Nutrition and the Role of Supplements in IBD

October 22, 2017

Seattle Children's IBD conference

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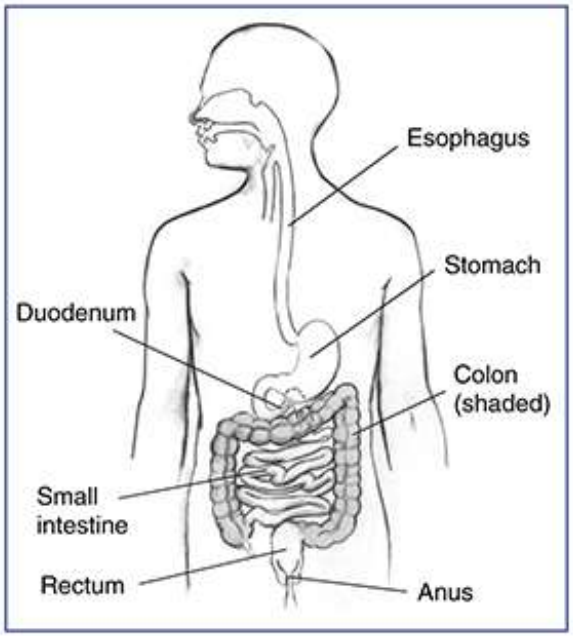
Learning Objectives

1) Review the role of location of disease
2) Discuss common misconceptions about diet and IBD: Fact vs. Fiction
3) Review low residue and high fat diets
4) Discuss special diets and dietary therapies
    a) Exclusive enteral nutritional (EEN)
    b) Specific carbohydrate diet

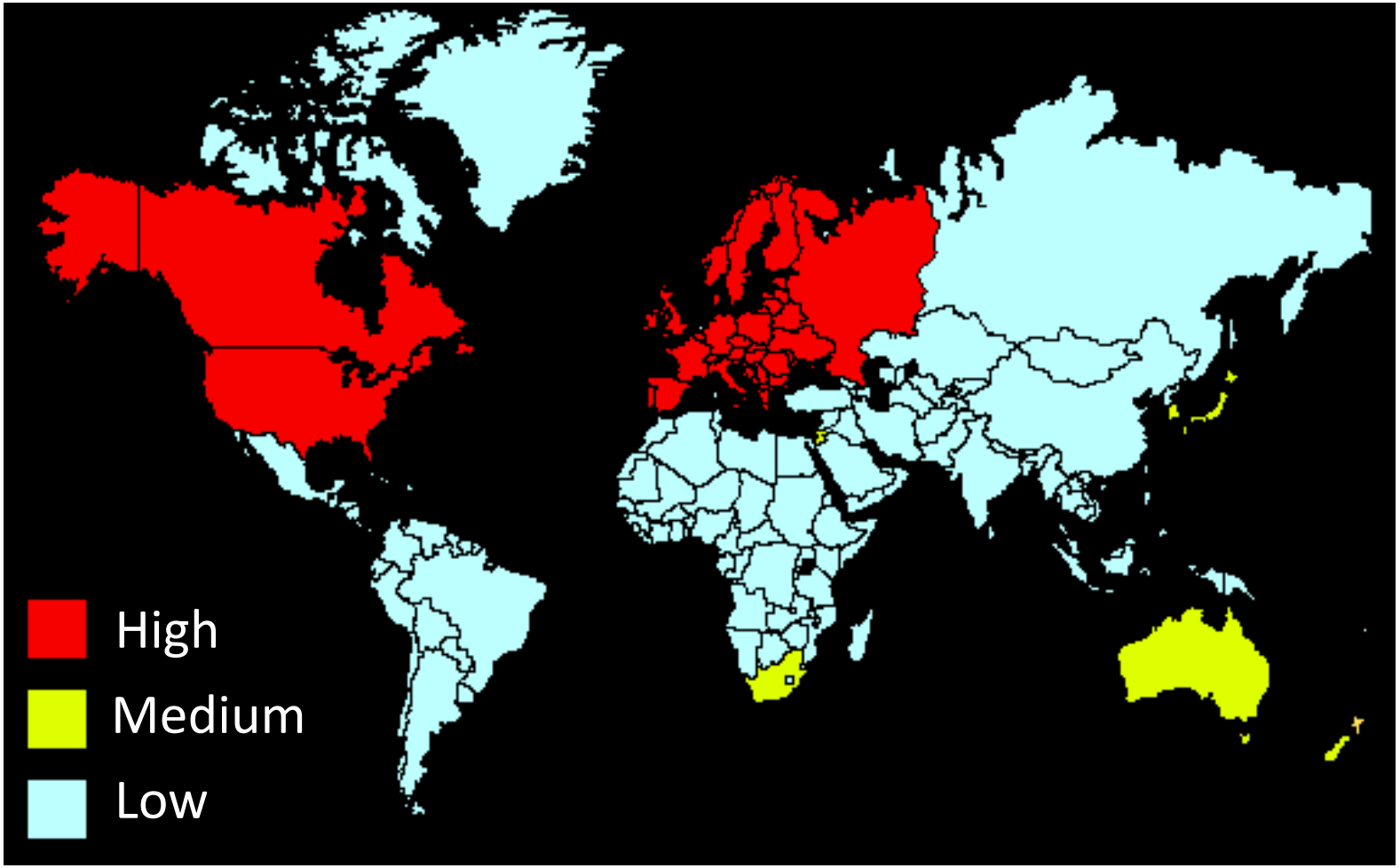
Inflammatory Bowel Disease (IBD)

- Definition: chronic inflammatory condition that can affect any portion of the GI tract
  - Includes systemic manifestations
  - Characterized by remitting, relapsing course

- Two types of IBD:
  - Crohn's disease (CD)
  - Ulcerative colitis (UC)

