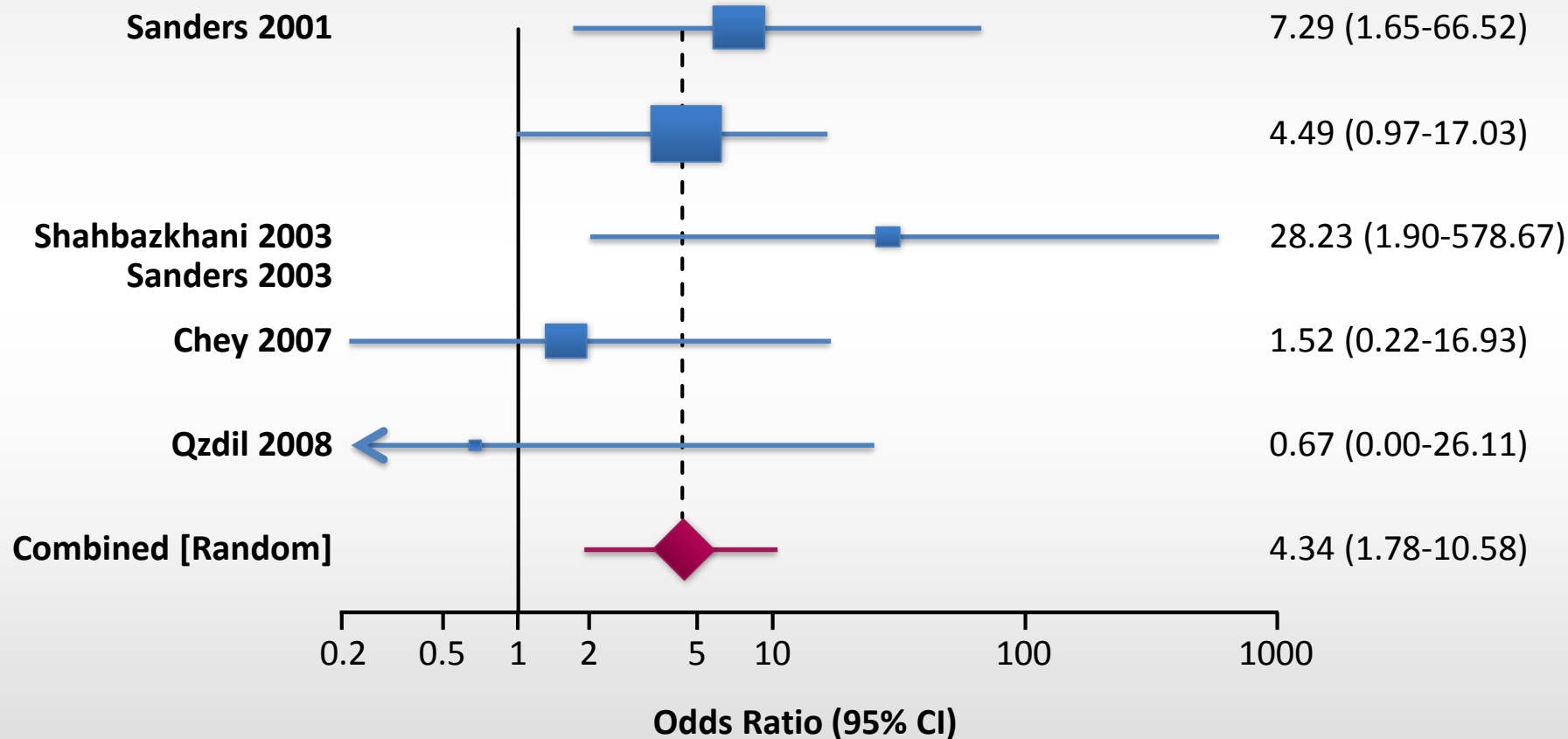
Adapted from Menees S, et al.  
*Am J Gastroenterol.* 2015;110:444-54.

- ESR is of no value
- CRP of <0.5 mg/dL confers a <1% risk of IBD
- Fecal calprotectin of <40 mg/g confers a <1% risk of IBD

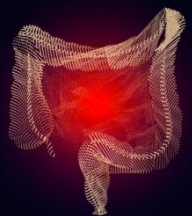


# Differential Diagnosis: Patients With IBS-D Symptoms Should Undergo Celiac Antibody Testing

Odds Ratio Meta-Analysis Plot [Random Effects]



Adapted from Ford AC, et al. *Arch Int Med.* 2009;169:651-865.

