November 2009 Issue | Alejandro Junger, MD Eleven Eleven Wellness Center

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Welcome to *Functional Medicine Update* for November 2009. What a year it has been so far in *Functional Medicine Update*. I hope you have enjoyed the last few months as much as I have. I think you'll agree that we have been traveling on a journey together that has been quite remarkable as it relates to the emergence of this systems biology approach-the functional medicine approach-to medicine. Certainly this journey is going to continue this month in our November issue, in which you will hear an extraordinary interview with Dr. Alejandro Junger from New York City, who will be speaking about his experiences with the functional medicine model in what we call a "tire-meets-the-road"-type of conversation about how the model really applies in clinical practice and how one can make this concept actually work in patient management.

Nationally (and even internationally), we are in the throes of one of the most remarkable debates about health care that I have experienced. What will the healthcare system look like as we move forward in the 21st century? Everybody has their view of the answer to that question (obviously with much room for debate, controversy, and discussion) about the scenario that will define the healthcare system of the future.

My colleague, Jay Johnson, found an insightful view that summarizes the present state healthcare reform, and I thought it would be fitting (with a degree of levity) to start off our November issue. If you will bear with me, I'll share this little humorous thought about the healthcare system:

> "Apparently the American Medical Association has weighed in on the new economic stimulus package and how it interrelates to the healthcare reform... The Allergists voted to scratch it, but the Dermatologists advised not to make any rash moves.
>
> The Gastroenterologists had sort of a gut feeling about it, but the Neurologists thought the Administration had a lot of nerve.
>
> The Obstetricians felt that they were laboring under a misconception.
>
> The Ophthalmologists considered the idea shortsighted.
>
> Pathologists yelled, 'Over my dead body!' While the Pediatricians said, 'Oh, grow up!'

> The Psychiatrists thought the whole idea was madness, while the Radiologists could see right through it.
>
> Surgeons decided to wash their hands of the whole thing.
>
> The Internists thought it was a bitter pill to swallow, and the Plastic Surgeons said, 'This puts a whole new face on the matter.'
>
> The Podiatrists thought it was a step forward, but the Urologists were pretty pissed off about the whole idea.
>
> The Anesthesiologists thought the whole idea was a gas, and the Cardiologists didn't have the heart to say no...
>
> In the end, the Proctologists won out, leaving the entire decision about what to do with health reform, up to the 'rear-end' people in Washington, DC."

A very interesting little insightful thought about the present healthcare debate and reform.

But with seriousness, now, let's move back to the real business at hand, which is how to make this system that has been a disease-care system balanced with a healthcare component. That has been the focus of *Functional Medicine Update*, and the efforts made on behalf of functional medicine through the Institute for Functional Medicine since its inception. To give you a little bit of an update as to what has happened over the last several months related to the topics we have been discussing, I'm now going to do kind of a "potpourri" discussion with you on a variety of topics. I think each one stands alone as a little weigh point on the overall view of the functional medicine matrix and might be considered a "node" in our understanding of how everything connects together to form the web of clinical practice that we called the systems biology in medicine functional medicine model.

Let's talk about toxicity first and review what's gone on over the last few months in this area. In each one of these little vignettes, I'm going to take you back to past discussions we've had in *Functional Medicine Update* and just kind of bring you up to speed. In the past, we talked about the extraordinary emerging idea that there seems to be a correlation between marginally elevated gamma glutamyl transpeptidase levels (GGTP levels) in serology (this would be in the upper quintile of even the normal range of this liver enzyme), and the association with overall chronic disease. And also how that connects together with body burden as it relates to various environmental lipid-soluble toxins, particularly things like polynuclear aromatic hydrocarbons (PAH) and other toxic substances.

In previous issues of *Functional Medicine Update*, we reviewed how this connection between chronic illness and marginally elevated (within the normal range) of GGTP also connects together with type 2 diabetes as a specific disease entity that is associated with this connection of what are called "POPs" (Persistent Organic Pollutants) that can be measured in the blood, and upper elevated levels of GGTP and serology.[1, 2]

There was another part of this story that was quite fascinating that I think had some pretty important

clinical implications. In evaluating the Health and Nutrition Examination Survey III data (the largest database that connects together health indices and nutrition status of the population), it was found that there was no direct correlation-I want to emphasize, NO direct correlation-between type 2 diabetes and obesity in the absence of elevated normal levels of GGTP in the serology. That's a fairly interesting observation because most of us have assumed that obesity, in and of itself, causes insulin resistance and leads to type 2 diabetes. But yet, this particular epidemiological statistical evaluation does not show a strong correlation between obesity and the onset of type 2 diabetes in the absence of elevated GGTP levels.[3]

We normally assume that GGTP is a measure of alcohol and drug-related abuse problems. In fact, it has been used as a way of actually following compliance with substance abuse programs. But now the evidence is suggesting that gamma glutamyl transpeptidase may be related more to an overall burden that the body has as it pertains to potential toxic exposure, as evidenced by a very strong correlation of serum levels of persistent organic pollutants and increased levels of GGTP, and then the subsequent connection to that of type 2 diabetes. As I mentioned, in the absence of this connection between GGTP and the level of persistent organic pollutants in the blood there was not a significant association with obesity and diabetes. It is only in those people who have increased body mass index and who also have increased levels of GGTP where there is a very strong correlation with type 2 diabetes.