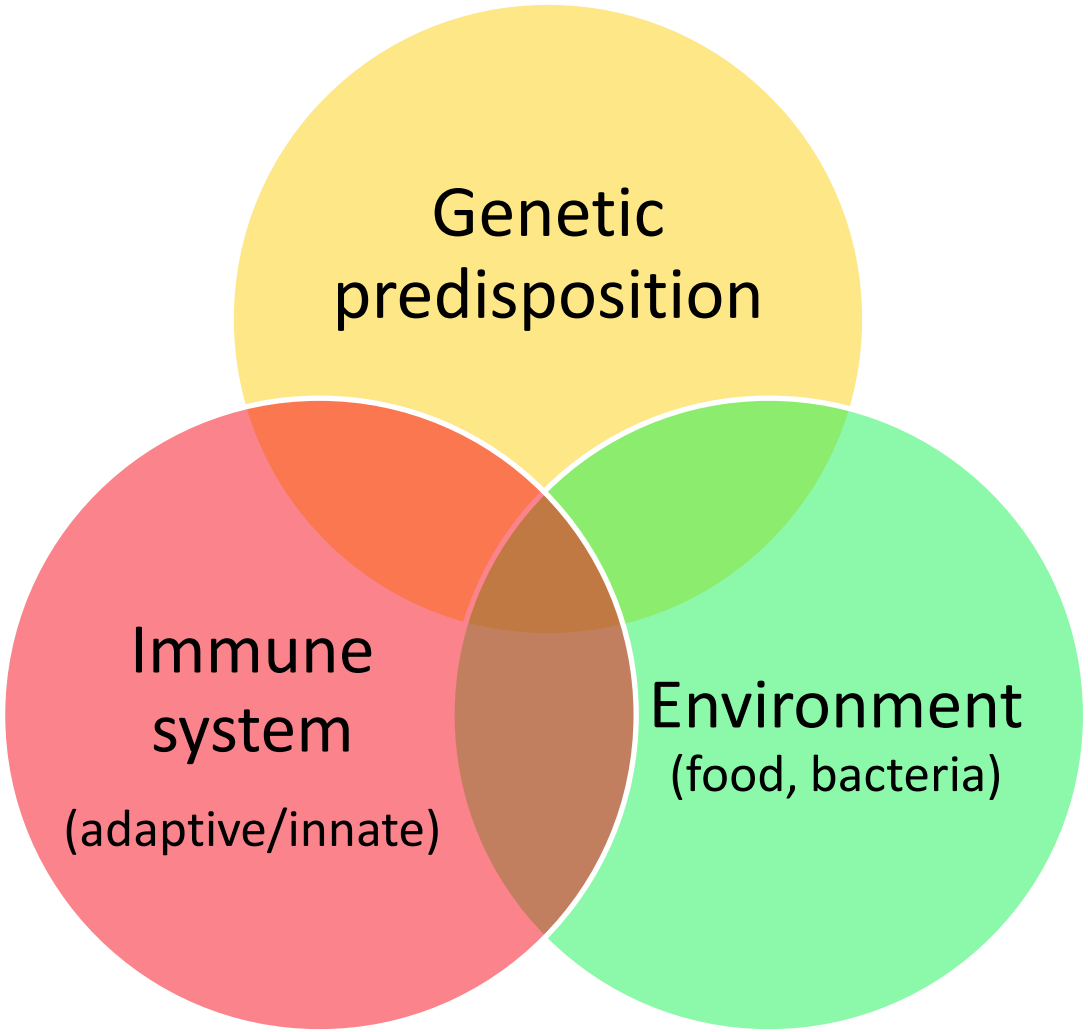


Epidemiology: geography



Lashner. Gastroenterol Clin North Am 1995.

What causes IBD?



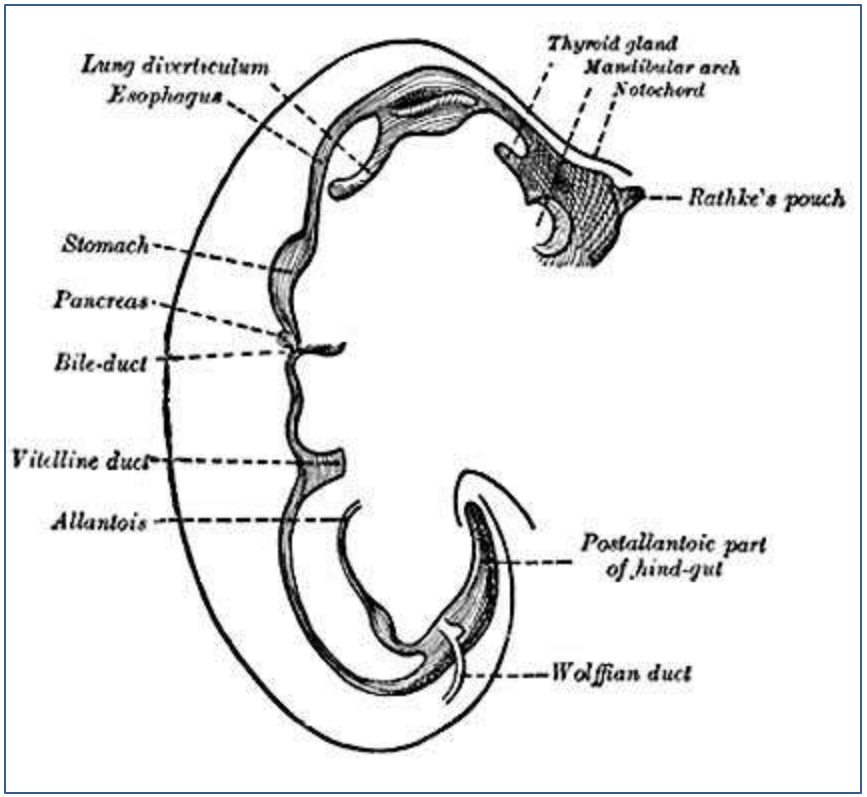
Risk of developing IBD

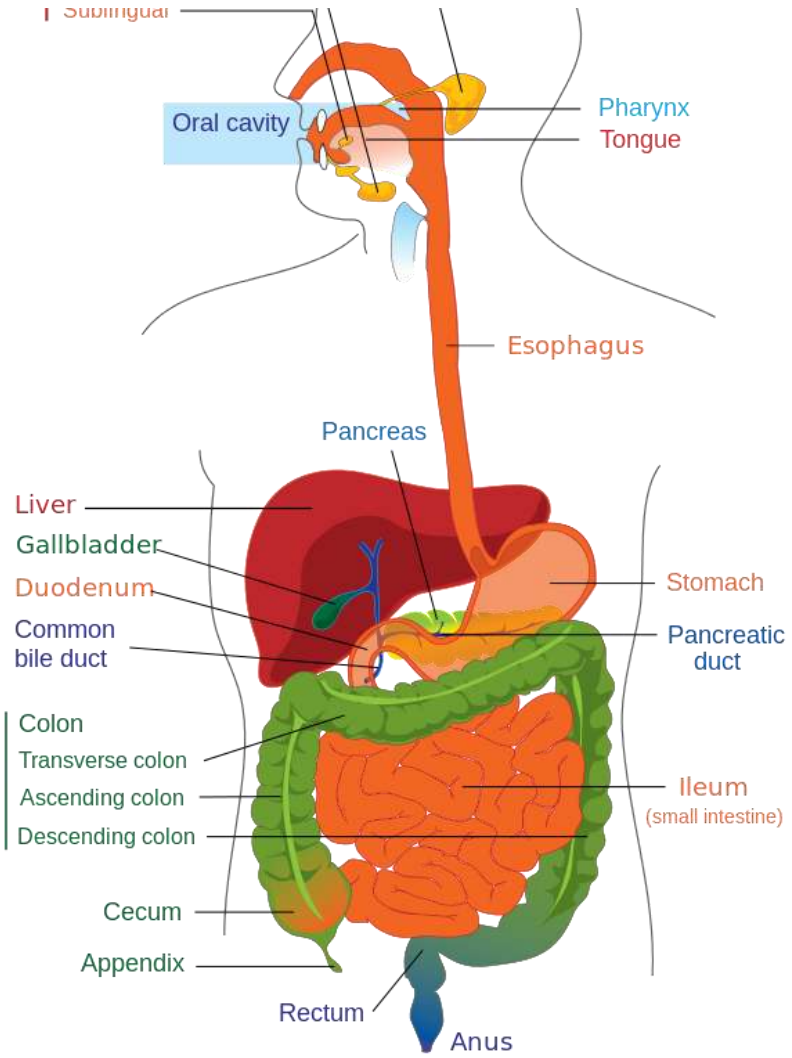
- Incidence of IBD is rising: typically occurring first in more industrialized countries
- Early life exposures are important in risk
  - Second-generation immigrants have a higher risk of developing IBD than first-generation
- Dietary factors associated with disease risk

Risk factor	Protective factor
Saturated fat	Fiber
Total PUFA	Fruits
Omega-6 PUFA	Vegetables
Meat	

Hou JK. Am J Gastro 2011.

