PLANT-BASED NUTRITION STRATEGIES for AUTOIMMUNE DISEASE

Michael Klaper, M.D.
www.DoctorKlaper.com

A common belief among rheumatologists about inflammatory joint disease:

“Diet doesn’t matter.”

“What the patient eats has no effect upon the course of the disease…”

“There have never been any studies that shows that diet makes any difference…”

WHAT FOSTERS THESE BELIEFS?

“Whole proteins don’t make it out of the stomach.”

“THEY ARE ALL DESTROYED BY STOMACH ACID AND PEPSIN.”

“Whole proteins can’t be absorbed into the bloodstream.”

“THEY ARE TOO LARGE TO CROSS THE INTESTINAL MEMBRANE AND ALL BROKEN DOWN INTO INDIVIDUAL AMINO ACIDS.”

COW’S MILK ALLERGIES
Cow’s milk allergy


Serum immunoglobulin E, IgA, and IgG antibodies to different cow’s milk proteins in children with cow’s milk allergy: association with prognosis and clinical manifestations.

Hidvegi E, Cserhati E, Kereki E, Savilahti E, Arato A.

Abstract: Diverse pathogenic mechanisms elicit different clinical manifestations in cow’s milk allergy (CMA). Our aim was to determine the concentration of serum immunoglobulin levels to different cow’s milk proteins in patients with CMA and to determine how these values were related to clinical symptoms and prognosis. Fifty children (mean age 10.9 months, range: 1-34 months) with previously confirmed CMA were enrolled in this study. All had clinical symptoms in response to cow’s milk. Cow’s milk-specific immunoglobulin G (IgG) antibodies were determined by enzyme-linked immunosorbent assay (ELISA) and total IgE, IgA, and IgG serum levels were measured by radioimmunoassay. Cow’s milk-specific IgG antibody levels were more sensitive indicators of disease activity than total IgE and IgG levels. The IgG antibody level to bovine serum albumin (BSA) was significantly lower in the patients than in the controls (median: 0.36 vs. 2.94, p < 0.01). There was a close correlation among all individual IgA and IgG antibodies to different cow’s milk proteins. The anti-alpha-casein IgG level (of 2.10) in children with a positive reaction at the re-challenge was significantly higher than in those with a negative reaction (0.89) (p < 0.05). The total IgG serum concentration was also significantly higher in those who had symptoms at the re-challenge compared to those who did not have any reaction at this time (22.9 vs. 6.8 kU/l, geometric mean, p < 0.02). There was no association between the clinical manifestations and the anti-alpha-casein antibody levels in the control group. However, there is considerable overlap among the values observed in different groups of patients, there is a limitation of these tests for predicting the prognosis.

CASEIN
199 amino acids


Antibodies against dietary antigens in rheumatoid arthritis patients treated with fasting and a one-year vegetarian diet.

Kjeldsen-Kragh J, Hvatum M, Haugen M, Førre O, Scott H.

METHODS:
Serum IgG, IgA and IgM antibody activity against several food antigens was measured by an enzyme immunoassay. Abnormally high antibody activity was defined as values above the 90th percentile of the measurements in 30 healthy controls. Serum IgE antibody activity was measured by a radioallergosorbent test.

RESULTS:
During the trial 10 of 27 patients suspected that certain food items aggravated their arthritis symptoms. Elevated antibody activity against one or more of the dietary antigens was found in all RA patients, but these measurements could not be used to predict which food would aggravate the symptoms. Elevated IgG and IgA antibody activity against alpha-lactalbumin was found in a significantly larger number of RA patients than in controls. With the exception of one patient, there was no concordance between the clinical course and antibody activity against the various dietary antigens.

HOW DO ANTIBODIES FORM AGAINST SUCH LARGE FOOD ANTIGENS?

Alpha-lactalbumin
– 123 amino acids

HOW IMPERMEABLE A BARRIER?
EVIDENCE OF THE GUT-JOINT CONNECTION HAS BEEN PRESENT FOR DECADES

Known examples of “Gut – Joint connection”

INFLAMMATORY BOWEL DISEASE

Up to 40% of patients with Inflammatory Bowel Disease (IBD) have associated inflammatory arthritis. (1)


REITER’S SYNDROME

“urethritis, conjunctivitis, arthritis”

Includes inflammatory arthritis after episode of infectious bowel inflammation.

The “Gut-Joint Connection - Reactive Arthritis after acute GE

In 1984 in Ontario, Canada, an outbreak of Salmonella typhimurium food poisoning occurred among police officers who were serving as security guards during a papal visit.

Of the 1,608 police officers involved, 432 had acute gastroenteritis.

