Chronic Disease Clinical and Nutrition Interventions

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Managing Disease-Related Lean Body Mass Loss through Clinical and Nutrition Interventions
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Chronic Disease Definition

• Chronic diseases are long-term diseases that are not contagious and largely preventable.
• They include diseases such as obesity, diabetes, cardiovascular diseases, cancer, dementia, autoimmune diseases, and present a growing burden for society.
• Account for 60% of deaths world-wide.
• In 2000, 125 M Americans had an identifiable chronic disease with projected prevalence of 171M in 2030.

Chronic Disease Impact

- Every 7 out of 10 natural deaths in the U.S. are caused by one or more chronic diseases,
- Out of the total spending on public and private health care in the U.S. approximately $2 trillion in 2005, more than 75% went toward treatment of chronic disease.
- According to the U.S. Center for Disease Control and Prevention (CDC), out of the major chronic diseases, almost 80% of heart disease and stroke; 80% of type 2 diabetes; and, 40% of cancer can be prevented by controlling the three major risk factors – poor diet, inactivity, and smoking.
Reported Cases in The United States, 2003
(and as % of population*)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cases</th>
<th>% of Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancers</td>
<td>10,555,000</td>
<td>(3.7%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>13,729,000</td>
<td>(4.9%)</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>19,145,000</td>
<td>(6.8%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>36,761,000</td>
<td>(13.0%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>2,425,000</td>
<td>(0.9%)</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>30,338,000</td>
<td>(10.7%)</td>
</tr>
<tr>
<td>Pulmonary Conditions</td>
<td>49,206,000</td>
<td>(17.4%)</td>
</tr>
</tbody>
</table>

* As % of non-institutionalized population. Number of treated cases based on patient self-reported data from 2003 MEPS. Excludes untreated and undiagnosed cases.

Milken Institute State Chronic Disease Index

States in the top quartile have the lowest rates of seven common chronic diseases.
Chronic illnesses
Most Americans believe heart disease is the leading chronic health condition today. The reality, in millions of sufferers:

- Irritable bowel syndrome: 40
- Depression: 19
- Asthma: 17
- Diabetes: 17
- Heart disease: 12.5

Source: TeleNation for Novartis Pharmaceuticals Corporation
The Whole Person: The Web of Chronic Disease

RISK FACTORS
- Tobacco use
- Alcohol use
- High cholesterol
- High blood pressure
- Diet
- Physical inactivity
- Obesity

CHRONIC DISEASES
- Cardiovascular Disease
- Cancer
- Chronic Lung Disease
- Diabetes

Among Alaska Adults with Cardiovascular Disease:
- 23% smoke
- 35% are inactive
- 42% are obese
- 25% have diabetes

Among Alaska Adults with Cancer:
- 20% smoke
- 30% are inactive
- 29% are obese
- 16% have a history of cardiovascular disease

Among Alaska Adults with Diabetes:
- 19% smoke
- 30% are inactive
- 59% are obese
- 19% have a history of cardiovascular disease

Chronic Disease
Malnutrition

• Obesity is a form of malnutrition that is spreading world-wide whereby the prevalence of obesity=undernutrition (33%).

• Approach to nutrition intervention to prevent and treat chronic disease needs to encompasses the whole spectrum of malnutrition.

• Western diets high in refined grains, sugars and meats are associated with proclivity towards chronic diseases.

• Distorted gut microbiome with reduced ecological biodiversity, pathogens and disruption in gut integrity common thread to many chronic inflammatory diseases.

*http://www.who.int/nutrition/topics/2_background/en/#diet2.1
Framework for Preventing Chronic Disease and Promoting Health

Life Span and Settings
- Worksites
- Schools
- Communities
- Health Systems
- Infants
- Children and Adolescents
- Adults and Older Adults

Priority Conditions
- Heart Disease
- Stroke
- Cancer
- Diabetes
- Obesity
- Arthritis
- Oral Health

Underlying Risk Factors
- Tobacco
- Nutrition
- Physical Activity
- Alcohol
- Genomics
THE SECRET KILLER

The surprising link between INFLAMMATION and
HEART ATTACKS, CANCER, ALZHEIMER'S and other diseases

