

# Physiology of the gut and mechanisms of prebiotic effect

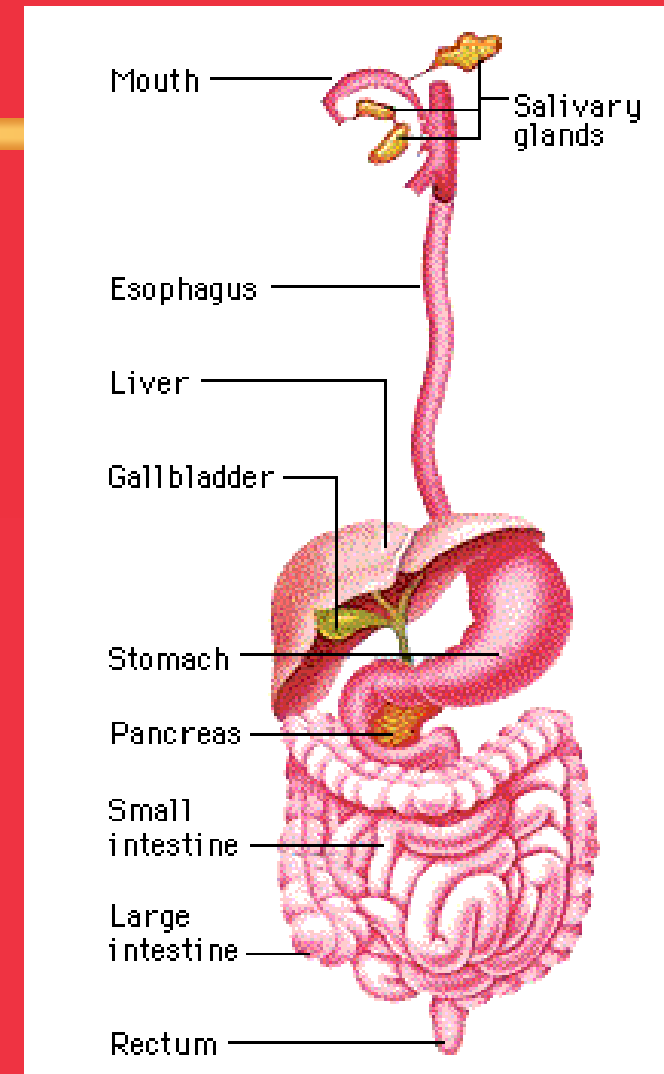
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# Fermentable carbohydrate: GI Tract

- Incompletely digested and partially absorbed in small intestine
  - Bonds resistant to digestive enzymes
- Fermented by bacteria in large intestine
  - SCFAs, H<sub>2</sub>, CH<sub>4</sub>, CO<sub>2</sub>
- 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)

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- Some celluloses and hemicelluloses
- Resistant maltodextrins
- Lignin (polyphenolic compound)



# Fiber balance studies

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- 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

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- 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

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- 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
- Slavin et al. *J Nutr* 1981;111:287-297.



# Can breath hydrogen and methane predict fiber digestibility?

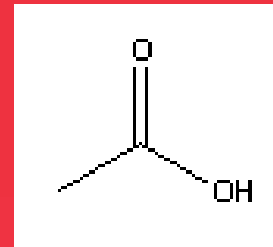
- Breath hydrogen and methane and fecal fiber were measured in human subjects consuming 0, 30, and 60 g soy fiber
- No relationship was found between breath gases and fiber digestion
- Breath gases were not changed with different fiber intakes
- McNamara et al. *Am J Clin Nutr* 1986;43:898-902.



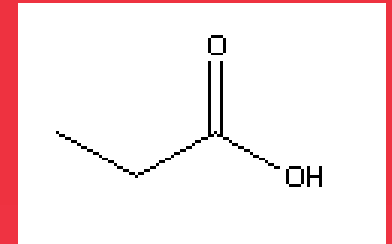


# Short-chain Fatty Acids

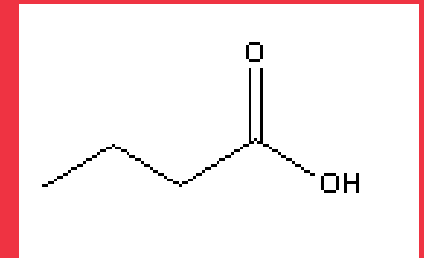
- Produced by bacterial fermentation of fiber in colon
- Physiological effects
  - Source of energy
  - Lowers colonic pH
    - Inhibits pathogenic bacteria growth
  - Butyrate promotes colon health
  - Propionate may lower cholesterol



Acetate



Propionate



Butyrate



# Are SCFAs and fiber digestibility related *in vivo*?

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- 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
- Fredstrom et al. *JPEN* 1994;18:14-19.



