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In this issue: Antioxidants & Autophagy; A Positive Perspective on Genetic Testing (video blog); Fiber: Partially-Hydrolized Guar Gum; SNiPpets: GLP-1; Prebiotic Yeast and IBD Mechanisms; Classic FMU: D. Barry Boyd, MD, MS



FMU KNOWLEDGEBASE

THE AUDIO ARCHIVE OF JEFFREY BLAND, PHD

"OUR LIFESTYLE CONTAINS INFORMATION FROM WHICH OUR GENES RECEIVE A MESSAGE THAT CREATES THE PHENOTYPE. CANCER IS NOT INEVITABLE."

> - JEFFREY BLAND, PHD JANUARY 2004

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The Curious Relationship Between Antioxidants and Autophagy



Recent research has clarified that caloric restriction triggers cellular housekeeping functions like DNA repair and organelle rejuvenation. Some of the metabolic aspects of fasting seem quite logical: that, done properly, restricting the intake of fats, carbohydrates, and less-healthy foods can help improve body composition, blood chemistry, overall health, and feelings of vitality. However, restricting food generally also means limiting intakes of necessary nutrients and valuable antioxidants—so how can that be good or helpful?

It turns out that the modest stress posed by discontinuous nutrition constitutes an important cue to the body to make use of stored resources, as well as an opportunity to

make cellular metabolism cleaner and more efficient. In fact, the contribution to this stress posed by reduced antioxidant intake may actually aid the transition into autophagy—the recycling, reorganizing, and remodeling of the cellular environment to optimize the use of its limited resources. The cellular program of autophagy allows cells to repair and/or clean out damaged proteins, membranes, DNA, and organelles, which ultimately greatly reduces oxidative stress in the cell, yet heightened oxidative stress within a given cell is what causes that cell to undergo autophagy (or cell death, alternatively, if damage is too metabolically costly to repair) rather than a less-stressed cell nearby. During a longer period of calorie restriction, the autophagy program can run continuously and dig more deeply into cellular damage, whereas in limited restriction it is switched on and off repeatedly, with less thorough cellular housekeeping results.

An interesting review of the <u>mechanisms underlying autophagy</u> describes laboratory research findings that certain antioxidants, including N-acetylcysteine, ubiquinone, glutathione, and vitamins C and E, can help facilitate certain steps in autophagy in damaged cells. However, cells enjoying habitually higher levels of such antioxidants (from higher dietary intakes) are generally more protected from damage, so antioxidants ultimately reduce the need for autophagy. <u>In this FMU interview</u>, functional neurologist David Perlmutter, MD and Dr. Bland discuss numerous ways of improving cognitive health and function, including caloric restriction to optimize mitochondrial energy production and integrity in the nervous system, which is especially vulnerable to energy deficit and oxidative stress.

Dr. Bland's Latest Video Blog

A Positive Perspective on Genetic Testing

When you think about genetic testing, does your mind veer directly toward concerns about disease? If so, you are not alone. Although genetic testing represents one of the greatest technological advances of the 21st century thus far, people can often feel apprehensive about participating in the testing process and learning about their results. But there is a different way to contextualize this experience, and it involves understanding how genetic testing can lead to empowerment and personalization. Dr. Bland shares his insights in this video blog.



Video Link: https://www.youtube.com/watch?v=dyX1nxYBhcI

Video is one of Dr. Bland's favorite communication tools. Subscribe to his <u>YouTube</u> <u>channel</u> to never miss an update, and also find many additional videos on the Personalized Lifestyle Medicine Institute <u>Vimeo page</u>.