Within three months following the outbreak, 27 of these officers had developed acute arthritis;


HOW IMPERMEABLE A BARRIER?
Bacterial balance is important!

Microbial Factors in IBD

**Beneficial**
- Bacteroidetes sp.
- Bifidobacterium Longum
- B. breve and Clostridia perfringens
- B. Thetaiotaomicron
- Clostridium cocoides
- Lactobacillus sp.
- B. brevete
- Clostridia
dificile
- E. Coli
- B. Thetaiotaomicron
- E. coli
- Lactobacillus sp.
- B. Thetaiotaomicron
- E. coli
- Lactobacillus sp.
- B. Thetaiotaomicron
- E. coli
- Lactobacillus sp.

**Detrimental**
- Pseudomonas sp.
- Clostridia difficile
- Clostridia perfringens
- E. coli
- Mycobacterium avium
- paratuberculosis
- Enterococcus sp.

We used to refresh our “intestinal garden” through our connection with the natural world:

- Eating fresh from the garden
- Drinking from streams
- Drinking from wells

Modern life is an assault on our friendly intestinal bacteria:

- Chlorinated drinking water
- Soft drinks with phosphoric acid
- Coffee, tea, etc.
- Foods with herbicides, etc.
- Alcohol
- Antibiotics – in animal foods and Rx’s
  + then add sugar

The problem is NOT with ½ tsp of sugar in one’s tea as a FLAVORING.

The problem is EATING SUGAR AS A FOOD!
**DYSBIOSIS**

“dys” = “bad”  
“biosis” = “life”

Disease-causing bacteria & yeasts

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**High-fat, high sugar diets increase**  
*Clostridium innocuum, Catenibacterium mitsuokai* and *Enterococcus spp.*


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**Protein-rich diets increase**  
the activity of bacterial enzymes such as *β-glucuronidase, azoreductase* and *nitroreductase*, which produce toxic metabolites that trigger inflammatory responses.


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*Intestinal Candida yeast overgrowth*
High n-6 PUFA from safflower oil decreases beneficial Bacteroidetes spp.


The type III toxins of Pseudomonas aeruginosa disrupt epithelial barrier function.

Strong B, Parker D, Magargee M, Prince AL.

Department of Pediatrics and Pharmacology, College of Physicians & Surgeons, Columbia University, 630 West 168th Street, New York, NY 10032, USA.

Abstract: The type III secreted toxins of Pseudomonas aeruginosa are important virulence factors associated with clinically important infection; however, their effects on bacterial invasion across mucosal surfaces have not been well characterized. One of the most commonly expressed toxins, ExoS, has two domains that are predicted to affect cytoskeletal integrity, including a GTPase-activating protein (GAP) domain, which targets Rho, a major regulator of actin polymerization; and an ADP-ribosylating domain that affects the EF-2 protein, which links the plasma membrane to the actin cytoskeleton. The activities of these two domains are thought to modulate the actin cytoskeleton, resulting in perturbation of epithelial barrier function. In this study, we investigated the effects of wild-type and toxin-negative mutants on the epithelial cells, suggesting that additional epithelial targets are involved. Confocal imaging studies demonstrated that ZO-1, occludin, and actin undergo substantial redistribution in human airway cells intoxicated by ExoS, T- and Y. These studies support the hypothesis that type III toxins enhance P. aeruginosa’s invasive capabilities by interacting with multiple eukaryotic cytoskeletal components.

Evidence that Tight Junctions Are Disrupted Due to Intimate Bacterial Contact and Not Inflammation during Attaching and Effacing Pathogen Infection In Vivo

Julien A. Gutierrez, F. Céline, N. Samji, Wayne Vogl, Brett Finlay.

Infect. Immun. 2006 vol. 74 no. 11 6075-6084
**ENDOTOXIN**

*Endotoxins are the lipid portions of lipopolysaccharides (LPSs) that are part of the outer membrane of the cell wall of gram-negative bacteria (lipid A; see Figure 4.12c). The endotoxins are liberated when the bacteria die and the cell wall breaks apart.*

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**ENDOTOXIN IS HEAT-STABLE**

*Interleukin-1 and interleukin-2\* Histamine\* Tumor necrosis factor* Activation of coagulation system\* Prostaglandin, thromboxane, leukotriene, and prostacyclin release\* Oxygen-derived free radicals\* Bradykinin\* Beta-endorphins*

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**FATTY MEAL INCREASES ENDOTOXIN ABSORPTION**

*Erridge C, Attina T, Spickett CM, Webb DJ.*

**A high-fat meal induces low-grade endotoxemia: evidence of a novel mechanism of postprandial inflammation.**

Intestinal permeability test:
positive result!

Dr. Klaper has no financial connection with any laboratory or product.

Intestinal permeability test:
positive result!

