Human Food For Thoughts

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Special Nutrition Issue

What to Eat Now

Uncovering the Myths about Food by Dr. Oz

Plus: Are Vitamins Worth It?
Vaginal delivery and C-section
Activation of lactation leads to the production of colostrum followed by milk.
Human milk composition

Lipids 40 g/L

Lactose 70 g/L

Proteins 8 g/L

HMO 5–15 g/L

Other 23%

1585.6 5%
1877.7 4%
2096.7 3%
1220.4 20%
855.3 1%
709.3 17%
1731.6 6%
1074.4 8%
1366.5 11%
1511.6 3%

Angela M. Zivkovic et al. PNAS 2011;108:4653-4658
Milk evolved to interact with microbes

Milk is a high glycosylated fluid

What are the functional components of milk?

Components of milk
- Lactose
- (Glyco)Lipids
- Oligosaccharides (HMO)
- (Glyco)Proteins
- (Glyco)Peptides
- Metabolites
- Minerals
- DNA
- RNA
- Cells
- Microbes
- Micelles

Milk evolved to shape the gut microbiota

To affect the microbiota, milk has:
- Antimicrobial
- Pathogen Block
- Prebiotic
- Probiotic

Which component is associated with what function?
Strong Consumers vs (weak) non-consumers of HMO

HMO are prebiotics selecting a specific bacteria

Strong Consumer          Weak or non-Consumers

<table>
<thead>
<tr>
<th>Bacteriodes</th>
<th>Bifidobacterium</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>B. infantis</em></td>
<td><em>B. bifidum</em></td>
</tr>
<tr>
<td><em>B. breve</em></td>
<td><em>B. animalis</em></td>
</tr>
</tbody>
</table>

*Bifido longhum infantis* evolved with the proteins to deal with HMO

```
(2) Sialidase
(3) Hexosaminidase
(5) Galactosidase
```

Sialidases ———— Sela et al JBC 2011
Fucosidases ———— Sela et al AEM 2012
Hexosaminidases ———— Garrido et al Anaerobe 2012
Galactosidases ———— Garrido et al Food Micro 2012

Zivkovic et al.  *PNAS* 2011

David Mills
Beneficial bacteria are diminishing in developed countries

Marker Gene Sequencing Studies of the Fecal Microbiota of Breast-fed Infants at ~1 Month of Age

Average % of Infant Fecal Microbiota

Country (Cohort Type)

- Bangladesh (Vitamin A supplement)
- Gambia (Random)
- Armenia (Random)
- Switzerland (Random, Values estimated from graph)
- Canada (Random, but at 4 months of age)
- Georgia (Random)
- Sweden (Healthy)
- Italy (Colicky infants)
- Davis, CA, USA (Non-secretor mother enriched cohort)
- Ireland (Healthy, Some formula feeding)

Legend:
- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria
- Other

Lewis et al, In Prep
What is the intestinal microbiota?

300 – 1000 species of bacteria, fungi, protozoa and viruses living in the human gastrointestinal tract

The total population of microbes in the intestine approaches 100 billion

100,000,000,000

That’s about 10 times more microbes than cells of the human body
Bifidobacterium Infantis

B. infantis
2,832,748 Mb

Fucosidase
Hexosaminidase
galactosidase
Sialidase

Glc
Gal
GlcNAc
Fuc
Neu5Ac

2 µm
The Human Infant Microbiome and a Changing Paradigm in Infant Nutrition

David J. Kyle
CEO
Evolve Biosystems Inc
Davis, CA, USA
The Infant Microbiome

- Exposure to microbes in early life is a key event
- Immune system is developing and being trained
- Physiology of infants inherently vulnerable to attack by pathogens

Early infancy microbial and metabolic alterations affect risk of childhood asthma


Early Life Adversity and Brain Development: Is the Microbiome a Missing Piece of the Puzzle?

S.M. O’ Mahony, G. Clarke, T.G. Dinan, J.F. Cryan

PII: S0306-4522(15)00895-7
DOI: http://dx.doi.org/10.1016/j.neuroscience.2015.09.068
Reference: NSC 16624
To appear in: Neuroscience

http://www.newyorker.com/magazine/2012/10/22/germs-are-us
## Summary of Differences between Milk

<table>
<thead>
<tr>
<th></th>
<th>Human milk</th>
<th>Animal milks</th>
<th>Infant formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>correct amount, easy to digest</td>
<td>too much, difficult to digest</td>
<td>partly corrected</td>
</tr>
<tr>
<td>Fat</td>
<td>enough essential fatty acids, lipase to digest</td>
<td>lacks essential fatty acids, no lipase</td>
<td>no lipase</td>
</tr>
<tr>
<td>Water</td>
<td>enough</td>
<td>extra needed</td>
<td>may need extra</td>
</tr>
<tr>
<td>Anti-infective properties</td>
<td>present</td>
<td>absent</td>
<td>absent</td>
</tr>
</tbody>
</table>

