Physiology of the gut and mechanisms of prebiotic effect

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Fermentable carbohydrate: GI Tract

- Incompletely digested and partially absorbed in small intestine
  - Bonds resistant to digestive enzymes
- Fermented by bacteria in large intestine
  - SCFAs, H₂, CH₄, CO₂
- And/or excreted in feces
Fermentable Carbohydrates

- Lactose and sucrose, on occasion
- Dietary fiber
- Functional fiber
- Oligosaccharides
- Resistant starch
- Sugar alcohols/rare sugars
Non-fermentable/Poorly Fermentable Carbohydrates (and Lignin)

- Some cellulososes and hemicellulososes
- Resistant maltodextrins
- Lignin (polyphenolic compound)
Fiber balance studies

• Must feed defined, controlled diet for a long enough time for adaptation
  – Wheat bran (56%)
  – Oat bran (96%)
  – Polydextrose (50%)
  – Pectin (100%)
  – Psyllium (25 – 50%)
Fiber fermentation measures

- Intubation studies – considered gold standard – very invasive
- Ileostomy model – different GI tract
- Hydrogen breath test – does not relate to symptoms
- SCFAs in venous blood or in feces
- Fiber in fecal samples
- Fecal microflora
Fate of fiber in the gut

- Fiber digestibility ranges from 2 – 100%
- Little Solka Floc (purified cellulose) is degraded during transit
- Difficult to measure fiber disappearance since microbial cell wall in feces inflate values
Can breath hydrogen and methane predict fiber digestibility?

- Breath hydrogen and methane and fecal fiber were measured in human subjects consuming 0, 30, and 60 g soy fiber
- No relationship was found between breath gases and fiber digestion
- Breath gases were not changed with different fiber intakes
Short-chain Fatty Acids

- Produced by bacterial fermentation of fiber in colon
- Physiological effects
  - Source of energy
  - Lowers colonic pH
    - Inhibits pathogenic bacteria growth
  - Butyrate promotes colon health
  - Propionate may lower cholesterol
Are SCFAs and fiber digestibility related *in vivo*?

- Measured fiber digestibility and colonic SCFAs (collected in dialysis bags in feces) on wheat bran and vegetable diets
- WB fiber more digestible – higher production of butyrate and propionate
- No correlation between fiber digestibility and SCFA concentrations
In vitro fermentation method

- Mimics colonic conditions in a closed laboratory system
- 0.5g fiber added to each 100mL serum bottle
  - Negative control = no fiber
  - Positive control = glucose
- Fecal samples obtained from 3 donors to provide representative colonic microflora
- Fecal slurry made to imitate colonic conditions
- Oxyrase® oxygen-reducing enzyme added to reducing solution
- Resazurin added to confirm anaerobic conditions
- Serum bottles flushed with CO₂ to remove oxygen
In vitro fermentation method

- Bottles incubated in shaking water bath at 37°C
- Fermentation stopped at 0, 4, 8, 12, and 24 hours, one bottle was removed for each fiber
- Duplicate samples removed from each bottle
- Samples analyzed by GC/MS for short-chain fatty acid content
In vitro fermentation - pros and cons

• Pros
  – Time-efficient
  – Non-invasive

• Cons
  – Static system
  – Slurry components may not adequately represent colon
Short chain FOS exhibit more rapid fermentation than long-chain inulin

- 3 FOS and 3 inulin (IN) compared
- The rate of FOS fermentation was higher than IN from 0-4 hours and rate of IN fermentation was higher than FOS from 12 – 24 hours
- The longest chain inulin produced the lowest amount of butyrate at 24 hours
Particle size and fraction of wheat bran influence SCFAs

- Compared particle size and fraction of wheat bran and SCFA production
- Greater SCFA production with small particle size bran
- Fine by-product produced most SCFAs
- Molar percentage of butyrate at 24 hours greater for large particle size bran
What is gut health?

