Western food habits and (un)health – the role of microbiota.

Stig Bengmark MD PhD

Institute of Hepatology, London, 2012-09-26

www.bengmark.com
MICROBIOTA, IMMUNITY, DISEASE

MICROBIOTA, IMMUNITY, DISEASE

Stressors like a calorie-rich diet:
activate epigenetic markers
modify histones,
add methyl groups to DNA strands,
turn genes on and off &
seem to affect what gets passed down to the offspring
DISEASE – IMPACT OF LIFESTYLE

The individual

- Early childhood
- Mother during pregnancy
- Mother at conception
- Grandfather & father
Acute and “chronic” phase reaction—a mother of disease

Stig Bengmark

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Received 23 July 2004

Summary The world is increasingly threatened by a global epidemic of chronic diseases. Almost half of the global morbidity and almost two thirds of global mortality is due to these diseases—approximately 35 million die each year from chronic diseases. And they continue to increase. Increasing evidence suggest that these diseases are associated with lifestyle, stress, lack of physical exercise, over-consumption of calorie-condensed foods rich in saturated fat, sugar and starch, but also under-consumption of antioxidant-rich fruits and vegetables. As a result the function of the innate immune system is severely impaired. This review discusses the
INFLAMMATION & INFECTION

• Inflammation paves way for acute and chronic disease espec. infections

• “the challenge in critical illness is less the infection than the exuberant inflammatory response”

Taneja et al Crit Care Med 2004; 32: 1460–1469
SYSTEMIC INFLAMMATION

Finch CE, Crimmins EM Science 2004; 305:1736–1739

Individuals without obvious disease, with higher levels of inflammatory markers/s:

C-reactive protein, fibrinogen, factor VIII activity, interleukin-6 and TNF-α etc.

are candidates to develop chronic diseases & complications to disease and treatments
INFLAMMATION, ORIGIN & MANIFESTATIONS

• Low intake of fresh plant foods; greens, vegetables, fruits, spices
• High intake of heat- and storage-induced proteotoxins: glycated (AGEs), lipoxidated molecules (ALEs)
• High intake of proteotoxins in certain foods: casein, gluten, zein (corn) etc.

leads to:
- Reduced numbers & diversity of microbiota
- Increased translocation through various body membranes: leaky gut, leaky airways, leaky skin, leaky vagina, leaky eye cavity, leaky nose, leaky placenta, leaky blood-brain barrier etc.
IGF & TOLL-STIMULATORY FOODS

Excess in refined, processed foods e.g.
- foods rich in IGF-1, and/or IGF-1 promoting &
- Toll-stimulatory (inflammation-inducing) foods:
  • increase expression of inflammatory messengers
  • reduce microbiota
  • increase membrane leakages
  • destabilize the immune system

Contributory are: Lack of physical activity, mental and physical stress, Vitamin D deficiency, lack of anti-inflammatory minerals; Mg, Zn, Se, lack of omega-3 fatty acids etc.
OBESITY - THE GLOBAL TZUNAMI
& ITS ASSOCIATION TO MODERN AGRICULTURE

THE GLOBAL OBESITY PROBLEM

Obese adults in population %
- 30 – 40%
- 20 – 30%
- 10 – 20%
- 5 – 10%
- 0 – 5%
- No data

An obese adult is classified as having a Body Mass Index equal to or greater than 30

SOURCE: World Health Organization, 2005
INDUSTRIAL & AGRICULTURAL REVOLUTION

100% increase in per person intake of saturated fats
5000% increase in consumption of dairy-derived foods
10000% increase in refined sugar intake (1 lb => 100 lb)

Figure 1. Scheme of the relative percentages of different dietary fatty acids (saturated fatty acids and n-6 and n-3 unsaturated fatty acids) in the diet and possible changes subsequent to industrial food processing, involving animal husbandry and hydrogenation of fatty acids. (Reprinted from Leaf and Weber), (14).

after Simopoulos (15).
Homo erectus
2 milj – 100 000 years bC
"diet consisted of green leaves, wild grasses, berries, flowers, nuts, honey, tubers, roots, occasional red meat, shellfish and bird's eggs."
PALEOLITHIC DIET

“Much support that our genes, adapted during million of years to the lifestyle of our prehistoric ancestors badly tolerate the dramatic changes, especially in food habits, which have occurred”.

**Contained more of:**

- (X = times more)
- Minerals: 2 X
- Fibers: 4 to 10 X
- Antioxidants: 10 X
- Omega-3 FA: 50 X
- Lactic acid bacteria: >10^{10} X

**Contained less of:**

- (X = times less)
- Protein: 2 X
- Saturated FA: 4 X
- Sodium: 10 X

VITAMIN D DEFICIENCY COMMON IN PATIENTS

Burkina Faso:

115 nmol/L

(> 70 nmol/L)

Vitamin D deficiencies (< 30 mol/L)

In Westerners undergoing surgery:

- 95% of Afro-Americans undergoing renal transplantation
  Tripathy SS et al Transplantation 2008;85: 767–770
- 85% of patients undergoing hip or knee replacement
- 77% of chronic pancreatitis patients
  Dujsikova H et al Pancreatology 2008;8:583–586
- 67% of renal transplantation patients
  Ducloux D et al Transplantation 2008;85: 1755–1759
- 57% obesity surgery patients (79% in black and Hispanic)
  Gemmel K et al Surg Obes Rel Dis 2009,5, 54–59
VITAMIN D DEFICIENCY & DISEASE

- Aging
- Allergy
- Alzheimer’s disease
- Asthma
- Athletic performance
- Autism
- Cancer
- Cavities
- Colds
- Crohn’s disease
- Cystic fibrosis
- Depression
- Diabetes 1 and 2
- Eczema
- Heart disease
- Hearing loss
- Hypertension
- Infertility
- Influenza
- Insomnia
- Liver diseases
- Macular degeneration
- Migraines
- Multiple Sclerosis
- Muscle pain
- Obesity
- Periodontal disease
- Pre-eclampsia
- Psoriasis
- Rheumatoid diseases
- Schizophrenia
- Seizures
- Septicemia
- Tuberculosis
VITAMIN D IN LIVER DISEASE

Malham M et al World J Gastroenterol 2011;17:922-925

ALCOHOLIC CIRRHOSIS

85% have serum levels below 50 nmol/L &
55% have levels below 25 nmol/L

BILIARY CIRRHOSIS

60% have serum levels below 50 nmol/L &
16% have levels below 25 nmol/L (P < 0.001).

Levels decrease with increasing severity of disease.
VITAMIN D, Hb A1c & LIVER FUNCTION


Figure 2  Graph of the relation between 25OHD and HbA1c in patients with T2DM. Lines in the graph represent the simple linear regression between values with their associated 95% confidence interval.

Figure 3  Graph of the relation between 25OHD and the log of ALT in patients with T2DM. Lines in the graph represent the simple linear regression between values with their associated 95% confidence interval.
to all European to 40 ng/mL would reduce the **direct** economic burden of disease by 11.4%, or EUR 105,000 000 000

the **indirect** economic burden of disease by 6.4 % or EUR 82,000 000 000

& reduce the economic burden of disease by 17.7%, or EUR 187,000 000 000
Western lifestyle; down-regulates immune functions through lack of beneficial microbial products, increasing systemic inflammation - inducing diseases. Microbiota contributes important anti-inflammatory and/or immuno-modulatory products such as SCFAs, polysaccharide A (PSA) and peptidoglycan (PTGN), vitamins, antioxidants etc.

