How Nutrition Can Relieve Pain
Part I

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UCSD, School of Medicine (vol.)

Past President,
Academy of Integrative Pain Management

@DrB_Well
<table>
<thead>
<tr>
<th>SAD</th>
<th>GLAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Fruits/Vegetables</td>
<td>Hi Polyphenol / Hi Micronutrient diet</td>
</tr>
<tr>
<td>Lo Fiber / Lo pre/probiotics &gt; lo diversity</td>
<td>Hi fiber Hi pre/probiotics → Hi Diversity</td>
</tr>
<tr>
<td>Hi processed (refined)</td>
<td>Fresh / minimally processed</td>
</tr>
<tr>
<td>Hi additives / preservatives (allergens)</td>
<td>Lo additives / preservatives</td>
</tr>
<tr>
<td>Inflammatory Fats / Glycation products</td>
<td>Healthy Fats / Healthy preparation</td>
</tr>
<tr>
<td><strong>Mindlessly</strong> Super Sized: Hi calorie / Hi glycemic</td>
<td><strong>Mindfully</strong> Sized: Lo GI / GL Diet</td>
</tr>
<tr>
<td>Hi liquid calories</td>
<td>Min to no liquid calories</td>
</tr>
<tr>
<td><strong>Mindlessly:</strong> Prepared and consumed</td>
<td><strong>Mindfully</strong> Prepared and Consumed</td>
</tr>
<tr>
<td><em>Eating on the GO! / Fast food</em></td>
<td></td>
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<tr>
<td>Hi caffeine / Hi ETOH</td>
<td>Little to none</td>
</tr>
<tr>
<td>Deficiency Prone</td>
<td>Individualized nutrients: Vitamin D, Omega-3, Probiotic, Coq10 . . .</td>
</tr>
</tbody>
</table>
Polyphenols
(Anti-oxidant / Anti-inflammatory)

Apples: Provide polyphenols
Blackberries: High levels of anthocyanins
Black tea: Theaflavins
Blueberries: High levels of anthocyanins
Broccoli: A range of health-giving polyphenols
Cereal bran: High in fibre and phenolic acids
Cherries: Contain antioxidant anthocyanins
Cherry tomatoes: High levels of quercatin
Coffee: Phenolic acids
Cranberries: Procyanadnin, which can prevent infections
Dark chocolate: Cocoa contains epicatechin
Green tea: Polyphenols
Oranges: Contain hesperedin, which aids a healthy heart
Peaches: Contain epicatechin and phenolic acids
Plums: Similar role to peaches
Raspberries: Contain anthocyanins
Red grapes: Anthocyanins and phenolic acids
Red onions: High levels of cancer-fighting quercatin
Spinach: Polyphenols
Strawberries: Contain anthocyanins and ellagic acid

www.EWG.org

Polyphenols

• *diallyl disulphide*, a compound found in garlic and other alliums, represses the expression of matrix-degrading proteases, providing a potential mechanism of action.

*Curr Drug Targets.* 2016 May 27.
Kaempferol, a dietary flavonoid, ameliorates acute inflammatory and nociceptive symptoms in gastritis, pancreatitis, and abdominal pain.

- *Kaempferol (KF) is the most abundant polyphenol in tea, fruits, vegetables, and beans.*


A Low-Glycemic Load Diet Reduces Serum C-Reactive Protein and Modestly Increases Adiponectin in Overweight and Obese Adults¹,²,³,⁴

- low-GL diets influence two critical mechanisms linked to adverse health outcomes: inflammation and synthesis of adipose-derived peptides.
- low-GL diet decreased serum *hs-CRP* concentrations and tended to increase serum *adiponectin* concentrations.