- Normal bowel function – subjective
- Regular bowel movements
- Desirable bowel movements – not diarrhea or constipation
- Absence of symptoms – bloating, gas, noises, pain
- Quality of life suffers greatly when gut health is compromised
Common gut health issues

- Constipation – how easily and how regularly you have a bowel movement
  - Low fiber diet
  - Sedentary lifestyle
  - Resisting the urge to have a bowel movement
  - Stress
  - Long-term laxative use
  - Some medications
Exit strategy – how to stay regular

- 15% adults report chronic constipation
- More common in older people
- At least twice as common in women
- Spend $750 million on laxatives and irregularity leads to 8 million trips to the doctor and $7 billion for evaluation and diagnostic testing
- *Nutrition Action Newsletter*, March 2009
Irritable bowel syndrome (IBS)

- Complex disorder of lower intestinal tract – accounting for 20-50% of referrals to GI clinics, majority being women 20-40 years old
- Mixed support for dietary fiber, probiotics, or prebiotics in treatment of IBS
- Conservative approach best - mixed fibers
Defining gut health

- Less than 3 stools per week or more than 3 stools per day – considered abnormal
- Stool weight greater than 200 g/day is clinically defined as diarrhea, but many vegetarians have stool weights of 300 g/day or more
- Stool consistency important to consumers – requires presence of water-insoluble fecal solids such as non-digested dietary fiber or bacterial cell walls
- *Gastroenterology* 1999;116:1464
The Scoop on Poop

- Feces are about 75% water – highly variable – much higher with diarrhea. Of the remaining feces, about 1/3 is dead bacteria, 1/3 is undigested carbohydrate, and 1/3 is protein, fat, mucus, dead cells, and inorganic material.

- Smell results from products of bacterial action – sulfur or nitrogen-rich compounds such as indole, skatole, and mercaptans, and the inorganic gas hydrogen sulfide.
Normal digestion and absorption

• Typically about 95% of macronutrients (carbohydrates, fats, proteins) get digested and absorbed
• Leftovers of digestion and absorption (feces) include fiber, bacteria, water
• Making nutrients less digestible (low digestible carbohydrates – starch, sugar alcohol, etc) – may lower calories but may create GI issues – intestinal gas, diarrhea, etc
Come check out our stool samples.

IKEA
<table>
<thead>
<tr>
<th>Celebrity KAKA</th>
<th>Who's Who of Poo</th>
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<tbody>
<tr>
<td>Martha</td>
<td>Paris and Tinkerbell</td>
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<tr>
<td></td>
<td>Keanu</td>
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<td>Brangelina</td>
<td>Arnold</td>
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<td>Tiger</td>
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<td>the Papal Pile</td>
<td>the Donald Dump</td>
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<td>Captain's Log</td>
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<td>Bush Bombs</td>
<td>Condoleezza's rice</td>
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<td>Oprah</td>
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<td>Description</td>
<td>Less than 100g</td>
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<tr>
<td><strong>Hard &amp; Formed</strong></td>
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<td>- hard or firm texture</td>
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<td>- retains a definite shape</td>
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<td>- like a banana</td>
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<td>- a cigar</td>
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<td>- or marbles</td>
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<td><strong>Soft &amp; Formed</strong></td>
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<tr>
<td>- retains general shape</td>
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<tr>
<td>- like peanut butter</td>
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<tr>
<td><strong>Loose &amp; Unformed</strong></td>
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<tr>
<td>- lacks any shape of its own</td>
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<td>- may spread easily</td>
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<td>- like porridge</td>
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<td>- or thick milkshake</td>
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<td><strong>Liquid</strong></td>
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<tr>
<td>- runny</td>
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<tr>
<td>- like water</td>
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*King's Stool Chart © 2001 King's College London*

www.kcl.ac.uk/stoolchart
Non-dietary factors that affect laxation

- Stress
- Smoking
- Coffee drinking
- Drugs (laxatives) (Lembo A, Camilleri M. New Eng J Med 2003;349:1360)
- Personality (Tucker et al. Gastroenterology 1981;81:879)
Nutrition and lifestyle and bowel movement frequency

- 20,630 subjects in EPIC
- Higher in men than women
- Higher in vegetarians – linked to fiber intake
- Positively associated with BMI
- Positively associated with vigorous exercise in women, not as clear in men
Fecal bulking index (FBI)