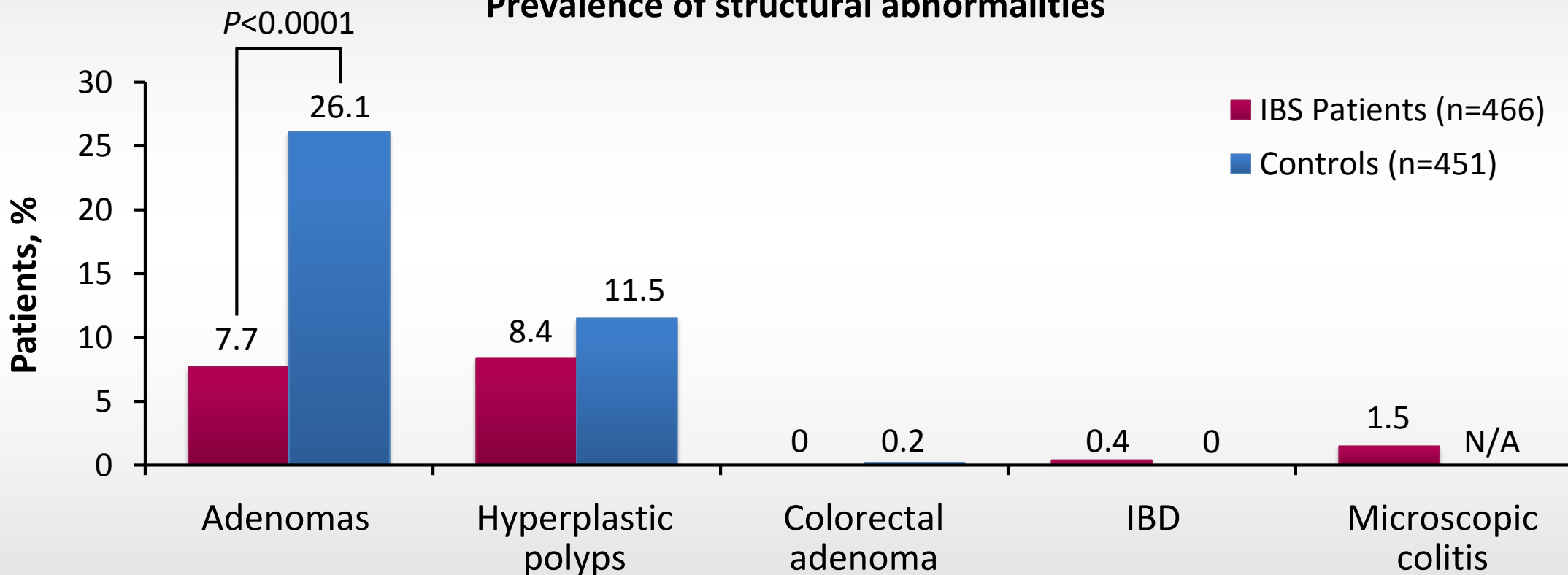


# Differential Diagnosis: Role of Colonoscopy

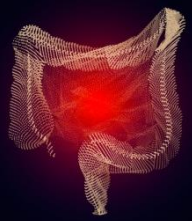
## Patients with IBS Symptoms Without Alarm Features Are Unlikely to Have IBD or Microscopic Colitis

Prospective, multicenter US study in nonconstipated IBS patients and controls undergoing colon cancer screening.

Prevalence of structural abnormalities



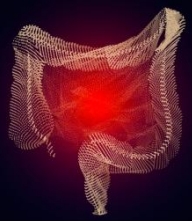
Microscopic colitis was more common in IBS-D patients aged  $\geq 45$  years



# Which patients should be evaluated for microscopic colitis?



- 1. Younger women or those who have intermittent symptoms**
- 2. Those with stress-associated symptoms or meal-related diarrhea**
- 3. Those with unrelenting symptoms or nocturnal diarrhea**



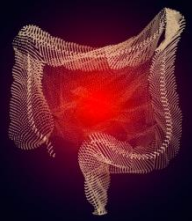
# Differential Diagnosis: Microscopic Colitis

## Who Should Be Evaluated?

Favors IBS	Favors Microscopic Colitis
Meal-related diarrhea	Nocturnal diarrhea
Intermittent symptoms	Unrelenting symptoms
Longstanding symptoms	Short symptom duration
Symptoms with stress	New drug in last 1-3 months
Family history of IBS	Other autoimmune disorders
Younger women	Older women

- **Majority of cases will be diagnosed with left-colon biopsies alone**





# Co-morbid Condition: SIBO

## Role of Breath Testing

- Breath tests are not validated to accurately detect SIBO
- There is insufficient evidence to recommend lactulose or glucose breath tests to identify SIBO in patients with IBS

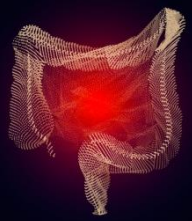


### Substrate

- Glucose breath test
- Lactulose breath test

SIBO = Small intestinal bacterial overgrowth.

