Food and the gut microbiome in IBD: Nourish the patient and the bugs

Lindsey Albenberg, DO
Attending Physician
The Children’s Hospital of Philadelphia
Hot Topic! The Human Microbiome

Comprised of Bacteria, Viruses, others (Archaea, Eukaryotes)

Distinctive microbiomes at each body site (gut, lung, skin, mucosa etc.)

The Gut Microbiome
- Human gut is home to ~ 100 trillion bacterial cells
- Density of $10^{11}$ to $10^{12}$ per gram in the colon
- Genome size of microbiota at least 100-fold greater than human
- Large numbers species present, most uncultured

How do the bugs get there?

- **Infant**
  - **Delivery mode**:
    - Vaginal delivery:
      - Colonization with vaginal microbiota such as *Lactobacillus* and *Prevotella*
    - Cesarean delivery:
      - Colonization with skin microbiota such as *Staphylococcus*, *Corynebacterium*, *Propionibacterium*

- **Feeding method**
  - Breastfeeding:
    - Increased aerobic organisms, increased *Bifidobacterium*, decreased *Clostridium*, decreased *Bacteroides*
  - Bottle feeding:
    - Increased anaerobes and facultative anaerobes, increased *Clostridium*, increased *Bacteroides*

- **Environmental exposures**

- **Toddler**

---

Relatively sterile gut  
Low diversity, unstable, chaotic  
Diverse, stable

The Gut Microbiota in Health and Disease

- Diverse and abundant microbiota
- Firmicutes, Bacteroidetes and Actinobacteria dominant
- Healthy levels of SCFA production
- Intact mucosal barrier
- No overt inflammation

Health

Therapeutic disruption of dysbiosis
- Antibiotics
- Probiotics
- Dietary intervention/Prebiotics
- Faecal transplantation

Dysbiosis-related diseases
- Chronic gastrointestinal infections
- Antibiotic-associated diarrhoea
- Pseudomembranous colitis
- Inflammatory bowel disease
- Necrotizing enterocolitis

Dysbiosis

- Microbiota diversity reduced
- Elevated Enterobacteriaceae/opportunistic pathogens
- Skewed SCFA profile
- Disruption of mucosal barrier
- Host inflammatory response initiated

Factors that affect gut microbiome composition

Factors:
- Diet
- Genetics
- Environment
- Other Host Factors
- Antibiotics
- Inflammation

Science. 2011 May 20;332(6032):970-4
Science. 2011 Jul 1;333(6038):101-4
Science. 2011 Oct 7;334(6052):105-8
Greatest change occurs with introduction of solid foods

Koenig et al. PNAS. 2010.
Day 1 is different from all other days
Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

PNAS 2010;107:14691–14696

Carolotta De Filippo9, Duccio Cavalieri9, Monica Di Paola9, Matteo Ramazzotti9, Jean Baptiste Poullet9, Sebastien Massart9, Silvia Collini9, Giuseppe Pieraccini9, and Paolo Lionetti9,1

9Department of Preclinical and Clinical Pharmacology, University of Florence, 50139 Firenze, Italy; 1Department of Pediatrics, Meyer Children Hospital, University of Florence, 50139 Firenze, Italy; 2Department of Biochemical Sciences, University of Florence, 50134 Firenze, Italy; 3DNA Vision Agrifood S.A., B-4000 Liege, Belgium; and 4Centro Interdipartimentale di Spettrometria di Masa, University of Florence, 50139 Firenze, Italy

Yatsunenko et al. Nature 2012

African Diet: High fiber and carbohydrate, low animal fat and protein.

European Diet: High animal fat and protein, low fiber.
Convinced that you are what you eat?
The gut microbiome is different in people with IBD
More evidence for the importance of the microbiome in IBD

- **Genetics**
  - Many of the genes that impart risk for IBD are involved in protection against bacterial invasion

- **Animal studies**

- **Targeted therapies**
  - Antibiotics
Is There a Relationship Between Diet, the Gut Microbiota, and IBD?

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.

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 normal food

Hypothesis: Formula diet-induced alterations in the gut microbiota are associated with therapeutic efficacy in the treatment of pediatric Crohn’s disease.

Design: Longitudinal prospective cohort study of patients with Crohn’s disease treated with either an elemental diet or anti-TNFα therapy.
Does Enteral Nutritional Therapy Work?
Polymeric Diet Alone vs. Steroids for Active Pediatric CD (Induction Therapy)

– Children newly diagnosed with Crohn’s disease received either exclusive enteral nutritional therapy (n=18) or steroids (n=19)

– Primary outcomes at 10 weeks
  • Clinical remission by symptom score
  • Healing of the tissue by endoscopy

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

- Clinical improvement
- Healing of GI tract


Legend:
- Red: Enteral nutrition (n=19)
- Blue: Corticosteroids (n=18)

P<0.05
To assess the capacity of EN therapy to induce small bowel mucosal healing by VCE

Methods: 15 children with active CD

8 ileocolonic
7 ileum

9 onset
6 relapse

In all patients VCE 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 VCE

Before

Ileocecal valve

Same ileal region

After
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
Does enteral therapy work for all IBD patients?

Clinical Remission at Week 8

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

Endoscopic Scores

- Ileocolonic: p=0.01
- Colonic: p=0.3

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</td>
<td>milk</td>
<td>vegetables</td>
<td>legumes</td>
<td>fruit</td>
</tr>
<tr>
<td>apple, mango, nashi, pear, tinned fruit in natural juice, watermelon</td>
<td>milk from cows, goats or sheep, custard, ice cream, yogurt</td>
<td>asparagus, beetroot, broccoli, brussel sprouts, cabbage, eggplant, fennel, garlic, leek, okra, onion, shallots, spring onion, cereals, wheat and rye</td>
<td>baked beans, chickpeas, kidney beans, lentils</td>
<td>apple, apricot, avocado, blackberry, cherry, lychee, nashi, nectarine, peach, pear, plum, prune, watermelon, vegetables, cauliflower, bell pepper, mushroom, sweet corn</td>
</tr>
<tr>
<td>sweetners</td>
<td>cheeses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fructose, high fructose corn syrup, concentrated fruit sources, large servings of fruit, dried fruit, fruit juice</td>
<td>soft unripened cheeses, such as cottage cheese, cream, mascarpone, ricotta</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>honey</td>
<td></td>
<td></td>
<td></td>
<td></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

Chiba M, et al. World J Gastroenterol 2010
Can a semi-vegetarian diet prevent relapse of Crohn’s disease?

\[ P = 0.0003, \text{ Log-rank test} \]

No. at risk

<table>
<thead>
<tr>
<th></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>
</tr>
</thead>
<tbody>
<tr>
<td>Semi-vegetarian</td>
<td>16</td>
<td>16</td>
<td>16</td>
<td>15</td>
<td>14</td>
<td>13</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Omnivorous diet</td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
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

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)
Conclusions

- Research is demonstrating that human health is closely linked to a balanced relationship with our gut microbes.
- There are numerous disorders, that have been linked to an abnormal gut microbiome.
- Diet impacts the composition of the gut microbiome.
- More research is needed to define the healthy gut microbiome, to better understand the alterations that occur in IBD, and to determine how diet impacts these alterations.
- The future is promising for diet-based IBD therapies!
Thank You!