The GI tract is a long tube

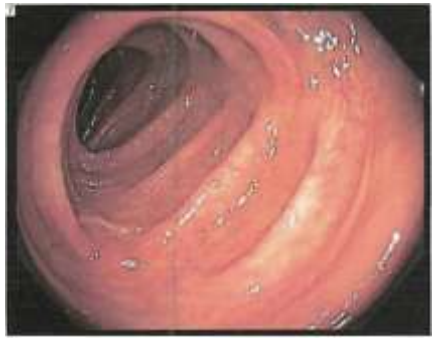




Disease Location: Ulcerative Colitis vs. Crohn's Disease

* Medical therapies are <u>similar</u> for both Crohn's disease and ulcerative colitis
* Efficacy of nutrition therapies may depend upon location.
    - -Exclusive enteral nutrition (EEN)
    - -Specific carbohydrate diet (SCD)

Location of disease can explain symptoms



Location	Symptoms
Mouth	Ulcers in mouth
Stomach	Pain immediately after eating
Small intestine	-Pain shortly after eating -Bloated/gurgling sensation -Vomiting -Diarrhea (or constipation)
Colon	-Frequent, loose, bloody stools -Waking up at night to stool
Perianal	-Drainage into underwear -Pain with stooling -Pain with sitting

Location of disease: Is EEN effective for UC and Crohn's?

- EEN: Poor outcomes in patients with UC, or CD involving the **colon**
- Comparing remission based on CD location (ileal, ileocolonic, or colonic)
  - **Lowest** rates of remission in exclusive colonic disease

- Conclusion: Data suggests that EEN is most effective for ileal or ileocolonic Crohn's

Seidman EG. Gastro Clin N Am 1989.
Afzal AN. Dig Dis Sci 2005.

Location of disease: Specific Carbohydrate Diet (SCD)

- The SCD is a whole-food based diet that restricts numerous foods
- SCD has been demonstrated to be effective in BOTH:
  - Crohn's disease
  - Ulcerative colitis

Suskind DL. JPGN 2014.
Obih C. Nutrition 2016.

Common misconceptions about diet and IBD

Common misconceptions about diet and IBD

Myth #1: A low fiber diet is good for my IBD

- Crohn's disease: Higher dietary fiber intake associated with 40% lower risk
  - Risk reduction greatest for fiber from fruit
- Ulcerative colitis: no worsened inflammation with fiber; increase in beneficial short-chain fatty acids

Ananthakrishnan A. Gastro 2013.

Fiber

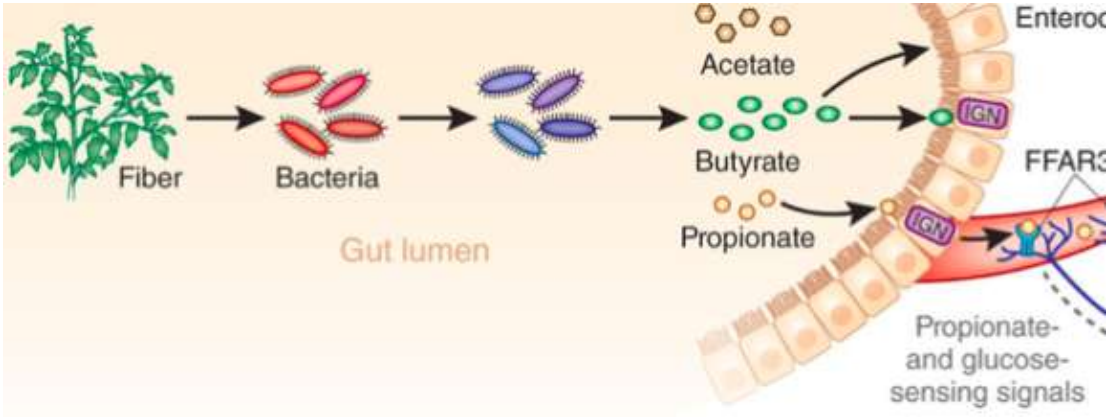
Fiber: the edible parts of plants and carbohydrates that are resistant to digestion and absorption in the intestine

- Soluble fiber: dissolves in water→ forms gel and slows intestinal transit time
  - Ex: oats, nuts, seeds, beans, lentils, certain fruit/veg

- Insoluble fiber: does not dissolve in water → increases volume of stool and speeds transit time
  - Wheat bran, vegetables, whole grains

Metabolism of fiber in the gut

Fiber is metabolized by bacteria to become short chain fatty acids (SCFAs), which nourish intestinal epithelial cells



Common misconceptions about diet and IBD

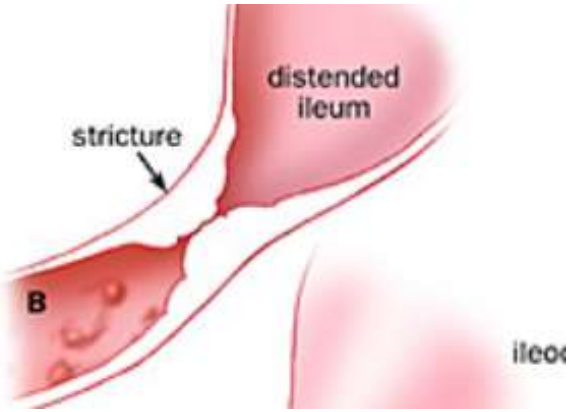
Myth #2: When in an IBD flare, I need to be on a low-residue diet

No!