What Does Gamma Glutamyl Transpeptidase Do?
What does this enzyme that is present in the blood-gamma glutamyl transpeptidase-really do? Why is it there? I think we have often assumed that it is similar to that of ALT and AST, the two principle liver function test enzymes that we use to measure liver pathology. Those enzymes, which are amino transferase enzymes, are found in hepatocytes in high levels because they are involved with amino acid metabolism and they are released into the blood when these cells die. It is recognized that there is a very strong correlation between liver cell death caused by cirrhosis and hepatitis and elevated ALT and AST levels, so that is part of our liver function test evaluation in serology for liver pathology.

The Three Personalities of Glutathione
I think we've also assumed that GGTP is elevated by the same route (the death of liver cells), but actually that is not totally true. Gamma glutamyl transpeptidase is an enzyme whose function in the body is involved glutathione recycling. As contrasted to your normal alpha amino acids, like alpha glutamic acid, the gamma glutamyl residue, gamma glutamic acid, is a unique amino acid that is found within the tripeptide that we call glutathione. Gamma glutamyl transpeptidase is actually used for recycling and reforming the glutathione molecule and it is upregulated in its activity when the body has greater turnover of glutathione. When would that be? That would be times when the body is under either oxidative stress or under xenobiotic load. Recall, if you would, that glutathione is a very important biomolecule that kind of has three personalities, one of which is the important role it plays in the glutathione recycling system pertaining to antioxidation through glutathione and glutathione disulfide. You remember the enzymes: glutathione reductase, which requires a flavin adenine dinucleotide for its activation (which is vitamin B2-derived cofactor), and the other is glutathione peroxidase, which you know as a selenium-requiring enzyme. So there are some nutritional relationships (through trace minerals and vitamins) for the proper support of glutathione activity through the glutathione peroxidase/glutathione reductase system.

The other part of this is glutathione's recycling/resynthesis. The gamma glutamyl residues get broken off and resynthesized through the GGTP activity in part, so when there is increased turnover of glutathione,

you have increased activity of GGTP. If one activity is related to oxidation, the other activity of glutathione is related to detoxification. It conjugates as a phase II conjugating nutrient with specific biotransformed intermediates in the detoxification process, which then conjugates with the specific biotransformed intermediates to form mercapturates (this makes it water soluble and then it can be excreted in the urine or transition to the bile to be excreted in the feces). So the second role of glutathione is that of detoxification. If you have a higher body burden of toxins and your body tries to upregulate its detoxification functions specific to those factors of phase II glutathione conjugation, then GGTP activity also rises to meet that need. And the third role of glutathione is it is used in the formation of various forms of what are called the leukotrienes (the proinflammatory mediators derived from arachidonic acid).

So there are multiple roles (three roles) for the glutathione molecule, and the one that I have been speaking to here that I think has a direct and interesting relationship to this story about toxicity, serum levels of persistent organic pollutants, increased serum levels of GGTP, and the association with chronic disease (particularly type 2 diabetes) has to do with the role that glutathione plays in detoxifying foreign chemicals or xenobiotics. With the elevation of GGTP, we are really talking about the nature of how the body might have a resident body burden of toxins, which means exposure to substances can correlate themselves with the relative risk to various chronic-related illnesses.

Bisphenol A and Dose Response Toxicity

One molecule that has received a considerable amount of attention is a plasticizer called bisphenol A (BPA). There is a wide body of literature supporting concern about bisphenol A as a toxicological material at a very low concentration. The concept of dose response toxicity, which often toxicologists think about, is at a slightly different level of story when we get to these very low levels of exposure because it is not a direct dose response; it has almost a xenohormetic effect. (Xenohormetic means having a much larger effect than we would anticipate based on the low level of that chemical, but if the chemical hits the right receptor, it has the right communication with the gene expression patterns, and it modulates function in a way that can amplify its effects across cell types.) With a xenohormetic effect, you might have a broader physiological outcome in terms of immunotoxicology or neurotoxicology than you would have anticipated just looking at the concentrations of material alone. One should not be misled into thinking that just because something is in the part-per-million level (or sub-part-per-million level) that it is necessarily safe and benign. And all of this ties together with the emerging recognition that toxins and toxicity can play a role as one of the triggering factors for modifying the web of physiology and inducing a transition in gene expression that is associated with alarm reactions and ultimately chronic illness.

Results from a New Animal Study on Low-Level Atrazine Exposure

With that as a backdrop, let me bring you up to speed on a number of the other papers that have been published recently in this area. One that is very consistent with this view that I have been describing is another nice paper from Dr. Pak and Dr. Lee's group, two of the investigators that really started looking at the connection between POPs and type 2 diabetes. This article was recently published in *PLoS* free access biomedical journal, and titled "Chronic Exposure to the Herbicide Atrazine and its Relationship to Mitochondrial Dysfunction and Insulin Resistance."[4] I think this a very important paper because, as the authors state, there is an overlap between areas in the United States where the herbicide Atrazine is heavily used and obesity-prevalent chronic illness. This is consistent with this model that I have been describing that ties together body burden of various toxins with altered function and how that ultimately translates into chronic illness.

