Diet and the Gut Microbiota

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Objectives

1. Describe key dietary influencers of the gut microbiota at different stages of the human life cycle
   - Infancy/early childhood
   - Adulthood

2. Explain the effect of dietary patterns on the composition of the gut microbiota

3. Understand benefits vs. risks of probiotic supplementation
The gut microbiota is made, not born

Gut presumed sterile at birth (but some evidence of early microbial colonization)

By age 3, gut microbiota is considered mature, will contain 100 trillion microbes from >1,000 different species

Numerous influences in first three years of life play a role in shaping the microbial ‘footprint’

Key influencers of early childhood gut microbiota

- Vaginal birth vs. C-section
- Siblings/daycare
- Pets/animals
- Urban vs. rural
- Sterilizing dishes, pacifiers
- Method of Delivery
- Method of Feeding
- Home Hygiene Practices
- Others
- Breastfeeding vs formula
- Weaning method?
- Dietary pattern on weaning
- Antibiotic use: Type, duration, frequency
- Genetics: gut microbial ecology may be inherited to some degree
(Cheat Sheet: Key Characters in the Human Gut Microbiota)

**Bacteroidetes**
- Prevotella
- Bacteroides
- B. fragilis

**Firmicutes**
- Bacillus (includes Lactobacillus)
- Enterococcus
- Streptococcus
- Clostridium
- L. acidophilus
- L. delbrueckii
- S. thermohillus
- S. mutans
- C. diff
- B. cereus

**Actinobacteria**
- Bifidobacterium
- B. infantis
- B. animalis

**Proteobacteria**
- Escherichia
- Salmonella
- Helicobacter
- Yersinia
- Vibrio
- Shigella
- E. coli
- H. pylori
- V. cholera

**Phylum:**
- Well known
- Genera:
  - Comprise vast majority of adult human gut microbiota
  - Higher ratio Firmicutes:Bacteroidetes associated with obesity

**Highest ratio**
- Bacteroidetes
- More dominant in infant gut microbiota, reduced prominence with age

**Enriched in**
- Malnutrition, inflammatory disease (IBD, allergies, e.g.) and advanced age
Long term macronutrient intake patterns influence ‘Enterotype’
Named for genera of predominant microbes

Type 1: Bacteroides (Phylum: Bacteroidetes)
Associated with diets high in animal protein and saturated/animal fats, lower in fiber
Western Diet

Type 2: Prevotella (Phylum: Bacteroidetes)
Associated with diets high in fiber from plants and starchy carbohydrates, and sugars
Agrarian society diet, possibly/presumably Vegans as well

Type 3?: Ruminococcus (Phylum: Firmicutes)
Also associated with Western-style diets;
Some consider this to be variation of Type 1 with higher ratio of Firmicutes: Bacteroidetes

Higher ratio of Firmicutes: Bacteroidetes is associated with obesity
Method of infant feeding

Breastfeeding associated with more beneficial “enterotype” vs. formula feeding
- Breastfed: Predominantly *Bifidobacteria*, also *Lactobacilli* & *Prevotella*
- Role of oligosaccharides → prebiotic effect that may nourish *Bifidobacteria*
- Skin to mouth → introduces maternal skin flora (promotes species diversity)

Formula feeding associated with reduced colonization with *Bifidobacteria*
- *Bifidobacteria* are less dominant, equally balanced with *Bacteroidetes* species
- More likely to be colonized with potentially pathogenic species like *E. coli* and *C. diff*

Unclear whether pre-mastication plays a meaningful role in development of infant gut microbiota
- Historically, pre-mastication was commonly practiced at weaning, but prevalence in Western societies now rare
- When studied in non Western societies, emphasis only on salivary microbiota (and limited studies suggest influence may be minimal)
- Saliva hypothesized to contribute to early childhood virome in particular at an immunologically optimal time (EBV)
Early childhood

Period of weaning associated with significant change, diversification in gut microbiome

• Year 1-2: microbiome undergoes “second shift” as complementary foods introduced
  • Prolonged breastfeeding into toddlerhood has strong effect on shaping adult microbiome profile
• Method of early infant feeding ceases to impact direction of microbiome development (but not future health risks)
• Developing microbial profile appears heavily influenced by diet
  • *Bacteroides plebeius* in Japanese gut microbiota, *Xylanibacter* in rural African microbiota → absent from North American/Western European microbiota

Gut microbiota stabilizes by ~age 3, more closely resembles adult

Antibiotic use is the factor most likely to provoke significant disturbances in development trajectory of gut microbiome in early childhood

• Frequency of antibiotic use also associated with increased risk of various allergic/autoimmune diseases in later life
• Presumably mediated by effect on microbiome

Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa

- Children aged 1-6 from Burkina Faso and Florence, Italy
- African kids ate ~2x more fiber and 60-70% less fat compared to European kids
- BF: 73% Bacteroidetes, 12% Firmicutes
- EU: 51% Firmicutes, 27% Bacteroidetes
- More SCFA in Burkina Faso kids’ stool
- BF children had significantly richer (more species) and more biodiverse microbiota vs IT children
High fiber intake promotes healthier, leaner enterotype