What you can do to fight it
Chronic Inflammation

Cardiovascular Disease
- Atherosclerosis
- Heart Failure
- Stroke
- Hypertension

Autoimmune Disorders
- IBD
- Crohn's Disease
- Colitis
- Lupus
- Multiple Sclerosis
- Type I Diabetes

Metabolic Disorders
- Type II Diabetes
- Fatty Liver Disease
- Renal Failure

Bone & Joint Disease
- Osteoarthritis
- Rheumatoid Arthritis
- Osteopenia
- Osteoporosis

All Cancer Stages
- Initiation
- Progression
- Metastasis

Neurological Diseases
- Depression
- Alzheimer's
- Parkinson's
- Multiple Sclerosis

Diabetic Complications
- Neuropathy
- Retinopathy
- Hypertension
- Atherosclerosis
- Heart Disease

Pulmonary Disease
- Asthma
- COPD
- Hay Fever
- Bronchitis
Role of Oxidative Stress in Chronic Disease

Exogenous sources: IR, UV, X, Y rays, a particles, air pollutants, Chemical drugs, ionizing radiation

Endogenous sources: O₂ metabolism, immune response, Inflammation, activated neutrophils, Respiratory burst of macrophages

Sources: Nutrient derived, Antioxidant enzymes, Metal binding proteins, Phytomutrients

Kidneys, Eyes, Reproduction system, Nervous system, Respiratory system

Shielding effects by AOs

ROS and RNS

Oxidative stress

Oxidation of protein amino acids

Altered oxidative metabolism

DNA strand break and mutations

Cancer

Atherogenesis

Autoimmune diseases

Diabetes and neurodegenerative diseases

Glycation of proteins

Oxidation of PUFA in cell membrane
Inflammatory Bowel Disease

• Chronic inflammation, tissue injury
• Gut repair is multimodal
• Increased oxidative stress both in the gut and systemically
• Uncontrolled inflammation leads to fibrosis in Crohn’s disease and higher risk of cancer in inflammatory bowel disease (IBD)
Pathogenesis of IBD

Initiating Events → Mucosal Damage → Abnormal Immune Response → Chronic Inflammation

- NSAIDs
- Antibiotics
- Infections
  - Viral
  - Bacterial
  - Parasitic
- Translocation of luminal contents
- Th1/Th17 vs. Th2
- Luminal antigens
- Food antigens
- Bacteria
- Bacterial products
  - FMLP
  - LPS
  - PGP5
Complex Interactions of the Pathogenesis of IBD
Environmental Triggers and IBD

Environmental Triggers

- Infections
- NSAIDs
- Antibiotics
- Diet
- Stress
- Smoking
Diet Research: Associations

Fats, Meats Refined Grains and Sugars
• High dietary intakes associated with an increased risk of IBD

Fiber and Fruits
• High dietary intakes were associated with decreased risk of CD

Vegetables
• High dietary intake was associated with decreased risk of UC

→Limitations with review (different studies, majority were retrospective)

Altered Microbiota in IBD
Skewing the Microbiome, Diet and IBD

Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in II10−/− mice

Suzanne Devkota¹, Yunwei Wang¹, Mark W. Musch¹, Vanessa Leone¹, Hannah Fehlner-Peach¹, Anuradha Nadimpalli¹, Dionysios A. Antonopoulos², Bana Jabri³ & Eugene B. Chang¹

The composite human microbiome of Western populations has probably changed over the past century, brought on by new environmental triggers that often have a negative impact on human health¹. Here we show that chylomicron-derived fat, but not nascent (that is, newly synthesized) fat, can perturb immune homeostasis. The data provide a plausible mechanistic basis by which Western-type diets high in certain saturated fats might increase the prevalence of complex immune-mediated diseases like inflammatory bowel disease in genetically susceptible hosts.

The data provide a plausible mechanistic basis by which Western-type diets high in certain saturated fats might increase the prevalence of complex immune-mediated diseases like inflammatory bowel disease in genetically susceptible hosts.