In this particular study, they used an animal model in which the dose response could be controlled. They used at Sprague-Dawley rats, which they treated with exposure to low levels (less than 30 part-per-billion) of Atrazine per day in their drinking water for five months. . The researchers then fed one group of rats a high-fat diet and the other a regular diet. Parameters of insulin resistance were measured, and then later morphological and functional activities of mitochondria were evaluated in tissues of both groups of Atrazine-exposed animals.

What the researchers found was that chronic administration of this low level of pesticide, Atrazine, decreased basal metabolic rate and was found to increase body weight, intra-abdominal fat, and insulin resistance without changing food intake or physical activity level. Let me say it again. The exposure to this specific environmental agent (this xenobiotic) at low levels of exposure with a high-fat diet resulted in blunting of the insulin signaling, increased body mass index (with intra-abdominal fat deposition), and decreased metabolic rate (meaning it had an adverse effect on mitochondrial function), without changing either food intake or physical activity.

I think we have been led to believe that the obesity epidemic is solely the manifestation of eating luxurious, calorie-rich, fast food diets. But could it be that the diets that we are eating, and the environment to which we are exposed, also contain other information (like this Atrazine or bisphenol A) that are blunting our physiology in such a way as to induce energy storage rather than energy utilization, and result in a contribution to the obesity/insulin resistance and type 2 diabetes epidemics? That is what this study appears to suggest, at least.

In this study, did they see any changes in mitochondrial oxidative phosphorylation (energy powerhouse activity) in these animals that were exposed at this very low level to this herbicide Atrazine? In looking at the mitochondria in skeletal muscle and liver, they found that the mitochondria had disrupted cristae. It was found to block the levels of oxidative phosphorylation complexes 1 and 2 in the electron transport chain, resulting in decreased oxygen consumption. This suggests, through this combination of information, that this low level of exposure to Atrazine suppressed the insulin-mediated phosphorylation and had an adverse effect on kinase signaling, the very important signaling process (intercellular signal transduction) that translates messages of insulin from the outside of the cells to the inside of the genes to result in appropriate glucose transport and bioenergetics of the cell. The results suggest that long-term exposure to the herbicide Atrazine might contribute to the development of insulin resistance, and then later result in obesity as a secondary (not a primary) effect, particularly exacerbated when a high fat diet is present.

I think mitochondrial oxidative phosphorylation is a very important part of this emerging story. What's the clinical outcome? I guess we'd call it metabolic detoxification. It is finding the way to lower the body burden in patients by improving their detoxification and excretory routes to eliminate these mitochondrial toxins, and to enhance, then, mitochondrial function, oxygen utilization, and ultimately induce more appropriate insulin signaling, kinase signaling, and glucoregulation.

That's my first little vignette. Let me now go to the second vignette. We had an extraordinary interview with a periodontist who told us about the amazing connection that is emerging between oral health and systemic health. This discussion focused on periodontitis and its relationship to atherosclerotic cardiovascular disease risk. I want to come back and revisit this just briefly. There was an amazing and well-written editorial that appeared in the July 2009 issue of the *Journal of Periodontology* that discusses

(and provides an extraordinary bibliography) this relationship between cardiology and periodontology.[5] In fact, this was a joint article written collaboratively by the editors of the *American Journal of Cardiology* and the *Journal ofPeriodontology*. Who would have believed there would be dentists co-collaborating with cardiologists to write an article about the connection between the oral health and the cardiovascular system? This is a very interesting example of the web in which disease names become less important than the soil in which these situations arose. This is the whole basis of our functional medicine thinking.

In this particular paper, which I think is beautifully written, there are some wonderful color illustrations showing the relationship between oral health and the appearance of cardiovascular disease. The article describes mechanistic proposals based upon the levels of proinflammatory cytokines found in individuals, and talks about the fact that these are non-cholesterol-related risk factors that are more inflammatory and associated with cardiovascular disease. By increasing oral hygiene, inflammatory burden is reduced from chronic infection and inflammation that results from periodontitis. That, then, lowers systemic inflammatory biomarkers--things like intercellular adhesion molecule 1, vascular adhesion molecule, and the things that relate to monocyte stickiness to the arterial endothelium and initiating the atherogenic process.

The Oral Cavity Can Be a Site of Focal Chronic Infection
I think this is emerging to be a well-understood connection. Specific recommendations came out of this article about how to manage patients and to preventively engage in proper oral health, and what treatment to use in those people who have periodontitis. Periodontitis is more than just a regional oral health problem; it has a systemic connection. When thinking about triggering factors that relate to altering or distorting metabolic webs that lead towards chronic disease, don't forget the sites of focal chronic infection: the oral cavity, sinus cavities, and the gastrointestinal tract. These are important areas within the body where low-grade, simmering infection can induce chronic inflammatory response, and there is at least a statistical relationship to increasing risk of various chronic diseases that have an inflammatory etiology.

We should probably also recognize, once again, that these situations are not uniform in their impact on all genotypes. There are specific genotypes that have higher levels of sensitivity, such as in people with specific IL-1 beta gene sensitivities (receptor site sensitivities) or specific TNFalpha (tumor necrosis factor) genotypic susceptibilities. What I'm saying is that people with certain SNPs (single nucleotide polymorphisms) may be at higher risk than others relative to a proinflammatory insult. We can't say all people are at risk to the same degree, but what we can say is that there is an increasing relative risk as you have increasing localized inflammatory processes going on (as to how that can spread to systemic disease etiology).