PHGG is a Fiber Worth Getting to Know



Fiber is one of the most commonly deficient nutrients in modern diets, and increasing intakes is one of the more inexpensive means of improving health outcomes. US authorities recommend that adults receive at least 25 grams of dietary fiber per day and prehistoric diets may have supplied several times that amount, yet most US adults ingest less than 15 grams daily. However, fiber can be challenging to incorporate sustainably into eating habits as it generally necessitates behavioral change (eating different foods or supplementing) and can result in discomfort

while digestive tracts adjust to increased amounts of fermentable food. Partially-hydrolyzed guar gum (PHGG) is derived from the beans of the guar plant and presents a realistic means of getting more fiber due to its combination of acceptable sensory qualities, wide range of healthful effects, and tolerability. The US Food and Drug Administration recognizes guar gum as a safe and physiologically beneficial fiber.

PHGG is a purified, low-viscosity soluble fiber, and like other soluble fibers is thought to slow gastric emptying and increase satiety. A recent Japanese study examined 12 total healthy, moderately glucose-intolerant, and pre-diabetic subjects taking 6 grams of PHGG in liquid with each of 3 meals daily for 12 months. Results overall showed significant drops in body weight, body mass index (BMI), and waist circumference, and in levels of postprandial glucose, fasting insulin, triglycerides, measures of inflammation and glucose intolerance, leptin, and LDL cholesterol, as well as significant increases in HDL cholesterol. Statistically significant changes were not seen in all study subgroups, though this may be attributable to the study's small size. Three of six glucose-intolerant subjects showed reversal of glucose intolerance by the end of the trial, and no GI disturbance was reported. In other clinical studies, PHGG improved symptoms of bloating in subjects with irritable bowel syndrome (a fine and rare trait for a dietary fiber!) and reduced gastrointestinal transit times in those with constipation. In preclinical research conducted on human feces, PHGG was found to encourage the growth of beneficial Bacteroidetes phylum members, and it has shown prebiotic effects on species of lactic acid bacteria; both of these effects could positively influence the composition of the microbiome.

SNiPpets

How significant to health are certain single nucleotide polymorphisms, also known as SNPs? SNiPpets is an ongoing exploration of this topic. This column is produced by Jeffrey Bland, PhD and the Personalized Lifestyle Medicine Institute.

This SNP May Increase Your Need for Prebiotic Fiber

In the body, production of the satiety hormone GLP-1 is stimulated by consumption of olive oil, pistachios, and non-digestible fibers like inulin, resistant starch, and oligosaccharides. The DPP4 gene codes for an enzyme that breaks down GLP-1, and the related SNP rs6741949 (substituting common allele G with variant allele C) has recently been shown to negatively impact GLP-1 levels and glucose and insulin metabolism in subjects with increased adiposity. This relationship suggests that individuals with elevated blood sugar levels, insulin resistance, or extra body fat may benefit from increasing intakes of

foods that help elevate GLP-1 levels such as those mentioned.



Prebiotic Yeast Beta-Glucans May Address IBD Mechanisms



In those with Crohn's disease, alterations in intestinal barrier function and the makeup of the gut microbiota are increasingly thought to reinforce one another and drive pathological processes of endotoxemia, intestinal cell death, and immune dysfunction. While increasing intake of dietary fiber can often improve the condition over time, it can be challenging to find fiber sources that are both effective and tolerable for those with it. To this end, sophisticated ex-vivo means of studying inflammatory bowel disease (IBD) are sometimes employed in researching these conditions, and one such recent study found

that a prebiotic beta-glucan derived from baker's yeast <u>improved measures of barrier integrity</u> between cells in intestinal samples removed from Crohn's surgical patients. Confirmation of these results is needed, but this preliminary success lends reasonable hope that beta-glucans might help improve the composition of the microbiome in IBD and/or other conditions manifesting both dysbiosis and impaired gut barrier function.

In <u>this edition of the FMU</u>, Dr. Bland describes the dynamic nature of epithelial barriers and how they are perturbed in disease, and talks with Kenneth Fine, MD about how Functional Medicine informed his practice of gastroenterology and is reflected in his service laboratory specializing in GI assessments.

Where in the World is Dr. Bland?

Every year, Dr. Jeff Bland speaks in front of



audiences around the world.