Milk Fat Induces Colitis in Genetically Susceptible Host via Dysbiosis

Milk Fat Induces Dysbiosis, and IBD in Susceptible Hosts
Reciprocal interaction of diet and microbiome in inflammatory bowel diseases.
Summary: Effectiveness of Nutritional Support for Crohn’s Disease

Enteral > Placebo
Enteral < GCS
Polymeric = Elemental

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment n/N</th>
<th>Control n/N</th>
<th>RR (random) 95% CI</th>
<th>RR (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barrall</td>
<td>15/19</td>
<td>12/18</td>
<td>1.18 [0.79, 1.77]</td>
<td></td>
</tr>
<tr>
<td>Seidrinen 1981</td>
<td>6/10</td>
<td>5/9</td>
<td>1.40 [0.98, 1.99]</td>
<td></td>
</tr>
<tr>
<td>Torin</td>
<td>9/10</td>
<td>5/10</td>
<td>1.80 [0.74, 4.36]</td>
<td></td>
</tr>
<tr>
<td>Seidrinen 1993</td>
<td>26/34</td>
<td>31/34</td>
<td>0.94 [0.48, 1.84]</td>
<td></td>
</tr>
<tr>
<td>Total (35%) CI</td>
<td>70</td>
<td>71</td>
<td>0.97 [0.60, 1.54]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 55 (Treatment), 57 (Control)
Test for heterogeneity: CH² = 4.90, df = 2 (P = 0.09), P = 88.1%
Test for overall effect: Z = 0.15 (P = 0.09)
## ESPEN Guidelines On Enteral Nutrition For Crohn’s Disease

<table>
<thead>
<tr>
<th>Subject</th>
<th>Recommendations</th>
<th>Grade</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indications</td>
<td>Indications for enteral nutrition are: prevention and treatment of undernutrition, improvement of growth and development in children and adolescents, improvements in quality of life, acute phase therapy, peri-operative nutrition, maintenance of remission in chronic active disease.</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Active disease</td>
<td>In adults use enteral nutrition as sole therapy for the acute phase mainly when treatment with corticosteroids is not feasible. Use combined therapy (enteral nutrition and drugs) in undernourished patients as well as in patients with inflammatory stenosis of the intestine. In children with CD enteral nutrition is considered as the first line therapy.</td>
<td>A</td>
<td>3.4</td>
</tr>
<tr>
<td>Maintenance of remission</td>
<td>In case of persistent intestinal inflammation (e.g. steroid dependent patients) use oral nutritional supplements. In longstanding (&gt;1 year) clinical remission and in the absence of nutritional deficits a benefit of enteral nutrition (oral nutritional supplements or tube feeding) or supplements (vitamins and trace elements) has not been demonstrated.</td>
<td>B</td>
<td>3.6</td>
</tr>
</tbody>
</table>
Remission rates compared between enteral nutrition, enteral nutrition plus drugs, drugs and no treatment groups.

<table>
<thead>
<tr>
<th>Years of cumulative clinical remission</th>
<th>Enteral Nutrition (n=22)</th>
<th>Enteral Nutrition plus Drugs (n=17)</th>
<th>Drugs (n=8)</th>
<th>No Treatment (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>94%</td>
<td>75%</td>
<td>63%</td>
<td>50%</td>
</tr>
<tr>
<td>2</td>
<td>63%</td>
<td>66%</td>
<td>42%</td>
<td>33%</td>
</tr>
<tr>
<td>4</td>
<td>63%</td>
<td>66%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

(Hirakawa *Gastroenterol Jpn*. 1993 Jun;28(3):379-84)
Mechanisms of Enteral Nutrition for the Induction of Remission of Crohn’s Disease

- Fat Composition
- Bowel Rest
- Antigenic Load
- Enteral Nutrition
- Glutamine
- Gut Flora
- Gut Permeability
### Elimination Diet Trials in IBD