Let me move to the next factoid I want to discuss, which relates to the emerging therapeutic potential for functional medicine and disease management and prevention. That relates to the extraordinary discussion we had recently with Professor Delzenne and Dr. Cani at Catholic University of Louvain. They were helping us to understand more about the microbiome and the complexity of the population of enteric flora that creates a very important community in our gastrointestinal tract and can either be friend or foe depending upon the species of bacteria, their relative population number, and their activity. We talked with Professor Delzenne and Dr. Cani about the role of probiotics and prebiotics in reestablishing appropriate gut enteric health and the influence this has on a healthy microbiome.

A New Study on Probiotic Use in Children

Since that discussion, a very interesting paper has been subsequently published, which I think bears on this whole story. This article was in *Pediatrics* in 2009 and titled "Probiotic Effects on Cold and Influenza-like Symptom Incidents and Duration in Children."[6] Let me give you the specifics of this study because I think it is a very interesting study with provocative, if not important, implications.

What was this study? The objective was to try to see if probiotic administration in healthy children could influence the appearance of cold and flu during the winter season. This was a double-blind placebo-controlled study in 326 eligible children, 3 – 5 years of age. They were assigned randomly to receive either a placebo or a supplement of *Lactobacillus acidolphilus* NCFM, or a combination of *Lactobacillus acidophilus* strain NCFM along with Bifidobacterium animalis (this is the Bi-07 strain). The children were treated twice daily for six months with either the placebo or one of the two arms of the treatment.

After the six months, the intervention with probiotics in these children 3 – 5 years of age was found to be very safe. There were no apparent ADRs (adverse reactions) that occurred in these children. It was also found to be very effective at statistically significant levels It was a cause-and-effect observation that the supplementation for six months was effective in reducing fever, rhinorrhea, coughing incidence, the duration of symptoms, and even the need for antibiotic prescriptions during the course of the cold and flu season with children 3 – 5 years of age.

What did they measure to come to this conclusion? The fever incidence was reduced by 53{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in the acidolphilus alone, and almost 73{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in the group that got the acidolphilus plus the bifido bacterium. Coughing incidence was reduced by 41{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in the acidophilus alone and 62{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in the combination of two strains of bacteria. Rhinorrhea, 28{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in acidophilus alone (NCFM strain) and 58.8{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} in the combination of acidophilus NCFM plus the bifido bacterium lactus 07. There is a story here: you get added clinical improvement by giving the combination of the *Lactobacillus acidophilus* NCFM along with the bifido bacterium. It seemed like in all clinical indicators, there was an improvement by the combination of the two strains. When you look at antibiotic use incidence, it was reduced relative to placebo by 68{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} with the single strain, and 84{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} with the combination strains. In terms of reductions in days absent from group childcare, there was about a 32{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} reduction in absenteeism (about a third less absenteeism days due to cold or flu-like symptoms when measured against the placebo).

I think this is a very compelling study that helps to validate that enteric bacteria and the microbiome have a role that is not just regional in terms of the GI function. It has a systemic effect. It has a functional effect on the whole of the body by modulating immune function. And this occurs throughout the gastrointestinal-associated lymphoid tissue (where more than 50{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of the body's immune

system resides) and the signaling to the rest of the body through the liver, the circulating immune cells, and the lymph tissue, and ultimately having an effect on overall systemic immunity. I think this is a very compelling story in support of this model that the gut is the center of the immune function. What we send as information to the gut, be it bad food, or toxins, or chronic infection, can have effects systemically on our overall immune integrity and function.

INTERVIEW TRANSCRIPT

Clinician of the Month
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Well, here we are once again at our clinician and/or researcher of the month component of the Functional Medicine Update. You're in for an extraordinary treat. This month I am speaking with a clinician who will describe his experiences and his interests to you in ways that I think makes functional medicine stand up and be real.

Sometimes I have been criticized (and I think justifiably so) for being a little bit in the blue sky, airy-fairy, idealistic, intellectual, and immersed in the world of theory, rather than taking things down to the ground level of where the tires meet the road, where the mechanics can deliver improved outcome and quality of care to patients. That role is going to be certainly fulfilled in my discussion in with this month's clinician of the month, Dr. Alejandro Junger. You may already have some identification with his name if you are familiar with his book, Clean: The Revolutionary Program to Restore the Body's Natural Ability to Heal Itself.11

There is so much more within this book than just a program. There is also the person behind the program and its philosophy, and how he has brought functional medicine into an interface with consumer and patient need through this remove-, restore-, rejuvenation-type of approach. Dr. Junger, it is really a great privilege to have you as a guest for Functional Medicine Update, and also to have you in the studio today. Thanks for being with us.

AJ: Thank you. It's an honor to be here talking to you.

JB: I always start with this question: With the many journeys that a person could be on in their life, the many different trails they could take-different pathways-you've selected a path that meets your particular background, interests, and needs. Your journey has led you to the broad matrix that we call functional medicine. Tell us a little bit what your path was and how your journey took you here.

Change in Lifestyle Leads to Change in Health
AJ: I went to medical school in Uruguay in South America. When I graduated, I traveled to New York to do my internship/residency in internal medicine, which I did at NYU Downtown Hospital in Manhattan. Then I moved to Lenox Hill Hospital (also NYU-affiliated at that time) to do my cardiology fellowship.

