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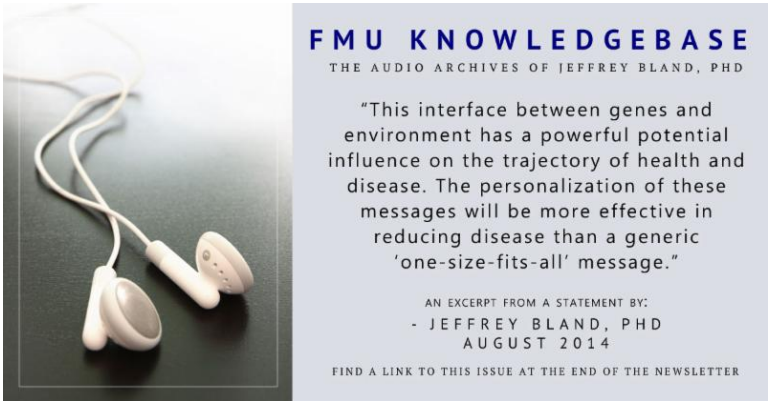

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A Brief History of Glucose

The medical traditions of India and China have long made note of dysglycemia; the former as a change in the kindling of digestive functions leading to altered storage of energy and toxicity, and the latter as a depleted condition involving pathogenic heat within vital organs causing mis-translation between appetite/thirst and physical energy production. From finding that glucose in chronic excess can be a toxin to observing that there are numerous subtypes of diabetes represents an enormous span of deep thinking. This somewhat revolutionary 1934

paper by Dr. HP Himsworth describes how dietary composition and periods of stress or starvation affect glucose tolerance in normal subjects, and even details the differential influence of fats and carbohydrates. By this time, doctors had seen that glycosuria and glucose intolerance did not always coincide, and Dr. Himsworth began to investigate how blood insulin and pH affected each of these signs. These Clinician-Scientists' studies led to the concept of insulin sensitivity and the further notion that diabetes had an insulin-resistant as well as an insulin-deficient form.

In this video, which is one part of a three-episode video series (links are provided in the next section of this newsletter), Dr. Bland highlights the contributions of visionaries like Dr. Gerald Reaven, who took a closer look at how insulin dynamics link to adolescent acne as well as serious conditions like inflammation, hypertension, dyslipidemias, and obesity. Dr. Reaven was an early advocate for functional (rather than static) testing of the glucose response, and was interested in how ketosis impacts glucose regulation. Among the most valuable ideas put forth by these researchers was the recognition that there are many actionable steps between the very earliest changes in pancreatic function and frank disease. More scientists and practitioners now understand that glucose toxicity arising from chronic hyperglycemia can directly damage organs and tends to feed inflammatory and carcinogenic processes—and that it induces more widespread metabolic disruption than previously realized. Because risk associated with glucose toxicity is epigenetically influenced by ancestral living experiences as well as our parents' lifestyles, functional pre-conception and prenatal evaluation is emerging as prime time for actionably assessing a child's later propensity for cardiometabolic disease while also supporting maternal welfare.

Much interest has lately focused on GLP-1 (glucagon-like peptide-1), an intestinal peptide stimulated principally by ingested saccharides. During a meal, GLP-1 initially aids insulin release and slows gastric emptying, but afterwards it helps shunt glucose towards liver glycogen storage. GLP-1 acts to some degree as an interlocutor between the central and enteric nervous systems, but this can be impaired by dysfunction or altered responsivity at virtually any intervening point. In adults, higher levels of GLP-1 signal the hypothalamus to reduce appetite and food intake. However, in 12-month-old babies, higher GLP-1 levels correlate to significant weight increase—yet rapid "catch-up" weight gain by small-for-gestational-age (SGA) babies confers greater risk for later diabetes and obesity. Recent research has discovered that SGA babies have higher GLP-1 levels compared to appropriate-for-gestational-age (AGA) babies at 12 months' age, and that formula-fed SGA infants have higher GLP-1 levels than those breastfed. Because GLP-1 activity relates to insulin dynamics, energy homeostasis, and appetite, researchers felt that higher GLP-1 levels in late infancy could negatively impact long-term GLP-1 signaling and thereby impair metabolic control in affected SGA infants.

Early clinical observations about interactions among insulin, glucose, dietary practices, and lifestyle inputs set the stage for intervention in diabetes. While rapid acquisition of knowledge in the Age of Big Data can feel dizzying, it provides analogous opportunity to intervene—now, prior to the subtlest signs of metabolic distress.

Food for Thought: Watch Dr. Bland's 3-Part Video Series

It's a complex topic with a complicated (but fascinating!) history. Dr. Jeff Bland recently completed a retrospective overview of the study of glucose metabolism and type 2 diabetes in his ongoing Food for Thought video series. The production of Food for Thought is made possible through through a generous educational grant from Metagenics Institute to the Personalized Lifestyle Medicine Institute.