1. Simren M, et al. *Gut*. 2013;62:159-176. 2. ACG Task Force on IBS. *Am J Gastroenterol*. 2009;104:S8-S35. 3. Saad R, et al. *Clin Gastroenterol Hepatol*. Dec;12(12):1964-1972.



# Co-Morbid Condition: Role of Bile Acid Diarrhea in IBS-D

- Up to 40% of patients with IBS-D may have bile acid diarrhea
- Bile acids are normally completely absorbed in terminal ileum; in the colon bile acids cause diarrhea
- Serum 7  $\alpha$ -hydroxy-4-cholesten-3-one (C4) (not complement) now available in US
- Bile acid malabsorption results in greater fat malabsorption and increased colon transit

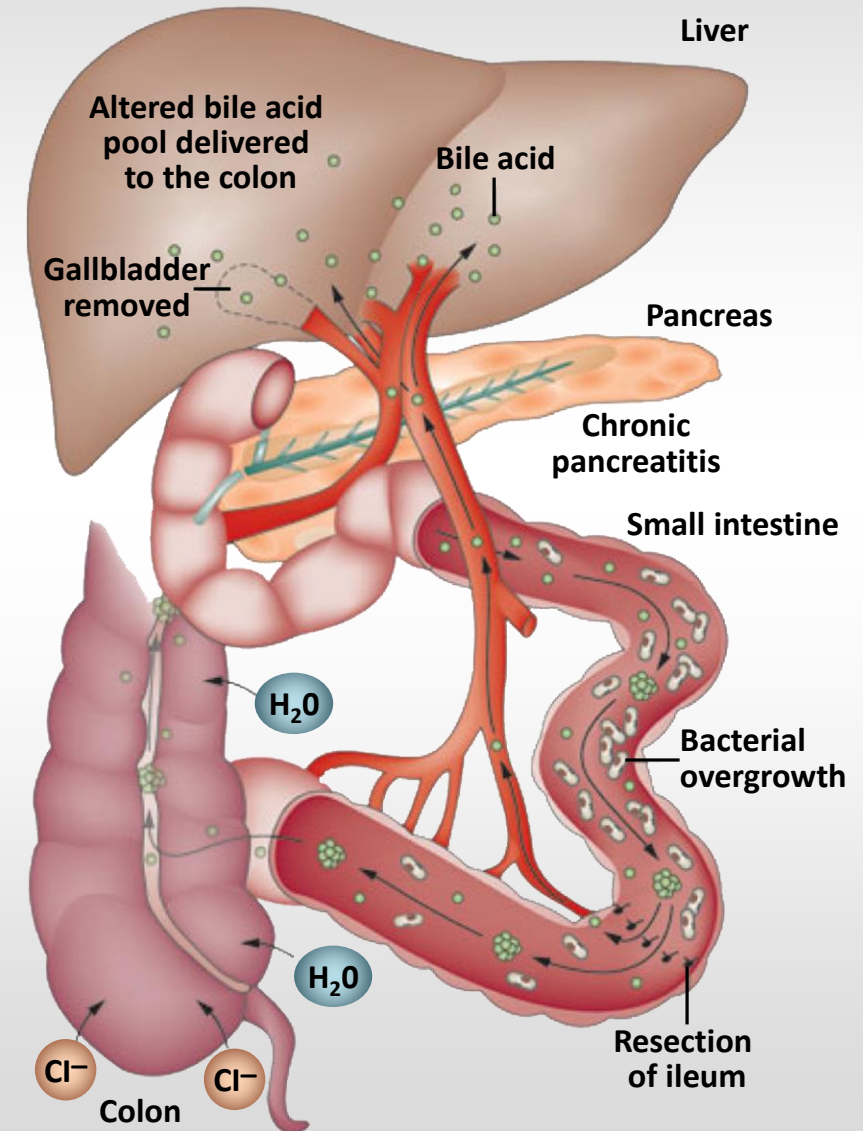
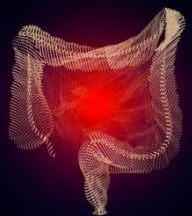
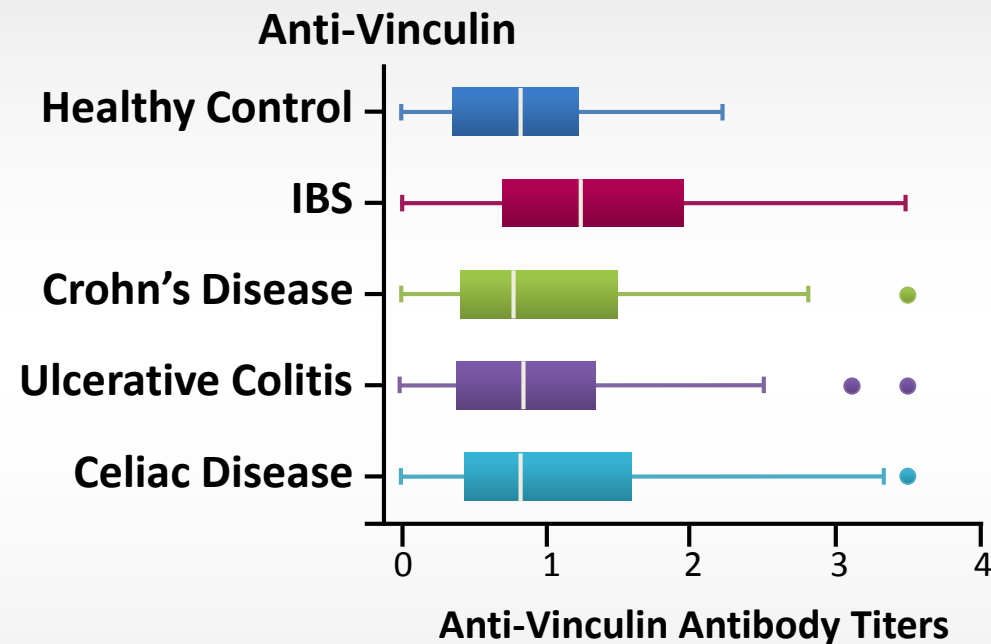
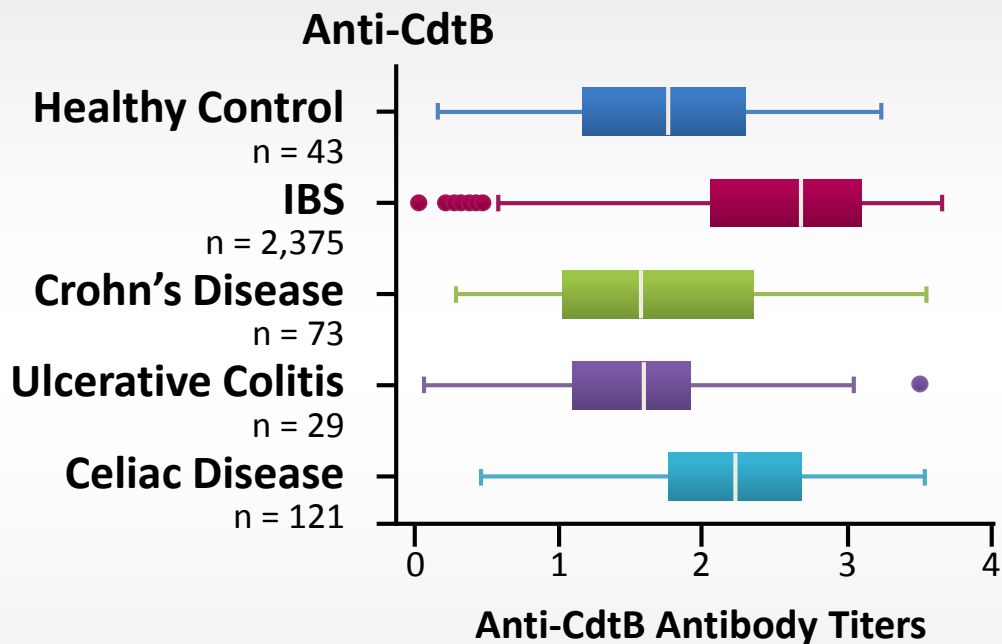


Figure adapted from Menees S, et al. *Nat Rev Gastroenterol Hepatol*. 2012 Nov;9(11):661-674.  
Camilleri M, et al. *Am J Gastroenterol*. 2014;109:1621-1630.



