

**State of the Art  
Therapeutic Treatments  
for IBS Patients**

*Understanding the Role of the  
Gastroenterologist, Dietitian, and  
GI Psychologist*

**William Chey, MD**  
**Kate Scarlata, MPH, RDN**  
**Megan Riehl, PsyD**



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**Disclosures**

**William Chey, MD**  
Research Support: Biomerica, Ironwood, Commonwealth Diagnostics, QOL Medical, Salix Pharmaceuticals, Urovant, Takeda, Zespri  
Consultant: Allergan, Biomerica, IM Health, Ironwood, QOL Medical, Salix/Valent, Phathom, Redhill, Ritter

**Kate Scarlata, MPH, RDN**  
Equity: Fody food co., Epicured  
Honorarium/Consultant: A2 Milk Company, Enjoy Life Foods, Green Valley Creamery, Monash University, Salix pharmaceuticals  
Published books and online low FODMAP educational handouts

**Megan Riehl, PsyD**  
Consultant: Gastro Girl, Inc



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**Learning Objectives**

1. Detail the state of the evidence for food intolerance and its role in IBS symptom induction.
2. Describe therapeutic behavioral therapies for IBS patients.
3. Explain the three phases of the low FODMAP diet.



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## Exclusion Diets for IBS

William D. Chey, MD, FACG, AGAF, FACP  
 Nostrant Collegiate Professor  
 Director: Nutrition & Behavioral Medicine Program  
 Michigan Medicine  
 Twitter: @umfoodoc



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## IBS: Rome IV Criteria

Recurrent abdominal pain at least 1 day per week associated with two or more of the following:

- Related to defecation
- Onset associated with a change in the frequency of stool
- Onset associated with a change in the form of stool

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

Mearin et al. Gastroenterology. May 2016



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## Food and IBS Symptoms

- 197 IBS patients (Rome III)
- Symptom severity correlates with number of food sensitivities
- No impact of IBS subgroup

Food Category	Percent
Any Food	84
Carbs	70
Fatty Foods	52
Histamine	68

Bohn et al. Am J Gastroenterol 2013;108:634



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## Dietary Interventions for IBS: What's the Evidence?

- **Gluten-free**
- Elimination diets
- Low-FODMAP



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## Celiac Disease and NCWI: Time Trends

Variable	2009-2010 Prevalence, % (95%CI) (n=7798)	2011-2012 Prevalence, % (95%CI) (n=6903)	P Value	2013-2014 Prevalence, % (95%CI) (n=7577)	P Value
<b>Celiac Disease</b>					
Patients with Celiac Disease (106 of 22278 [0.69%] 95% CI, 0.53% - 0.84%)	0.70 (0.58 to 0.83)	0.77 (0.41 to 1.13)	.72	0.58 (0.30 to 0.86)	.49
<b>People Without Celiac Disease Avoiding Gluten</b>					
Patients Without Celiac Disease Avoiding Gluten (213 of 22277 [1.08%] 95% CI, 0.80% - 1.35%)	0.52 (0.24 to 0.80)	0.99 (0.63 to 1.35)	.06	1.69 (1.10 to 2.31)	.001

• 22,278 Persons Participating in National Health & Nutrition Exam Surveys  
 • While the prevalence of Celiac Disease was stable from 2009 - 2014, the prevalence of persons without CD avoiding gluten steadily and significantly increased  
 Kim et al. JAMA Int. Med 2016;176:1716

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## Wheat Sensitivity vs. Controls: Differences in Symptoms & Conditions

	Self-reported wheat sensitivity % (95% CI)	No self-reported wheat sensitivity % (95% CI)
Abdominal pain relieved by bowel motion	54.3 (49.7-59.0)	34.8 (32.9-36.7)
Bloating	36.9 (32.5-41.5)	8.3 (7.3-9.5)
Abdominal distention	30.7 (26.5-35.1)	8.2 (7.2-9.3)
Abdominal pain with loose bowel motions	29.7 (25.5-34.1)	16.6 (15.1-18.1)
Abdominal pain	26.9 (22.9-31.2)	7.5 (6.5-8.5)
Abdominal pain with more bowel motions	26.2 (22.2-30.5)	13.7 (12.3-15.1)
Loose or watery bowel motions	22.6 (18.8-26.7)	9.0 (8.0-10.2)
Post prandial fullness	22.5 (18.7-26.5)	6.0 (5.1-6.9)
Straining with bowel motion	19.0 (15.5-22.8)	9.0 (7.9-10.1)
Hard or lumpy stool	16.8 (13.5-20.5)	8.9 (7.8-10.0)
Greater than three bowel motions per day	16.2 (13.0-19.9)	6.6 (5.6-7.6)

- 3542 randomly selected Australians filled out a mail survey
- 14.9% had self reported wheat sensitivity
- 1.2% had celiac disease

Variable	SRWS (%)	No SRWS (%)	Odds ratio (95% CI)
IBS	35.1	8.9	3.55 (2.71-4.65)
Female gender	75.0	49.3	2.46 (1.95-3.11)
Food allergy	12.1	5.2	1.84 (1.28-2.64)
FD	31.3	13.6	1.48 (1.13-1.94)
Age (years)	51.4 years	58.1 years	0.98 (0.98-0.99)

Potter et al. Am J Gastroenterol 2018;113:1036-44

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## Gluten Free Diet for IBS: Meta-Analysis

- Two RCTs of a GFD, involving 111 participants
- Patients who responded to a GFD randomized to continue GFD or receive diet with gluten
- Conclusion: There is currently insufficient evidence to recommend a GFD for IBS symptoms

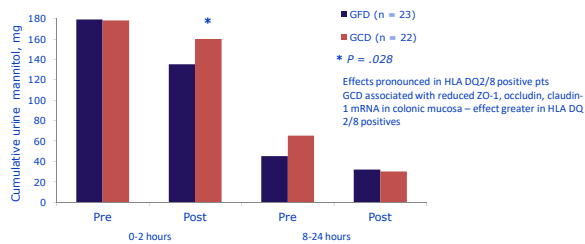


Donne et al. Am J Gastroenterol 2018, online early.