- Fiber is an important part of gastrointestinal tract health.
- Though certain raw fruits/vegetables can worsen symptoms, they do not worsen inflammation
- Fiber *should* be eaten when in a disease flare

Common misconceptions about diet and IBD

Myth #3: I cannot eat any nuts or seeds if I have IBD



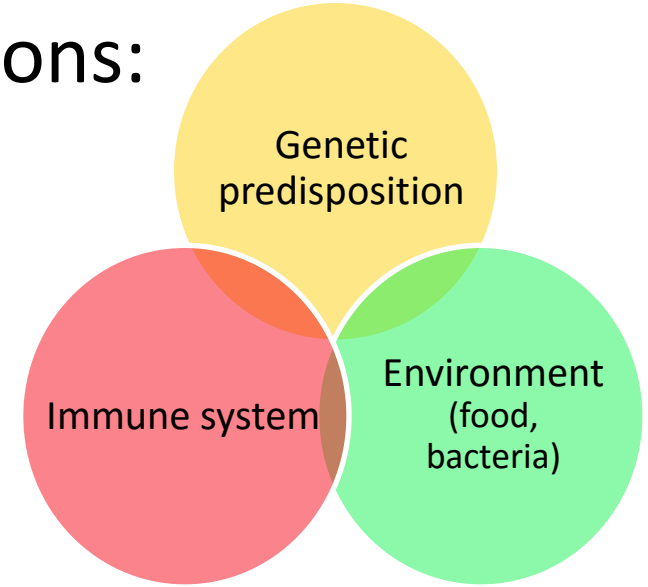
In IBD, foods that can cause a blockage in a narrowed area of intestine should be avoided

- Small seeds (like on strawberries) are ok to eat!
- Nut butters and flours are fine as well

Common misconceptions about diet and IBD

Myth #4: Diet is **not** important if I am taking immunosuppressive medications:

- Prednisone
- Azathioprine
- Methotrexate
- Remicade



1) Diet plays a broad role in everyone's health.
2) In IBD, diet may play a more important role
3) Diet + medications can work together

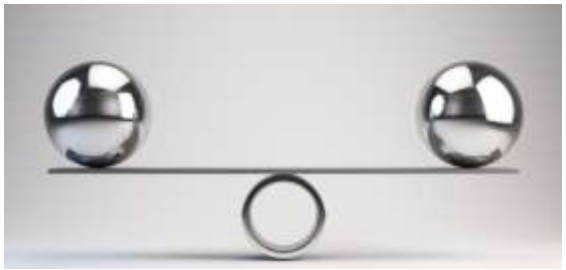
Common misconceptions about diet and IBD

Myth #5: Dietary therapy for IBD can help *anyone* avoid medications

- Diet therapy alone does **not** work for everyone
- It is important to follow objective parameters with your medical team to assess for healing:
  - Labs
  - Stool markers
  - Endoscopy
  - Imaging

Common misconceptions about diet and IBD

<u>Myth #6:</u> A high fat diet is harmful for patients with Crohn's or ulcerative colitis



Types of fat:

- Unsaturated fat—liquid at room temp; generally felt to be healthy fats
  - Omega-3: improve cholesterol, decrease inflammation (found in coldwater fish, walnut, flax)
  - Omega-6: increase inflammation (found in refined vegetable oils)
- Saturated fat—mainly found in animal foods

Common misconceptions about diet and IBD

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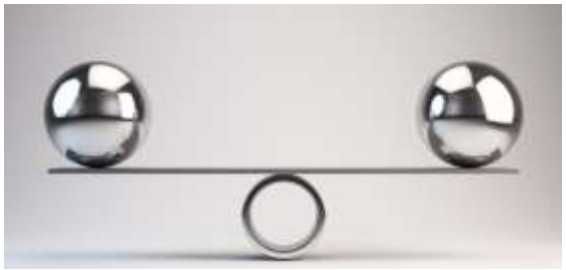


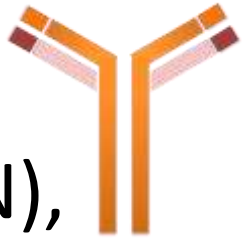
- A diet high in healthy fats can be quite healthy and well-balanced.

→ This can be beneficial for individuals with IBD

Dietary Therapy for IBD

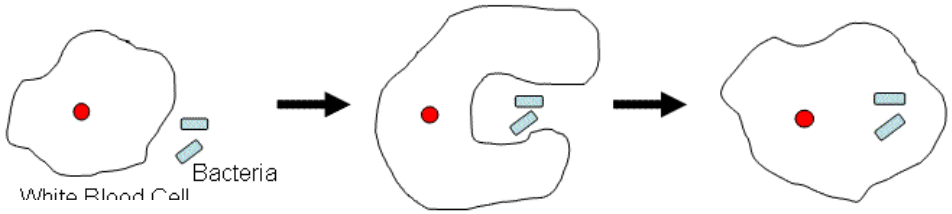
Strategies for treating IBD

- 5-ASA/Antibiotics
- Immunosuppression
  - Corticosteroids
  - Immunomodulator: azathioprine, methotrexate
  - Biologics: anti-TNF-alpha
- Nutrition—Exclusive Enteral Nutrition (EEN), Specific Carbohydrate Diet (SCD)



The conventional approach: Suppress the immune system

- Can be effective at controlling symptoms and even induce mucosal healing
- But, does not address environmental triggers
- Immunosuppression is associated with:
  - Infection
  - Increased risk of **cancer**
  - Other medication-specific side-effects



Siegel CA. Clin Gastro Hepatol 2009

Risk of developing IBD

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Risk factor	Protective factor
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Hou JK. Am J Gastro 2011.

Exclusive enteral nutrition (EEN)

- The one nutritional therapy that has been rigorously studied in IBD
- Also known as “defined formula diet”
- Provides 90-100% daily calories via a formula
  - Can be taken by mouth, or by feeding tube
  - Small amount of drink/food allowed

History: Use of Nutrition in IBD

- 1930s: EEN used for nutritional rehabilitation of patients with IBD in surgical units
- 1960s: Parenteral nutrition (PN) developed at Penn
- 1973: Votik et al reported on 13 patients with IBD successfully treated with EEN
  - Weight gain and ↓ inflammatory indices
  - Avoided risks associated with PN
- Subsequent use of EEN as therapy and studies designed to compare EEN with steroids

Votik AJ. Arch Surg 1973.
Kansal S. Gastro Research and Prac 2013.

Questions about EEN

1) Is EEN effective in adults and children?

2) What formulas should be used for EEN?

3) What are the barriers to using EEN?

What is the data for EEN efficacy in CD?

- Cochrane Systematic Review 2007:

