Importance of the developing gut microbiota for the infant.

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ILSI SEA Region - Conference: Gut feelings - what can we learn from recent research on gut microbiota?
Australia December 2013
(www.ilsi.org/SEA_Region)
Overview

- Describe the microbiota
- Successive development from birth
- Factors affecting the microbiota
- Host-microbiota interactions
- Impact on the health of the infant
- Harnessing the potential of the microbiota for long term health benefits.
- **Microbiota (microflora)**
  
a collection of microbial communities colonizing a particular ecological niche

- **Microbiome**
  
the collective genome of the microbial symbionts in a host.
Methods for studying the microbiota

Which microbes are there?
- Nucleic Acids
  - SSU rRNA Approaches

What are the microbes doing?
- RNA
  - Metatranscriptomics
- Proteins
  - Metaproteomics
- Metabolites
  - Metabonomics

What is the genetic potential?
- DNA
  - Metagenomics

Holistic & High Throughput Avenues - Cohorts & Controlled Interventions - MetaAnalysis Approaches
Are we there yet?

Reduce intestinal putrefaction
Increase longevity (1907)
Nobel prize – macrophages

**MICROBIOTA EVOLUTION**

**OUR OTHER GENOME**
- Karyome
  - $10^{12}$ human cells
  - single genome
  - 3 Gbase sequence
  - 30-100 k proteins

- Mitochondriome
  - $10^{14}$ mitochondria
  - single genome
  - 17 kbase sequence
  - 13 proteins

- Microbiome
  - $10^{34}$ microbial cells
  - $10^6 - 10^8$ species
  - 500 Gbase sequence
  - now reference genome of 3 M genes – proteins
The important first years

- At birth:
  - digestive tract is sterile (no microbes)
  - immune system Th2 bias (prevents foetus rejection)
- First few days of life:
  - microbes establish successively
- Breast fed infants have mostly bifidobacteria
- Maturation of immune system with Th1 development to balance the Th2 of the newborn
- Microbes of the intestine contribute to Th1 development, needed for development of oral tolerance
Acquisition

Maternal and environmental eg hospital, siblings, pets
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The function of our microbiota: who is out there and what do they do?

Noora Ottman1, Hauke Smidt1, Willem M. de Vos1,2 and Clara Belzer1
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Impact of gestation time

### PREMATURE

- 2 days: p.value 0.007
- 10 days: p.value < 0.001
- 30 days: p.value 0.002
- 90 days: p.value 0.048

### FULL-TERM

- Facultative anaerobes
- Strict anaerobes
Microbiota of infants in Europe & Africa
Window of sensitivity around 4-6 months of age
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The gut microbiota – masters of host development and physiology

Sommer and Backhed, 2013, Nature Reviews, Microbiology, 11:227
Effects of gut microbiota: nutrition, immunomodulation and neuromodulation

Hemarajata and Versalovic *Ther Adv Gastroenterol* (2013) 6(1) 39–51
Effects gut microbiota on immunomodulation
Gut–brain axis (GBA).

Health conditions affected by the GBA.

Microbiota and MS

Link between commensal filamentous bacteria and MS (rodent study)

Savidge TC et al. Laboratory Investigation 2007.

Booth 2013
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Impact of C-section on health

(Chang et al 2006)
http://www.plosone.org/article/info:doi/10.1371/journal.pone.0020647
Infants of 6 to 11 months old are more prone to diarrhea than older children

(Kosek, WHO Bulletin, 2003)
Colicky Infants

- Slower colonization
- Lower diversity and stability
- Increased proteobacteria (including species producing gas and inflammation)
- Decreased butyrate-producing species
- Decreased lactobacilli & bifidobacteria (including species with anti-inflammatory effects)
Microbiota and the emerging pandemic of NCDs (Non-Communicable Diseases)

NCDs: Allergy, obesity, diabetes, cardiovascular disease, mental health and auto-immune diseases

Early life exposures
- Mode of delivery
- Infant diet
- Antibiotic usage
- Environmental factors

Gut microbiota

Dysbiosis

Disease
- Immune: atopy, asthma, multiple sclerosis, respiratory
- Metabolic: Diabetes, obesity
- Intestinal: Inflammatory bowel disease, Diarrhoea, Necrotising enterocolitis, Colon cancer