FOREIGN PROTEINS
“LEAKING” INTO
BLOOD STREAM

MAY INCITE AUTO-IMMUNE DISEASE
INFLAMMATORY ARTHRITIS ETC.
OTHER AUTOIMMUNE DISEASES
MAY INCITE ALLERGIC RESPONSES
ASTHMA

Arthritic manifestations of inflammatory bowel disease.

Rheumatologic conditions associated with inflammatory bowel disease may be divided into four clinical categories.

First, a unique form of peripheral arthritis occurs in 15-20% of patients with inflammatory bowel disease. The incidence is higher in Crohn's disease than in ulcerative colitis. This is a self-limited, nondeforming, arthropathy that waxed and waned with bowel flares. It characteristically involves knees and ankles. Persistent erosive monoarthritis is described.

Second, spondylitis clinically and radiographically indistinguishable from idiopathic ankylosing spondylitis occurs in 3-6% of patients with inflammatory bowel disease. HLA-B27 positivity occurs in 53-75% of cases, fewer than in idiopathic ankylosing spondylitis.

Third, a bilateral, symmetrical sacroiliitis is seen in 4-18% of patients. This may not progress to clinical spondylitis.

The fourth category encompasses rheumatologic complications of inflammatory bowel disease. These include granulomas of bones and joints, granulomatous vasculitis, clubbing, amyloidosis, osteoporosis, septic arthritis, and complications of corticosteroid therapy.


Intestinal permeability is increased in bronchial asthma.

Hani Z, Molla AM, Al Hayashi IJ, Muharrad WM, Molla AM, Sharma PH.

Abstract: Thirty two asthmatic children, and 32 sex and age matched controls were recruited. The dual sugar (lactulose and mannitol) test was used to evaluate intestinal permeability, and the percentage of ingested lactulose (L) and mannitol (M) in the urine, and the L:M ratio were determined. All patients were skin prick tested for common aeroallergens, and specific IgE to some food items was determined.

RESULTS: The median value of L in asthmatic children (2.29, IQR 0.91-4.07) was significantly higher than that in controls (0.69, IQR 0.45-1.08), and that of M was almost similar. The ratio L:M was significantly higher in asthmatic children (0.20, IQR 0.11-0.40) than in controls (0.06, IQR 0.04-0.09). Intestinal permeability did not correlate with eczema, inhaled steroids, positive skin prick test to aeroallergens, or severity of asthma.

CONCLUSIONS: Intestinal permeability is increased in children with asthma, suggesting that the whole mucosal system may be affected.


Vegan regimen with reduced medication in the treatment of bronchial asthma.

Lindahl O, Lindwall L, Spångberg A, Stenram A, Ockerman PA.
PLANT-BASED DIETS in TREATMENT OF ASTHMA

Thirty-five patients who had suffered from bronchial asthma for an average of 12 yr, all receiving long-term medication, 20 including cortisone, were subject to therapy with vegan food for 1yr. In almost all cases, medication was withdrawn or drastically reduced. There was a significant decrease in asthma symptoms. Twenty-four patients (69%) fulfilled the treatment. Of these, 71% reported improvement at 4 months and 92% at 1 yr. There was a significant improvement in a number of clinical variables; for example, vital capacity, forced expiratory volume at one sec and physical working capacity, as well as a significant change in various biochemical indices as haptoglobin, IgM, IgE, cholesterol, and triglycerides in blood.

FOREIGN PROTEINS “LEAKING” INTO BLOOD STREAM

MAY INCITE AUTO-IMMUNE DISEASE
INFLAMMATORY ARTHRITIS ETC.
OTHER AUTOIMMUNE DISEASES
MAY INCITE ALLERGIC RESPONSES
ASTHMA
URTICARIA

ATOPIC DISEASES

Eczema, asthma, etc.

Identical intestinal permeability changes in children with different clinical manifestations of cow’s milk allergy.

STRATEGIES for INFLAMMATORY JOINT DISEASE

+ OTHER AUTO-IMMUNE CONDITIONS
WHY THE IMPROVEMENT IN RHEUMATIC/AUTOIMMUNE DISEASES with PLANT-BASED DIETS?

Possible Factors: WHAT ISN'T THERE:

Neu5Gc – a highly inflammatory sialic acid found only in animals

Neu5Cg incites antibody formation and inflammation and is implicated in autoimmune and inflammatory diseases

Neu5Gc – sialic acid found only in animals


ARACHIDONIC ACID OMEGA -6

PRO-INFLAMMATORY

Eicosapentaenoic Acid

Arachidonic Acid

Dihomoγ-Linolenic Acid

COX-2

NSAID'S

Eicosapentaenoic Acid

Arachidonic Acid

Dihomoγ-Linolenic Acid

COX-2

PRO-INFLAMMATORY

ANTI-INFLAMMATORY

PGE

PGE

PGE

PGE
(Omega-6) Arachidonic acid is

Found mostly in:
- Chicken
- Eggs
- Beef & Pork

Arachidonic acid is pro-inflammatory.


Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis.


Sixty patients completed the study. In AID patients, but not in WD patients, the numbers of tender and swollen joints decreased by 14% during placebo treatment. In AID patients, as compared to WD patients, fish oil led to a significant reduction in the numbers of tender (28% vs 11%) and swollen (34% vs 22%) joints (P<0.01). Compared to baseline levels, higher enrichment of eicosapentaenoic acid in erythrocyte lipids (244% vs 217%) and lower formation of leukotriene B(4) (34% vs 8%, P<0.01), 11-dehydro-thromboxane B(2) (15% vs 10%, P<0.01) and prostaglandin metabolites (21% vs 16%, P<0.003) were found in AID patients, especially when fish oil was given during months 6-8 of the experiment.

CONCLUSION:
A diet low in arachidonic acid ameliorates clinical signs of inflammation in patients with RA and augments the beneficial effect of fish oil supplementation.

REMOVAL OF ANIMAL TISSUE ANTIGENS AS TRIGGERS

CROSS REACTIVITY WITH CARTILAGE, LIGAMENT, ETC?

ANTIGEN-ANTIBODY COMPLEXES IN JOINTS?


Controlled trial of fasting and one-year vegetarian diet in rheumatoid arthritis.


Department of General Practice, University of Oslo, Norway.

27 patients were allocated to a four-week stay at a health farm. After an initial 7-10 day subtotal fast, they were put on an individually adjusted gluten-free vegan diet for 3.5 months.

After four weeks at the health farm the diet group showed a significant improvement in number of tender joints, Ritchie's articular index, number of swollen joints, pain score, duration of morning stiffness, grip strength, erythrocyte sedimentation rate, C-reactive protein, white blood cell count, and a health assessment questionnaire score. In the control group, only pain score improved significantly. The benefits in the diet group were still present after one year, and evaluation of the whole course showed significant advantages for the diet group in all measured indices.

PUT THE FIRE OUT!

NSAID's
- Methotrexate
- Steroids
- DMARD's
- Biologics

BUT ALSO WATER-ONLY FASTING

See “Fasting” at DoctorKlaper.com

Fasting and vegetarian diets have potent anti-inflammatory effects in RA and other maladies


...we tested the effect of fasting for 7-10 d, then consuming an individually adjusted, gluten-free, vegan diet for 3.5 mo,

For all clinical variables and most laboratory variables measured, the 27 patients in the fasting and vegetarian diet groups improved significantly compared with the 26 patients in the control group who followed their usual omnivorous diet throughout the study period. (and maintained 1 year later.)

Fasting is effective in initial therapy for inflammatory and autoimmune diseases


**Fasting followed by vegetarian diet in patients with rheumatoid arthritis: a systematic review.**

Müller H, de Toledo FW, Resch KL.

PUT THE FIRE OUT!

NSAIDS
Methotrexate
Steroids
DMARD’s
Biologics

have a role, but

success depends upon preventing a flare-up as these drugs are tapered off.

APPLIED CLINICAL NUTRITION and MEDICAL THERAPY for IBD

 товаров: Meat, dairy, wheat, processed foods, oils, fried foods

Food

OLD MODEL of NUTRITION

CARBOHYDRATES = ENERGY
(via KREBS CYCLE => ATP, etc.)

PROTEIN = STRUCTURAL COMPONENTS
and ENZYMES

FATS = ENERGY STORAGE

OLD MODEL of NUTRITION

CARBOHYDRATES = ENERGY
(via KREBS CYCLE => ATP, etc.)

PROTEIN = STRUCTURAL COMPONENTS
and ENZYMES

FATS = ENERGY STORAGE
Our food is chemically “alive,” and as it flows through every cell in our body, it interacts with us and plays our DNA like a piano – turning genes on and off that create and inhibit the protein enzymes in every cell that make us – us.

**EPIGENETICS**
changes in gene expression or cellular phenotype, caused by mechanisms other than changes in the underlying DNA sequence.

**NUTRIGENOMICS**
the study of the effects of foods and food constituents on gene expression.

**HISTONE ACETYLATION**

- **QUERCETIN**
  - Inhibits PKC (protein kinase C) - cell proliferative

- **RESVERATROL**
  - Inhibits TNFα, IL-6, COX-2

- **CURCUMIN**
  - Inhibits Nuclear Factor kB

**EPIGENETICS**
changes in gene expression or cellular phenotype, caused by mechanisms other than changes in the underlying DNA sequence.