Part 1: November 2018

Video Link: https://vimeo.com/298038853

Part 2: December 2018

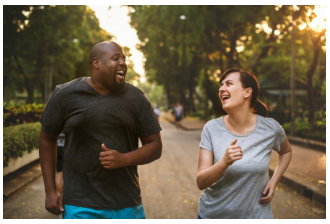
Video Link: https://vimeo.com/303166322

Part 3: January 2019

Video Link: https://vimeo.com/308619261

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

To Cultivate Metabolic Flexibility, Honor the Past



At a fundamental level, the human body is designed to allow individuals to adapt to changing conditions and survive them. It's also one of the main reasons it's difficult to lose weight, as metabolism quickly adapts to altered energy intake to try to maintain weight and preserve long-term fertility despite the new limitations. Though the body's remarkable cleverness in reusing and recycling fats within its metabolic pool has been crucial for helping humans survive times of famine, it doesn't help weight loss resolutions. And especially since dietary fat has, in evolutionary terms, only recently become commonly plentiful, many struggle to shed depots of fat stored in belly, thighs, arms or have high cholesterol levels. Even type 2 diabetes, which directly affects around 15% or more of the US population, reflects exceptional efficiency in conserving caloric nutrient resources, and has for decades been called "the thrifty genotype" as a result.

A 2016 study investigated how natural genetic selection responds to survival pressures (like widespread exposure to infectious pathogens, mass migration, food scarcity, and climate change) at the population level, and compared what happens to these genes in stable populations over time. Migration increased selection pressure for genes associated with increased immune defense responsivity, and genes involved in efficient glucose metabolism were more highly preserved in populations experiencing frequent fasting conditions. In stable populations with food security, however, there appeared to

be some genetic adaptation to attenuate 'excessive' thriftiness, but the speed of this change lagged behind increases in metabolically 'thrifty' conditions like obesity, insulin resistance, and diabetes.

The mental and physical stresses experienced during periods of upheaval may contribute to this slow adaptation by activating long-term stress responses in the brain, the immune system, and metabolic regulation in what is termed "selfish" metabolic behavior that temporarily prioritizes a particular function over others. All of these systems 'want' energy in order to carry out their functions, and do not easily 'sacrifice' their highly-evolved mechanisms for ensuring that they have sufficient energy to support normal function with reserves to spare for times of higher need. Over time, however, times of insufficiency are survived at the expense of developing chronic health conditions related to overaccumulation of energy currency during times of plenty.

While the pace of genetic change is slow compared to that of living circumstances, Dr. Bland reminds us that behaviors can make up some of this difference by influencing how genes they carry out their programming. In this FMU, he describes how intense individual engagement in one's own health care can transform physical and mental health while reducing care and medication costs; in fact, Functional Medicine was deliberately designed to improve metabolic flexibility by reducing biological aging and building functional reserves. Success in personalizing health engagement is reflected by a nationwide lifestyle intervention program for reversing metabolic syndrome among abdominally obese individuals in Japan. Out of over 19 million subjects initially screened, 907,909 were studied as non-participants and 111,779 were studied as participants. Participants were examined, screened for cardiometabolic conditions, educated about lifestyle impacts on health, given diet and lifestyle suggestions, helped to set their own health goals, trained to measure their weight and abdominal circumference, and followed up periodically. After 3 years, a significantly greater portion of participants showed clinical reductions in BMI and waist circumference and significant improvements in abdominal and overall obesity, systolic and diastolic blood pressures, HDL cholesterol, triglycerides, fasting blood glucose, and glycosylated hemoglobin compared to non-participants.

Smoke Muddies the Waters for Genes—Across Generations

Though fetuses are well-protected from many toxins, they are surprisingly susceptible to the effects of tobacco smoke, and prenatal exposure can hurt future lung function. Ethical considerations make it difficult to investigate these influences, but recent study employing an animal model found that maternal exposure to tobacco smoke slowed delayed lung development and dysregulated hundreds of genes and microRNAs within fetal lungs. MicroRNAs often silence genes, and thus a pregnant mother's exposure to smoke can inappropriately alter fetal gene expression in both direct and indirect ways.

A particularly important discovery was that, particularly in female fetuses, expression of the gene coding for insulin-like growth factor-1 (IGF1) was strongly affected by smoke exposure. IGF1 is related to cellular growth and body weight throughout life, and altered IGF1 signaling is implicated in obesity, cancer, and other disorders. Earlier research had found that grandparents' smoking habits during pregnancy with their own children might even affect weight gain in their grandchildren. The impacts of secondary smoke are fairly well understood, but the current study helped clarify that even 'tertiary' smoke—maternal exposure to secondary smoke—has significant effects on children.

The results of these various genomic studies related to tobacco smoke reveal that its effects are among the most pervasive and lasting, regardless of whether one chooses to ingest it directly or is introduced to it through genomic changes that occurred in generations past. They also reinforce that nicotine, cotinine (the main metabolite of nicotine), carbon monoxide, and smoke all contribute to the transgenerational effects of

tobacco. It seems that our genes, and perhaps especially those of our female ancestors, take careful note of this experience.

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

FMU KNOWLEDGEBASE

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 free to explore on Dr. Bland's website, and this extraordinary collection is now known as the FMU Knowledgebase.

To access the **August 2014** issue, which is featured at the start of this newsletter, click here or use this link: https://jeffreybland.com/knowledgebase/august-2014-issue-dr-bland/.

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