- Increase over baseline in rehydrated fecal weight induced by a food, as a percentage of the increase induced by an equal weight of wheat bran reference.
- Fecal weight required for health – 200 g/day (Spiller 1993)
- Fecal weight/g wheat bran fiber - 5.11 g (Cummings 1993)
Average increase in fecal weight per gram fiber fed

- Wheat: 5.4 g/g fiber fed
- Oats: 3.4 g/g fiber fed
- Corn: 3.3 g/g fiber fed
- Legumes: 2.2 g/g fiber fed
- Pectin: 1.2 g/g fiber fed

Cummings JH. 1993. CRC Handbook of Dietary Fiber in Human Nutrition
Inulin and stool weight

• 12 healthy males consumed a controlled diet for 3 weeks with and without 20 grams of inulin/day
• Significant increase in flatulence
• No differences in stool weight – 20 g/day inulin increased daily stool weight less than 20 g/day
• Slavin & Feirtag. *Food Funct* 2011 2:72
Limitations to fecal samples

- Not practical in epidemiological studies
- No accepted standard
  - Stool weight
  - Stool chemistry
  - Microflora – methods, what is best
  - Stool frequency (easy to collect)
  - Quality of life (used in IBS trials)
Gut health and fiber

• Central question:
  – Does dietary fiber from increase stool weight and speed gastrointestinal transit?

  – Generally accepted
  – Not supported by evidence-based review:
    • Dietary Reference Intakes for fiber are based on epidemiologic studies on protection against CVD
    • *J Am Diet Assoc* (2008) evidence-based review – fiber and laxation given a low score – Grade III - Fair
Gut health and fiber

• Confounding Issues:
  – Many other diet factors affect laxation
  – Confounding effects of laxative use
  – Difficult to collect stool samples in these settings
    • Wet and dry stool weight, transit time, fecal chemistry, microflora, how long to collect
  – Are subjective measures enough support?
    • Frequency, ease of elimination, bloating, flatulence
Side effects of gut fermentation

Gastrointestinal effects

- Abdominal pain/cramps
- Bloating
- Colic
- Distention
- Flatulence/borborygmi
- Laxation
  - Frequency increased
  - Consistency more watery
- Diarrhea

Livesey, Brit J Nutr 2001;85(Suppl 1):S7-S16
Subjective methods

- Symptom questionnaires where subjects report the occurrence and severity or intensity of GI symptoms and frequency and consistency of bowel movements
- Need to define bloating, diarrhea, flatulence and describe rating scale
- Vary greatly among studies/subjects
Summary of tolerance data

- Dietary fiber – up to 80 g/d in vegetarians – no UL
- Polydextrose – 50 g
- Resistant starch – 80 g
- Fructo-oligosaccharides – 10-15 g – diarrhea at 40 g
- Sugar alcohols
  - No effect dose – 20-50 g
  - Laxation threshold – 50-70 g
Disclaimers

- Definitions of tolerance – how much intestinal gas is acceptable
- Adaptation
- Habitual or background diet
- Total exposure to low digestible carbohydrates – dietary fiber, resistant starch, oligosaccharides, polyols, etc.
No recommended UL for fiber

- Occasional adverse GI symptoms are observed when humans consume some of the isolated or synthetic fibers (Grabitske and Slavin. *J Am Diet Assoc* 2008;108:1677)
- Due to the bulky nature of fiber in foods, excess consumption is likely to be self-limiting.
Dietary fiber and laxation

- Not all fibers are equally effective in increasing stool weight
- Wheat bran is most effective and fibers that are extensively fermented during gut transit time (inulin, pectin, etc) have little effect on stool weight
Conclusion

• Fermentation of fiber difficult to study *in vivo*
• Fermentation rates of interest – since quick fermentation causes unwanted GI side effects
• Markers of fiber fermentation *in vivo* – breath gases, SCFAs – not shown to reliably measure fiber fermentation
• *In vitro* models for fermentation need to be developed and optimized