**NUTRIGENOMICS**
the study of the effects of foods and food constituents on gene expression.
THE STANDARD AMERICAN DIET
“S.A.D.”

Meat and Dairy-based meal

A WITCH’S BREW OF MEAT-SPECIFIC TOXINS

Endotoxins
Pro-inflammatory Neu5Gc
Oxidized muscle proteins
Bio-concentrated pesticides
Herbicides and heavy metals
Hormones and antibiotics
Food chemicals – flavorings, colorings, etc.

The genes that will be turned on by this fuel mixture and the protein/enzymes they create will be much different than the proteins and enzymes created by this fuel mixture:

Polyphenols, alkaloids, and phenolics: tea polyphenols, genistein, curcumin, resveratrol, sulforaphane, isothiocyanates, silymarin, diallyl sulfide, lycopene, rosmarinic acid, apigenin, and gingerol.

Therapeutic Dietary Program for RA:

“The Paddison Program“

http://www.paddisonprogram.com/”

“The Paddison Program”

dietary recommendations

2-3 days on water or cucumber-celery juice (optional)

then,
Food Reintroduction program
“DYNAMIC TRIO” INTERACTION
“Nutrigenomics”

Food
Genetics
Intestinal biome

Enzyme induction inflammation, membrane permeability, other effects

Plant-based diets shift fecal flora to less pro-inflammatory species


Lignans have anti-microbial effects:

Diets rich in complex carbohydrates show less pathogenic species such as Mycobacterium avium subspecies paratuberculosis and Enterobacteriaceae than diets higher in fat or protein.


Complex carbohydrates also increase levels of beneficial Bifidobacteria spp. such as B. longum subspecies longum, B. breve and B. thetaiotaomicron.

Refined sugars, on the other hand, mediate the overgrowth of opportunistic bacteria like C. difficile and C. perfringens.

Changing the diet changes gut flora


A vegan or vegetarian diet substantially alters the human colonic faecal microbiota.

Zimmer J., Lange B., Frick JS., Sauer H., Zimmermann K., Schwartz A., Rusch K., Klosterhalfen B. Department of Internal Medicine VI, University Hospital, Tübingen, Germany.

Abstract: We examined faecal samples of vegetarians (n=144), vegans (n=105) and an equal number of control subjects consuming ordinary omnivorous diet who were matched for age and gender. We used classical bacteriological isolation, identification and enumeration of the main anaerobic and aerobic bacterial genera and computed absolute and relative numbers that were compared between groups.

RESULTS: Total counts of Bacteroides spp., Bifidobacterium spp., Escherichia coli and Enterobacteriaceae spp. were significantly lower (P<0.001, P<0.002, P<0.006 and P<0.008, respectively) in vegan samples than in controls, whereas others (E. coli Enterobacteriaceae spp., Enterobacter spp., other Enterobacteriaceae, Enterococcus spp., Lactobacillus spp., Clostridium spp. and Costridium spp.) were not. Subjects on a vegetarian diet ranked between vegans and controls. The total microbial count did not differ between the groups. In contrast, counts of beneficial anaerobic bacteria such as Faecalibacterium prausnitzii and total numbers of streptococci were significantly correlated across all subgroups.

CONCLUSIONS: Maintaining a strict vegan or vegetarian diet results in a significant shift in the microbiota while total cell numbers remain unaltered.

Vegetarianism alters intestinal microbiota in humans because high amounts of fiber result in increased short chain fatty acid production by microbes which decrease the intestinal pH. This prevents the growth of potentially pathogenic bacteria such as E. coli and other members of Enterobacteriaceae.

**Abstract**

Colorectal cancer (CRC) is one of the most common cancers and a leading cause of cancer-related mortality in developed countries. Many ingredients of apples have been proven to have anti-inflammatory and anti-carcinogenic characteristics, and show benefits for CRC prevention. The aim of this study, therefore, was to evaluate inhibitory effect of an apple oligogalactan (AOG) on inflammation in Caco-2 cells through regulation of gene expressions of TOLLIP, SOCS1, SOCS3, and IRAK-1. These data may provide another molecular basis for understanding how apples act to prevent CRC and indicate that AOG may be useful for treatment of colitis and prevention of carcinogenesis.

**Colon bacteria digest fiber – liberate short-chain fatty acids**

- Butyric acid
- (methyl) butyrate

**BUTYRATES ARE ABSORBED INTO BLOODSTREAM AND EXERT ANTI-INFLAMMATORY EFFECT**

- Butyric acid
- (methyl) butyrate

Vegetarians diets foster more butyrate-producing colon bacteria

**PROBIOTICS**

**LACTOBACILLUS PLANTARUM**

Lactobacillus plantarum MYL26 induces endotoxin tolerance phenotype in Caco-2 cells.