  EEN for Induction of Remission in CD

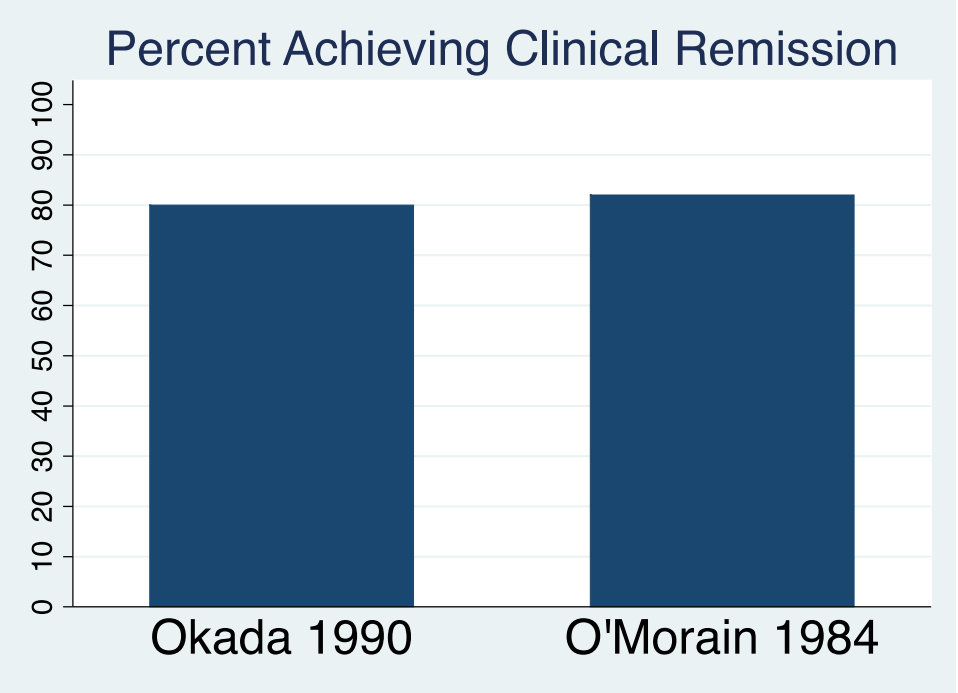
  - Conclusion: EEN is less effective than steroids
  - Limitations:
    - Mostly adult study subjects
    - Evaluating *clinical* outcomes
- Review of EEN in pediatric CD: effective in 70-80%
- Efficacy of EEN in adult CD has been questioned

Zachos M. Cochrane Review 2007.
Heuschkel RB. JPGN 2000.

1) Is EEN effective in adults and children?

- A recent review of EEN in adults with Crohn's disease:
  - Poor compliance: poor palatability and motivation
- Adults generally have longer disease duration and prior exposure to medications
- EEN in treatment-naïve adults with CD

- Conclusion: EEN can be effective in adult CD
  - but studies limited by poor compliance



Wall CL. World J Gastro 2013.
Okada M. Hepatogastroenterology 1990.
O'Morain C. Br Med J 1984.

2) What formula should be used for EEN?

- No significant differences in outcomes based on formula composition:
  - Protein: elemental, semi-elemental, or polymeric
  - Carbohydrate: variety of formulations
  - Low vs. high fat (<20 g vs. >20 g fat per 1000 kcal)
- Considerations:
  - Palatability
  - Osmotic load

Zachos M. Cochrane Review 2007.

2) What formula should be used for EEN?

- **Great variability** in formulas used, and protocols
- International questionnaire: 35 centers*
  - 23 different formulas used
  - Protein content of formulas used:
    - 90% polymeric formulas
    - 32% semi-elemental
    - 48% elemental
  - 81% permitted addition of flavorings
  - 68% allow clear fluids: ice, carbonated beverage, soup
  - Duration of EEN: mean 8.5 weeks (range <6 to >12)

Whitten KE. J Dig Dis 2012. *16 UK centers, 9 Europe, 8 Asia, 2 USA

3) What are the barriers to using EEN?

- Usage of EEN greatly varies:
  - 4% N. American pediatric GI physicians
  - 62% European counterparts
- Clinician perception about efficacy and/or difficulty of EEN therapy
  - Lack of exposure during training
- Cost, and lack of insurance support
- Lack of satisfactory exit strategy based on nutritional therapy (but, more to come…..)

Levine A. J Pediatric Gastro Nutrition 2003.
Stewart M. J Pediatric Gastro Nutrition 2011.
Critch. J Pediatric Gastro Nutrition 2012.

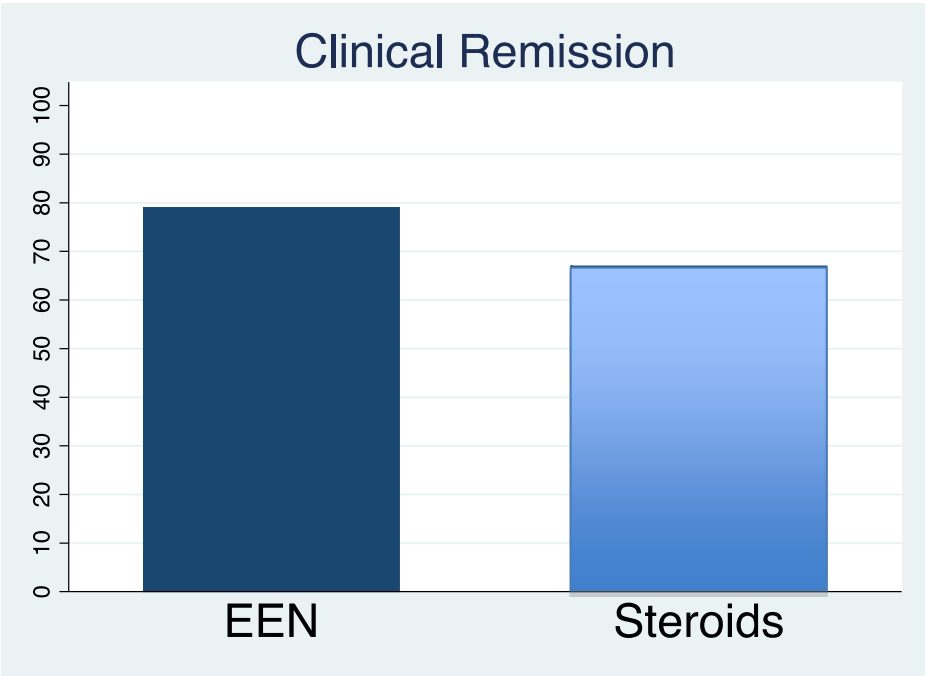
Questions about EEN

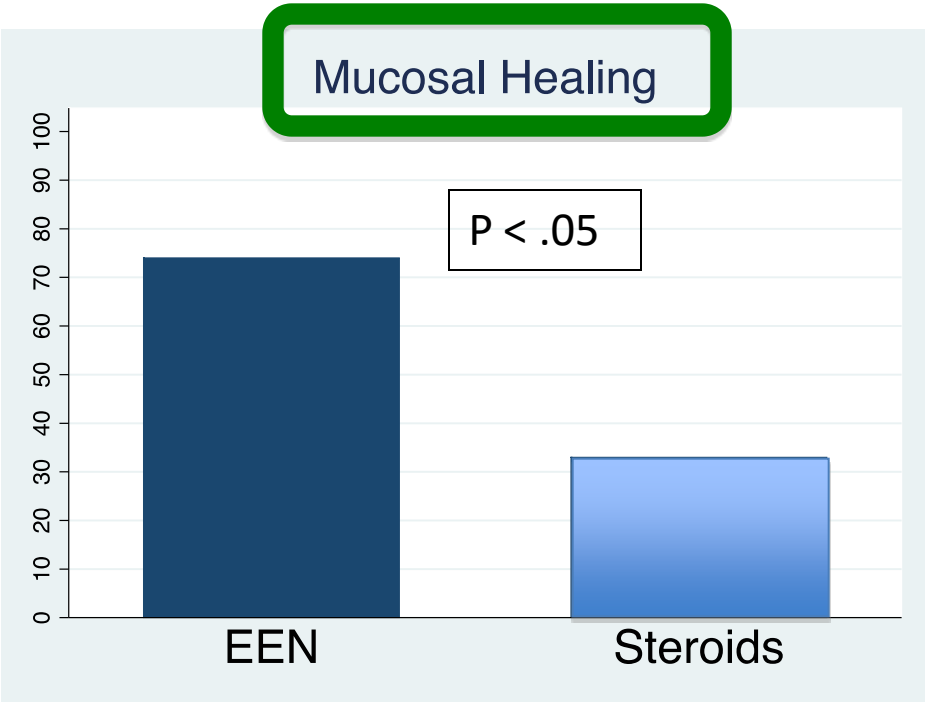
1) Is EEN effective in adults and children?
   - Both (but for adults better in treatment naïve)
2) What formulas should be used for EEN?
   - Formula type does not seem to matter
3) What are the barriers to using EEN?
   - Numerous: but practitioner perceptions are key

Inducing Remission with EEN

– 37 children with newly diagnosed Crohn's disease

– 10 week <u>randomized</u> trial: steroids vs. EEN





Borrelli O. Clin Gastro Hep 2006.

