Inflammatory Bowel Disease and Diet

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*With help from Sarah Weston, RD, CSP, LDN
Etiologic Theories for IBD

- Genetic Predisposition
- Mucosal Immune System (Adaptive/Innate)
- Environmental Triggers (Luminal Bacteria, Infection)
Dysbiosis of Gut Microbiota in IBD

- Gut microbiota in patients with IBD are enriched for taxa belonging to the *Proteobacteria* and *Actinobacteria* phyla with a decrease in representation of *Firmicutes*.
Is There a Relationship Between Diet, the Gut Microbiota, and IBD?

Clinical Relevance of Diet and IBD

• CCFA maintains an Information Resource Center that receives more than 14,000 inquiries per year, of which approximately 65% ask for dietary advice.

• Patients with IBD frequently identify dietary components that cause increased symptoms (lactose, gluten, etc.) and often follow very restricted diets.

• Patients desire therapies that do not suppress the immune system.

• Diet and the gut microbiota are the two biggest environmental factors to which the gut is exposed.
Diet is Associated with New Onset IBD

- High dietary intakes of total fats, PUFAs, omega-6 and meat were associated with an increased risk of CD and UC.

- High fiber and fruit intakes were associated with decreased CD risk.

- High vegetable intake was associated with decreased UC risk.

Dietary Factors and UC

- Study of 191 patients with UC in remission
- Followed over 1 year
- 52% of patients relapsed during this time period
- Consumption of meat, particularly red and processed meat increased the likelihood of relapse


Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in Il102/2 mice

Devkota et al. Nature 2012;487:104
## Diet in animal models of IBD

<table>
<thead>
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<th>Methods/animal model</th>
<th>Results</th>
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<td>Devkota, S.</td>
<td>Dietary-fat-induced</td>
<td>Did wild type and IBD-/- animals were fed a high-fat diet.</td>
<td>Cholesterol levels were significantly reduced in the IBD-/- group compared to the wild type group.</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>Gao, Y.</td>
<td>Atherosclerotic diet</td>
<td>Feeding mice a high-cholesterol diet resulted in atherosclerotic plaque formation.</td>
<td>Plaque formation was significantly reduced in mice fed the statin formulation.</td>
</tr>
<tr>
<td>High Fat</td>
<td>Gruber, H.</td>
<td>High-fat diet</td>
<td>Mice fed a high-fat diet showed increased body weight and reduced insulin sensitivity.</td>
<td>The high-fat diet group had higher fasting glucose levels compared to the control group.</td>
</tr>
<tr>
<td>Green tea polyphenols</td>
<td>Ozawa, T.</td>
<td>Green tea polyphenols</td>
<td>Feeding mice green tea polyphenols resulted in reduced inflammation and oxidative stress.</td>
<td>Green tea polyphenols improved antioxidant levels and attenuated severity of colitis analogous to sulfasalazine.</td>
</tr>
<tr>
<td>Semi-synthetic diet</td>
<td>Wagener, S.</td>
<td>Semisynthetic diet</td>
<td>Feeding mice a semi-synthetic diet improved colonic inflammation.</td>
<td>The semi-synthetic diet group showed reduced inflammation compared to the control group.</td>
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<td>Omega-3 fatty acids</td>
<td>Boss, W.</td>
<td>Omega-3 fatty acids</td>
<td>Dietary supplementation with omega-3 fatty acids improved colonic inflammation.</td>
<td>Omega-3 supplementation reduced pro-inflammatory cytokine levels.</td>
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<td>Feeding mice omega-3 fatty acids reduced pro-inflammatory cytokines.</td>
<td>Omega-3 supplementation reduced the severity of colitis.</td>
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<td>TGF-beta</td>
<td>Schirren, W.</td>
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<td>Feeding mice TGF-beta reduced colonic inflammation.</td>
<td>TGF-beta treatment significantly reduced the severity of colitis.</td>
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<td>Curcumin treatment significantly reduced pro-inflammatory markers.</td>
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### Chemicals used:

- Cholesterol
- Omega-3 fatty acids
- TGF-beta
- Curcumin
- Olive oil
- Green tea polyphenols

### Results:

- Dietary milk fat and high cholesterol diets significantly increased body weight and reduced insulin sensitivity.
- Green tea polyphenols and omega-3 fatty acids significantly reduced inflammation and oxidative stress.
- TGF-beta and curcumin treatments significantly reduced the severity of colitis.
- Olive oil supplementation improved colonic inflammation.
- Red meat consumption was associated with increased colonic inflammation.
- Green tea polyphenols and olive oil showed beneficial effects on colonic inflammation.
- Curcumin treatment significantly reduced pro-inflammatory markers.
- MCT-rich formula treatment significantly reduced pro-inflammatory markers.
Diet studies in humans with IBD

- Eliminate Foods
- Add anti-inflammatory substances or prebiotics
- Enteral nutritional therapy
Enteral Nutritional Therapy For IBD