The change in lifestyle from Uruguay to New York put me in a state-a physical, and mental, and emotional state-that was diseased. In looking for help I consulted a gastroenterologist for digestive problems that were diagnosed as irritable bowel syndrome. I saw an allergist due to my severe allergies, which at times required prednisone. And then I saw a psychiatrist for what was diagnosed as depression. All in all, within three consultations, I was left with seven prescription medications, which did not make sense to me.

I had a shock at that time, not only because I saw myself with a future of depending on drugs, but also because I realized this was the type of medicine that I was practicing. The shock was double. At that point I decided to stop everything and look for a different solution to my problems.

JB: I think this is a point that differentiates, to me, individuals who finally get to functional medicine from those who have maybe similar thoughts but never get there. There is a point of action, and some people are afraid to pull the trigger, or take the step, or make the commitment. And people like you make a commitment. Your action took you where?

AJ: Some people say, "How courageous of you." But the truth is, I had no option. I really, literally, was just looking to ease my disease. One of the first things that I noticed was that my mind was constantly producing thoughts. I say, "My mind was producing thoughts," as opposed to saying, "I was thinking," because that's when I realized that there was nobody there initiating those thoughts. In fact, if I had a choice, I wouldn't have been thinking 95{56bf393340a09bbcd8c5d79756c8cbc94d8742c1127c19152f4230341a67fc36} of the thoughts that were appearing in my mind. My burning desire was to answer, "Where are these thoughts coming from? Who is deciding about these thoughts? Why do I wake up in the morning and I think about the check I have to pay, and I remember this and that, and if I'm thinking of things in the future I become anxious, and if I'm thinking of things in the past I become sad? These thoughts that are just appearing in my mind are playing my emotions like a symphony with a life of its own." So that was my burning desire, to answer those questions: Where are these thoughts coming from? Who is producing them? And how can I get rid of them?

I started studying everything I could about where thoughts come from. I used to go to libraries (the psychiatry and psychology sections). I read and I underlined anything that made sense and resonated with me. The references that I was finding were from the New Age section. I was shifting from the psychology and psychiatry section to the New Age section, then to the Eastern Philosophy section, and finally found a book on meditation, which said, basically, that meditation was the way to slow down and even stop the thinking process. I said, "This is what I need." I found a meditation teacher and ended up in a monastery in India, trying to, basically, shut my mind.

JB: So tell us a little bit about that. It must have been quite an interesting transformation from New York.

From New York City to an Ashram in India

AJ: That was an incredible experience. I ended up directing a group of healthcare practitioners from different modalities who came from all over the world. I always say that without even ever hearing the term "integrative medicine," I was directing a team of practitioners from different philosophies and modalities from all over the world. This was my experience of integrative medicine.

JB: In that capacity, I think you were serving as a teacher and as a student simultaneously. Did you actually have, through that kind of involvement, some relationship to patient care, or was this more just talking about where one should go?

AJ: Oh no, no, no. We were actually running a clinic in the ashram, in the monastery. We were seeing up to 2000 people at any given time, who were living there, from all over the world. We were running the first aid station (the clinic). We would get a patient and we would sit him in the middle, with all of us around asking questions-Ayurvedic medicine, Chinese medicine, the chiropractor, the hands-on healer. And then we would discuss how each one could contribute to the treatment of this patient with the best tools that we had without conflicting with each other. At times, the Ayurvedic doctor prescribed a diet, and at times I had to take patients to the hospital in Bombay, which was four hours away. For example, there was a patient that was having severe bleeding. The Ayurvedic doctor wanted to start him on a certain diet and I said, "This is for later. Let's take this patient, let's cauterize that artery or vein that is bleeding, and then we'll start on a diet."

JB: As you did this, this must have been very interesting from a pedagogical or learning system basis. What you were almost realizing is a different educational system from the kind of top-down, lecture-series-type of approach (a didactic system) of Western medicine to a participatory collaborative system. It probably spoke to your mind and the thoughts you were having in a very different way, I would imagine.

Learning About Different Approaches to Heath Care

AJ: More than speaking to my mind, it cracked my mind open. One of the things that I base my life on is that you cannot argue with success. When you see that meditation is successful in treating a certain state, there is no argument there. I learned from Chinese medicine some things that were very effective: I learned how needles and certain herbs work very powerfully. I learned how Ayurvedic doctors divide the dosages according to the constitution and how diet influences them powerfully. I learned how meditation has a place in achieving a state of well being. I couldn't deny it. This was imprinted in me so powerfully that I still carry it around with me today.

From India Back to New York City

JB: We're going to jump forward for a second and then come back and fill in the gap. The jump forward is now I want the listener to be thinking, "Okay, we're now in an ashram in India. Dr. Junger is overseeing and collaborating with this group of integrative practitioners." Now we are going to segue really quickly, time-feed forward, to this very successful medical clinic that you and Dr. Lipman share in Manhattan, one of the most busy, energy-intensive, time-compressed centers in the universe (or at least in the known universe, as it relates to the world). In between those two places resides your life. As they say, life is what happens in between our plans. Tell us a little bit about how you got to this extraordinarily thriving practice from the ashram.