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<td>Lactobacillus plantarum MYL26 induces endotoxin tolerance phenotype in Caco-2 cells</td>
<td>De Palma G., Nadal I., Collado M.C., Sanz Y.</td>
<td>Effects of a gluten-free diet on gut microbiota and immune function in healthy adult humans. Br. J. Nutr. 2009;102:1154–1160. However, a gluten-free diet may not completely restore the natural balance of the microbiota normally seen in healthy individuals in those patients that have experienced dysbiosis due to gluten sensitivity.</td>
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Lactobacillus plantarum MYL26 induces endotoxin tolerance phenotype in Caco-2 cells.

Chiu YH, Liu YC, Ou CC, Lin SL, Tsai CC, Huang CT, Lin MY
Science and Biotechnology, National Chung Hsing University, Taichung 40227, Taiwan.

Abstract: Crohn's disease and ulcerative colitis are the major types of chronic inflammatory bowel disease occurring in the colon and small intestine. A growing body of research has proposed that probiotics are able to attenuate the inflammatory symptoms of these diseases in vitro and in vivo. However, the mechanism of probiotic actions remains unclear.

RESULTS: Our results suggested Lactobacillus plantarum MYL26 inhibited inflammation in Caco-2 cells through regulation of gene expressions of TOLLIP, SOCS1, SOCS3, and IkBα, rather than SHP-1 and IRAK-3.

CONCLUSIONS: We proposed that live/heat-killed Lactobacillus plantarum MYL26 and bacterial cell wall extract treatments impaired TLR4-NFκb signal transduction through Tollip, SOCS-1 and SOCS-3 activation, thus inducing LPS tolerance. Our findings suggest that either heat-killed probiotics or probiotic cell wall extracts are able to attenuate inflammation through pathways similar to that of live bacteria.

LACTOBACILLUS RHAMNOSUS

J Biol Chem. 2013 Sep 16. [Epub ahead of print]

A Lactobacillus rhamnosus GG-derived soluble protein, p40, stimulates ligand release from intestinal epithelial cells to transactivate EGFR receptor.


Abstract: p40, a Lactobacillus rhamnosus GG (LGG)-derived soluble protein, ameliorates intestinal injury and colitis, reduces apoptosis and preserves barrier function by transactivation of the EGFR receptor (EGFR) in intestinal epithelial cells. The aim of this study is to determine the mechanism by which p40 transactivates EGFR in intestinal epithelial cells. Here we show that p40-conditioned medium activates EGFR in young adult mouse colon (YAMC) epithelial cells and human colonic epithelial cell line. TLR4 stim, p40 up-regulates a damage and metaproteinidase domain-containing protein 17 (ADAM17) catalytic activity and broad spectrum metaproteinidase inhibitors block EGFR transactivation by p40 in these two cell lines. In ADAM17 deficient mouse colonic epithelial (ADAM17-MICe) cells, p40 transactivation of EGFR is blocked, but can be rescued by co-expression with ADAM17. Furthermore, p40 stimulation release of laminin binding (HB)EGF, but not transforming growth factor (TGFα) or amphiregulin, in YAMC cells and ADAM17-MICe cells.

LACTOBACILLUS CASEI


Immunomodulatory effects of lactobacillus casei administration in a mouse model of gliadin-sensitive enteropathy.

D'Arienzo R., Stefanile R., Maurano F., Mazzarella G., Ricca E., Troncone R., Auricchio S., Rossi M.

LACTOBACILLUS CASEI

Lactobacillus casei has been found to be effective in restoring normal mucosal architecture and gut-associated lymphoid tissue homeostasis in a mouse model of gliadin-induced enteropathy.


BIFIDOBACTERIA SPP

Bifidobacteria spp. enhance the maturation of the mucosal slgA system.

Diet-Induced Dysbiosis of the Intestinal Microbiota and the Effects on Immunity and Disease

Kirsty Brown, Daniella DeCoffe, [...], and Deanna L. Gibson
Timing of probiotics

Take probiotics between meals -
- one hour before
- two hours after
- Or at bedtime...

NOT with an antibiotic!

Use probiotics if:
If the patient has taken a course of antibiotics recently, take probiotics during the treatment and for 3-4 weeks afterwards.
If the patient has known “leaky gut” or autoimmune disease until improved.
If the patient drinks chlorinated water, alcohol, sugary drinks – take probiotics once or twice a month?

EATING YOGURT FOR PROBIOTICS?
Most have high fructose corn syrup for sweetness and often cornstarch and gelatin for texture and artificial sweeteners.