• Low Glycemic load diet increased kynurenate by ~40%
  – compared with the HGL diet

Kynurenic and Quinolonic Acids Bind to NMDA Receptors

- KYNA is NMDA receptor antagonist
- QUIN is NMDA receptor agonist

MINIREVIEW

Quinolinic acid, the inescapable neurotoxin

Gilles J. Guillemin$^{1,2}$

Rapid Resolution of Chronic Back Pain with Magnesium Glycinate in a Pediatric Patient

Christine Lamontagne\textsuperscript{1}, John A Sewell\textsuperscript{2}, Régis Vaillancourt\textsuperscript{2} and Cyrus Kuhzarani\textsuperscript{3,4}

Magnesium supplementation, metabolic and inflammatory markers, and global genomic and proteomic profiling: a randomized, double-blind, controlled, crossover trial in overweight individuals\textsuperscript{1–3}
Foods can have deleterious effects for patients with IBD. …

certain nutrients can reduce intestinal inflammation
Dietary intervention impact on gut microbial gene richness

- **low glycemic index carbohydrates & soluble fiber (increased consumption of fruits and vegetable)** … associated with high bacterial richness.

A Diet Low in FODMAPs Reduces Symptoms of Irritable Bowel Syndrome

- Shift in microbiota occurs within 1 day …
A low fermentable oligo-di-mono saccharides and polyols (FODMAP) diet reduced pain and improved daily life in fibromyalgia patients

- 4 mo. on FODMAP
- 70% had IBS symptoms
- Significant ($p < 0.01$) declines in scores in VAS, FSQ, and RFIQ scores, in all domains measured.
- 50% reduction in IBS symptoms
## Non-celiac Gluten Sensitivity and Rheumatic Diseases

### Symptoms of Non-celiac Gluten Sensitivity.

<table>
<thead>
<tr>
<th><strong>Intestinal</strong></th>
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<tbody>
<tr>
<td>Abdominal pain</td>
<td>68%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>33%</td>
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<tr>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td></td>
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<tr>
<td>Bloating, flatulence</td>
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<table>
<thead>
<tr>
<th><strong>Cutaneous</strong></th>
<th>40%</th>
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<tbody>
<tr>
<td>Erythema</td>
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<tr>
<td>Eczema</td>
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<table>
<thead>
<tr>
<th><strong>General</strong></th>
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<tbody>
<tr>
<td>Headache</td>
<td>35%</td>
</tr>
<tr>
<td>Bone and joint pain</td>
<td>11%</td>
</tr>
<tr>
<td>Muscle contractures</td>
<td>34%</td>
</tr>
<tr>
<td>Numbness of hands and feet</td>
<td>20%</td>
</tr>
<tr>
<td>Chronic tiredness</td>
<td>33%</td>
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<table>
<thead>
<tr>
<th><strong>Behavioral</strong></th>
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<tbody>
<tr>
<td>Attention deficit</td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>22%</td>
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<tr>
<td>Hyperactivity</td>
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</table>
Effect of one year of a gluten-free diet on the clinical evolution of irritable bowel syndrome plus fibromyalgia in patients with associated lymphocytic enteritis: a case-control study

- FMS occurs in 20-32% of those IBS
- IBS 32-70% of those with FMS
- LE 16% of those IBS, and 56% IBS+FMS
- GFD: + Marsh stage 1 group: 26 to 29% ↓ in the TPs, FIQ, HAQ and VAS scales
- 27% in the SF-36 scores
- Marsh stage 0 group: the GFD ~ 3% improvement
The Effects of a Gluten-free Diet Versus a Hypocaloric Diet Among Patients With Fibromyalgia Experiencing Gluten Sensitivity–like Symptoms

• 24 wks of GF or 1500 cal/day diet
• Both diets associated with similar beneficial outcomes in reducing gluten sensitivity symptoms and FMS
• Sig drop in FIQ:
  – 54% of GFD group; 37.5% HCD group.
• However, despite its specificity, GFD was not superior to HCD in reducing the number of gluten sensitivity symptoms or secondary outcomes.
The gut microbiota as a key regulator of visceral pain

O'Mahony, Siobhain M.; Dinan, Timothy G.; Cryan, John F.