Maslowski KM, Mackey CR
Nature Immunol 2011;12:5-9
LEAKY BARRIERS

- Gastrointestinal tract
- Airways
- Skin
- Oral cavity
- Vagina
- Nose
- Eye cavity
- Placenta
- Blood brain barriers

Maccaferri S et al Dig Dis 2011;29:525–530
LEAKY PLACENTA

A shocking 9/20 (43 %) of umbilical cord blood, cultivated from healthy neonates born by cesarean section, demonstrated positive growth:

Enterococcus faecium,
Propionibacterium acnes,
Staphylococcus epidermidis &
Streptococcus sanguinis

“We have become accustomed to the idea that the major disorders of adult life, including coronary heart disease, stroke and diabetes, arise through interaction between influences in our adult lifestyle and genetically determined susceptibility. Recent research, however, suggest that growth in utero may also play an important role.”

“Even brief periods of undernutrition may permanently change or `programme` the body........................................ and lead to persistent changes in blood pressure, cholesterol metabolism, insulin response to glucose, and in a range of other metabolic, endocrine and immune parameters.”
Live intestinal bacteria found present in large numbers in adipose tissue (MAT), mesenteric lymph nodes (MLN) and blood after only one week on a high-fat diet (HFD)
LEAKY GUT – TRANSPORT OF ENDOTOXIN (LPS)

ATHEROSCLEROSIS & BACTERIAL DEBRIS


Bacteria & bacterial debris in human atheroma, in the past considered harmless, seems to contribute to disease progression via TLR-dependent lipid body formation in macrophages

![Graph showing cholesterol ester (ng per µg protein)]
Boutenko V. Green for Life.
North Atlantic Books Calif, USA, 2010

FOOD PATTERN UGANDIAN CHIMPANZEEs
Potts KB et al Int J Primatol 2011;32:669-690

ripe fruits = RF
unripe fruits = UF
young leaves = YL
seeds, flowers
## DIET & LONGEVITY

*Robbins J: Health at 100. USA 2007*

<table>
<thead>
<tr>
<th></th>
<th>Abkhasia</th>
<th>Vilcabamba</th>
<th>Hunza</th>
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<tr>
<td>Percent of calories from carbohydrate</td>
<td>69%</td>
<td>74%</td>
<td>73%</td>
</tr>
<tr>
<td>Percent of calories from fat</td>
<td>18%</td>
<td>15%</td>
<td>17%</td>
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<tr>
<td>Percent of calories from protein</td>
<td>13%</td>
<td>11%</td>
<td>10%</td>
</tr>
<tr>
<td>Overall daily calories</td>
<td>1,800</td>
<td>1,700</td>
<td>1,800</td>
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<tr>
<td>Percentage of diet from plant foods</td>
<td>90%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Percentage of diet from animal foods</td>
<td>10%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Salt consumption</td>
<td>low</td>
<td>low</td>
<td>low</td>
</tr>
<tr>
<td>Sugar consumption</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Processed food consumption</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Incidence of obesity</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
80/10/10/10 DIET

80 % raw greens
10 % vegetable fats
10 % vegetable proteins
President Bill Clinton – now a vegan radically changed diet, lost 20 lbs. in weight & improved his health, Clinton tells CNN. After experiencing periodic heart problems leading up to the 2004 surgery, the former junk food lover now calls himself a vegan, shunning meat, eggs, dairy and almost all oil saying: "I like the vegetables, the fruits, the beans, the stuff I eat now," "I feel good, and I also have ... more energy."
Employees (insurance company) with overweight and/or diabetes received either a low-fat vegan diet or regular food for 22 weeks. The vegan group reported improvements in:

- general health \((p = 0.002)\)
- physical functioning \((p = 0.001)\)
- mental health \((p = 0.03)\)
- general vitality \((p = 0.004)\)
- overall diet satisfaction \((p = 0.001)\)
- reduced food costs \((p = 0.003)\), but
- increased difficulty finding foods when eating out
Saddleback Church & Loss of 260,000 lbs
Rick Warren - The Daniel Plan
DIFFERENT MICROBIOTA IN OBESE vs LEAN


Figure 6. Population of bacteria found to increase in obese and lean individuals.
Fig. 2 Possible links between the gut microbiota and metabolism. Details, see main text. Continuous lines, likely pathway; dotted lines, putative pathway.
INFLAMMATION IN OBESE PREGNANT WOMEN

Basu S et al Obesity 2011;19:476-482
ENDOTOXIN-ASSOCIATED DISEASES


Cognitive impairment Lee JW et al. J Neuroinflammation 2008; 5: 37

Arterio-/Coronary Diseases Heo SK et al Immunol Lett 2008;120:57-64

Diabetes type 1 Nymark M et al Diabetes Care 2009 32(9): 1689–1693

Diabetes type 2 Andreasen AS Intensive Care Med. 2010;36:1548-1555


• DHD, allergy, ALS, autism, autoimmune diseases, bipolar disease, cataracts, chronic fatigue syndrome, COPD, fibromyalgia, glaucoma, gulf war syndrome, HIV, iritis, macular degeneration, minimal encephalopathy, multiple sclerosis, nephropathies, obesity, osteoporosis, paradontosis, Parkinson, polycystic ovary syndrome, rheumatoid disease, stress, schizophrenia, stroke, uveitis
MICROBIOTA-INDUCED METABOLIC DISORDERS

Cani PD et al Diabetes 2008;57:1470-1481

Bacteria induced metabolic disease hypothesis

High fat feeding

Change Gut flora

Increased permeability

Increased LPS absorption

Increased endotoxemia

Inflammation

Metabolic disorders

LPS concentration 10 to 50 X higher than those obtained during septic shock


Bifidobacterim spp.
CASEIN & GLUTEN IMPAIRS LACTOBACILLUS GROWTH

Without casein and gluten

With casein and gluten

GLUTEN & SURFACE MOLECULE EXPRESSIONS
GS seen in well-defined chronic diseases such as therapy-resistant epilepsy & in patients with Alzheimer-like symptoms. Often in diffuse often ignored distresses; fatigue, lack of energy, mental depression, encephalopathy/‘foggy mind’, diffuse abdominal pain, bloating, diarrhea, eczema and/or rash, undefined headache, numbness in the legs, arms or fingers, joint pain and other manifestations.

Gluten-free diet increases energy, enthusiasm, well-being & frequently also improve clinical signs.
Gluten increases systemic inflammation & is associated with diseases such as:

ADHD, arthritis, Addison´s disease, allergy, autoimmune disorders, autism, bipolar disease, depression, dermatitis herpetiformis, diabetes mellitus, epilepsy, Graves´disease, infections, inflammatory bowel diseases - IBD, irritable bowel syndrome – IBS, lupus erythematosus, myasthenia gravis, osteoporosis and increased risk of fractures, pernicious anemia, polymyalgia rheumatica, psoriasis, schizophrenia, scleroderma, sepsis, Sjögren’s syndrome, thyreotoxicosis, vitiligo
A close association between celiac disease & autoimmune liver disorders is well-known. Celiac disease observed in
- 3 to 7% in primary biliary cirrhosis
- 3 to 6% in autoimmune hepatitis
- 2 to 3% in primary sclerosing cholangitis

Will as known today, & much in contrast to cryptogenic liver disorders, not improve on a gluten-free diet.
Gluten-free diet tried in 15 individuals with diabetes but no gluten intolerance. Insulin sensitivity increased significantly in 12/14 subjects after six months on gluten-free diet ($P=0.04$) & decreased again in 10/13 subjects after 6 months on “normal” diet ($P=0.07$).
GLUTEN-FREE DIET in IRRITABLE BOWEL SYNDROME

Biesiekierski Jr et al. Am J Gastroenterol 2011;106: 508-514
EXCLUSION (GLUTEN-REDUCED) DIET IN ADHD