All yogurts - “acidophilus,” “probiotic” or not - have DAIRY protein.

Why consume dairy protein and sugar that work against weight loss and diabetes control?

IF ONE WANTS A PROBIOTIC - TAKE A NON-DAIRY PROBIOTIC

LACTOBACILLUS SPECIES CURDLES MILK!

PROBIOTICS ARE THERE ENOUGH ORGANISMS PER DOSE?
At least 5 BILLION CFU (colony forming unit)
**SIMPLE “KITCHEN CHEMISTRY!”**

**TEST IT!**

In ONE of the bowls…

OPEN 3-4 CAPSULES OR 1/2 TSP LIQUID OR POWDER AND STIR IN TO THE MILK WITH A FORK.

(IF TABLETS, CRUSH TO POWDER)

LET BOTH BOWLS SIT OUT AT ROOM TEMPERATURE OVERNIGHT

After 24 – 48 hours:

(in the bowl with the probiotics)

1. Chunks of curdled milk
   or
2. A film of yogurt
   or
3. Bubbles of CO₂
   AND
4. A smell of sour milk

Probiotics should be able to curdle milk.

WHAT ABOUT FISH OIL?

*Rheumatol Int. 2003 Jan;23(1):27-36. Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis.***

Sixty patients completed the study. In AID patients, but not in WD patients, the numbers of tender and swollen joints decreased by 14% during placebo treatment. In AID patients, as compared to WD patients, fish oil led to a significant reduction in the numbers of tender (28% vs 11%) and swollen (34% vs 22%) joints (P<0.01). Compared to baseline levels, higher enrichment of eicosapentaenoic acid in erythrocyte lipids (244% vs 217%) and lower formation of leukotriene B(4) (34% vs 8%, P=0.01), 11-dehydro-thromboxane B(2) (15% vs 10%, P<0.05), and prostaglandin metabolites (21% vs 16%, P<0.003) were found in AID patients, especially when fish oil was given during months 6-8 of the experiment.

**CONCLUSION:**

A diet low in arachidonic acid ameliorates clinical signs of inflammation in patients with RA and augments the beneficial effect of fish oil supplementation.
**LINOLEIC ACID**
(Walnuts, flax, hemp, dark greens, chia, etc.)
CARBON ATOMS = 18

**EPA**
CARBON ATOMS = 20

**DHA**
CARBON ATOMS = 22

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**FISH-OIL MAY CONTAIN:**
HYDROCARBON CONTAMINANTS (PCB’s, PESTICIDES, etc.)
and
PROLONG BLOOD CLOTTING

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**DHA/EPA IS MADE BY ALGAE CELLS IN THE OCEAN**
FISH SWIM IN THE OCEAN WITH THEIR MOUTHS OPEN AND SWALLOW ALGAE.
THE ALGAL DHA/EPA DEPOSITS IN THE FISH’S MUSCLE
THE OMEGA-3 DHA/EPA IN “FISH OIL” IS REALLY DERIVED FROM ALGAE.

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**FISH**
DO NOT MAKE EPA OR DHA.

---

**ALGAE-DERIVED DHA/EPA**
200 MG. – 300 MG. DAILY
DR. KLAPER HAS NO FINANCIAL CONNECTION WITH ANY NUTRITIONAL SUPPLEMENT OR SUPPLIER

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**J T Ashley, J S Ward, C S Anderson, M W Schafer, L Zaoudeh, R J Horwitz, D J Velinsky.**

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(Heavier brominated ethers, and halogenated natural products – not distilled.)

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**2. Arteriosclerosis, Thrombosis, and Vascular Biology.**
2004; 24: 1734-1740
Variable Hypocoagulant Effect of Fish Oil Intake in Humans: Modulation of Fibrinogen Level and Thrombin Generation, Kristof Vanschoonbeek, et.al.
PLANT-BASED THERAPIES IN AUTOIMMUNE DISEASES

MINIMIZE PRO-INFLAMMATORY MOLECULES
- NootKo – salk acid (found only in animals)
- Arachidonic acid → pro-inflammatory prostaglandin-2 series
- Food-based antigens → whole-food plant-based diet (Pattison Program)

OPTIMIZE ANTI-INFLAMMATORY MOLECULES
- High-potassium foods increase endogenous cortisol
- DMA & EPA → long chain omega-3 fatty acids (consider supplements?)
- Curcumin → in foods and supplements

IMPROVE MICROBIAL BALANCE
- MINIMIZE BACTERIES – alcohol, antibiotics, chlorinated water, etc.
- PLANT-BASED DIET → PROBIOTICS? ANTIBIOTICS?