FIGURE 1: Neuron Growth & Connections Over Time

- Newborn
- 1 Month
- 9 Months
- 2 Years
- Adult

Source: Corel, JL. The postnatal development of the human cerebral cortex. Cambridge, MA: Harvard University Press; 1975
Glia Make up >80% of Human Brain Cells
<table>
<thead>
<tr>
<th>Types of Neuroglia</th>
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</thead>
<tbody>
<tr>
<td><strong>Central Nervous System</strong></td>
</tr>
<tr>
<td>Ependymal cells</td>
</tr>
<tr>
<td>Oligodendrocytes</td>
</tr>
<tr>
<td>Astrocytes</td>
</tr>
<tr>
<td>Microglia</td>
</tr>
<tr>
<td><strong>Peripheral Nervous System</strong></td>
</tr>
<tr>
<td>Satellite cells</td>
</tr>
<tr>
<td>Schwann cells</td>
</tr>
</tbody>
</table>
From Man to.... Cook!
Pleasure Centers
We Only Eat What We Like
IF ADAM AND EVE HAD BEEN CHINESE

We would still be in Paradise. Because they would have eaten the snake instead of the apple!
Jean-Anthelme Brillat-Savarin

The pleasures of the table are for every man, of every land, and no matter of what place in history or society; they can be a part of all other pleasures and they last the longest, to console us when we have outlived the rest.
Diet after surgical operation

Apfelbaum M Presse Med 1971;79:2027-2032

Seminal study demonstrating that artsy and tasting food shortens hospital stay of surgical patients by an average of 3 days. All constituents/calories were identical in both diets.
Good Food Makes People Happy, and Healthy

The effect of the palatability of a meal was tested on the post-prandial release of several gut hormones or neuropeptides that are known to effect intake and satiety. Hormonal response was measured in plasma for 3 h after a highly palatable and energy-rich meal, or after the same meal served cold in a poorly acceptable form, as well as fasting. The early post-prandial pancreatic polypeptide and neurotensin response was significantly higher after the highly palatable meal than after the cold one.
Mood improved during the palatable meal

![Graph showing mood ratings over time for palatable and cold meals.](image)
Pancreatic Polypeptide level was higher in the palatable meal than in the cold meal (p<0.03)
We are SUPRAORGANISMS!

- **Microorganisms**: ~100 trillion cells, ~3 million genes
- **Human**: ~10 trillion cells, ~23,000 genes
- **Environment**: Toxins and beneficial metabolites
- **Immunity and nutrition**: Health status
  - Health
  - Transition
  - Disease

Nature Reviews | Microbiology
What’s Happening in the Oral Cavity?

A wide variety of microbes regularly enter the oral cavity. Saliva, pH, temperature, immune system prevent many species from surviving. Oral antibiotics inhibit growth. Brushing and flossing teeth clears some built up biofilm.

Symbiosis of the oral microbes that are able to survive these conditions form an elaborate scaffold that lives on the tooth enamel and at the interface with the gums. It forms a barrier for incoming bacteria.
Ruminococcus sp. bacteria can be found in significantly high numbers in the gut flora. They break down cellulose in the gut, helping with digestion.

Helicobacter pylori bacteria has a helical shape and colonizes the stomach and upper G.I. tract. It is known to be a major cause of stomach ulcers, although many with H. pylori do not get ulcers.
Gut Microbiome & Gene Expression

Figure 1

Lorenza Putignani
doi:10.1038/pr.2014.49
**The Gut-brain Axis**

- Within the first few days of life, the human gut is colonized by commensal intestinal microbiota.

- Studies show that commensal, probiotic, and pathogenic bacteria in the gastrointestinal tract can activate neural pathways and central nervous system signaling systems.
How the Gut-brain Axis works

✓ The microbiome is affected by our experiences and emotions.

✓ In turn microbes in the gut send chemical signals (including neurotransmitters) affecting memory, emotions and behavior in important parts of the brain.

✓ Gut microbes even alter gene expression in the gut.
Altered intestinal microbiota

- Antibiotics
- Lifestyle
- Diet
- Hygiene

Hyperimmunity
- IL-6
- IL-12
- TNF

Immunodeficiency
- NOD2
- IL-10

Chronic inflammation

Metabolic dysfunction
A developmentally abnormal gut microbiota may in turn affect both the gut-brain axis and brain development and contribute to the etiology of autism.

Propionic acid (PA) found as a metabolic product of gut bacteria has been reported to mimic/mediate the neurotoxic effects of autism.

Results from animal studies may guide investigations on human populations toward identifying environmental contaminants that produce or drugs that protect from neurotoxicity.
Gut-Brain Axis

Brain - to - Gut Microbiota

Motility & barrier function
Mucus secretion & neurotransmitters
Stress response system

composition of gut microbiota

Enteroendocrine cells
Hormonal signals

Gut Microbiota - to - Brain

Vagus nerve activation

Activation of mucosal immune system

Bacterial metabolites
Bacterial like neuropeptides
Mechanism of Atherosclerosis

A

Carnitine

Gut flora

TMA

Atherosclerosis

Choline

FMO

TMAO

B

ASCVD

Atherosclerosis

TMAO

FMO

Gut microflora

Choline

TMA
Global Food Production

The graph shows the trend of total production and per capita production from 1960 to 2000. The total production line is represented in black, while the per capita production line is in light blue. The base year for comparison is 1989–91, with a value of 100.
A Symposium