Pelsser LMJ et al Lancet 2011;377:494-503
Crossover study 100 children, aged 4-8 yrs, 9 weeks + 4 weeks
A. Total, B. Inattention, C. Hyperactivity  D. Abbreviated Connor Scale scores (ACS)
PROLAMINS & TRYPTOPHAN/CORTEX

Choi S et al Physiol Behav 2009;98:156-162

Up to 8-fold decrease in cortex tryptophan & similar decrease in serotonin after feeding:

• Zein (corn) marked reductions
• Casein (dairy) & Gluten (wheat, rye, barley) significant reductions
• Lactalbumin (dairy) small reductions
• Vegetable protein (soy) small increases

No effects were observed in regional catecholamine synthesis rates
• **Amaranth** – Aztec culture, high protein & mineral content
• **Quinoa** – Inca culture, high protein & mineral content
• **Sorghum (durra, jowari, milo)** - 5th in world, versatile, low energy, most cost-effective
• **Millet** – 6th highest in world, versatile, mild flavor
• **Teff** – staple in Ethiopia, tiny seed, high mineral content
### Table V. Antioxidant activity (ORAC) of sorghum grains and brans compared to common fruits and vegetables

<table>
<thead>
<tr>
<th>Commodity</th>
<th>ORAC (μmol TE/g, dry wt.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tannin sorghum (grain)</td>
<td>868</td>
</tr>
<tr>
<td>Tannin sorghum (bran)</td>
<td>3124</td>
</tr>
<tr>
<td>Black sorghum (grain)</td>
<td>219</td>
</tr>
<tr>
<td>Black sorghum (bran)</td>
<td>1008</td>
</tr>
<tr>
<td>Red sorghum (grain)</td>
<td>140</td>
</tr>
<tr>
<td>Red sorghum (bran)</td>
<td>710</td>
</tr>
<tr>
<td>White sorghum (grain)</td>
<td>22</td>
</tr>
<tr>
<td>White sorghum (bran)</td>
<td>64</td>
</tr>
<tr>
<td>Blueberry, lowbush</td>
<td>842</td>
</tr>
<tr>
<td>Strawberry</td>
<td>402</td>
</tr>
<tr>
<td>Plum</td>
<td>495</td>
</tr>
<tr>
<td>Watermelon</td>
<td>18</td>
</tr>
<tr>
<td>Apple, red delicious</td>
<td>295</td>
</tr>
<tr>
<td>Orange, navel</td>
<td>137</td>
</tr>
<tr>
<td>Broccoli</td>
<td>173</td>
</tr>
<tr>
<td>Carrot</td>
<td>108</td>
</tr>
<tr>
<td>Onion, red</td>
<td>93</td>
</tr>
<tr>
<td>Sweet pepper, green</td>
<td>105</td>
</tr>
<tr>
<td>Radishes</td>
<td>217</td>
</tr>
<tr>
<td>Potatoes, russet</td>
<td>63</td>
</tr>
</tbody>
</table>

\[a\] Adapted from Dykes and Rooney [18].
\[b\] Sumac.
HEAT-INDUCED DYSFUNCTIONING PROTEINS – smoking with the stomach

Bengmark S JPEN 2007;31:430-440

FIGURE 3. Schematic depiction of the multiple sources of AGEs. Beyond the known conditions associated with elevated circulating and tissue AGEs, exogenous sources—namely, diet and tobacco—constitute significant contributors.

Review

Advanced Glycation and Lipoxidation End Products—Amplifiers of Inflammation: The Role of Food

Stig Bengmark, MD, PhD, PRACS (hon), FRCP (hon)

From UCL Institute of Hepatology, University College, London Medical School, London, United Kingdom

ABSTRACT. Background: High levels of glycated and lipoxidized proteins and peptides in the body are repeatedly associated with chronic diseases. These molecules are strongly associated with activation of a specific receptor called RAGE and a long-lasting exaggerated level of inflammation in the body. Methods: PubMed reports over 5000 papers plus disease. Its activation is associated with high levels of dysfunctioning proteins in body fluids and tissues, and is strongly associated with a series of diseases from allergy and Alzheimers to rheumatoid arthritis and urogenital disorders. Heat treatment, irradiation, and ionization of foods increase the amount of dysfunctioning molecules. Conclusions: Max...
Toasted bread contains several-fold more of acrylamide than untoasted Wheat: 11–161 vs < 5 mg/kg. Rye: 27–205 vs 7–23 mg/kg

Granby K et al Food Additiv Contamin 2008; 25:921–929
AGEs/ALEs IN FOODS

HEATED DAIRY: powdered milk (rich in ice cream, baby & clinical nutrition formulas) & cheese, espec. hard cheeses

HEATED GRAIN PRODUCTS: Toasted bread, bread crusts & crisp breads

HEATED MEAT (espec. bacon, sausages), POULTRY, FISH: content increases with exposure to temperature: boiling (1000 kU/serving) frying (9000 kU/serving)


HEATED VEGETABLE OILS: heated olive oil ca 8000 kU

OTHERS: Egg yolk powder, lecithin powder, coffee, espec dark roasted, hard-cured teas, roasted and salted peanuts, dark and sugar-rich alcoholic beverages, broth, Chinese soy, balsamic vinegar, Cola drinks etc
AGEs IN VARIOUS MILK PRODUCTS

Baptista J, Carvalho R Food Res Int 2004;37:739-747
AGES/ALES IN TISSUES

Dys-functioning, glycated proteins induce about 50 times more free radicals than non-glycated proteins (AGEs and ALEs), which:

- accumulate in tissues (amyloid) &
- make the body auto-fluorescing
- impair DNA repair mechanisms
- induce tissue accumulation of toxins
- reduce antioxidant defense
- induce inflammation & infection
- weaken immune system &
- accelerate development of various diseases

### Table 2. Cytokines and cellular events associated with AGE or RAGE activation

<table>
<thead>
<tr>
<th>Cytokine/Event</th>
<th>Cell Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>VCAM-1 ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>ICAM-1 ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>E-selectin ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>PDGF ↑</td>
<td>Pancreatic cancer cells</td>
</tr>
<tr>
<td>eNOS ↓</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>Tissue factor ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>TGF-β ↑</td>
<td>Mesangial cells, proximal tubular cells, vascular smooth muscle cells, macrophages</td>
</tr>
<tr>
<td>TNF-α ↑</td>
<td>Endothelial cells, mesangial cells, mononuclear macrophages</td>
</tr>
<tr>
<td>IGF-1 ↑</td>
<td>Mesangial cells</td>
</tr>
<tr>
<td>MCP-1 ↑</td>
<td>Mesangial cells, endothelial cells</td>
</tr>
<tr>
<td>CTGF ↑</td>
<td>Fibroblasts, mesangial cells</td>
</tr>
<tr>
<td>IL-6 ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>PAI-1 ↑</td>
<td>Endothelial cells</td>
</tr>
<tr>
<td>RAGE ↑</td>
<td>Mesangial cells, endothelial cells, podocytes</td>
</tr>
<tr>
<td>VEGF ↑</td>
<td>Podocytes, endothelial cells, mesangial cells</td>
</tr>
<tr>
<td>ANG II-dependent cell activation ↑</td>
<td>Vascular smooth muscle cells</td>
</tr>
<tr>
<td>Type IV collagen expression ↑</td>
<td>Mesangial cells</td>
</tr>
<tr>
<td>Fibronectin ↑</td>
<td>Mesangial cells</td>
</tr>
<tr>
<td>Cell cycle progression ↓</td>
<td>Fibroblasts, mesangial cells</td>
</tr>
</tbody>
</table>

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eNOS, endothelial nitric oxide synthase; TGF-β, transforming growth factor-β; MCP-1, monocyte chemotactic protein-1; CTGF, connective tissue growth factor; PAI-1, plasminogen activator inhibitor-1.
DISEASES WITH ELEVATED AGES/ALEs