Will this be the year your paths cross?

View Appearances Calendar



For more than three decades, Dr. Jeff Bland recorded and self-published a monthly audio journal called Functional Medicine Update (FMU). Although he is no longer recording new issues, an archive of content spanning 1997-2016 is <u>free to explore</u> on Dr. Bland's website, and this extraordinary collection is now known as the FMU Knowledgebase.

To access the **January 2004** issue, which is featured at the start of this newsletter, click here. That issue features an interview with D. Barry Boyd, MD, MS, integrative oncologist.

More about what you'll hear: Though more hospitals are adding integrative therapy programs and more medical schools are providing nutrition education, mainstream adoption of functional medical paradigms has yet to catch up. The onus for developing optimal individualized treatment plans still falls to practitioners in many cases, and perhaps especially in oncology—ironic, since cancer is increasingly understood as an intensely genetically unique condition. As a result of this confusion, much cancer research, which examines findings across populations rather than within individuals, has not been designed to guide doctors in understanding which dietary or drug approach may be best for a given person at a given point in their treatment. In this classic FMU interview, integrative oncologist D. Barry Boyd, MD, MS talks with Dr. Jeffrey Bland about how behavioral and dietary factors (including food preservation and preparation methods) positive and negative interact with insulin- and immune-related signaling axes to guide life-and-death balance in cells and tissues—and in people. They discuss the cross-ties between obesity and cancer dynamics, and how to unwind them through nutrition.

Classic FMU Top Ten Clinical Pearls From This Issue:

- 1. Dr. Bland: "Food is information. Our lifestyle contains information from which our genes receive a message that creates the phenotype. Cancer is not inevitable. It is modifiable through the information you send to your genes."
- 2. Fewer than 15% of cancers beyond prostate, breast, and colorectal cancer appear genetically hard-wired; thus environment and experience relate to cause in many cancers and modulate risk even in genetically-driven cancers.
- 3. Dietary contributions to cancer risk: refined foods with natural anticarcinogens (fiber, vitamins, phytonutrients, minerals, etc.) removed, deep-fat fried foods, many fatty foods, char-grilled meat.
- 4. Dietary cancer preventatives: perishable nutrient-dense foods; unrefined, intact fruits, vegetables, and grains with full natural complement of fiber, phytonutrients, vitamins, and minerals.
- 5. Macrobiotic diets may present advantage to those at increased risk for breast and prostate cancer, while the Mediterranean eating style can aid chemotherapy response and improve cancer prognosis.
- 6. Methylenetetrahydrofolate reductase polymorphisms can increase cancer risk

- (possibly through altering homocysteine detoxification), but genetically-individualized nutrition is safer than simply increasing intake.
- 7. Phytonutrients like isoflavones, resveratrol, phytosterols, glucosinolates (and their metabolites), limonene, ellagic acid, vitamin C, and catechins can improve metabolic dynamics related to inflammation, lipid metabolism, angiogenesis, gene expression, and metastasis in cancer.
- 8. Appropriate insulin, insulin-like growth factor (IGF), MAPK (mitogen-activated protein kinase), and PI3K (phosphoinositide-3-kinase) signaling can influence cell proliferation and tumor promotion, and relates to cancer mortality in obesity; caloric restriction may help address this relationship.
- 9. Chronic stress affects insulin status and inflammatory mediators and can thereby impact cancer incidence. In obese or hypertensive mice, extract of licorice (a traditional stress management herb) improved glucose regulation, blood lipid profiles, and visceral adiposity—even with no change in caloric intake.
- 10. Upregulating PPAR (peroxisome proliferator-activated receptor) activity aids insulin sensitivity and may help limit obesity; natural PPAR modulators include omega-3 fatty acids, conjugated linolenic acid, and dehydroepiandrosterone (DHEA).

Interview Link:

http://jeffreybland.com/knowledgebase/january-2004-issue-d-barry-boyd-md-ms/

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