Proposed mechanism of action for EEN

Hypotheses:

- Nutritional restitution
- Direct effect on mucosa
- Reduction of pro-inflammatory cytokines
- Alteration of gut microbiota
- Avoidance of harmful food substances

How “exclusive” does EEN need to be?

Daily calories from formula:

EEN: 90-100%

PEN: partial enteral nutrition ~50%

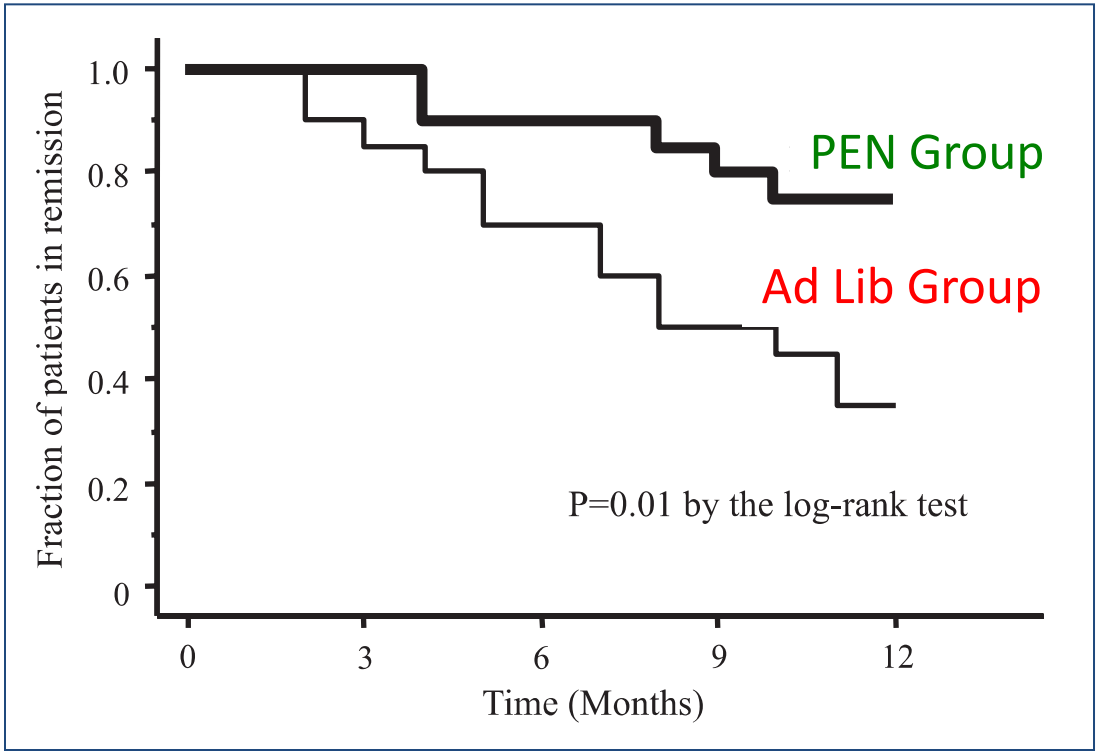
- PEN is less restrictive, and easier to continue long-term

PEN not effective at *inducing* remission

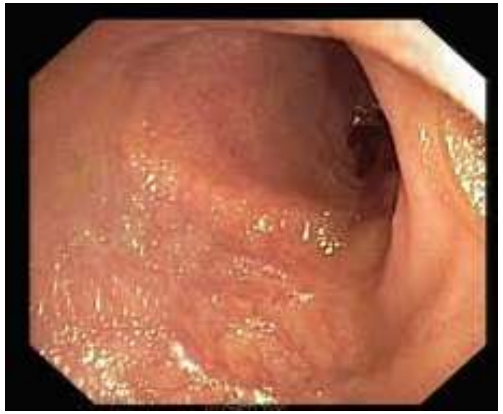
→ But, beneficial for *maintenance* of remission

PEN vs. ad lib diet for maintenance therapy

- 40 subjects with Crohn's disease in remission
- Two study groups:
  1) Ad lib diet + Pentasa
  2) PEN group: 50% calories from formula



Mucosal healing superior in PEN group (P = 0.04)