<table>
<thead>
<tr>
<th>Author</th>
<th>Subjects</th>
<th>Design-Treatment</th>
<th>Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Riordan et al 1994</td>
<td>N=78 CD active</td>
<td>Placebo controlled, elimination diet (ED) and placebo drug vs. control - normal diet and prednisolone 40 mg/D, 24 months (mo.)</td>
<td>Induction, Maintenance of Remission (MOR), Time in Remission. Tx. 37% vs. Control 25% 24 mo.</td>
</tr>
<tr>
<td>Pearson et al 1993</td>
<td>N=42 CD active</td>
<td>Placebo controlled, elimination diet (ED) vs vivonex, 60 mo.</td>
<td>Induction, MOR No Difference (ND)</td>
</tr>
<tr>
<td>Thomas et al 1993</td>
<td>N=36 CD active</td>
<td>Placebo controlled; ED, elemental diet (ELD), EL&amp;ELD. Control normal diet/meds 24 weeks</td>
<td>ED improved disease activity index vs control. Duration of remission ND</td>
</tr>
<tr>
<td>Jones et al 1987</td>
<td>N=26 CD active</td>
<td>Placebo controlled 26 mo.</td>
<td>MOR, ESR, orsomucoid 40% 24 mo. 28% 36 mo.</td>
</tr>
<tr>
<td>Strange 1990</td>
<td>N=27 CD active</td>
<td>Placebo controlled, ED vs. fiber rich low refined carbs 12 mo.</td>
<td>ND Clinical inflammatory markers</td>
</tr>
<tr>
<td>Giagger 1991</td>
<td>N=27 CD active</td>
<td>Placebo controlled; Tx. (ELD, Polymeric, ED) vs normal diet 36 mo.</td>
<td>MOR, (40% Tx. vs. 18% control 23 months. MOR 40% vs. control 18% 23 mo.</td>
</tr>
<tr>
<td>Workman 1894</td>
<td>N=33 CD active</td>
<td>ED 32 mo.</td>
<td>MOR 78% ED 6-32 months</td>
</tr>
<tr>
<td>Jones 1985</td>
<td>N=20 CD active</td>
<td>Placebo controlled; ED vs control diet 6 mo.</td>
<td>MOR, ESR, orsomucoid improved over control at 3, 6 months (p&lt;0.05)</td>
</tr>
<tr>
<td>Jones 1985</td>
<td>N=77 CD active</td>
<td>ED alone-no meds 51 months</td>
<td>MOR 100% 3 mo., 86% 22 mo., 2% 51 mo., reduced ESR (p&lt;0.02), reduced...</td>
</tr>
</tbody>
</table>
In patients who responded to EEN, the magnitude of the observed changes was greater and the concentration of Bacteroides/Prevotella group also decreased. All these changes reverted to pre-treatment levels when the children returned to their free habitual diet.
UCNS Formula per 8 oz.

- 310 kcal [16.1/49.7/6.5% protein/CHO/lipid]
- Fish oil (1.09 g EPA/0.46 g DHA)
- 3.5 g EPA/DHA per day
- FOS 2.9 g
- Gum arabic 2.2 g
- Calcium (mg)- 432
- Phosphorus (mg)- 300
- Magnesium (mg)- 108
- β-carotene (μg)- 1185
- Vitamin A (IU)- 1320
- Vitamin D (IU)- 192
- Vitamin E (IU)- 72
- Vitamin K (μg)- 32
- Vitamin C (mg)- 156
- Folic acid (μg)- 456
- Zn (mg)- 7
- Se (μg)- 22
An Oral Supplement Enriched With Fish Oil, Soluble Fiber, and Antioxidants for Corticosteroid Sparing in Ulcerative Colitis: A Randomized, Controlled Trial

Figure 1. Plasma phospholipid concentrations of AA, EPA, and DHA in completed patients receiving either placebo (n = 50) or UCNS (n = 36) at baseline and after 3 and 6 months of study. Values are means ± SE. *P < .001 vs. placebo.

Figure 2. Plasma concentrations of α-tocopherol and β-carotene in completed patients receiving either placebo (n = 50) or UCNS (n = 36) at baseline and after 3 and 6 months of study. Values are means ± SE. *P < .001 vs. placebo.
An Oral Supplement Enriched With Fish Oil, Soluble Fiber, and Antioxidants for Corticosteroid Sparing in Ulcerative Colitis: A Randomized, Controlled Trial

Intent-to-Treat Patients

- Placebo = -0.72, p = 0.08
- UCNS = -1.24, p = 0.003

Mean Prednisone Dose (mg/day) Change from Baseline

The Effects of an Oral Supplement Enriched With Fish Oil, Prebiotics, and Antioxidants on Nutrition Status in Crohn’s Disease Patients

- Increased fat-free and fat mass deposition,
- Improved vitamin D status
- Improvement in quality of life and lower disease activity
- Open label; high drop out rate; small sample

Vitamin D and PTH levels

Plasma phospholipid FA levels

Clinical trial: vitamin D3 treatment in Crohn’s disease – a randomized double-blind placebo-controlled study

108 patients with Crohn's disease in remission, of which fourteen were excluded later. Patients were randomized to receive either 1200 IU vitamin D3 (n = 46) or placebo (n = 48) once daily during 12 months. The primary endpoint was clinical relapse.