- Aging
- Allergy
- Autoimmune diseases
- Alzheimer’s disease
- Parkinson’s disease
- Amyotrophic lateral sclerosis
- Huntington’s disease
- Stroke
- Familial amyloidotic polyneuropathy
- Creutsfeldt-Jakob disease
- Down’s syndrome
- Atherosclerosis
- Cardiovascular diseases
- Cataract
- Glaucoma
- Macula degeneration
- Diabetes
- Hormone deficiencies
- Polycystic Ovary Syndrome
- Chronic liver diseases
- Chronic pulmonary disorders
- Rheumatoid diseases
- Fibromyalgia
- Ruptured Achilles tendon
- Osteoporosis
- Nephropathies
- Paradontosis
- Sepsis
### AGEs IN VARIOUS MILK PRODUCTS

*Baptista J, Carvalho R* Food Res Int 2004;37:739-747

<table>
<thead>
<tr>
<th>Milk-based Products</th>
<th>Furosine mg/g of Protein</th>
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</thead>
<tbody>
<tr>
<td>Powder Milk (a)</td>
<td></td>
</tr>
<tr>
<td>Powder Milk (b)</td>
<td></td>
</tr>
<tr>
<td>UHT Milk</td>
<td></td>
</tr>
<tr>
<td>Evapor. Milk</td>
<td></td>
</tr>
<tr>
<td>Pasteur. Milk</td>
<td></td>
</tr>
<tr>
<td>DIF (c)</td>
<td></td>
</tr>
<tr>
<td>DIF (d)</td>
<td></td>
</tr>
<tr>
<td>Powder Milk (e)</td>
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<td>DIF (d)</td>
<td></td>
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<td>Powder Milk (e)</td>
<td></td>
</tr>
<tr>
<td>UHT lact. Free</td>
<td></td>
</tr>
<tr>
<td>Powder Milk (f)</td>
<td></td>
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<tr>
<td>UHT Homog.</td>
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<tr>
<td>DIF with Milk</td>
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<tr>
<td>DIF lact. Free</td>
<td></td>
</tr>
<tr>
<td>Soya Milk</td>
<td></td>
</tr>
<tr>
<td>Milk (g)</td>
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AGEs IN NASH

AGE & GRAFT SURVIVAL

Hartog JWL et al Transplantation 2009;87:1069-1077

Accumulation of AGEs studied, during > six years in 302 renal transplant patients

Stronger predictor of graft loss than proteinuria & creatinine clearance
Eating cured meats: (bacon, cured hams, sausage) induces inflammation & reduces FEV1

<table>
<thead>
<tr>
<th>Intake</th>
<th>Reduction (ml)</th>
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<tbody>
<tr>
<td>3 - 4 X/mo</td>
<td>12 ml</td>
</tr>
<tr>
<td>5 - 13 X/mo</td>
<td>42 ml</td>
</tr>
<tr>
<td>≥ 14 X/mo</td>
<td>110 ml</td>
</tr>
</tbody>
</table>

Jiang R et al, Am J Respir Crit Care Med 2007;175:798–804

Intake of solid fruits & esp. catechin (tea & apple) reduces inflammation and increases FEV1 + 130 ml & reduces main COPD symptoms: chronic cough, phlegm, breathlessness (p < 0.001)

Tabak C et al, Am J Respir Crit Care Med 2001;164:61–64
DAIRY-INDUCED INFLAMMATION

Dietary proteins of cow’s milk induce inflammation:
• release inflammatory mediators
• increase intestinal permeability
• induce leakage of large molecules; albumin, hyaluronan etc

BOVINE MILK & CHRONIC DISEASES

- **Allergy**  Rautava S, Isolauri EJ  

- **Breast cancer**  Outwater JL et al  
  *Int J Cancer* 2001;93:888-893

- **Colorectal cancer**  
  Manousos O et al  
  *Int J Cancer* 1999;83:15-17, Ma et al  
  *J Nat Cancer Inst*;2001;93:1330-1336

- **Coronary heart disease**  
  Briggs RD et al.  
  *Circulation* 1960;21:538-542, Marshall T  
  *BMJ* 2000;320:301-305

- **Chronic constipation**  
  Iacono G et al  

- **Diabetes type 1**  
  Gimeno SGA, De Souza JMP  
  *Diabetes Care* 1997;20:1256-1260, Virtanen SM et al  

- **Malabsorption**  O’Keefe SJD et al  

- **Ovarian cancer**  Larsson SC et al  
  *Am J Clin Nutr* 2004;80:1353-1357,  
  Ganmaaa D, Sato A  

- **Parkinson disease**  Park M et al.  
  *Neurology* 2005;64:1047-1051

- **Testicular and prostate cancer**  
  Ganmaaa D et al  
  *Med Hypotheses* 2003;60:724-730, Qin LQ et al  
  *Nutrition and Cancer* 2004;48:22-27
ESTROGENS IN MILK

Background: The dramatic increase in testicular, breast, prostate, ovarian, and corpus uteri, and large bowel cancers.

60-80% of the intake of oestrogens originates in the Western world from milk and other dairy foods.

The daily intake of oestrogens through milk is 372 ng, “dramatically more than currently recognized.”

The content is twice as high in 3.5 % fat milk than in non-fat milk & extremely high in butter!
# FREE ESTROGENS IN DAIRY

<table>
<thead>
<tr>
<th></th>
<th>PG/G</th>
<th>E1</th>
<th>E2 - 17B</th>
<th>E3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole milk</td>
<td>3.7</td>
<td>6.4</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>Skimmed milk</td>
<td>20.2</td>
<td>3.4</td>
<td>8.2</td>
<td></td>
</tr>
<tr>
<td>Whey</td>
<td>3.6</td>
<td>1.5</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>Cottage cheese</td>
<td>34.9</td>
<td>10.8</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>Butter</td>
<td>539.4</td>
<td>82.3</td>
<td>86.8</td>
<td></td>
</tr>
</tbody>
</table>

*Wolford ST, Argoudelis CJ  J Dairy Science 1979;62:1458-1463*
Fig. 1 Relation between national per capita fat intake and breast cancer mortality rate (from Carroll, 1975, reproduced with permission).
DAIRY CONSUMPTIONS & IGF-1

The Endogenous Hormones and Breast Cancer Collaborative Group
Lancet Oncol 2010; 11: 530–42

• a positive association between consumption of dairy products or milk and IGF-I concentrations reported in several cross-sectional studies (11, 12, 17, 18, 31, 32)

• IGF-I concentrations found significantly lower in vegans compared with lactoovo-vegetarians and omnivores in the EPIC-Oxford cohort (16, 21)

• increase in IGF-I in response to a higher intake of milk and dairy products observed in both younger (33-35) and older (36-38) participants
HOW DO YOU MANAGE YOUR CONDITION?
I DON’T eat dairy, and minimal wheat and fibre, and stay away from anti-inflammatory drugs.
INFLAMMATION REDUCTION - ECOBIOLOGICALS