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## Effect of a GFD on Small Intestinal & Colonic Permeability by Mannitol Excretion in IBS-D

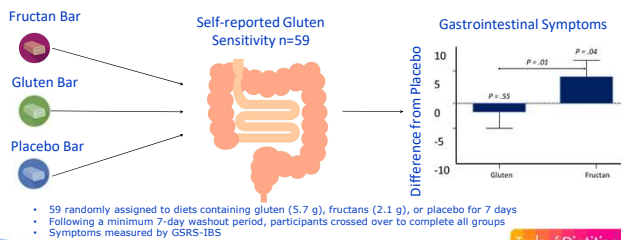
Single center, parallel group 4-week RCT in 45 gluten ingesting IBS-D pts



Vazquez-Roque ML, et al. Gastroenterology 2013;144:903

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## Non-Celiac Wheat Intolerance: Fructan, More Than Gluten, Causes Symptoms

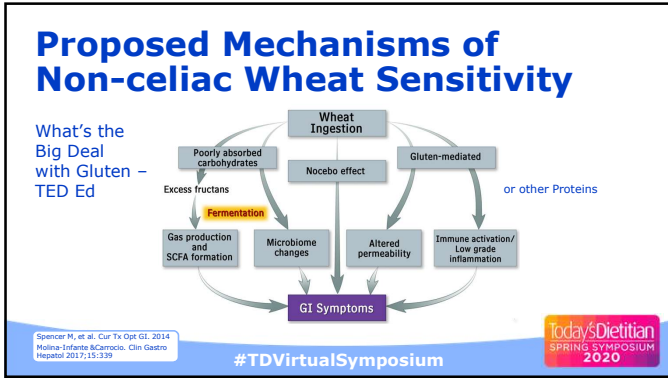


Skodje et al. Gastroenterology 2018;154:529-539

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### Dietary Interventions for IBS: What's the Evidence?

- Gluten-free
- **Elimination diets**
- Low-FODMAP

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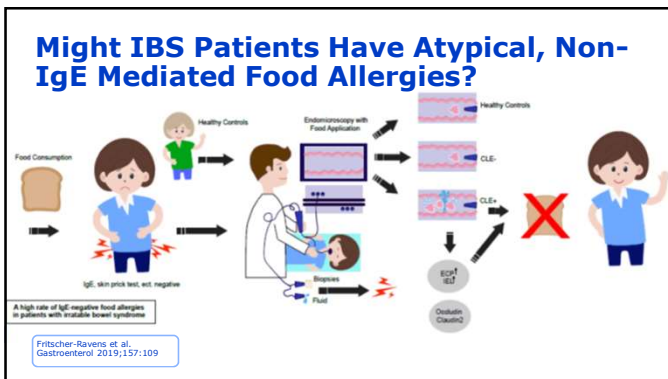
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### Might IBS Patients Have Atypical, Non-IgE Mediated Food Allergies?

Prevalence of atopic disorders or family history of atopic disorders

CLE before and after exposure to wheat, milk, soy, yeast, or egg white and a control (simethicone)

76/108 pts CLE + (70%)

- 46 (61%) reacted to wheat
- 4-fold higher rate of atopic conditions
- More IELs than controls
- Expression of claudin-2 up regulated & increased from crypt to villus tip (P < .001)
- Levels of Occludin were reduced
- No differences in inflammatory cytokines or eosinophils but degranulating eosinophils increased

Fritscher-Ravens et al. Gastroenterol 2019;157:109

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### Leukocyte Activation Test Elimination Diet

(A) IBS-GIS (B) IBS-SSS

Food	Frequency n (%)	High FODMAP
Strawberry	15 (26)	
Cinnamon	15 (26)	
Almond	12 (21)	X
Apple	12 (21)	X
Orion	12 (21)	X
Pear	11 (19)	X
Buckwheat	11 (19)	
Chickpea	11 (19)	
Ginger	11 (19)	
Raspberry	11 (19)	
Blackberry	10 (17)	
Hops	10 (17)	
Oats	10 (17)	
Olive	10 (17)	
Quinoa	10 (17)	
Sorghum	10 (17)	
Yellow squash	10 (17)	

- Peripheral blood taken from 58 IBS pts
- LAT (n=29) vs. Sham (n=29) elimination diet x 4 weeks
- No significant benefits for adequate relief or IBS-QOL scores

Ali A et al. BMJ Open Gastroenterology. 2017;0:e000164.

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### Dietary Interventions for IBS: What's the Evidence?

- Gluten-free
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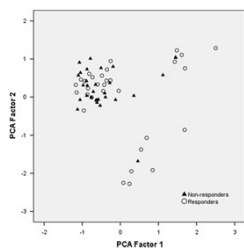






## Fecal Microbiome Predicts Response to LFD

- 61 Norwegian IBS patients underwent dietician led FODMAP exclusion x 4 weeks
- 32/61 (52%) Responses: >50% reduction in baseline IBS-SSS score
- Stool samples analyzed for 54 markers by 16S rRNA sequencing
- Responders had higher levels of *Bacteroides fragilis*, *Acinetobacter*, *Ruminiclostridium*, *Streptococcus*, and *Eubacterium* (all  $p < 0.05$ )



Valeur et al. Dig Dis Sci 2018;63:429-436

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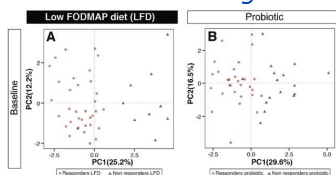
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## Low FODMAP and Probiotics for IBS: Predictive Value of Volatile Organic Compounds



Baseline model	Accuracy (%)				Sensitivity (%)				Specificity (%)					
	Responders	Non-responders	Median	Mean	CI	Median	Mean	CI	Median	Mean	CI	Median	Mean	CI
Low FODMAP diet (n = 46)	35	9	100	97	99-100	100	100	100-100	100	95	80-100			
Probiotic (n = 42)	29	16	89	88	86-92	100	93	90-95	75	82	75-87			

Rossi et al. Clinical Gastroenterology and Hepatology 2016;16:385-391

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## The Low FODMAP Diet: Key Points

- Teaching is ideally provided with the assistance of a trained dietician.
- In the absence of a dietician, appropriately vetted books, web-based resources & mobile apps can help patients to implement the Low FODMAP diet in a medically responsible manner. A one page handout is NOT sufficient to implement the diet.
- A 2-4 week trial is usually sufficient to gauge clinical response.
- Bloating and abdominal pain are the most likely symptoms to respond. Diarrhea is more likely to improve than constipation.
- The full Low FODMAP diet is NOT intended to last a lifetime. Responders should be instructed to implement a stepwise reintroduction of foods containing individual FODMAPs to identify triggers and allow diversification of their diet.
- The Low FODMAP diet is NOT intended for persons who do not experience GI symptoms

Chey. Am J Gastroenterol 2016;111:366

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## Sucrase-Isomaltase (SI) Deficiency: Is Sucrose an Unrecognized FODMAP?