AJ: My family is Jewish and from South America. Actually, my parents are both Holocaust survivors. When I told them that I was going to an ashram-their golden boy, just graduated from cardiology training, now going to fulfill their dreams of achieving something in the world and suddenly I'm dropping out and leaving--they were desperate. My father made me promise him that a year later I would meet him in New York and we would recap. Once I was in New York, I realized that I needed to make some money to live. I applied for work, and I found a job in a very busy cardiology practice in Palm Springs. I went back to practicing medicine. I said, "I'm going to bring everything that I learned in the ashram into my practice,"

which was an impossible thing to do. I realized that in order for me to be in competition and to be considered profitable as a partner in this practice, I had to see a certain quota of patients, which left me with about 7 to 10 minutes per patient. Two years into this, I was literally hating medicine again. Not only that, I was back to eating foods from a hospital cafeteria, and back to being depressed, allergic, and having irritable bowels.

At that time, just by chance, a friend of mine had gone to a detox cleansing center and had an incredible experience. I had seen him ten days before he went. In ten days, he dropped about 15 pounds, he looked younger, and it was such a transformation. I said, "I have to learn what this guy did that put him in this state." This was what I wanted to be able to do for people when I went to medical school.

I went to the center, which was called the We Care Center in Desert Hot Springs, near Palm Springs. I saw what other people were going through. I immediately signed up for the program, and in 14 days, basically, my allergies, my depression, and my irritable bowel syndrome completely disappeared. I was so blown away that I started going to the center regularly, and sending my friends, my family, and then my patients. The owner of the center asked me to start lecturing there, or at least sharing with the clients there what I was finding that could explain, from a medical point of view, the results that we were seeing. But it wasn't until I did my first AFMCP that I understood-that I was able to translate, physiologically and biochemically-what I was seeing that was kind of miraculous, in a way, because I didn't have the scientific language to explain it.

Finding Functional Medicine

JB: I know when a lot of doctors go through the course, Applying Functional Medicine in Clinical Practice, they have kind of an "a-ha" or an epiphany experience, and it kinds of hits them at a level of saying, "Well, this is actually why I went to medical school. This is what I thought I was going to be doing when I got out into practice." And then the translation of that (and incorporation of it) into their lives becomes the real challenge. It's like having a feel-good experience and you then have to return back to the real world. What happened after AFMCP for you?

AJ: For me, it was different. For me, the high moment of "This is what I wanted to do when I went to medical school" came before, but the intellectual understanding of what was happening to people was not there. That was the "a-ha" moment for me. Functional medicine and AFMCP gave me the language, and the intellectual tools to understand the physiology behind what I was witnessing, which was kind of magical to me. Functional medicine gave me the translation. It gave me the explanation of something. You know when a magician explains the trick it seems so easy, but when you see it for the first time, you are just blown away? This is what functional medicine did for me.

JB: From there, you and Dr. Lipman have developed an incredible repartee-a partnership-which is not always easy with very creative people who have a lot of sense as to what the universe should look like. Partnership can be the best of all worlds, and it can be challenging as well. But your clinic has just started to radiate goodness to patients of all types and dispositions and backgrounds. Tell us a little bit about what goes on for you in Manhattan.

AJ: I actually moved to New York from Palm Springs, where I was practicing. I left my practice, basically. I left three months before becoming a partner in a very busy practice with a very big promise of monetary remuneration. I actually went to We Care, and became the medical director, which was

basically nothing more than sitting under a tree with people and talking about (what I didn't know) was functional medicine at that time (what I was trying to understand): how to integrate fasting, cleansing, and detoxification into a wellness plan, and how to think of it in terms of not contradicting what their doctors were telling them.

I moved to Los Angeles, kept working at We Care, and met a Chinese medicine practitioner there, Dr. Drew Francis, who introduced me to functional medicine. That was when the "a-ha" moment happened. I worked with Dr. Francis for awhile, and then was invited by Donna Karan to speak at her Urban Zen Initiative. She is trying to change medicine in the United States after a very bad experience with her late husband, who had lung cancer. She wanted to give him other aspects of care that Western medicine was not providing in the hospital, and she was denied. Even with all her power and all her contacts, she was not able to give her husband access to acupuncture and other modalities that would have made his demise easier. She is on a crusade to change medicine. She created this movement called the Urban Zen movement. She invited me, through a patient that I have, to speak at this conference where Frank Lipman was one of the speakers. After we heard each other speak, we became curious about each other. Frank came to me and basically asked me, "What's your name?" "Alejandro." He said, "You know, I've been looking for a partner for ten years, and I think it's you. I know you live in Los Angeles, but you've got to come and work with me." So I did. I sometimes compare this to a rookie playing basketball and Michael Jordan comes and says, "Come play with me." You're not going to say no. That's what I felt like when Frank invited me to work with him.

What has happened is we work in offices next to each other, and we just basically run from room to room. When he has a patient he comes and he says, "Alex, listen, come," and he puts me in the room and the patient has two opinions in one. And I do the same thing: I pull him into my room. That's how we work in a very simple and interactive way that patients really like. That's a big part of the success that we have been seeing in the clinic. Not that Frank hasn't seen it before, because Frank was a very established practitioner before he met me, but these are some of the things that are happening now with both of us in the clinic.

JB: I think it is interesting how circles work within circles. Things come 360 and remorph themselves. This Lenox Hospital experience you had that was your residency in cardiology...it kind of remorphed in your life, it seems, now that you are back in practice. Tell us a little bit about Lenox Hospital.