Examples: bioflavonoids, polyphenols

Isothiocyanates in **cruciferous vegetables**, anthocyanins and hydroxycinnamic acids in **cherries**, epigallocatechin-3-gallate (EGCG) in **green tea**, chlorogenic acid and caffeic acid in **fresh coffee beans** and also **fresh tobacco leaves**, capsaicin in **hot chili peppers**, chalcones in **apples**, euginol in **clove**, gallic acid in **rhubarb**, hesperidin in **citrus fruits**, naringenin in **citrus fruits**, kaempferol in **white cabbage**, myricetin in **berries**, rutin and quercetin in **apples** and **onions**, resveratrol and other procyanidin dimers in **red wine** and **virgin peanuts**, various curcumenoids, the main yellow pigments in **turmeric curry foods**, and **daidzein and genistein from the soy bean**
ABSTRACT. Background: The world suffers a tsunami of chronic diseases, and a typhoon of acute illnesses, many of which are associated with the inappropriate or exaggerated activation of genes involved in inflammation. Finding therapeutic agents which can modulate the inflammatory reaction is the highest priority in medical research today. Drugs developed by the pharmaceutical industry have thus far been associated with toxicity and side effects, which is why natural substances are of increasing interest. Methods: A literature search (PubMed) showed almost 1500 papers dealing with curcumin, most from recent years. All available abstracts were read. Approximately 300 full papers were reviewed. Results: Curcumin, a component of turmeric, has been shown to be non-toxic, to have antioxidant activity, and to inhibit such mediators of inflammation as NFκB, cyclooxygenase-2 (COX-2), lipooxygenase (LOX), and inducible nitric oxide synthase (iNOS). Significant preventive and/or curative effects have been observed in experimental animal models of a number of diseases, including arteriosclerosis, cancer, diabetes, respiratory, hepatic, pancreatic, intestinal and gastric diseases, neurodegenerative and eye diseases. Conclusions: Turmeric, an approved food additive, or its component curcumin, has shown surprisingly beneficial effects in experimental studies of acute and chronic diseases characterized by an exaggerated inflammatory reaction. There is ample evidence to support its clinical use, both as a prevention and a treatment. Several natural substances have greater antioxidant effects than conventional vitamins, including various polyphenols, flavonoids and curcumenoids. Natural substances are worth further exploration both experimentally and clinically. (Journal of Parenteral and Enteral Nutrition 30:45–51, 2006)
12
Control of Systemic Inflammation and Chronic Diseases—The Use of Turmeric and Curcuminoids

Stig Bengmark

ABSTRACT

The world suffers an epidemic of both critical illness (CI) and chronic diseases (ChDs), and both groups of diseases increase from year to year, and have done so for several decades. It is strongly associated to the modern, so-called Western, lifestyle: stress, lack of exercise, abuse of tobacco and alcohol, and the transition from natural unprocessed foods to processed, calorie-condensed, and heat-treated foods. There is a strong association between reduced intake of plant fibers and plant antioxidants and increased consumption of industrially produced and processed products especially dairy, refined sugars, and starch products and ChDs. Heating up foods such as milk (pasteurization) and production and storage of milk powder produce large amounts of advanced glycation end products (AGEs) and advanced lipid oxidation end products (ALEs), known as potent inducers of inflammation (see further Chapter 20).

Numerous plant-derived, but also microbe-derived, substances, often referred to as chemopreventive agents, have documented anti-inflammatory

AN EPIDEMIC OF CHRONIC DISEASES AND CRITICAL ILLNESS

Modern medicine has to a large extent failed in its ambition to control both acute and chronic diseases. The world suffers an epidemic of chronic diseases of a dimension never seen before, and these diseases are like a prairie fire also spreading to the so-called developing countries. As an example, there are more cases of diabetes reported in China (24 million) and India (44 million) than in the United States (17 million), and the increase in incidence is faster in these countries than in Western societies. Today, chronic diseases—for example, diseases such as cardiovascular and neurodegenerative conditions, diabetes, stroke, cancers, and chronic respiratory diseases—constitute 46% of the global disease burden and 59% of the global deaths; each year approximately 35 million individuals die in conditions related to chronic diseases, and the numbers are fast increasing and have done so for several years (World Health Organization 2003).
CURCUMIN-REDUCED DISEASES
Curcumin attenuates endotoxin-induced coagulopathy & prevents disseminated intravascular coagulation

*Chen HW et al J Endotoxin Res 2007;13:15-23*

Curcumin pretreatment for 3 d before CLP
- Prevents cellular alterations in macrophages
- Decreases expression of TNF-α,
- Down-regulates PPAR-γ in organs (liver) &
- Reduces tissue injury and mortality

*Siddiqui AM et al Crit Care Med 2006 34:1874-1882*
HYPOMAGNESESEMIA & SEPSIS

• Magnesium replacement provides significant protection against endotoxin
  

• Administration of Mg to animals with sepsis improves organ function and survival time
  
52% of patients show Mg-deficiency on admission to MICU & suffer increased:

- Mortality rate (57.7% vs 31.7%)
- Need for ventilatory support (73% vs 53%)
- Duration of mechanical ventilation (4.27 vs 2.15 days),
- Rate of sepsis (38% vs 19%)
- Hypocalcemia (69% vs 50%)
- Hypoalbuminemia (80.76% vs 70.8%)
THE 1986 EXPERIENCE

Review of 81 major liver resections

Morbidity: 33% (17% major)

No antibiotics, by clinical error, to 24/81 patients

Prophylactic antibiotic (ampicillin, cephalosporin, tetracyclines) given to 57/81 patients

All infections were in antibiotic-treated patients

No infections observed in non-antibiotic-treated patients

Ekberg, PhD thesis, Lund University 1986
Synbiotics in Human Medicine

Thirty years have passed since Gilliland and Speck reported that patients with inflammatory bowel disease (IBD) had a significantly different microbiota from that of healthy individuals (Gilliland and Speck, 1977). Finegold and Sutter reported in the following year an altered microbiota in 75% of healthy omnivorous and 35% of vegetarian Americans (Finegold and Sutter, 1978). Similar observations were later made for European populations (Ahrne et al., 1998).

Numerous attempts during the last 30 years to reconstitute or remodel the microbiota in order to prevent or treat diseases were repeatedly made. However, these often produced dissatisfying results. One obvious explanation suggested by recent reviews (Sartor, 2004; Marteau, 2006) is that the majority of clinical studies thus far have been underpowered.

Factors Influencing Clinical Study Outcomes
Several factors might contribute to differences in the outcome of interventions with probiotics and prebiotics.

Regenerative Capacity
The spontaneous regenerative capacity of the gastrointestinal tract is much greater in young experimental animals and in animals with induced disease. Regenerative capacity is greater in humans with acute disease than in humans with chronic disease.

Differences in Daily Doses
The daily dose related to body weight or to the gastrointestinal mucosal surface is generally much larger in experimental animals and in pediatric cases. In the majority of studies, the daily dose used in humans has been 1 billion lactic acid bacteria (LAB) once or twice per day, up to 10 billion organisms/day. Larger doses delivered more impressive results. Large-scale doses in liver transplantation (Rayes et al., 2003) and trauma (Spindler-Vesel et al., 2007) with Synbioric 2000 and Synbioric 2000 Forte (see below) included 40 and 400 billion LAB per day. In IBD, VSL#3 was administered at a dosage of 1,200 billion LAB per day (Venturi et al., 1999). A total of 80 billion LAB of Synbioric 2000 per day were administered to patients with chronic liver disease, according
LOCATION OF IG-PRODUCING IMMUNOCYTES
Brandtzaeg, P et al Gastroenterology 1989;97:1562-1584
FLORA IN WESTERNERS

- *Lb plantarum*, a dominating LAB, in only 25% of omnivorous Americans & in 65% of vegetarian Americans


- Common colonic LAB species present only in about 50% or less of healthy Scandinavians:
  *Lb plantarum* 52%,
  *Lb rhamnosus* 26%,
  *Lb paracasei ssp paracasei* 17%

### MICROBIOTA & OBESITY


<table>
<thead>
<tr>
<th>Strain</th>
<th>Obese (n=68)</th>
<th>Controls (n=44)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>L. plantarum</em></td>
<td>0 (0%)</td>
<td>8 (18.2%)</td>
<td>0.0004</td>
</tr>
<tr>
<td><em>L. paracasei</em></td>
<td>10 (14.7%)</td>
<td>17 (38.6%)</td>
<td>0.004</td>
</tr>
<tr>
<td><em>L. reuteri</em></td>
<td>6 (8.8%)</td>
<td>1 (2.3%)</td>
<td>0.16</td>
</tr>
<tr>
<td><em>L. rhamnosus</em></td>
<td>3 (4.4%)</td>
<td>4 (9.1%)</td>
<td>0.27</td>
</tr>
<tr>
<td><em>L. ruminis</em></td>
<td>3 (4.4%)</td>
<td>4 (9.1%)</td>
<td>0.27</td>
</tr>
<tr>
<td><em>L. salivarius</em></td>
<td>5 (7.4%)</td>
<td>2 (4.5%)</td>
<td>0.43</td>
</tr>
</tbody>
</table>
THE GREAT Ps

- *Plantarum*
- *Paracasei*
- *Pediococcus pentosaceus*
*Lb paracasei* – the master?