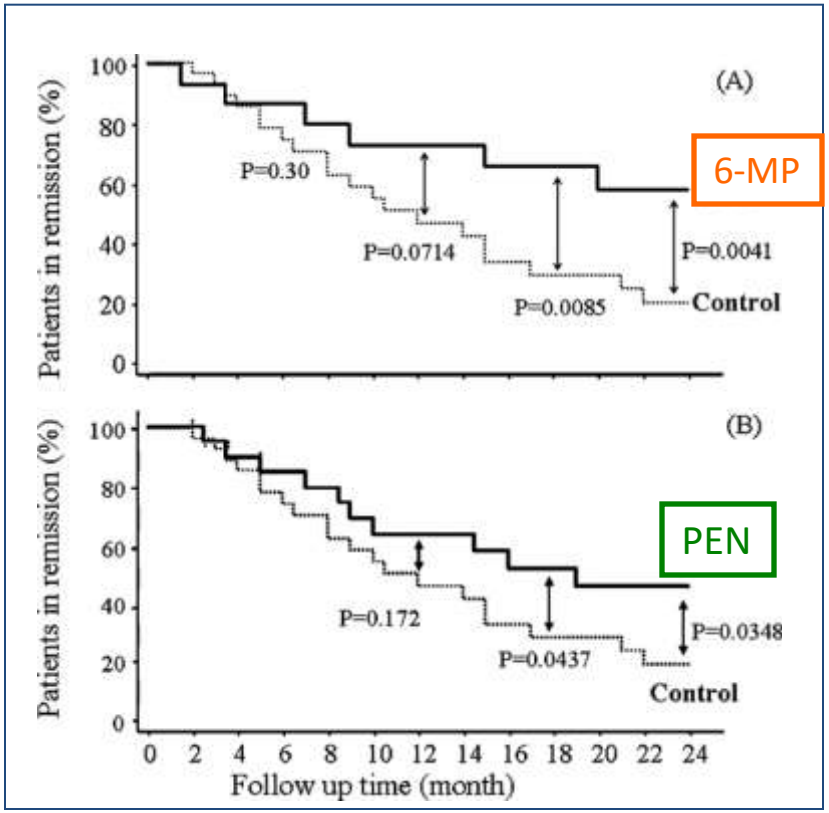


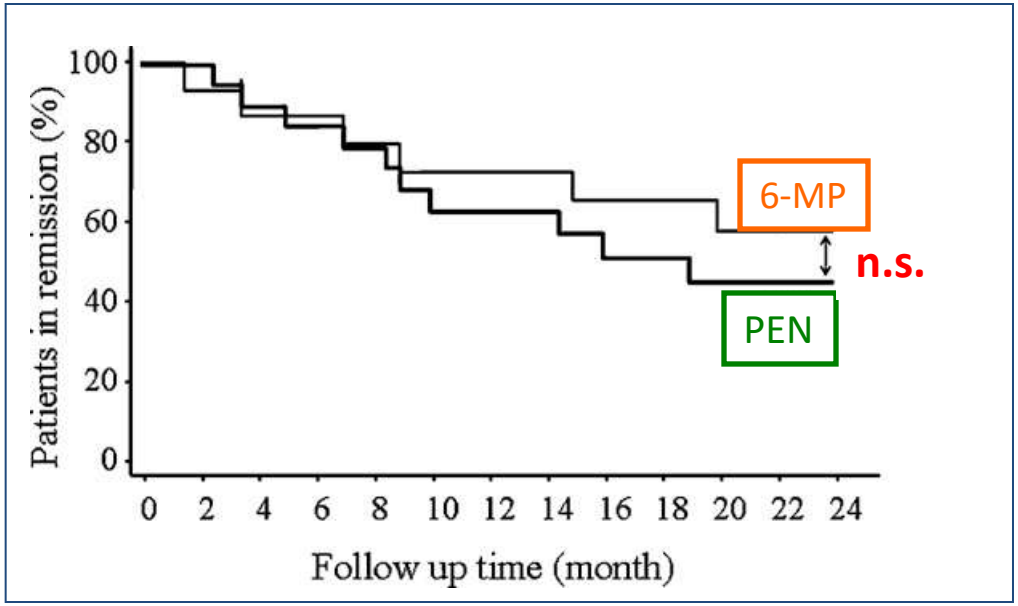
Yamamoto T. Inflamm Bowel Dis 2007.

PEN vs. 6-MP for maintenance therapy

Three therapies followed for 24 months (95 patients)

1) 6-MP (immunosuppressive medication)
2) PEN—diet with ~900 kcal/day formula
3) No therapy





No difference between PEN and 6-MP

Hanai, H. Digest and Liver Dis 2012.

EEN and Table Food

- EEN is infrequently used for maintenance therapy—it is a restrictive therapy
- Table foods are gradually introduced as formula is decreased
- Disease relapse occurs with food introduction
- **Question**: are certain foods associated with ↓ intestinal inflammation?

Table Foods and IBD

- Clinical studies have evaluated foods/components

Elimination Diets	Specific foods
Specific carbohydrate diet	Omega-3 PUFA
“Crohn’s disease exclusion diet”	Curcumin
Allergen elimination diet	Prebiotics (inulin, fructose-oligosaccharides)
Semi-vegetarian diet	Fiber
Low residue diet	Processed food components
FODMAP	

Conclusion: **Further** definitive data needed, but numerous exciting, ongoing studies

Food-based interventions for Crohn's

Clinical studies:

- Specific carbohydrate diet (SCD)
- "Crohn's disease exclusion diet"
- Semi-vegetarian diet
- Allergen elimination diet
- Low residue diet

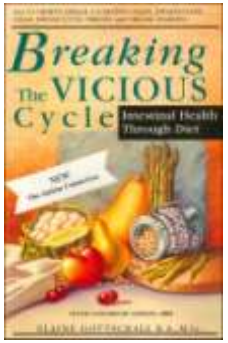
Case report and anecdote

- FODMAP exclusion
- Paleolithic diet
- Processed food

Hou JK. Clin Gastro and Hep 2014.

The specific carbohydrate diet (SCD)

- SCD limits:
  - All grains
  - Refined sugars
  - Cow's milk products (fully fermented yogurt ok)
  - "Processed foods"



- Popular following in the community for variety of GI illnesses
  - *Anecdotal* evidence plentiful
- <u>Concerns</u>:
  - Elimination of whole food groups from diet
  - Inadequate calories
  - Emotional well-being