Fiber a primary energy substrate for colonic bacteria, so intake impacts composition of microbiota
- Higher fiber diets associated with increased microbial diversity and increased SCFA production
- Increased SCFA content in stool associated with leaner enterotypes (lower ratio Firmicutes: Bacteroidetes)
- High fiber diet $\rightarrow$ ↑ SCFAs $\rightarrow$ protects gut mucosal barrier from damage by the microbiota

High fiber, lower calorie diets associated with greater microbial diversity (taxonomic, functional) vs. Western style diets
- Small, short term feeding studies suggest a variety of whole, plant based foods have a prebiotic effect on gut microbiota: whole grain cereals, apples, fruits/veg…
- Available research limited as to specific effects of other high fiber food groups or types of fiber (e.g., soluble vs. insoluble)

Prebiotic fiber intake (inulin) has narrow but notable impact on Bifidobacteria and Lactobacilli species
- Bifidobacteria typically minority genus in adult human gut microbiota but may have protective role vs. IBD, metabolic diseases
Other dietary factors with observed effect on gut microbiota

Dairy intake?
  • Eliminating dietary intake of dairy correlated with reduced *Lactobacillus* levels (is this good or bad?)

Iron supplementation?
  • Iron fortification/supplementation to cereal in 6 month old Kenyan children resulted in increased pathogen abundance and inflammatory diarrhea compared to infants fed unfortified cereal

Malnutrition and assorted micronutrient deficiencies?
  • Increased prevalence of microbes in the *Proteobacteria* phylum (pathogens) in context of malnutrition, RYGB surgery, choline deficiency
  • Iron depletion associated with increased *Lactobacilli* and *Enterobacteriaceae* (pathogenic family in the Proteobacteria phylum), decreased *Roseburia spp.* (SCFA producing microbes in phylum *Firmicutes*).

Researchers are just beginning to scratch the surface as to complex relationship between dietary factors and the gut microbiota!
Limited Role of Supplemental Probiotics in Shaping Gut Microbiota

Commercialized probiotic supplements problematic on many levels

- **Strain selection:**
  - Based on convenience/ “culturability,” not necessarily efficacy → vast majority of microbes in human gut are not able to be cultured!
  - Single strain vs. multi-strain

- **Evidence basis:** Limited testing to verify efficacy and beneficial “probiotic” effect for most products on market
  - E.g., *Lactobacillus*: helpful or harmful?

- **Lax regulation:** numerous studies have shown mislabeling of commercial probiotic supplements is rampant

Supplemental probiotics have not shown to have significant or lasting impact on microbiota

- When studies have shown benefits, they’re typically “small & transient” → benefits typically cease when supplementation ceases
Benefits vs Risks of Supplemental Probiotics

Any demonstrated benefits of probiotic supplements are product and symptom specific

- Best evidence available supports role of various species/strains in managing pediatric gastroenteritis/AAD
- Align (B. infantis) → constipation
- VSL #3 (Bifidobacterium spp., Lactobacillus spp., S. thermophilus) → UC, Pouchitis
- Florastor (S. boulardii Iyo CNCM I-745) → preventing AAD/C. diff
- Cardioviva (L. reuteri NCIMB 30242) → lowers LDL and TC by ~10%

Supplemental probiotics not without risk

- SIBO in predisposed individuals → PPI use/hypochlorhydria; slow transit
- Populations at risk of sepsis: immunocompromised infants/children, those with IVs/central line

Future of supplemental probiotics likely to be:

- Personalized, customized (not mass market)
- Symbiotic cocktails vs. single strains
- FMT
Adult gut microbiota both stable and dynamic

Mature gut microbiota remarkably stable, trends back to baseline enterotype even after disruptions
- Assuming relatively stable dietary patterns, health status, environment
- Baseline enterotype rebounds after course of antibiotics within ~4 weeks, and may be faster after repeated exposure to same drug
  - Exception: Ciprofloxacin (6 months or more)

Major change in dietary patterns can alter gut microbiome within days...
- Plant based→ high sugar Western diet changes microbiota within a single day in terms of relative proportion of species/strains, but enterotype remains stable in the short run

...But longer-term dietary practices are what dictate enterotype
- Longer term dietary patterns could produce more profound, significant changes at the enterotype level...
- ...but responsiveness to significant dietary change may be hampered by baseline enterotype
- (Need lots more research!)
Care & Feeding of Your Gut Microbiota

Consume the highest fiber, “highest FODMAP” diet you can comfortably tolerate

- Aim for variety of sources from whole foods: vegetables, whole grains, fruits, nuts, seeds, beans/legumes, tubers…
- Seek out naturally rich prebiotic foods, such as artichokes, sunchokes, jicama, alliums, chicory, rye

Cook/store grains/starches to maximize resistant starch content

- Rice/potatoes: cook → cool → reheat (do so safely to avoid “fried rice syndrome” from B. cereus!)

Include cultured/fermented foods in your regular diet

- Cultured beverages (kombucha, kvass, e.g.,), fermented vegetables, fermented soy/beans…
- Cultured dairy (?)

Limit exposure to antibacterial personal care products and unnecessary antibiotic medication
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References (I)


References (II)