• the strongest inducer of Th1 & repressor of Th2 cytokines when more than 100 strains are compared

SYNBIOTIC 2000

Synbiotic AB, Sweden, contact; synbiotic@gmail.com

- 400 billion Lactic acid bacteria:
  - $10^{10}$ of *Pediococcus pentosaceus* 5-33:3
  - $10^{10}$ of *Leuconostoc mesenteroides* 32-77:1
  - $10^{10}$ of *Lactobacillus paracasei sbsp. paracasei*
  - $10^{10}$ of *Lactobacillus plantarum* 2362

- 10 gram bioactive fibers:
  - 2.5 g of betaglucan
  - 2.5 g of inulin
  - 2.5 g of pectin
  - 2.5 g of resistant starch
SYNBIOTIC 2000 IN LUNG INJURY


Placebo

Only fibres

Synbiotic 2000
NEUTROPHILS IN LUNG TISSUE

Tok D et al J Trauma 2007;62:880-885

• Synbiotic 2000  9.00±0.44
• Only LAB       8.40±0.42
• Only the fibres 31.20±0.98
• Placebo        51.10±0.70
• p< 0.05
MYELOPEROXIDASE – MPO

Tok D et al J Trauma 2007;62:880-885

U/g

• Synbiotic 2000 25.62±2.19
• Only LAB 26.75±2.61
• Only the fibres 56.59±1.73
• Placebo 145.53±7.53

p< 0.05
MALONALDEHYDE – MDA

Tok D et al J Trauma 2007;62:880-885

nmol/mg

- Synbiotic 2000  0.22±1.31
- Only LAB  0.28±3.55
- Only the fibres  0.48±5.32
- Placebo  0.67±2.94

p< 0.05
NITRIC OXIDE
micromol/g

- Synbiotic 2000 17.16±2.03
- Only LAB 8.91±2.24
- Only the fibres 47.71±3.20
- Placebo 66.22±5.92

p< 0.05
SYNBIOTIC 2000 IN LIVER TRANSPLANTATION

50 to 85 % of transplant patients develop nosocomial infections within 30 days.

Synbiotic 2000 or Only fibres daily from the day before surgery + during 14 postop. days

30 day-infection rate:

Synbiotic 2000 1/33 - 3 %
Only fibres 17/33 - 51 %

### SYNBIOTIC 2000 in LT

<table>
<thead>
<tr>
<th>Isolated bacteria</th>
<th>Synbiotic 2000</th>
<th>Fibres only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**(total 1)**  **(total 18)**

SYNBIOTICS IN ACUTE PANCREATIS

Oláh A et al Hepato-gastroenterology 2007;54:36-41

Isolated Microorganisms:  

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>SYNBIOТИC 2000</th>
<th>Fibres Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Candida spp</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus haemolyticus</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Serratia spp</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

(Total 7) (Total 17)
SYNBIOTICS IN ACUTE PANCREATITIS

Oláh A et al Hepato-gastroenterology 2007;54:36-41

<table>
<thead>
<tr>
<th>Isolated Microorganisms</th>
<th>SYNBIOTIC 2000</th>
<th>Fibres Only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Enterobacter spp</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Streptococcus spp</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Candida spp</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Staphylococcus haemolyticus</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Serratia spp</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Klebsiella spp</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

(Total 7) (Total 17)
## SYNBIOTIC 2000 IN TRAUMA PATIENTS

*Spindler-Vesel A et al. JPEN 2007;31:119-126*

### Total number of infections:

<table>
<thead>
<tr>
<th>Product</th>
<th>Total Infections</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synbiotic 2000</td>
<td>2/14</td>
<td>14%</td>
</tr>
<tr>
<td>Only fiber</td>
<td>16/28</td>
<td>57%</td>
</tr>
<tr>
<td>Nutricomp Braun (peptide)</td>
<td>1/21</td>
<td>52%</td>
</tr>
<tr>
<td>Alitraq Abbott-Ross (glut +arg)</td>
<td>19/37</td>
<td>51%</td>
</tr>
</tbody>
</table>

### Number of chest infections:

<table>
<thead>
<tr>
<th>Product</th>
<th>Total Infections</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synbiotic 2000</td>
<td>1/14</td>
<td>7%</td>
</tr>
<tr>
<td>Only fiber</td>
<td>11/28</td>
<td>9%</td>
</tr>
<tr>
<td>Nutricomp Braun (peptide)</td>
<td>10/21</td>
<td>48%</td>
</tr>
<tr>
<td>Alitraq Abbott-Ross (glut +arg)</td>
<td>12/37</td>
<td>32%</td>
</tr>
</tbody>
</table>

Both Alitraq and Synbiotic 2000 down-regulated Il-6 but not Il-8 and TNF
SYNBIOTIC 2000 IN CHRONIC LIVER DISEASE

One month supply of Synbiotic 2000 reduced:

- Mucosal pH

- PPM flora: *E. coli* (*p*<0.001) *Staphylococcus* (*p*<0.01) and *Fusobacterium* (*p*<0.05),

- Endotoxin, ammonia/s, ALT/s, bilirubin/s

& improved:

- albumin/s and prothrombin

- Child classification &

- degree of encephalopathy/psychometric test in half of the patients

A NOVEL THERAPY

Drs. Steven F. Solga and Anna Mae Diehl of Johns Hopkins University commented: “the researchers have made a major contribution to the application to gut flora therapy to humans with liver disease,”

“it is even more exciting that altering the gut flora may improve not only HE but also liver disease.”

Solga S, Diehl AM. Hepatology; 2004;39:1197-1200
Log Viable Count of *Lactobacillus* spp

*Riordan SM et al Microb Ecol Health Dis 2007;19:7-16*

(CFU/g faeces)

Synbiotic 2000 (p=0.001)  Placebo (p=0.21)
Indocyanine Green Retention at 15 mins

Riordan SM et al Microb Ecol Health Dis 2007;19:7-16

(ICGR15) (%)

Synbiotic 2000 (p=0.003) Control (p=0.37)
LIVER FUNCTION CHANGES
Riordan SM et al Microb Ecol Health Dis 2007;19:7-16

Serum Bilirubin (umol/L)
P=0.002

Serum Albumin (g/L)
P=0.003

Pre-Synbiotic Treatment
Post-Synbiotic Treatment
Pre-Synbiotic Treatment
Post-Synbiotic Treatment
Emelie – a child with cystic fibrosis