# Post-infectious Antibody Titers May Differentiate IBS-D from IBD, Celiac Disease

## Antibody Titers in IBS Compared With Healthy Subjects and IBD

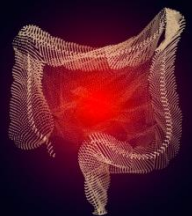


### IBS-D vs IBD

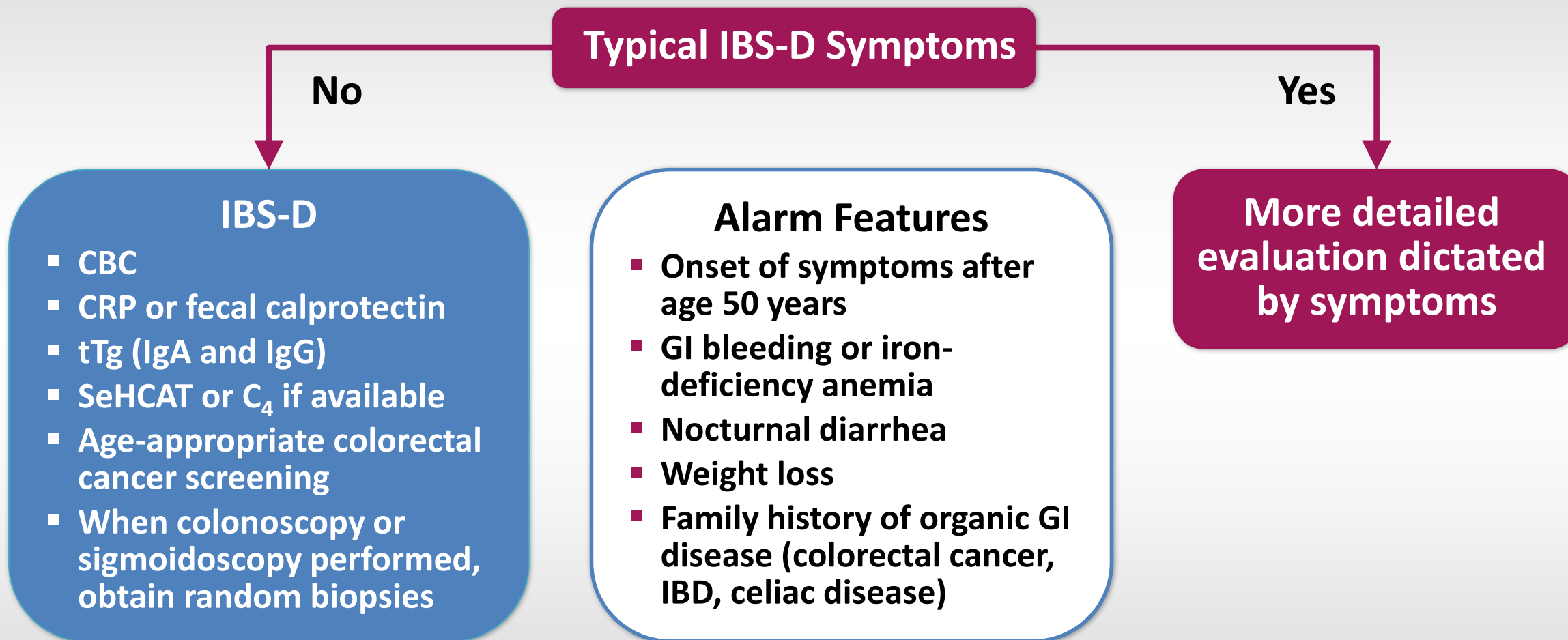
Optical Density	Specificity %	Sensitivity %
CdtB (cutoff $\geq 2.80$ )	91.6	43.7
Vinculin (cutoff $\geq 1.68$ )	83.8	32.6

$P < .001$  for titers in IBS subjects vs other groups.

Adapted from Pimentel M, et al. *PLoS ONE*. 2015;10:e0126438.

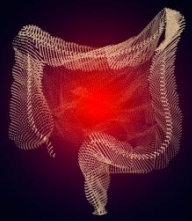


# Work-Up of Patients With Suspected IBS-D



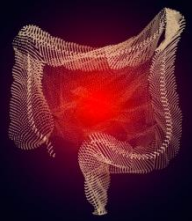
CBC = complete blood count; CRP = C-reactive protein; tTg = tissue transglutaminase.

Chey WD, et al. *JAMA*. 2015;313:949-958.



# Alan: Diagnosis

- **Based on Alan's symptoms, history, and physical exam, the following tests are performed :**
  - tTg IgA antibody, CBC, CRP, stool calprotectin
- **After evaluation of the results (all negative), a diagnosis of IBS-D is made, allowing the physician to recommend appropriate and effective treatment**



# Summary

- **IBS-D can be diagnosed using symptom-based criteria, a detailed physical exam, and select tests to exclude organic diseases**
- **Tests to consider include: CBC, CRP/stool calprotectin, tTg (IgA and IgG), and stool analysis**
- **Assessment for bile acid malabsorption should be considered where available**
- **Role of breath testing remains unclear**