Symbiosis

Health
- Immune tolerance
- Intestinal homeostasis
- Healthy metabolism

(Conway, 2013)
Overview

- Describe the microbiota
- Successive development from birth
- Factors affecting the composition/function
- Host-microbiota interactions/immune triggers
- Impact on the health of the infant
- Ways to harness the potential of the microbiota for long term health benefits.
"All" disease begins in the gut

**Poor diet**
- Antinutrients and too much insoluble fiber
- Disrupted gut physiology and leaky gut
- Excess fiber found in grains, legumes, and nuts
- High-density carbohydrates, and cellulose
- Large amount of food
- Hugle metabolites, and cellular carbohydrates
- Growth of food gut microbes
- Bacteria by foods (e.g., grains and white flour) and foods with a high sugar content
- Certain hormones and inflammatory agents are able to breach the gut barrier
- Fat and sugar in milk, and fats in processed, refined foods
- Modified gut flora composition

**Drugs**
- Antibiotics and other antimicrobials, NSAIDs, steroids, drugs, analgesics, contraceptives, and other drugs alter gut flora composition and disrupt normal gut physiology

**"Clean" lifestyle**
- Regular cleaning (e.g., hands, body, clothes, surfaces) reduces exposure to new microbial strains. The western food system is built on the premise that "bacteria are bad."

**Chronic stress**
- Chronic stress can change the balance of microorganisms that live in the gut

**Disease**
- Infectious diseases and microbial infections (e.g., bacteria, parasites) can cause lasting damage to the gut flora

**Caesarean section, bottle-feeding, and poor hereditary gut flora**
- Children pick up microorganisms during birth and breastfeeding that shape their gut flora. Children also come in touch with microorganisms from other humans and animals (e.g., kissing, pre-chewed food). Dysfunctional gut flora is hereditary.

**Treatment**

**The Gut Diet**
- A diet based on meat, fish, seafood, eggs, vegetables, fruits, berries, nuts, and other foods that have a high amount of fiber will limit the consumption of problematic food components processed foods, high-density carbohydrates, etc. Most people can also include butter, cream, and creamed dairy products in their diet.
- Avoid foods you have an intolerance towards, and slowly include them in the diet when gut flora improves.

**Probiotics**
- Probiotics are beneficial microorganisms that live in the digestive tract. They improve the health of the gut flora. Fermented dairy products, and other processed foods (e.g., vegetables with citrus seeds, raisins, and honey) are possible sources of microorganisms. Contact with healthy humans and animals (e.g., kissing, petting, etc.) is a source of new microbial strains. Microorganisms are also obtained from the rest of the environment (e.g., surfaces, soil, and transferred onto hands, face, etc.).

**Prebiotics**
- Prebiotics are non-digestible food ingredients that stimulate the growth of beneficial bacteria in the digestive tract. Common root, onions, and garlic are some foods that contain prebiotics. Prebiotics can also be supplemented. It's advised to start with a small quantity of probiotics since they usually promote some type of initial reaction (e.g., gas, bloating).

**Inflammation and oxidative stress**
- Dysfunctional gut flora or gut dysbiosis
- Increased intestinal permeability (leaky gut)

**Poor health and disease**
- Improved gut flora and decreased intestinal permeability (no leaky gut)
- Decreased inflammation and reduced oxidative stress

**Good health and no disease**
Probiotics
(strain dependent)

- Restore/achieve gut homeostasis
- Immune modulation and down regulation of inflammation
- Decreased infection
- Improved growth and development
- Valid outcomes and measurable parameters needed.
  - reduced risk of disease OR health indicators/benefits
    eg immune triggering; structure/function benefits

Well documented probiotic strains can promote infant growth and development and potentially assist in reversing the pandemic of NCDs.
**B. lactis** results in healthier gut microbiota

Full term infants

Bifidobacteria similar to that in fully breastfed

Preterm infants (88.4% C-sections)

More bifidobacteria and less clostridia

Future Perspectives

- Need to understand host-microbe interactions
- Targeted immune regulation
- Regulate metabolism and behaviour
- Identify healthy responses/populations
- Re-programing to reverse the pandemic of NCDs
- Hollistic approach including maternal and infant nutrition, life style and exposures.
There is no single silver bullet
Thank You