• A therapy which has been used for almost 4 decades
• Involves the use of a specific enteral formula as nutritional therapy
• Formula most often administered through an NG tube
• Exclusive (100% of calories) for a defined period of time versus...
• Partial (80-90% of calories) with the remainder of calories from whole foods

EN Therapy: “European” Protocol

**Induction**

- **Exclusive** enteral nutrition with an elemental, semi-elemental, or polymeric formula
  - Duration: 4 – 12 weeks

**Maintenance Therapy**

- **Nutritional therapy**: Repeat 4 week cycle of exclusive enteral nutrition every 3 – 4 months
- **Medical therapy**: 6-MP/AZA/MTX
CHOP Enteral Nutrition Therapy (ENT)

**Induction**
- 8-12 weeks
- 80-90% of estimated needs from ENT
- 10-20% food
- NG tube/oral/combo

**Maintenance**
- Post induction to . . . ?
- Lower % EN by 10-15% in 8-10 week intervals
  - \(\downarrow\) # of days
  - \(\downarrow\) volume
- Repeat as able
- Liberalize oral intake
## Formula Selection

**THERE IS NO MAGIC FORMULA!**

<table>
<thead>
<tr>
<th>Suggested Formulas</th>
</tr>
</thead>
<tbody>
<tr>
<td>NG tube</td>
</tr>
<tr>
<td>Whey predominant 1.5kcal/ml</td>
</tr>
<tr>
<td>Oral??</td>
</tr>
<tr>
<td>Intact protein 1.5kcal/ml</td>
</tr>
<tr>
<td>Milk allergy</td>
</tr>
<tr>
<td>Soy or amino acid 1.0kcal/ml</td>
</tr>
</tbody>
</table>
http://www.youtube.com/watch?v=4xwRrezN9Qw
A Novel Enteral Nutrition Protocol for the Treatment of Pediatric Crohn’s Disease

Kernika Gupta, BA,* Angela Noble, MD,† Kelly E. Kachelries, RD,* Lindsey Albenberg, DO,* Judith R. Kelsen, MD,* Andrew B. Grossman, MD,* and Robert N. Baldassano, MD*

• Retrospective review of CHOP ENT protocol
• 43 patients with CD treated from 1998-2010
• 87% response rate and 65% remission rate
• Decreases in ESR and CRP, increase in albumin
• Increases in weight and height
How Does Enteral Nutritional Therapy Work?

- Reduction in luminal antigens and food exclusion
- Direct anti-inflammatory effects of the formula
  - Improved nutrition
  - Changes in the gut microbes
- Ongoing studies at CHOP
Open

An Altered Gut Microbiome Profile in a Child Affected by Crohn’s Disease Normalized After Nutritional Therapy

Valeria D'Argenio, MD\textsuperscript{1,2}, Vincenza Precone, PhD\textsuperscript{1,2}, Giorgio Casaburi, MS\textsuperscript{1,2}, Erasmo Miele, MD\textsuperscript{3}, Massimo Martinelli, MD\textsuperscript{3}, Annamaria Staiano, MD, PhD\textsuperscript{3}, Francesco Salvatore, MD, PhD\textsuperscript{1,4} and Lucia Sacchetti, PhD\textsuperscript{1,2}
Is Enteral Nutritional Therapy Effective?
Polymeric Diet Alone vs. Steroids for Active Pediatric CD (Induction Therapy)

• Methods (n=37)
  – Prospective 10 week randomized controlled open-label trial
  – Newly diagnosed children receive:
    • polymeric formula (n=18) or steroids (n=19)
  
  – Primary outcomes at 10 weeks
    • Clinical remission (PCDAI≤10)
    • Mucosal healing
      – Decrease in both endoscopic and histologic scores by > 50% when compared to baseline

Polymeric Diet Alone vs. Steroids for Active Pediatric CD (Induction Therapy)

Clinical improvement

- Enteral nutrition: n=19
- Corticosteroids: n=18

Healing of GI tract

P<0.05

To assess the capacity of EN therapy to induce small bowel mucosal healing by CE

Methods: 15 children with active CD

- 9 onset
- 6 relapse

In all patients CE was performed before and after an 8 week course of exclusive EN with a polymeric formula
To assess the capacity of EN therapy to induce small bowel mucosal healing by CE

**Before**

Ileocecal valve

**After**

Same ileal region
Safety of EN therapy for Crohn’s Disease

• No immunosuppression and beneficial effects on microbiota
• Generally well tolerated
• Most common side effects: Nausea, flatulence, abdominal pain, diarrhea

Nutritional therapy vs. 6-MP as maintenance therapy in CD

- Prospective 24 month randomized controlled open-label trial (n=95)
  - Inclusion: CDAI ≤ 150
  - Randomly assigned to:
    - 6-MP (0.5-1.5 mg/kg/day n=30)
    - ED (elemental diet ≥ 900 kcal/day n=32)
    - Control (5-aminosalicylic acid n=33)
  - Relapse: ≥ 200 CDAI