# 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 CO<sub>2</sub> to remove oxygen



# In vitro fermentation method

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- 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

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- 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

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- 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
- Stewart et al. *Nutr Res* 2008;28:329-334.



# Particle size and fraction of wheat bran influence SCFAs

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- 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
- Stewart & Slavin. *Br J Nutr* 2009 102:1404-7



# What is gut health?

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- 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

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- 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

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- 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)

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- 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
- Williams & Slavin. *Topics in Clin Nutr* 2009;24:262-271



# Defining gut health

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- 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

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- 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

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- 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



ELLER

Come check out  
our stool  
samples.



# CELEBRITY KAKA

a who's who of poo.



Martha.



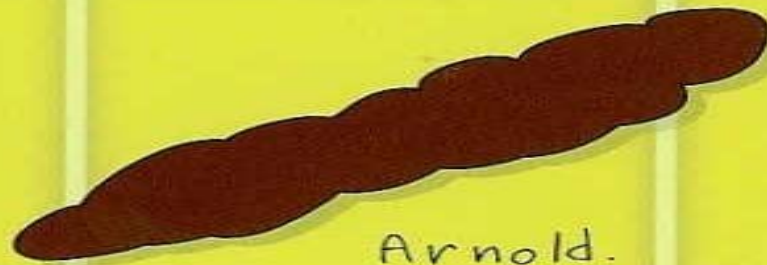
Paris and  
Tinkerbell.



Keanu.



Brangelina.



Arnold.



Tiger.



the  
Papal Pile.



the  
Donald Dump.



Captain's Log.



Bush Bombs.







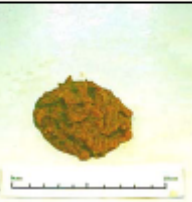

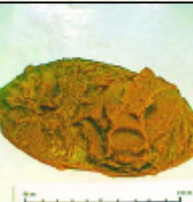
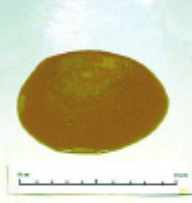
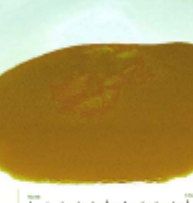



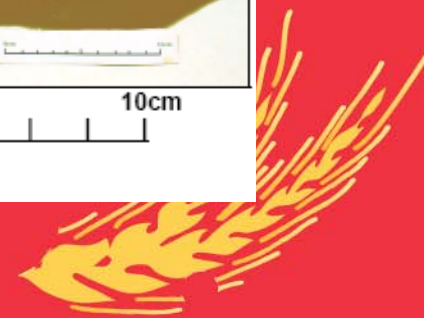
Condoleezza's  
rice.



Oprah.



	Less than 100g	Between 100 – 200g	More than 200g
<b>Hard &amp; Formed</b> - hard or firm texture - retains a definite shape - like a banana a cigar or marbles	<b>A</b> 	<b>B</b> 	<b>C</b> 
<b>Soft &amp; Formed</b> - retains general shape - like peanut butter	<b>D</b> 	<b>E</b> 	<b>F</b> 
<b>Loose &amp; Unformed</b> - lacks any shape of its own - may spread easily - like porridge or thick milkshake	<b>G</b> 	<b>H</b> 	<b>I</b> 
<b>Liquid</b> - runny - like water	<b>J</b> 	<b>K</b> 	<b>L</b> 



# Non-dietary factors that affect laxation

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- Stress
- Exercise (Oettle. *Gut* 1991;32:941)
- 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

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- 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
- Sanjoaquin et al. *Pub Health Nutr* 2004;7:77-83.



# Fecal bulking index (FBI)

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- 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)
- Monro. *Eur J Clin Nutr* 2004;58:32-39



# Average increase in fecal weight per gram fiber fed

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- 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

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- 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

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- 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

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- 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

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- 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

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## 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

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- 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

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- 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
  - Grabitske & Slavin. *Cr Rev Food Sci Nutr* 2009; 49:327-360.



# Disclaimers

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- 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

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- 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

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- 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

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- 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