PROMOTE INTESTINAL WALL INTEGRITY
- AVOID NSAID’s (they increase intestinal permeability)
- GLUTAMINE
- AVOID BACTERICIDES
- DHA & EPA

REPAIR GUT INTEGRITY

1. REMOVE ONGOING INJURY
   SUGARS, ALCOHOL, ANTIBIOTICS, NSAIDS, ETC.

2. REMOVE IMMUNOGENIC FOODS:
   MEAT, DAIRY, WHEAT, etc.

3. REPAIR BARRIER FUNCTION
   QUERCETIN 500 - 1000 mg bid (x 6 wks)
   GLUTAMINE 500 - 1000 mg bid (x 6 wks)
   PROBIOTICS (non-dairy)

GLUTAMINE HEALS INTESTINAL MUCOSA

- Turmeric, the King of Spices – Digestive Regulatory Mechanisms in the Prevention of Cancer, Neurological, and Inflammatory Diseases.

QUERCETIN

- Quercetin Enhances Intestinal Barrier Function through the Assembly of Zonula Occludens-2, Occludin, and Claudin-1 and the Expression of Claudin-4 in Caco-2 Cells!
- Quercetin increases ZO-2, occludin, and claudin-1 expression in Caco-2 cells, indicating a potential therapeutic role in the management of inflammatory bowel disease.

TURMERIC

Usual dose: 300 mg – 600 mg 2 – 3 times/day

"Curcumin, the King of Spices" – Digestive Regulatory Mechanisms in the Prevention of Cancer, Neurological, and Inflammatory Diseases.

AUTOIMMUNE PROTOCOL

1. CONSIDER 2-3 DAY WATER OR JUICE FAST (or longer medically-supervised fast)
2. “Paddison Program" food re-introduction
   Whole food, plant-based diet. (Gluten free?)
3. Anti-inflammatory foods and supplements – turmeric, DMA/EPA
4. Restore intestinal microbial balance and gut wall integrity
If flare occurs despite all the above

CONSIDER ANTIBIOTIC TREATMENT
FOR
Proteus mirabilis
AND/OR
Yersinia enterocolitica

Proteus as main cause of RA via cross-reactivity with synovial tissue and bacterial cell wall

A Ebringer, T Rashid. Rheumatoid arthritis is caused by a Proteus urinary tract infection. APMIS. 2014 May;122(5):363-8.

Decrease in anti-Proteus mirabilis but not anti-Escherichia coli antibody levels in rheumatoid arthritis patients treated with fasting and a one year vegetarian diet.

Keldsen-Kragh J1, Rashid T, Dybwad A, Sioud M, Haugen M, Forre O, Ebringer A.

Yersinia is a key pathogen in Reiter’s syndrome (inflammatory arthritis)


Behavior of Yersinia enterocolitica in Foods.
Bari ML1, Hossain MA, Isshiki K, Ukuku D.

“GENETICS LOADS THE GUN… DIET AND LIFESTYLE CHOICES PULL THE TRIGGER.”

ARE WE REALLY TREATING THE CAUSES OF OUR PATIENTS’ PROBLEMS?

Kaiser Permanente Urging Adoption of Plant-Based Diets!

Nutritional Update for Physicians: Plant-Based Diets

Phillip J Tuso, MD; Mohamed H Ismail, MD; Benjamin P Ha, MD; Carole Bartolotto, MA, RD

Perm J 2013 Spring; 17(2):61-66

Research shows that plant-based diets are cost-effective, low-risk interventions that may lower body mass index, blood pressure, HbA1c, and cholesterol levels. They may also reduce the number of medications needed to treat chronic diseases and lower ischemic heart disease mortality rates. Physicians should consider recommending a plant-based diet to all their patients, especially those with high blood pressure, diabetes, cardiovascular disease, or obesity.”
Physician Competencies for Prescribing Lifestyle Medicine

JAMA, July 14, 2012 – Vol304, No. 2 202-203

YOU DON’T HAVE TO DO THIS IS ALL YOURSELF!
THERE IS HELP AVAILABLE!

FIND PLANT-BASED NUTRITION COUNSELORS,
COOKING INSTRUCTORS, LIFESTYLE COACHES,
ETC. IN YOUR COMMUNITY:

PCRM.ORG
DRMCDougall.COM
DRFuhrman.COM
T.Colin Campbell
Center for Nutrition Studies

"ALL TRUTH PASSES THROUGH THREE STAGES:
FIRST, IT IS RIDICULED…
THEN, IT IS VIOLENTLY OPPOSED…
THEN, IT IS ACCEPTED AS SELF-EVIDENT"

- Schoepenhaur

PLANT-BASED NUTRITION STRATEGIES
for AUTOIMMUNE DISEASE

Michael Klaper, M.D.
www.DoctorKlaper.com