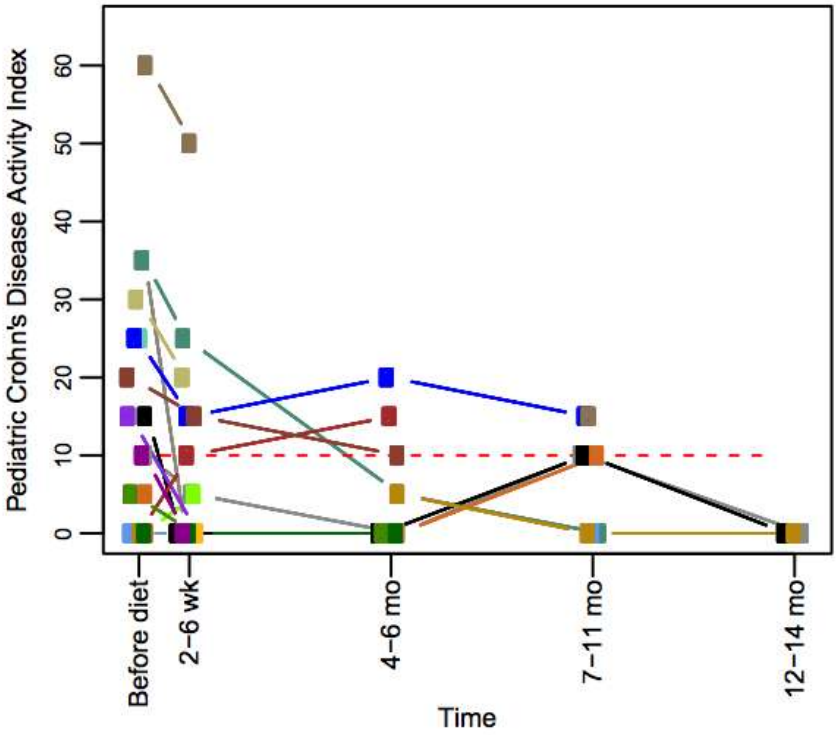
Studies on the SCD

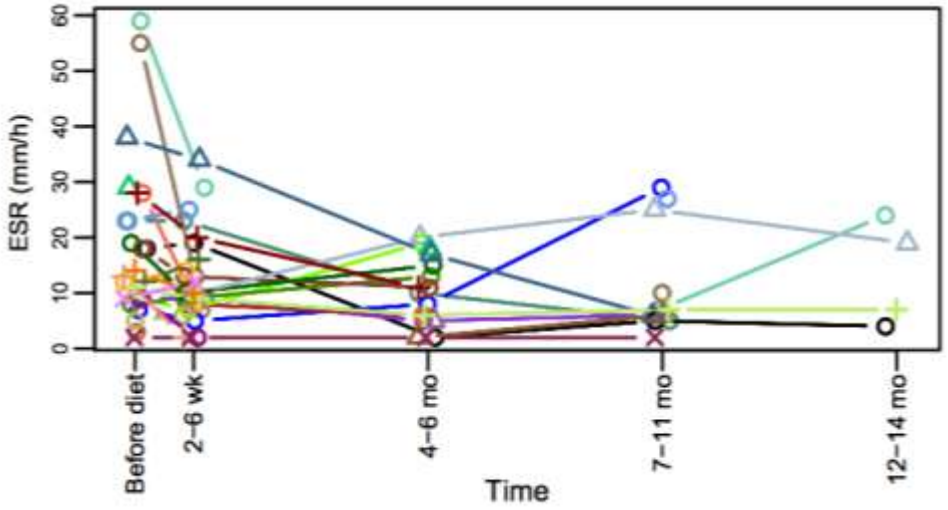
Author	Year	n	Summary
Obih, C	2016	26	20 children with CD, 6 with UC; Mean PCDAI at baseline, week 4, and month 6: 32.8 → 20.8 → 8.8
Kakodkar, S	2015	50	36 adults with CD, 9 UC, 5 IC; -Survey of those in remission on the SCD -High quality of life -12 subjects on immunosupp. medications
Suskind, DL	2014	7	Children with CD; Improvement in clinical + lab parameters (Hct, CRP)
Cohen, SA	2014	16	Children with CD; 12 week trial -Mean PCDAI: 21.1 → 7.8 -Capsule endoscopy showed improvement in mucosal inflammation

Efficacy of the SCD

- 26 children with IBD (20 Crohn's, 6 UC)
  - Peds Crohn's Disease Activity Index: 32.8 → 8.8
  - Peds Ulcerative Colitis Activity Index: 28.3 → 18.3

**Baseline to 6 months

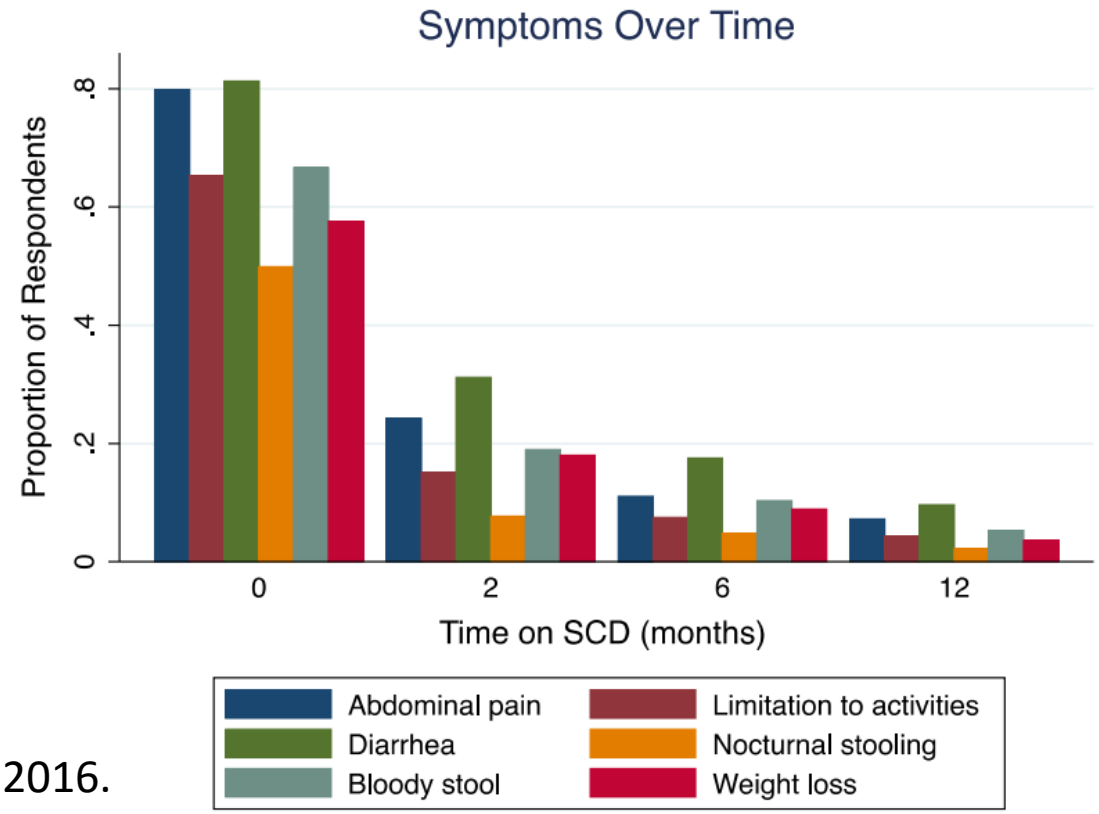




Obih C. Nutrition 2016.

The SCD is gaining popularity

- Online survey with 417 respondents
- Respondents described improvement over time



Suskind DL. Dig Dis Sci 2016.

Nutritional Adequacy of the SCD

Table 1. Percent of Specific Carbohydrate Diet (SCD) patients and National Youth Fitness Survey (NYFS) participants achieving nutritional adequacy

Nutrient	Percent Achieving Nutritional Adequacy	
	SCD Patients (N=8)	NYFS Patients (N=605)
Vitamins		
B1	37.5	79.2
B2	87.5	83.6
B3	87.5	81.0
B5	75.0	--
B6	87.5	77.2
B7	75.0	--
B9	37.5	6.1
B12	87.5	79.3
C	100	52.9
A	100	83.6
D	0	5.1
E	75.0	12.2
K	62.5	34.7
Minerals and Trace Elements		
Calcium	12.5	26.8
Iron	75.0	70.1
Magnesium	50.0	30.9
Phosphorus	37.5	46.6
Selenium	100	89.3
Zinc	50.0	52.4
Energy	62.5	--
Protein	100	84.3

Braly K. JPGN 2017.

Upcoming SCD studies

- Multi-center, David Suskind: SCD n-of-1 study
  - 120 participants with active Crohn's
  - Followed over 32 weeks
  - Crossover between SCD and "liberal SCD"
  - Outcomes: disease activity, fecal calprotectin
- UPenn, James Lewis: SCD vs. Mediterranean diet
  - 194 participants with active Crohn's disease
  - Randomized 1:1 to the two diets
  - For 6 weeks: 3 meals and 2 snacks delivered to home
  - Endpoints: disease activity and fecal calprotectin change

Conclusion

- Disease location can explain symptoms and guide therapy
- Many myths are out there about diet and IBD
- Exclusive enteral nutrition (EEN) can be effective therapy for Crohn's disease
- The specific carbohydrate diet (SCD) is a whole food based diet that can treat IBD

Thank you