Cooperative Work with Lenox Hill Hospital

AJ: I did my fellowship in cardiology at Lenox Hill Hospital. One of the attending physicians, who was one of my dearest professors/teachers there, was a doctor called Dr. Rony Shimony. He is the cardiologist with the biggest heart that I known. Even though he practices Western medicine in a very extreme way-he really uses interventional cardiology a lot, angioplasties and angiograms-he gets results above the statistics of Western medicine because of his open heart, because he loves his patients, and because he's such a good man. I had established a close friendship with him, and when I came back to New York 15 years later, we established contact. Through our interaction, he actually invited me to help him at the office one day a week, and basically was exposed to everything I am doing with Frank. That led him to be willing to start an integrative service at the cardiology department at Lenox Hill Hospital. That's what we are working on right now. We are working on, basically, in my mind, bringing functional medicine into Lenox Hill Hospital.

JB: There is a thread that ties all of this together that should be fairly obvious to the listener, and that thread is that you are man of passion, you are a man of principle, you are a person that is directed by experience, and you are guided by a series of deep objectives as to where you want your life to go, but you are not necessarily a guy that runs his life off a set of plans out of the "seven ways to be successful" or the "motivational seminar series of the month" club. Tell us a little bit about how that has worked for you.

AJ: Well, when I was doing my fellowship and I was depressed and had irritable bowel syndrome I wish I could have gone to a course and within five days resolve everything and make a plan for my life, but I had to actually do it the hard way. I was desperately looking for a solution for my problems, and that led me to find functional medicine. And because it helped me so much, first my friends and then my family, and then my patients started to ask for it, I had no choice. This is what organically happened to my practice, and I'm happy that it did.

JB: I know for a lot of people who come into this field, they are very enthusiastic about it. They know that it resonates correctly with their sense of what they want to do, but often they don't know exactly how to structurally pound it into the model to make it a success financially or procedurally and from a tactical point of view. Do you have any guidance as to how that-not that there is a master design but just from your experience--kind of led you into what appears to be escalating success?

AJ: The only thing that I can say is that if you focus on results, if you focus on giving to your patients what is going to bring them to a better state, that's really the formula that I use. Word of mouth spreads. People are looking for results. When you have good results with patients, everything else happens on its own.

JB: I've been criticized over the years, and I'll share this criticism with you (I'd like to offload some of it off my shoulders). The criticism is: "Jeff you have spoken for years and years," (in my case, now over 30 years), "about this functional medicine concept, but you have been a little irresponsible in doing this because you don't have any long-term outcome studies to demonstrate that patients really will live longer, or they are really better off than if they would have just stayed the course, stayed with the prescription and done a traditional standard of care. Don't you think, Jeff, you are misleading people into thinking this is the Holy Grail or they are going to get something that they wouldn't have gotten by just following what everybody else (by board certification) feels is the right path?" What would be your response to a person who criticizes me for that?

AJ: My response to that person would be, "You should really take a look at those double-blind, clinical, placebo-controlled studies-how they are done, why they are done, who are they done with, how the meta-analysis is made." There is this idea that science and Western medicine have the answer for everything and is the gold standard to compare things to. And if you really understand how those numbers are gotten, and the many things that are omitted from these studies, then you actually lean on to something like functional medicine to guide yourself.

JB: Now tell us a little bit about what you've seen in the patients you've been applying this construct of Clean and the functional medicine kind of personalization. Give us kind of a Rorschach test as to how this looks to a patient who has gone through your program.

Patient Success Stories from the Clean Program

AJ: I have so many stories, but I can think of a few that are really remarkable. For example, I had this 28-year-old lady. She is an architect. She came to me with a cough that was persistent for like three years. She had gone through several courses of antibiotics. She had even had a bronchoscopy with a biopsy taken. She went to every extreme and came to me as a final resource to deal with her problem. I put her on a detox program (on the Clean program), and within three weeks her cough had completely disappeared. But then she called me and she said, "Doctor, something really strange happened." I said, "What happened?" She said, "Well, I started really getting blurred vision, and I didn't really understand what was happening, so I went to my ophthalmologist." Basically, what ended up happening is she had worn glasses for the last five years, and she didn't need her glasses anymore. Her blurred vision was because her glasses were not needed anymore. So that was an incredible result.

And there is another one. This lady recently-a 38-year-old who was sent by one of my celebrity clients-said, "Doctor, I come to you. I don't believe in what you do, but Western medicine, which is what I believe in, wants to give me chemotherapy." I said, "What's the problem?" "I have something called ankylosing spondylitis, which is an autoimmune disease, and it is characterized by the finding of anti-Ro antibody." One of the things that I now understand is that the confusion of the immune system in attacking yourself many times is originating in your gut, with the leaky gut syndrome, which is not recognized by Western medicine. Basically I put this lady through the process (through the program). She did really, really well, and then later on we found that she had very, very high levels of mercury. I started treating her with oral chelation. To make a long story short, not only did she avoid chemotherapy, but her anti-Ro basically turned negative. Her rheumatologist, who was one of the top rheumatologists in the United States (and I'm not going to name any names), basically sent her an email saying that she was committing suicide and that the doctor that was doing this to her should be put in jail and his license should be taken away. So we are going to frame the anti-Ro negative, and we are going to send it to him. And she actually, clinically, looks incredible, much better. Her pains from the ankylosing spondylitis-her hip pains-have completely disappeared, and she is a new person.