- Congenital SID
- Genetic SID
- Acquired/Secondary SI Deficiency

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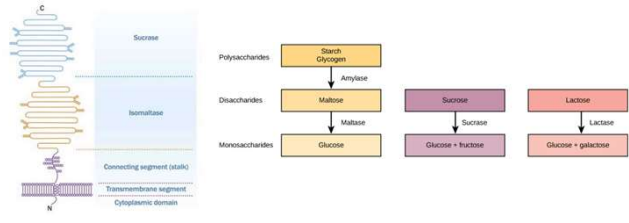
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## Congenital Sucrase-Isomaltase Deficiency (CSID)

Recessive mutations in the sucrase-isomaltase (SI) gene



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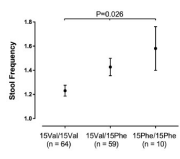
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## CSID Mutations are Associated with IBS

Association of known CSID mutations with IBS

IBS Subtype	IBS		CSID		EAC	
	No. IBS	Subtype	No. CSID	p Value*	No. EAC	p Value**
pAbTFRGy	14	4 BS-D, 5 BS-M, 5 BS-C	4	0.12	100	0.0029
pAbTFRAla	3	3 BS-D	3	0.57	109	0.42
pAbTFRSer	1	1 BS-D	0	-	8	0.07
pAbTFRGly	4	1 BS-D, 3 BS-M, 1 BS-C	1	0.35	110	0.42
Any mutation	22	9 BS-D, 10 BS-M, 1 BS-C, 1 BS-U	10	0.016	400	0.0001

Correlation between p.Val15Phe genotype and stool frequency



Association of 15Phe variant with IBS

IBS Subtype	IBS		IBS-C		IBS-D		IBS-M		IBS-DM	
	No. IBS	Subtype	No. IBS-C	p Value*	No. IBS-D	p Value*	No. IBS-M	p Value*	No. IBS-DM	p Value*
Case-control	0.36	0.0001	1.26	0.275	0.42	1.09	0.312	0.0002	1.30	0.319
Stratified	0.20	0.47	0.46	1.49	0.40	1.12	0.409	0.20	1.16	0.555
Combined	0.30	0.0071	1.27	0.301	0.39	1.10	0.314	0.0002	1.30	0.319

SIGVs associated with reduction in sucrase activity of 40-45% & Palatinase activity of 25-70%

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### Reduced Efficacy of LFD in patients with SID When Sucrose Becomes a FODMAP...

- 46 pts from US RCT randomized to LFD
- Primary endpoint: Adequate relief of IBS symptoms
- SI gene variants analyzed
- In a separate analysis the number of gene variants present predicted non-response to LFD or mNICE: 2>1>0

Group	Sample Size (N)	Symptom Relief (%)
All patients	46	52.2
Non-carriers	23	60.9
Carriers	23	43.5

Zheng et al. Gut 2020;69:397+ #TDVirtualSymposium Today'sDietitian SPRING SYMPOSIUM 2020

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### Summary

- Elimination diets may provide benefits to a subgroup of
- IBS patients
- The greatest weight of evidence supports the low FODMAP diet
- Other elimination diets require adequate validation
- Emerging data suggests that atypical food allergy may be important
- Sucrase isomaltase deficiency can cause GI symptoms in a small percentage of IBS patients and may be enriched in patients with meal related symptoms who do not respond to the low FODMAP diet

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### Practical Applications of Diet Strategies for Food Intolerance in IBS

Kate Scarlata, MPH, RDN  
Twitter: @katescarlata\_RD  
Instagram: @katescarlata

KATE SCARLATA RDN FODMAP + IBS EXPERT  
FOR A DIGESTIVE PEACE OF MIND

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## Finding Suitable Substitutions

Meals/snacks—high FODMAP	Meal substitutions --low FODMAP
Bran cereal with milk and raisins	Corn flakes with lactose free milk + strawberries
Wheat toast with almond butter and apricot jam	Slow leavened wheat toast (Iggy's Francese) with peanut butter and strawberry (chia) jam
Salad with onion, tomatoes, cucumber, carrots and ranch dressing, topped with tuna.	Salad with scallion greens, tomatoes, cucumber, carrots, Fody Maple Dijon Salad Dressing, topped with tuna.
Yogurt and granola (with added chicory root)	Lactose free yogurt and granola without chicory root
Italian sausage with onion and peppers in bun	Suitable onion and garlic free sausage, tri-color pepper sautéed in Fody Shallot Oil in suitable bun
Bowl of pistachio ice cream	Bowl of vanilla lactose free ice cream
Lara bar (dates, apples)	Fody bars: Dark Chocolate Nuts & Sea Salt, Almond Coconut, Blueberry Almond, Peanut Butter Chocolate Quinoa

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## When Food is Confusing: *The Soy Example*

### High FODMAP

- Soy flour, whole mature soybeans, silken tofu



### Low FODMAP

- Edamame (1 cup), firm tofu, soy milk made with soy protein (8<sup>th</sup> Continent @), soy sauce, soy lecithin

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## The Reintroduction Phase: *Basic Guidelines*

- Test one FODMAP group (lactose, excess fructose, etc.) at a time and choose foods that contain only one FODMAP
- Consume a food amount that represents a normal intake (not excessive amounts)
- Continue to restrict all FODMAPs (maintain a low FODMAP diet) except the food that is being tested until tolerance or intolerance is confirmed
- Record symptoms experienced for each challenge
- Use the same food for each of the 3 challenge days

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**Determine Sensitivities with the Following Foods**

- Lactose: ½ -1 cup milk
- Fructose: 1-2 tbsp. honey or ½ mango
- Fructans: 2 slices of wheat bread, 1 tbsp onion, ½ garlic clove
- GOS: ½ cup beans
- Polyols: ½ cup mushrooms, ½ cup cauliflower (mannitol) or 1 peach, 5 blackberries (sorbitol)

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**What is a Failed Challenge?**

-  A failed challenge should be a noticeable and significant change in symptoms
-  Symptoms may resemble an IBS flare: diarrhea, cramping, return of constipation, bloating
-  = Undesirable outcome

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**Why Reintroduce FODMAPs?**

- Research has shown that the low FODMAP diet reduces bifidobacteria and other probiotic gut bacteria (butyrate-producing Clostridium cluster XIVa and mucus-associated Akkermansia muciniphila)
- Stool pH increases slightly on the low FODMAP diet---this may allow pathogenic microbes to grow
- The low FODMAP has been shown in 2 studies to increase gut microbial diversity—perhaps a good thing!