- **2000** – severe cystic fibrosis, repeat chest infections, diarrhea, loosing weight, supplemented Synbiotic 2000
- **2 months later** – gained 2.5 kg in weight, no diarrhea, no chest infections, no antibiotics
- **2006** – still on Synbiotics, undergone liver transplantation, no complications, won 2 Gold and one Bronze medal at World Championship in Western horse-riding.
Parenteral nutrition increases mortality significantly (63% vs 26%) in patients with burns.
Enteral nutrition induces loss of mucosal protein content, intestinal microbial overgrowth & translocation:

- Vivonex (Nestle) 53%
- Criticare (Mead-Johnson) 67%
- Ensure (Ross Lab) 60%
  \((p < .05)\)
Enteral nutrition with Nutrison (Nutricia) induces significant elevations of pro-inflammatory cytokines:

**TNF-alpha:**
- day 3 \( (P=0.006) \)
- day 7 \( (P<0.001) \)

**IL-1beta:**
- day 7 \( (P<0.001) \)
- day 14 \( (P=0.022) \)
Immunomodulatory nutrition with Stresson (Nutricia) leads elevations in anti-inflammatory cytokines:

**IL-8:**
- day 1 (P=0.011)
- days 3, 7, 10, & 14 (P<0.001)

**IL-10:**
- days 3 & 10 (P<0.001)

**IL-1ra/s:**
- day 7 (P<0.001)

**IL-6:**
- day 10 (P=0.017)
Chemicals incl. pharmaceutical drugs suppress innate immune functions. 

Antibiotics suppress:
- Lymphocyte proliferation
- Macrophage functions:
  chemiluminescence response, chemotactic motility, bactericidal & cytostatic ability
PHARMA & MICROBIOTA – INCOMPATIBLE!

**Antibiotics** destroys about 90% of microbiota functions: bile acid metabolism, eicosanoid and steroid hormone synthesis etc


Chemotherapeutics reduces microbiota 100-fold; decrease anaerobic bacteria up to 10,000-fold & increase in PPMs 100-fold


Proton pump inhibitors during pregnancy increase the risk of offspring getting asthma

*Andersen AB et al. Aliment Pharmacol Ther 2012;35:1190-1198*

**Anti-hypertensives** induce gastrointestinal dysbiosis & reduce mucosa protection espec mucus production

Table 5. ORs of Developing Lip Cancer According to the Amount of Drugs Dispensed, Measured in Years Supply, Regardless of Whether Other Drugs Were Given

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;1-Year Supply</th>
<th>1-Year to &lt;5-Year Supply</th>
<th>≥5-Year Supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>0.98 (0.66-1.45)</td>
<td>2.03 (1.54-2.68)</td>
<td>4.22 (2.82-6.31)</td>
</tr>
<tr>
<td>Hydrochlorothiazide-triamterene</td>
<td>0.91 (0.60-1.39)</td>
<td>1.87 (1.37-2.57)</td>
<td>2.82 (1.74-4.55)</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>1.04 (0.74-1.46)</td>
<td>1.60 (1.25-2.04)</td>
<td>1.42 (0.95-2.13)</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>1.77 (1.20-2.59)</td>
<td>2.26 (1.58-3.23)</td>
<td>2.50 (1.29-4.84)</td>
</tr>
<tr>
<td>Atenolol</td>
<td>0.88 (0.62-1.26)</td>
<td>0.88 (0.63-1.21)</td>
<td>1.93 (1.29-2.91)</td>
</tr>
<tr>
<td>Atenolol only</td>
<td>0.68 (0.30-1.55)</td>
<td>0.42 (0.15-1.14)</td>
<td>0.54 (0.07-4.08)</td>
</tr>
</tbody>
</table>
INFLAMMATION INVOLVES ABOUT 1200 GENES & affects a wide range of effector molecules; pro-inflammatory cytokines, chemokines, MMPs and metabolic proteins

- **Biologicals aimed to target single genes**: anti-TNF-α, anti-IL-1β, anti-HER2, IL-12/IL-23, IFN-γ, IL-17A, IL-2 and IL-6, and inhibitor of NF-KB
- **Uni-targetting**
- **Immediate powerful effects**
- **Limited by toxicity**
- **Negative to microbiota**
- **Sometimes short-lasting effects**
- **Substantial adverse effects**
- **Indicated - aggressive diseases**

- **Eco-biologicals**: utilizes the anti-inflammatory effects of microbes and plants; greens, vegetables, fruits & spices to support microbiota
- **Multi-targetting**
- **Slower and weaker effects**
- **GRAS – e.g. no toxicity**
- **Support microbiota**
- **For-ever lasting effects**
- **No adverse effects**
- **Indicated - prevention and early disease**
HEALTH – TEN COMMANDMENTS

Seven NOS & three YES!

1. Restrict intake of insulinotrophic foods (refined carbohydrates)
2. Restrict intake of highly pro-inflammatory fructose
3. Restrict intake of dairy products
4. Restrict intake of foods heated above 100°
5. Restrict exposure to in microb-derived highly inflammatory endotoxin
6. Restrict exposure to chemicals including pharmaceutical drugs
7. Eliminate/Minimize intake of foods rich in proteotoxins such as casein, gluten and zein (corn)
8. Increase the intake of fresh and raw greens, fresh spices and vegetables -
9. Increase intake of ancient anti-oxidant-rich, high fiber, low-calorie containing grains
10. Supplement vitamin D and omega fatty acids in large doses
FRUCTOSE & MEMORY LOSS


Omega-3 oil mg/200 calorie foods

- Flaxseed, oil: 12059
- Flaxseed, seeds: 8543
- Fish, salmon: 7828
- Chia, seeds: 7164
- Fish, menhaden: 6236
- Fish, caviar: 5388
- Fish oil, cod liver: 4375
- Nuts, butternuts: 2850
- Nuts, walnuts, English: 2776
- Basil, fresh: 2747
- Oregano, spices: 2732
- Cloves, spices: 2649
- Grape leaves: 2443
- Marjoram, spices: 2384
- Broccoli, Chinese: 2346
- Spinach, frozen: 2183
- Canola oil: 2067
THE DILEMMA!
The sickest patient, the critically ill & often elderly patient:

- Is in constant mental & physical stress
- Cannot exercise
- Receives the worst "food"
## NUTRITIONAL VALUE - GREENS vs ROOTS

*Boutenko V. Green for Life. North Atlantic Books Calif, USA, 2010*

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Beats</th>
<th>Greens</th>
<th>Beets</th>
<th>Greens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>43.0</td>
<td>22.0</td>
<td>0.35</td>
<td>0.38</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>1.6</td>
<td>2.0</td>
<td>4.9</td>
<td>30.0</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>0.17</td>
<td>0.13</td>
<td>0.03</td>
<td>0.30</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>9.56</td>
<td>4.33</td>
<td>0.04</td>
<td>0.22</td>
</tr>
<tr>
<td>Fiber (g)</td>
<td>2.80</td>
<td>3.70</td>
<td>0.33</td>
<td>0.40</td>
</tr>
<tr>
<td>Sugar (g)</td>
<td>6.76</td>
<td>0.50</td>
<td>0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>Calcium (mg)</td>
<td>16.0</td>
<td>117.0</td>
<td>109.0</td>
<td>15.0</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>0.8</td>
<td>2.6</td>
<td>0.00</td>
<td>0.0</td>
</tr>
<tr>
<td>Magnesium (mg)</td>
<td>23.0</td>
<td>70.0</td>
<td>33.0</td>
<td>6326.0</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>78.0</td>
<td>226.0</td>
<td>0.04</td>
<td>1.50</td>
</tr>
<tr>
<td>Copper (mg)</td>
<td>0.1</td>
<td>0.2</td>
<td>0.20</td>
<td>400.0</td>
</tr>
<tr>
<td>Selenium (mg)</td>
<td>0.7</td>
<td>0.9</td>
<td>0.70</td>
<td>0.9</td>
</tr>
</tbody>
</table>
# Foods For Health 1