Nutritional therapy vs. 6-MP as maintenance therapy in CD

Results:
• At 24 months, patients who maintained remission were 60%, 46.9% and 27% for 6-MP, ED and Controls
• No significant difference between 6-MP and ED

Prevention of Post-op Recurrence with Enteral Nutrition for CD

• Methods: (prospective, non-randomized)
  – After resection for ileal or ileocolonic CD

  – Patients received either:
    • 50% of caloric needs from overnight elemental NG feed for 1 year (n=20)
    OR
    • Normal diet (n=20)

Prevention of Post-op Recurrence with Enteral Nutrition for CD

Clinical Recurrence

% Clinical Recurrence

At 1 year

Endoscopic Recurrence

% Endoscopic Recurrence

Physician Attitudes in Pediatrics

Does enteral therapy work for all IBD patients?

**Clinical Remission at Week 8**

- Ileal: 92%
- Ileocolonic: 82%
- Colonic: 50%

\[ p=0.05 \]

**Endoscopic Scores**

- Ileocolonic: \[ p=0.01 \]
- Colonic: \[ p=0.3 \]

Enteral Nutritional Therapy: Where should this be in our treatment algorithm?

• Should be offered to all newly diagnosed patients with CD who can tolerate nutritional therapy
  – Special groups
    • Malnourished patients
    • Younger patients
    • Growth failure
    • History of cancer
    • Family history of lymphoma?

• Consider when failing other therapies
Other diets for IBD

The FODMAPS Diet

<table>
<thead>
<tr>
<th>Excess Fructose</th>
<th>Lactose</th>
<th>Fructans</th>
<th>Galactans</th>
<th>Polyols</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit: apple, mango, nashi, pear, tinned fruit in natural juice, watermelon</td>
<td>Milk from cows, goats or sheep, custard, ice cream, yogurt</td>
<td>Vegetables: asparagus, beetroot, broccoli, brussel sprouts, cabbage, eggplant, fennel, garlic, leek, okra, onion, shallots, spring onion</td>
<td>Legumes: baked beans, chickpeas, kidney beans, lentils</td>
<td>Fruit: apple, apricot, avocado, blackberry, cherry, lychee, nashi, nectarine, peach, pear, plum, prune, watermelon, vegetables: cauliflower, bell pepper, mushroom, sweet corn, sweeteners: sorbitol, mannitol, isomalt, maltitol, xylitol</td>
</tr>
</tbody>
</table>
Can a Semi-vegetarian Diet Prevent Relapse of Crohn’s Disease?

- Adult patients with Crohn disease
- S/P medically or surgically induced remission
- Only treated with 5-ASA after remission achieved
- All were prescribed semi-vegetarian diet

Can a semi-vegetarian diet prevent relapse of Crohn’s disease?

![Graph showing remission rates for semi-vegetarian and omnivorous diets.](image)

- **Remission (%)**
- **Semi-vegetarian diet**
- **Omnivorous diet**

**No. at risk**

<table>
<thead>
<tr>
<th>Diet Type</th>
<th>0</th>
<th>100</th>
<th>200</th>
<th>300</th>
<th>400</th>
<th>500</th>
<th>600</th>
<th>700</th>
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<td>Semi-vegetarian</td>
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<td>16</td>
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<td>14</td>
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<tr>
<td>Omnivorous</td>
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<td>5</td>
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<td>3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
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</tr>
</tbody>
</table>

*P = 0.0003, Log-rank test*
Sigall-Boneh and colleagues recently found that a combination of partial enteral nutritional therapy and a restricted diet could induce remission and mucosal healing in 70% of patients.

So What do I tell my patients?

• Enteral nutritional therapy is an effective therapy for certain patients with IBD

• Other general messages (but not enough data to know for sure!)
  – Red meat in moderation
  – The typical “Western” diet is probably not good.
    • Processed foods, preservatives, long shelf life
  – Fiber may be beneficial (fruits, vegetables, whole grains)
  – Less restrictive exclusion diets may be future therapies
  – Constantly reassess!
Dietary changes to manage symptoms and diets to treat disease are not the same!!

**Symptoms**
- Low fiber diet (low residue diet) when disease is very active
- Low lactose if small bowel disease
- Low gluten or gluten free
- Work with a dietician and constantly reassess
- Should not be long-term!

**Treatment (decreases inflammation)**
- Enteral nutritional therapy
Conclusions

• In the future, diet might be used to treat active IBD, maintain remission, or even prevent disease
• ENT has consistently demonstrated effectiveness in CD and so interest has turned towards exclusion diets
• Patients often create, in essence, their own exclusion diets based on foods that exacerbate symptoms. This does not treat inflammation in contrast to ENT.
• We need to better understand the mechanism of ENT so that less restrictive diets can be designed
• We need better mechanisms of studying diet
• The future is promising!
Thank You!