Halmos, Gut. 2015  
McIntosh Gut. 2016

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## Non-Responder

Assess symptoms:

- Bloating and post prandial fullness: r/o SIBO, gastroparesis
- Constipation: assess for slow transit constipation and/or dyssnergic defecation, high colonic stool burden, methane + SIBO
- Diarrhea: parasitic infection, bile acid malabsorption, SIBO
- Other food intolerance/sensitivities: gluten, fat, sucrose, food chemicals-histamine, milk protein (A1 vs A2)
- Consider probiotics, gut-directed hypnotherapy + other gut-brain directed therapies

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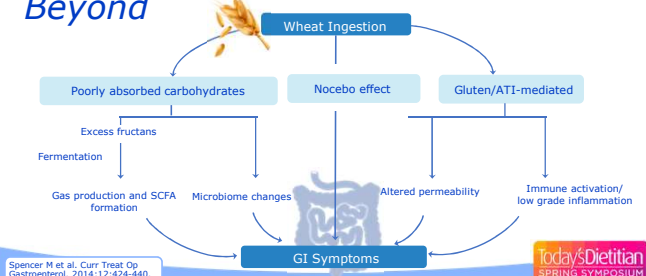
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## Wheat Intolerance: FODMAPs & Beyond



Spencer M et al. *Curr Treat Op Gastroenterol.* 2014;12:404-440.

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## Amylase Trypsin Inhibitors (ATIs)

Activate innate immunity and may fuel gut inflammation<sup>1,2</sup>




- ATIs
- Pest-resistance molecules in wheat<sup>1</sup>
- Family of 17 proteins constituting 4% of total wheat protein<sup>1</sup>
- Highly resistant to intestinal proteases and heat<sup>1</sup>

Associated with non-celiac wheat intolerance?<sup>1,2</sup>

Modern gluten-containing staples (hybridized wheat) have levels of ATIs 100-fold higher than gluten free food<sup>3</sup>

- Older wheat variants (Emmer, Einkorn) have lower ATI bioactivity
- GF grains lowest ATIs



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## Atypical Wheat Allergy

Learn more on [foodallergy.org](http://foodallergy.org)

**Avoid these wheat foods:**

Wheat (flour, breadcrumbs, grass, bran), wheat protein isolate, bulgur, cereal extract, couscous, cracker meal, durum, emmer, einkorn, farina, freekeh, hydrolyzed wheat protein, kamut, matzoh, pasta, seitan, semolina, spelt, triticale...

May contain wheat:

Glucose, oats, soy sauce, starch, surimi

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### What If It's A1 B-Casein Intolerance?



A2




A1/A1  
A1/A2  
A2/A2

Goats, sheep, water buffalo and human breast milk contain A2-type β-casein protein

- Most dairy operations pool all of this milk together so conventional milk is a mix of A1/A2 β-casein proteins
- It is possible to identify cows that produce A2/A2 through a simple genetic test
- Milk produced by these cows is generally considered A1 protein-free

Due to a genetic mutation, cows can produce milk with 3 variations of casein (A1/A1, A1/A2, A2/A2)


  
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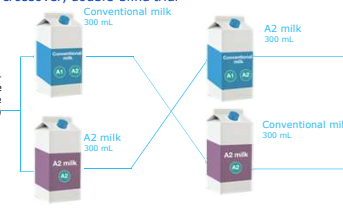
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### Milk Containing A2 β-Casein Reduces GI Symptoms of Milk Intolerance

Randomized, crossover, double-blind trial

Patients with self-reported lactose intolerance (N=600)



At 12 hours, A2 milk associated with significantly (P<0.0001) lower GI symptoms

- Bloating
- Abdominal pain
- Stool frequency
- Stool consistency

Baseline
3 days washout
12 hours
7 days washout
12 hours

He M et al. Nutr J. 2017;16:72.

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## Histamine Intolerance

- Histamine: chemical released from our immune cells, in foods, created by gut microbes from amino acid
- Histamine intolerance results from a disequilibrium of accumulated histamine and the capacity for histamine degradation
- In healthy persons, dietary histamine can be rapidly detoxified by diamine oxidase (DAO), whereas persons with low amine oxidase activity are at risk of histamine toxicity
- DAO is synthesized by mature apical enterocytes-located on upper intestinal villi. Mucosal damage (gastroenteritis, SBS) may reduce DAO

Maintz L, Novak J. Am J Clin Nutr. 2007;85(3):1185-1196. 2. Enck D et al. Can J Gastroenterol Hepatol. 2016;Article ID: 4892501.

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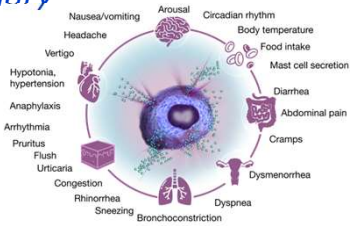
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## Histamine-Mediated Symptoms: A Summary



Maintz L, Novak J. Am J Clin Nutr. 2007;85:1185-1196.

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## Foods Rich in Histamine



### Fruits

Citrus fruits, strawberries, kiwifruit, papayas, pineapples, dried fruits



### Vegetables

Tomatoes, spinach, eggplants



### Fish

Mackerel, tuna, sardines, anchovies, herring



### Aged cheeses

Cheddar, Gouda, Roquefort, Parmesan



### Other

Alcohol, nuts, eggs, cured meats, chocolate, leftover meat or fish

Spencer M et al. Curr Treat Op Gastroenterol. 2014;12:424-440.