Alimentary Pharmacology & Therapeutics Volume 32, Issue 3 pages 377-383, 11 MAY 2010
The data provide a plausible mechanistic basis by which Western-type diets high in certain saturated fats might increase the prevalence of complex immune-mediated diseases like inflammatory bowel disease in genetically susceptible hosts.
Diet, Microbiome and IBD

• Animal fat, milk fat, iron, emulsifiers flare IBD in rodent models
• High fat-sugar diet leads to dysbiosis, leaky gut, AIEC, leaky gut in IL-10 KO
• High-fat diet promotes more severe ileitis, dysbiosis, Th17 cells in animal model of CD
• Maltodextrin promotes AIEC adhesion and biofilms
• Iron and red meat promotes IBD in animal models but mitigated by resistant starches
Nutritionals Showing Efficacy in IBD

Solid Evidence
• Elimination Diet
• Oral Nutrition Supplements
• Prebiotics
• Probiotics
• Turmeric
• Boswellia
• Fish Oils
• Butryate enemas

Promising
• UCNS
• CDNS
## Therapeutic Modalities for IBD

<table>
<thead>
<tr>
<th>Modality</th>
<th>Level of Evidence</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omega-3 fatty acids</td>
<td>B</td>
<td>Low</td>
</tr>
<tr>
<td>Curcumin</td>
<td>A</td>
<td>na</td>
</tr>
<tr>
<td>Probiotics</td>
<td>B</td>
<td>low</td>
</tr>
<tr>
<td>Butyrate enemas</td>
<td>B</td>
<td>na</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>A</td>
<td>na</td>
</tr>
<tr>
<td>Infliximab</td>
<td>B</td>
<td>high</td>
</tr>
<tr>
<td>Aminosalicylates</td>
<td>A</td>
<td>moderate</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>A</td>
<td>high</td>
</tr>
</tbody>
</table>
Schematic representation of the causes and manifestations of PEW in children with CKD


Results suggest that people with CKD who received MNT were less likely to start dialysis and had improved nutritional biomarkers than participants who did not receive MNT.
Chronic Disease
Malnutrition/Undernutrition

• 30% of world is suffering from one or more form of malnutrition
• Some 60% of the 10.9 million deaths each year among children aged under five years in the developing world are associated with malnutrition
• Intrauterine growth retardation (IUGR), affects 23.8% or approximately 30 million newborn babies per year, profoundly influencing growth, survival, and physical and mental capacity in childhood.
• Iodine, Iron, Vitamin A deficiency impacts affects > 1B people and may have long-term consequences.
• It also has major public health implications in view of the increased risk of developing diet-related chronic diseases later in life

*http://www.who.int/nutrition/topics/2_background/en/#diet2.1
Overall differences between microbial communities residing in the gut of a malnourished and a healthy child

Ped Rese 2015 Jan;77;0:256-262.
Causes of Malnutrition in IBD

- Diet Intolerance
- Therapeutic Fasting
- Chronic Disease Processes
- Extensive Intestinal Involvement
- Greater GI Losses
- Catabolic Inflammatory Cytokines (TNF-α, IL-1, IL-6)

- Dietary Limitations
- Increased Energy Requirement
- Malabsorption (poor absorption)
- More Catabolism (more breakdown)
- Anorexia (diminished appetite)

Resultant MALNUTRITION in Inflammatory Disease
Conclusions

• Chronic diseases impart a major economic burden, afflict >125 M Americans and are on the rise
• Chronic inflammation mediates a number of pathophysiological consequences
• The gut microbiome has a major controlling influence over immunity, immunoregulation, inflammation, epigenetic regulation and the development of chronic diseases
• Distortions in the gut ecosystem resulting in disruptions in the communities of microbes and biodiversity of the gut contribute towards barrier disruption and disease development and outcome
• Nutrition can modify the development and course of chronic diseases by improving the gut terrain, epidemic regulation and combat inflammation-related chronic diseases