**Magnesium-rich foods mg/100 gr**

<table>
<thead>
<tr>
<th>Food</th>
<th>Mg/100 gr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pumpkin &amp; Squash seeds</td>
<td>540</td>
</tr>
<tr>
<td>Cacao 20-22 %</td>
<td>520</td>
</tr>
<tr>
<td>Sesami seeds</td>
<td>350</td>
</tr>
<tr>
<td>Almonds</td>
<td>280</td>
</tr>
<tr>
<td>Soya beans</td>
<td>265</td>
</tr>
<tr>
<td>Cashew nuts</td>
<td>260</td>
</tr>
<tr>
<td>Rosehip, dry</td>
<td>240</td>
</tr>
<tr>
<td>Oat bran</td>
<td>235</td>
</tr>
<tr>
<td>Peanuts</td>
<td>190</td>
</tr>
<tr>
<td>Peas</td>
<td>150</td>
</tr>
<tr>
<td>Lentils</td>
<td>80</td>
</tr>
<tr>
<td>Spinach</td>
<td>79</td>
</tr>
<tr>
<td>Prunes</td>
<td>52</td>
</tr>
<tr>
<td>Avocado</td>
<td>41</td>
</tr>
<tr>
<td>Banana</td>
<td>35</td>
</tr>
<tr>
<td>CHEESE</td>
<td>35</td>
</tr>
<tr>
<td>Broccoli</td>
<td>23</td>
</tr>
<tr>
<td>FRENCH FRIES</td>
<td>35</td>
</tr>
<tr>
<td>BREAD, whole</td>
<td>24</td>
</tr>
<tr>
<td>HAMBURGERS</td>
<td>20</td>
</tr>
<tr>
<td>KETCHUP</td>
<td>18</td>
</tr>
<tr>
<td>MILK</td>
<td>15</td>
</tr>
<tr>
<td>CREAM</td>
<td>14</td>
</tr>
<tr>
<td>BUTTER</td>
<td>3</td>
</tr>
</tbody>
</table>
## Foods for Health 2

### Tryptophan in foods mg/100 g foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Tryptophan (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sesame seeds</td>
<td>470</td>
</tr>
<tr>
<td>Dry yeast</td>
<td>430</td>
</tr>
<tr>
<td>Pumpkin seeds</td>
<td>430</td>
</tr>
<tr>
<td>Cheese, 10%</td>
<td>400</td>
</tr>
<tr>
<td>Wheat germs</td>
<td>330</td>
</tr>
<tr>
<td>Peanuts</td>
<td>310</td>
</tr>
<tr>
<td>Tuna fish</td>
<td>270</td>
</tr>
<tr>
<td>Turkey</td>
<td>250</td>
</tr>
<tr>
<td>Feta cheese</td>
<td>240</td>
</tr>
<tr>
<td>Chicken</td>
<td>240</td>
</tr>
<tr>
<td>Beef</td>
<td>220</td>
</tr>
<tr>
<td>Hazelnuts</td>
<td>220</td>
</tr>
<tr>
<td>Salmon</td>
<td>210</td>
</tr>
<tr>
<td>Walnuts</td>
<td>190</td>
</tr>
<tr>
<td>Soya bean sprouts</td>
<td>180</td>
</tr>
<tr>
<td>HAMBURGERS</td>
<td>165</td>
</tr>
<tr>
<td>Alfa sprouts</td>
<td>135</td>
</tr>
<tr>
<td>Soya, cooked</td>
<td>135</td>
</tr>
<tr>
<td>Beans, cooked</td>
<td>108</td>
</tr>
<tr>
<td>Tofu</td>
<td>94</td>
</tr>
<tr>
<td>Yellow Peas, cooked</td>
<td>87</td>
</tr>
<tr>
<td>FRENCH FRIES</td>
<td>53</td>
</tr>
<tr>
<td>KETCHUP</td>
<td>35</td>
</tr>
</tbody>
</table>
FOODS FOR HEALTH 3

Lutein-rich foods mg/portion

- Kale, raw 26.3
- Kale, cooked 23.7
- Spinach, cooked 20.4
- Collards, cooked 14.6
- Turnip Greens, cooked 12.2
- Green peas, cooked 4.1
- Spinach, raw 3.7
- Broccoli, raw 1.3
- Romaine lettuce, raw 1.1
- Egg 0.2
- Orange, raw 0.2
FOODS FOR HEALTH 4

Vitamin K-rich foods mcg/portion

- Brussels sprouts, 1/2 cup 460
- Broccoli, 1/2 cup 248
- Cauliflower, 1/2 cup 150
- Swiss Chards * 1/2 cup 123
- Spinach, raw, 1 cup 120
- BEEF, 3.5 oz 104
- PORK, 3.5 oz 88
- EGGS, whole, large 25
- Strawberries, 1 cup 23
- Oats, 1oz, dry 18
- MILK, 8 oz, whole 10
  * mangold
**FOODS FOR HEALTH 5**

*Glutatione in foods Nmol/g foods*

<table>
<thead>
<tr>
<th>Food</th>
<th>Glutatione (Nmol/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broccoli (flower)</td>
<td>440</td>
</tr>
<tr>
<td>Parsley (leaf)</td>
<td>400</td>
</tr>
<tr>
<td>Spinach</td>
<td>400</td>
</tr>
<tr>
<td>Yellow squash (fresh)</td>
<td>320</td>
</tr>
<tr>
<td>Yellow squash (frozen)</td>
<td>70</td>
</tr>
<tr>
<td>Potato (raw)</td>
<td>230</td>
</tr>
<tr>
<td>Potato (boiled 15 min)</td>
<td>110</td>
</tr>
<tr>
<td>Tomato</td>
<td>170</td>
</tr>
<tr>
<td>Green pepper</td>
<td>170</td>
</tr>
<tr>
<td>Tangerine</td>
<td>140</td>
</tr>
<tr>
<td>Broccoli (stem)</td>
<td>140</td>
</tr>
<tr>
<td>Cauliflower</td>
<td>130</td>
</tr>
<tr>
<td>Food</td>
<td>Chlorophyll (microgram/cup)</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Parsley</td>
<td>380</td>
</tr>
<tr>
<td>Spinach</td>
<td>240</td>
</tr>
<tr>
<td>Cress, garden</td>
<td>160</td>
</tr>
<tr>
<td>Green beans</td>
<td>80</td>
</tr>
<tr>
<td>Arugula</td>
<td>80</td>
</tr>
<tr>
<td>Leeks</td>
<td>80</td>
</tr>
<tr>
<td>Endive</td>
<td>50</td>
</tr>
<tr>
<td>Sugar peas</td>
<td>50</td>
</tr>
<tr>
<td>Chinese cabbage</td>
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</tr>
<tr>
<td>Vegetable</td>
<td>Nitrate (mg/kg)</td>
</tr>
<tr>
<td>--------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Fennel</td>
<td>3200</td>
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<tr>
<td>Lettuce</td>
<td>2900</td>
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<td>Celery</td>
<td>2700</td>
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<td>Mangold</td>
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<tr>
<td>Dill</td>
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<tr>
<td>Spinach</td>
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<tr>
<td>Nettle</td>
<td>1600</td>
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<tr>
<td>Radish</td>
<td>1300</td>
</tr>
<tr>
<td>Chinese cabbage</td>
<td>1300</td>
</tr>
<tr>
<td>Savoy cabbage</td>
<td>1100</td>
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</table>
FUTURE NUTRITION OF CRITICALLY ILL?
Hospital-made nutrition solutions?
Fresh fruit and vegetable juices?
Green Smoothies? Gaspacho?
The danger of wallowing in the past