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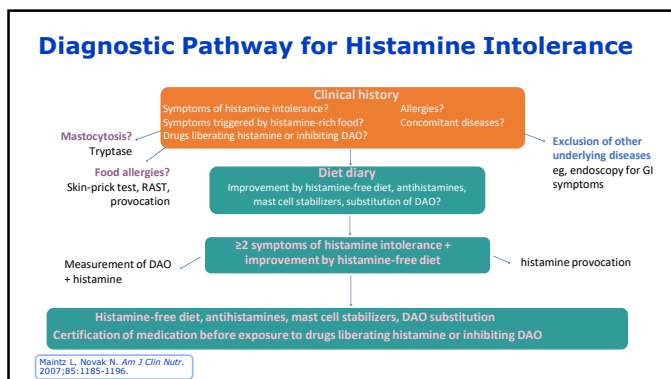
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### Reducing Dietary Histamine: *Tips*

- Minimize fermented foods (aged cheeses, soybean paste, kimchi, alcoholic drinks due to higher histamine content)
- Don't allow foods to linger outside the refrigerator – especially meat products, as histamine content can increase due to microbial degradation; freeze leftovers for later use
- Minimize grilling and frying, as this method of cooking increases histamine; instead choose raw or boiled
- Choose fresh foods when possible: fresh *not aged* meats, fresh caught fish; avoid canned or leftover meats/fish (e.g. canned tuna, anchovies)
- Consult a registered dietitian to help manage diet, nutritional needs

Chung BY, et al. Ann Dermatol. 2017;29(6):706-714. doi:10.5021/ad.2017.29.6.706

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### Sucrose Intolerance

- Starch and sucrose use sucrase-isomaltase enzyme complex for digestion
- Congenital sucrase isomaltase deficiency screened in pediatrics
- May be called (GSID) in adults, presents similarly

Food	Choose
Dairy	Cow's milk, cream cheese, hard cheeses, plain cottage cheese, ricotta cheese, plain yogurt
Protein	Eggs, chicken, beef, lamb, pork, tofu, turkey
Vegetables	Alfalfa sprouts, artichokes, asparagus, cabbage, cauliflower, celery, chard, cucumber, eggplant, endive, green beans, kale, lettuce, peppers, snow peas, spinach, tomatoes, summer squash, zucchini
Fruit	Avocado, blackberries, blueberries, cherries, currents, grapes, kiwifruit, lemon/lime, strawberries, rhubarb, raspberry, pomegranate.
Sweeteners	Dextrose, glucose
Nuts, seeds	Almond, Brazil, hazelnut, peanut, pecan, flaxseed, pumpkin seed
<b>AVOID</b>	<b>Baked goods, beans, breads, grains, pasta, crackers</b>

<https://www.csidcares.org/treatmen/diet/>  
<https://www.sucroseintolerance.co/ny/choosing-your-food/>

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### SI in Kids

- Sx sucrose intolerance doesn't appear in infants until they start ingesting sucrose- and starch-containing foods (fruit juices, solid foods, common baby foods, milk-based formula)
- Breastfed infants may not show symptoms until a milk-based formula is introduced into their diet, or they begin eating solid foods
- Present w/ FTT, chronic abdominal pain, watery diarrhea
- Abdominal distention, gassiness, chronic colic, irritability, diaper rash, and vomiting can all be signs of pediatric sucrose intolerance

<https://www.sucroseintolerance.com/symptoms/>

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### SI in Adults

- Adult symptoms may be limited to increased frequency of loose stools, abdominal distention, and flatulence
- Some people are almost "used to it" – expect diarrhea to be normal
- Episodic watery diarrhea may occur when ingesting foods containing high levels of sucrose
- Also, diarrhea may alternate with constipation, which can contribute to an IBS misdiagnosis
- Testing: sucrose breath test, genetic markers, biopsy for disaccharidase assay

<https://www.sucroseintolerance.com/symptoms/>

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- Encourage healthy fats: omega 3, monounsaturated fats via olive oil, nuts, seeds
- Fat malabsorption or intolerance does not necessitate a fat free diet!
- May be indicator of SIBO, pancreatic insufficiency, BAD- work with GI doctor!
- Spread fats out including some at each meal; this will aid satiety and provide balance to diet
- Essential fats: omega 6: Linoleic acid (safflower), omega 3: alpha-linolenic acid (walnut, soybean, flax, chia)

## Fat Intolerance/ Maldigestion

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### Food Intolerance: *Recap*

- Often portion driven. Example: Lactose intolerance: many people can tolerate 4 grams + per serving of lactose; can use over the counter lactase enzymes to aid digestion. Fat intolerance does not necessitate a fat free diet!
- Histamine: stress management, reduce histamine in diet, mast cell stabilizers and anti-histamines to manage symptoms
- FODMAPs: reduce, re-challenge and personalize to least restrictive diet. Select correct candidate, utilize FODMAP gentle or alternative therapy as indicated.
- Sucrose isomaltase deficiency triggers bowel symptoms similar to IBS. 4 genetic variants associated with 3-4 fold reduction in the likelihood of response to LFD.<sup>1</sup>
- Beta-casein: choose goat or sheep milk/cheese; trial A2 milk in dairy intolerant.

Eswaran S, et al Is Sucrose the Sixth FODMAP in a Subset of Patients with Irritable Bowel Syndrome with Diarrhea and Sucrose Sensitivity Deficiency. IBSW 2019, presentation 347.

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### Psychogastroenterology: Brain-Gut Therapies for IBS

Megan E. Riehl, PsyD  
 Assistant Professor of Medicine  
 Clinical Director, GI Behavioral Health Program  
 Michigan Medicine  
 Twitter & Instagram @DrRiehl



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### What is Psychogastroenterology?

The application of evidence-based psychological interventions and scientific practice for the management of gastrointestinal conditions.



Keefe L, et al. Gastroenterology 2018;134:1249-1257

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## The Burden of Chronic GI Conditions

**SUBSTANTIAL**

- Cost our health care system **billions** of dollars
- Cannot be disentangled from psychosocial factors requiring multidisciplinary care

Van Duijnhoven L, et al. Gastroenterology 2016;151:2255-2263  
Kao R, et al. Gastroenterology 2018;154:1249-1257  
Joshi M, et al. Gastroenterology 2018;154:1249-1257

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## Who Do We Treat?

### Disorders of Gut-Brain Interaction (DGBI):

- No pathophysiology to identify the underlying cause of symptoms
- Medical workup = "normal;" "unremarkable;" "reassuring"
  - Irritable Bowel Syndrome (IBS)
  - Functional Dyspepsia
  - Functional Heartburn

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## Who Do We Treat?