Probiotics in Functional Pain

- Children 4-18 with Functional abdominal pain
- L reuteri DSM 17938 10B CFU daily vs placebo
- Significantly less abdominal pain with probiotics 2\textsuperscript{nd}-4\textsuperscript{th} Month (P<0.01)


Anti-inflammatory effects of bifidobacteria by inhibition of LPS-induced NF-κB activation

Christian U Riedel, Franziska Mauch, Christiane Riedel, Christiane Knechtges, Stephanie Blum

Pathogen binding

Probiotics

Anti-bacterial substance

Pathogens

↑ Barrier integrity

↑ Survival

↑ Hsp, Mucins, Defensins

↓ Pathogen binding

↑ IL-8

TNF

IL-1β

△ Innate immunity

↑ TNF, γ-IFN, IL-2, IL-3, IL-4, IL-5, IL-6, IL-12.

↑ IL-10

T<sub>r</sub>1/T<sub>H</sub>3

↑ TNF, γ-IFN, IL-2, IL-3, IL-4, IL-5, IL-6, IL-12.

T<sub>H</sub>1/T<sub>H</sub>2

Mφ

Inflamm Bowel Dis ● Volume 14, Number 11, November 2008
Probiotic supplementation improves inflammatory status in patients with rheumatoid arthritis

- RDBPCT N=46 subjects with RA
- 10(8) CFU of L. casei x 8 wk. vs placebo
- Well tolerated; Sig decreased DAS, TNF-\(\alpha\), IL-6, & IL-12 vs placebo
- **Further studies are warranted to confirm these results, and such confirmation may lead to the introduction of probiotics as adjunctive therapy for this population.**

Effect of Probiotic Administration on Acute Inflammatory Pain

• reducing edema (P = 0.0009), hyperalgesia (P = 0.0002), serum levels of TNF-α (P = 0.0004) and IL-1β (P = 0.0004) and NF-κB expression (P = 0.0007) during the acute phase of inflammatory pain caused by CFA.

RESEARCH ARTICLE

The effect of probiotic Lactobacillus casei Shirota on knee osteoarthritis: a randomised double-blind, placebo-controlled clinical trial
Myth: Amount of weight loss for pain relief is not feasible

- **11%** weight loss = **50%** decrease in pain across 8 weeks in patients with mean BMI of 36.

- 18 MO. ADAPT trial, weight loss + plus moderate exercise provided more improvement obese adults with knee OA
  - A **5%** weight loss = **24%** improvement in function and a **30%** reduction in pain.


The IDEA Trial 18 Month randomized trial of 450 osteoarthritis subjects to: Diet Exercise or Combination
Dietary Influence on Pain via the Immune System

- Omega-3 PUFA
- Curcumin
- Omega-3 PUFA
- Omega-6 PUFA
- Arachidonic acid
- PGE$_2$
- COX-2
- Broccoli lycopene
- TRPV1
- TNFR
- TRPA1
- EGFR
- TLRs
- P2Xs
- EGCG
- Saturated fats
- EGCG, ginger, broccoli, turmeric
- Grape seed extract, bilberries, soy proteins, broccoli, lycopene, curcumin, ginseng
- NFκB
- Pro-IL-1β
- IL-1β

Inhibitors of Microglial Neurotoxicity: Focus on Natural Products

ANTI-INFLAMMATORY FOODS/FOOD COMPOUNDS*

- GARLIC
- FIBER
- CAROTENOIDs
- OMEGA-3 FATTY ACIDS
- TURMERIC
- FLAVONOIDs
- TEA
- GINGER
- MAGNESIUM

LIMIT

- Inflammatory foods
  - × Saturated fat
  - × Trans fat
  - × Cholesterol

How the Mediterranean diet and some of its components modulate inflammatory pathways in arthritis

- Many of the anti-inflammatory effects of the MDP are linked to the intake of foods that are rich in PUFAs with a lower n-6 to n-3 fatty acid ratio and extra-virgin olive oil which, with its high content of MUFAs and non-fat micro-components such as phenolic compounds, has been found to have important anti-inflammatory effects ...
Inflammation

- Microbiome
- Obesity
- Immune
- Anti-Oxidant / Mitochondrial
- Genetic
- Deficiency