### Organic Disease

Structural or chemical abnormalities

- Inflammatory Bowel Disease (IBD)
  - Crohn's Disease
  - Ulcerative Colitis
- Gastroesophageal Reflux Disease (GERD)

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## Brain ↔ Gut: A Bi-Directional Pathway


**DGBI**

- Higher rates of depression and anxiety in patients with DGBI
- GI-specific anxiety is a predictor of symptom severity and disability

**IBD**

- 6-fold increase in anxiety symptoms in those with normal anxiety but active IBD
- 2-fold increase in the risk of IBD flares in patients with anxiety, but with inactive disease at baseline

Genovese et al. Gastro 2018;134:1533-1540.  
Lalonde et al. Psychosom Med 2017;59:99-105.  
Lee et al. J Neurogastroenterol Motil 2017;23:349-362.  
\*Slide used with permission from Dr. Sarah Kivimäki

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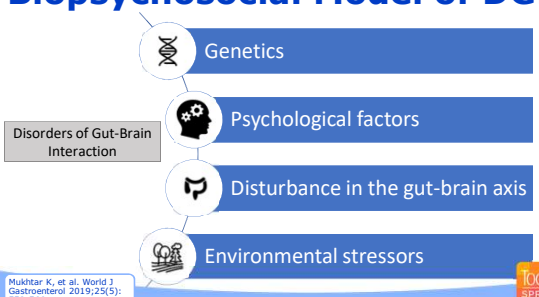
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## Biopsychosocial Model of DGBI



Disorders of Gut-Brain Interaction

- Genetics
- Psychological factors
- Disturbance in the gut-brain axis
- Environmental stressors

Mukhtar K, et al. World J Gastroenterol 2019;25(5): 552-566.

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## The Second Brain

“Trust your gut”  
“I’ve got butterflies in my stomach”

The Little Brain  
Enteric Nervous System (ENS)



- The ENS is two thin layers of more than 100 million nerve cells lining your gastrointestinal tract from esophagus to rectum.

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## Mood Disorders in IBS: Prevalence Rate

Patients with IBS have a three-fold increased odds of either anxiety or depression, compared to healthy subjects

Anxiety

Depression

- Symptoms = 39.1%
- Disorders = 23%

- Symptoms = 28.8%
- Disorders = 23.3%

Zamani M, et al. Aliment Pharmacol Ther 2019; 50(2):132-143.

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## Disordered Eating in GI Conditions

- 23.4% of patients with GI disease (n=691) displayed disordered eating patterns
- Dietary-controlled GI disorders:
  - Lifelong modifications to diet may aid in reducing symptoms associated with disruptions to the GI tract: nausea, bloating, diarrhea, constipation, weight changes, abdominal pain

Celiac Disease	IBS and IBD
Necessary to follow strict, life-long gluten free diet.	Trial and error regimens to identify food triggers.

Satherley et al. Appetite, 2015; 84:240-50.

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## Orthorexia Nervosa & ARFID

**Table 1 Emerging eating disorders relevant to gastroenterologists**

Orthorexia nervosa (4)	Obsessive focus on "healthy" eating marked by exaggerated emotional distress in relationship to food choices perceived as unhealthy. Weight loss may occur related to dietary choices, but this is not the primary goal as evidenced by the following: <ol style="list-style-type: none"> <li>1. Compulsive behavior and/or mental preoccupation regarding restrictive dietary practices believed to promote optimum health.</li> <li>2. Violation of self-imposed dietary rules causes exaggerated fear of disease, sense of personal impurity, and/or negative physical sensations, along with anxiety and shame.</li> <li>3. Dietary restrictions escalate over time and may lead to elimination of entire food groups and involve progressively more frequent and/or severe "cleanses" (partial fasts) regarded as purifying or detoxifying.</li> </ol>
Avoidant/restrictive food intake disorder (5)	A problem with eating or feeding (e.g., seeming disinterest in food or eating, repulsion to certain foods based on their sensory qualities, fears about aversive effects of eating) leading to recurrent inability to take in adequate nutrition and/or energy coupled with one (or more) of the following: <ol style="list-style-type: none"> <li>1. Major nutritional deficiency</li> <li>2. Substantial weight loss</li> <li>3. Reliance on NG or G tube feeding or oral nutritional supplements</li> <li>4. Impaired psychosocial function</li> </ol>

Chey W. Am J Gastroenterol, 2019; 114(2):201-203.

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## ARFID in Adult GI Population

- Nine Item ARFID Screen (NIAS) prospectively administered (cutoff score of 24 = positive ARFID screen)
- 19.6% of patients in outpatient GI clinic screened positive
- IBS patients 2x as likely to screen positive compared to non-IBS patients

**Table 3: Patient Demographic and Clinical Characteristics**

	Enterocolitis (n=37)	Positive ARFID Screen (n=42)	Negative ARFID Screen (n=255)	p-value
<b>Age (years)</b>				0.32
<20	1 (0.3%)	0 (0%)	1 (0.3%)	
20-29	81 (21.9%)	111 (26.2%)	54 (21.1%)	
30-39	87 (23.5%)	111 (26.2%)	46 (18.0%)	
40-49	51 (13.8%)	14 (3.3%)	58 (22.7%)	
50-59	41 (11.1%)	11 (2.6%)	44 (17.2%)	
60-69	41 (11.1%)	11 (2.6%)	50 (19.6%)	
≥70	10 (2.7%)	1 (0.2%)	13 (5.1%)	
<b>Gender</b>				0.04
Male	89 (23.9%)	11 (2.6%)	60 (23.5%)	
Female	206 (56.1%)	47 (11.0%)	195 (76.5%)	
<b>Race/Ethnicity</b>				0.54
White/Caucasian	149 (40.3%)	41 (9.7%)	214 (83.9%)	
Black/African American	18 (4.8%)	1 (0.2%)	14 (5.4%)	
Hispanic/Latino	17 (4.5%)	2 (0.5%)	4 (1.5%)	
American Indian	4 (1.1%)	0 (0%)	4 (1.5%)	
Native Pacific Islander	1 (0.3%)	0 (0%)	1 (0.3%)	
Multiple races	1 (0.3%)	1 (0.2%)	1 (0.3%)	
Other	1 (0.3%)	1 (0.2%)	1 (0.3%)	
Unknown/declined	21 (5.7%)	1 (0.2%)	1 (0.3%)	
<b>IBS*</b>				0.42
General GI	217 (58.4%)	44 (10.5%)	172 (67.4%)	
Medical Subspecialty	100 (27.1%)	48 (11.4%)	82 (32.1%)	

Harer et al., Am J Gastroenterol, 2018; 113(suppl):S247-S248.

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## Self-Report Screening Measures

### Nine Item ARFID Screen (NIAS)

- S** Do you make yourself SICK (vomit) because you feel uncomfortably full?
- C** Do you worry that you have lost CONTROL over how much you eat?
- O** Have you recently lost more than ONE stone in a 3 month period?
- F** Do you believe yourself to be FAT when others say you are too thin?
- F** Would you say that FOOD dominates your life?

	Strongly Disagree	Disagree	Slightly Disagree	Slightly Agree	Agree	Strongly Agree
1. I am a picky eater	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. I dislike most of the foods that other people eat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. The list of foods that I like and will eat is shorter than the list of foods that other people eat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. I am not very interested in eating. I seem to have a smaller appetite than other people	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. I have had pain (especially in the upper middle throughout the day) or to eat a large enough amount of food at meals	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6. Even when I am eating a food I really like, it is hard for me to eat a large enough volume anyway	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. I avoid or put off eating because I am afraid of getting indigestion, choking, or vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. I restrict myself to certain foods because I am afraid that other foods will cause GI discomfort, choking, or vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. I eat small portions because am afraid of discomfort, choking, or vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Morgan et al., BMJ, 1999; 319(7223):1467-8. Zickgraf & Ellis, Appetite, 2018; 123:32-42.

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## The Underweight Patient (BMI <17)

- CBT in setting of GI Behavioral Health is NOT indicated in this population
- Patients require intensive outpatient disordered eating treatment

**National Institutes for Clinical Excellence (NICE) Guidelines for Management of Refeeding Syndrome**

**Patients at risk for refeeding syndrome**

ONE or more of the following: -OR- TWO or more of the following:

BMI < 16 kg/m <sup>2</sup>	BMI < 18.5 kg/m <sup>2</sup>
Unintentional weight loss of >15% in the previous 3-6 months	Unintentional weight loss of >10% in the previous 3-6 months
Little or no nutritional intake for >10 days	Little or no nutritional intake for >5 days
Low levels of potassium, phosphorus, or magnesium before refeeding	History of alcohol abuse or drugs including insulin, chemotherapy, antacids, or diuretics

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### Treatment Considerations

- Progressive restriction within an already restrictive diet
- Refusal to reintegrate foods during reintroduction protocol
- Discordance of clinical presentation of hx of clinical data
- Evidence of body dysmorphia
- Lack of concern with a severely restrictive diet or weight loss



Harer K. Gastroenterol Hepatol. 2019; 15(5):280-82. #TDVirtualSymposium Today'sDietitian SPRING SYMPOSIUM 2020

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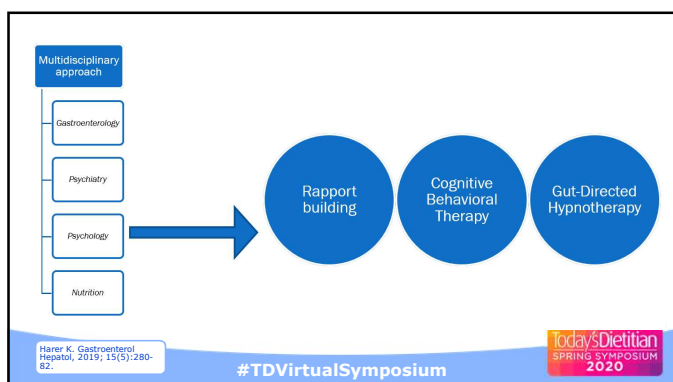
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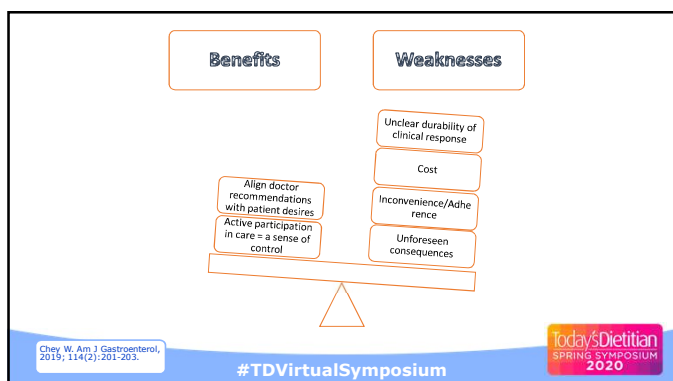
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## Brain-Gut Psychotherapies

Meta-analyses conclude that psychological therapies reduce GI symptoms in adults with IBS. These effects remain significant after short-term and long-term follow-up periods:

- Based on >30 years of research and > 30 RCTs
- Cognitive Behavioral Therapy and Gut-Directed Hypnotherapy have the strongest empirical support
- 60-70% patients in clinical trials are treatment responders

Ford et al. *Am J GI* 2014; 109: 1350-65  
 Laird et al. *Clin Gastroenterol Hepatol* 2016; 14: 937-947

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## Cognitive Affective Processes

Illness Anxiety	Global Tendency to worry about current and future bodily symptoms
Symptom-Specific Anxiety	Worry/hypervigilance around the likelihood/presence of specific symptoms and the contexts in which they occur
Hypervigilance/ Attentional Bias	Altered attention toward, and increased engagement with, symptoms and reminder of symptoms
Catastrophizing	2-pronged cognitive process in which an individual magnifies the seriousness of symptoms and consequences while viewing themselves as helpless

van Dulmen-Huisman L, Chowell R, Steeman EA, et al. *Gastroenterology*. 2016; 150(5):1350-1357.  
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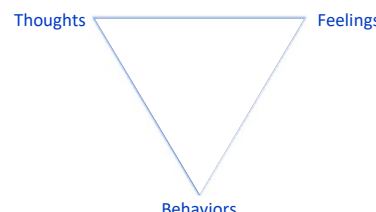
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## Cognitive Behavioral Therapy (CBT)



The diagram shows a triangle with 'Thoughts' at the top left, 'Feelings' at the top right, and 'Behaviors' at the bottom center. Lines connect each vertex to the other two, forming a continuous cycle.

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## Considerations for CBT

- Patient must be invested and participatory
- Untreated mental health disorders should be prioritized
- Change will not happen immediately
- Insight regarding the manner in which the patient's thoughts, feelings and behaviors impact their health is necessary

Kinsinger S. Psychol Res Behav Manag 2017;10:231-237.

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## CBT for IBS

- First applied to IBS in 1992
- ~20 RCTs across spectrum of DGBIs in pediatric and adult patient populations
- 40-65% of patients achieve significant symptom reduction
- Number Needed to Treat: 4-5

Kinsinger S. Psychol Res Behav Manag 2017;10:231-237.

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## GI-CBT

Psychoeducation	Relaxation Strategies	Cognitive Restructuring	Problem-Solving Skills	Exposure Techniques
<ul style="list-style-type: none"> <li>• GI problem education</li> <li>• Brain-gut axis</li> <li>• Physiological stress response</li> <li>• Rationale for behavioral treatment</li> </ul>	<ul style="list-style-type: none"> <li>• Diaphragmatic breathing</li> <li>• PMR, Guided Imagery, etc.</li> <li>• Relaxation activates the PNS, which can downregulate pain thresholds and normalize gut motility</li> </ul>	<ul style="list-style-type: none"> <li>• Assist patient in generating more accurate cognitive responses to stress and symptoms</li> <li>• De-catastrophizing</li> <li>• Symptom related anxiety</li> <li>• Address hypervigilance</li> </ul>	<ul style="list-style-type: none"> <li>• Emotion-focused coping for uncontrollable stress</li> <li>• Encourage flexible coping</li> </ul>	<ul style="list-style-type: none"> <li>• Face situations that patient has avoided because of fear of symptom</li> <li>• Goal: decrease avoidance behaviors and reduce appraisals that symptoms will be harmful</li> </ul>

Kinsinger S. Psychol Res Behav Manag 2017;10:231-237.

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## Gut-Directed Hypnotherapy

- Thorough explanation of medical hypnosis with patient
- **This is not exploratory hypnosis**
- Discuss limits of hypnosis
- Contraindicated for untreated trauma





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## Gut-Directed Hypnotherapy

Benefits and Limitations of Gut-Directed Hypnotherapy for DGBIs	
Benefits	Limitations
<ul style="list-style-type: none"> <li>• Highly effective in refractory patients</li> <li>• Very safe</li> <li>• Important in management of extra-intestinal symptoms</li> <li>• Reduced healthcare utilization</li> <li>• Socioeconomic benefits (ex: reduced absenteeism)</li> <li>• Reduced need for medication</li> <li>• Improves resilience</li> <li>• Teaches self management skill</li> <li>• Improves QOL</li> <li>• Improves psychological and cognitive function</li> </ul>	<ul style="list-style-type: none"> <li>• Time intensive (6-12 sessions + daily home practice)</li> <li>• Requirement of working with a trained therapist</li> <li>• Stigma, misconceptions and negative perception</li> <li>• Relatively expensive</li> <li>• Requires highly motivated patients</li> <li>• Limited availability</li> </ul>

Vasant D & Whorwell P. Neurogastroenterol Motil. 2019; epub.



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## Effectiveness of Hypnotherapy

- RCTs demonstrate benefits from 3 months to 1 year post treatment
  - 10 RCTs and over 30 studies since the 1980s
- >50% improvements for >70% of patients
- Continued improvements and durability
- Patient feels empowered and hopeful through home practice

Miller V, et al., Alimentary Pharmacol Ther. 2015;41(9):844-853. Paterson D. Am J Clin Hygn. 2015;58(2):134-136.



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**GDH v. LFD: Randomized Controlled Trial**

- Hypnotherapy (n=25) → clinically-significant improvements in overall GI sxs = 72%
  - 6 months post treatment = 74%
- Diet (n=24) → clinically-significant improvements in overall GI sxs = 71%
  - 6 months post treatment = 82%
- Hyp + Diet (n=25) → clinically-significant improvements in overall GI sxs = 73%
  - 6 months post treatment = 54%

Peters S., et al., Aliment Pharmacol Ther. 2016; 44(5):447-59.  
Hill D., Muir J., & Gibson P. Gastroenterology Hepatol (N Y). 2017; 13(1):35-45.

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**GDH v. LFD: Randomized Controlled Trial**

- IBS QOL improvements across groups
- Hypnotherapy resulted in superior improvements in psychological indices
- Hypnotherapy should be considered an alternative to dietary management

**Hypnotherapy may be a better treatment option for individuals with IBS: takes the focus off restrictive diet and eating practices**

Peters S., et al., Aliment Pharmacol Ther. 2016; 44(5):447-59.  
Hill D., Muir J., & Gibson P. Gastroenterology Hepatol (N Y). 2017; 13(1):35-45.

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**Potential Mechanisms**

- Evidence for central mechanisms
  - Decreased somatization and general distress
- Improvements in cognition
  - Changing beliefs about the significance of the symptoms
- Normalizes central processing of visceral sensations and signals
- Limited evidence for direct impact on GI physiology
  - Reduction in autonomic nervous system activity
  - Change in motility
  - Improvement in visceral pain sensitivity

Palsson O., et al., Dig Dis Sci. 2002;47(11):2605-14.

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**“I don’t think I am hypnotizable.”**

- Reduced attention to bowel symptoms
- Altered perception of your experience with symptoms
- Increase overall sense of health and comfort
- Immunity to intestinal disturbance from internal and external stimuli
- Normalization of bowel functioning

Pelsson O & van Tilburg M. Am J Clin Hypn, 2015; 58(1):5-21.

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**Reduced Attention to Bowel Symptoms**

“You pay less and less attention to unpleasant feelings inside you every day, as your sensitivity to bowel pain and discomfort steadily fades away and disappears.”

Pelsson O & van Tilburg M. Am J Clin Hypn, 2015; 58(1):5-21.

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**Normalization of Bowel Functioning**

“You will probably notice after you leave here today that your intestines are more and more functioning with a healthy, steady, comfortable rhythm that does not cause you problems, a healthy natural rhythm that does not disturb your comfort.”

Pelsson O & van Tilburg M. Am J Clin Hypn, 2015; 58(1):5-21.

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## Summary

- GDH is an evidence-based intervention strongly supported for use in IBS
- With careful explanation of the intervention, patients are receptive and enjoy use
- Hypnotherapy should not be used until a patient has had a medical work up
- Patients respond well to virtual delivery of GDH
- Treatment typically 5-7 sessions

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## A Mindful Minute

Foster a mindful environment of compassion and empathy

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## In Conclusion

- Psychogastroenterology should be included early and often in the treatment of IBS
- Behavioral interventions are effective and well received by patients
- Allow the GI psychologist to determine the appropriate treatment plan for each patient
- A holistic approach to IBS can aid patients in learning adaptive health strategies for long term QOL improvements

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### Case Study #1

- 45 yo female with intractable IBS-D for past 5 years
- Preliminary GI w/u normal includes: colonoscopy, lab + stool tests
- Labs/testing WNL, weight is stable but she has to force eating because she feels full.
- Sx: severe bloating, post-prandial fullness, abdominal pain, diarrhea, anxiety
- GI doctor does not "believe" in SIBO diagnosis but patient had read online about it and feels this makes sense
- Tx: Psyllium husk not helpful. Probiotic trial made her more bloated. Has removed most raw vegetables from diet with some improvement. Has heard of LFD but has not tried it yet. States: "You are my last-ditch effort"

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### Multi-Disciplinary Approach to Care in IBS



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### Questions?

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