JB: It's really fascinating, isn't it? It's hard for any of us to know what we don't know. We're told what we should know, but we're not told what we don't know. I was very intrigued in the August issue of 2009 of Scientific American, which I would consider a fairly conservative, science-for-the-average-person-type journal, had a wonderful article on gluten authored by Alessio Fasano, who is in pathology now at Maryland (he was at gastroenterology at the University of North Carolina School of Medicine and now he's in GI and pathology at Maryland). He is, I think, considered one of the top experts in the world on celiac disease. In that article there is a fascinating diagram, as only Scientific American can do with beautiful medical illustrations (color) of a leaky gut. And he's talking about the fact that once you have opened the portals of entry with a gluten sensitivity, that many other middle molecular weight molecules can swim across the gut into the blood and have access to the immune system and can initiate systemic effects. This thing that was so vehemently rejected for years as not factually correct is now starting to get traction because we don't know what we don't know until we start to know it.

AJ: Not only that, we often find what we look for, but we only look for what we know. Right?

JB: That's very well said.

AJ: So that's one of the big problems that we have-that Western medicine only looks at a certain spectrum

of problems and has a way of detecting them, but they only look for what they know. That is where the confusion comes.

JB: In the few moments we have remaining, I'd like to ask just one last question that I think could be very helpful for some of our listeners: As a person who is watching this field unfold, watching the national healthcare debates be raging, recognizing that we are in a demographic transition with aging baby boomers, knowing that we're in a global economic kind of meltdown, and re-annealing with a new alloy probably coming out of this time into the 21st century, what's your view of medicine for your colleagues? What's your view of getting up every morning, putting your shoes and socks on and doing your work, and is there anything that you would pass on from your path that might be helpful for some of us who are still on our path.

AJ: Yes. People ask me, "Do you like your work?" I don't really consider my work and my life different. I wouldn't be doing anything else. When I'm not working, when I'm not in the office, I'm doing the same thing. In a way, to find what you really, really like to do--to find what you really want to do--is one of the most important things. And this is important because what I see is all my colleagues that are still trapped in the Western system-in the modern, Western medical system-actually hate their jobs. Many, many times they went into medicine with these ideas, with these principles, and then find this system that is, in a way, prostituted by competition and the politics inside the hospital. It degenerates the whole thing so much that they end up looking at their work as a job. They can't wait to get out of the hospital, and they can't wait to sign off their beepers and get the hell out of there. I don't see that in my life anymore. I consider myself so fortunate because from the time I wake up until I go to sleep, for me life and work is the same thing. This is, I think, one of the most important things that one should look for: What is it that you really, really want to do? What is it that you really like to do? And then everything happens on its own.

JB: Do you worry at all about losing touch with "medicine"? In other words, losing touch with all the skills that you developed-the bioscience, the hours that you spent developing certain types of understanding and knowledge?

AJ: The thing is, if you get the Textbook of Functional Medicine, you see that actually you will be much more versed in those things than if you were in medical school. Another aspect of that question is the whole aspect of how hospitals work and how these technologies can be used. The thing is this: Of the 100 percent of diseases that exist today, 10 percent are actually very, very well treated with Western medicine. If I am having a heart attack, I'm not going to take any anti-inflammatory herbs or going to meditate. I'm going to the first cath lab that can open my artery and save my myocardium. Now, afterwards, then I'm going to meditate and I'm going to do the nutrigenomic aspect of switching my genes, but that 10 percent of acute problems are actually very well treated by Western medicine. There is nothing comparable to it. The 90 other percent of diseases, which are the chronic diseases that we are trying to force the Western medicine tools into solving-that's what we have to change. That is where functional medicine has a place and a role that is very, very important for us to bring in.

JB: And how about the voices that were there that started you down this path, that kind of became the master of your change? Have they changed?

AJ: Again, you can't argue with success. When people see results, they start looking at you with more respect and with more interest. Actually, whenever you touch them in their personal life, and you resolve

any problem that they have or their family members have, then you have a convert. That's what I'm doing. I'm just spreading the word and trying to help as many people as possible.

JB: I can't tell you how much I, personally-and I think every listener-appreciates this inspirational sharing. I mean you went well below (or well above, actually) the normal kind of reductionistic discussion that often pertains to bioscience and 21st century medicine. It's really the connections. It's really the sense of the principle, the purpose: What is healing all about? Where does it come from? It comes from an intentionality that radiates from everything you talk about.

AJ: And for me to be sitting here with you is really an honor, and coming full circle because you gave me the possibility of expressing myself and of understanding what I was witnessing as miraculous, as weird, and understand that this is actually very, very well explained.

JB: Thank you, Dr. Junger. We look forward to seeing Clean continue to do its job of cleaning and hearing of your success, and of course, what a great partnership with Dr. Lipman. I can see the two of you really would be a force to reckon with.

AJ: Thank you.

JB: Thank you so much. The best to you.

Once again we really thank Dr. Junger for an extraordinary contribution to understanding how this functional medicine model can be applied successfully in managing patients and developing a very exciting and rewarding practice.

In Closing: High-Level Supplementation of Essential Fatty Acids

Let me talk a little bit about one of the aspects that has been on our radar screen for some time-probably the most well-understood, well-researched, and widely accepted nutritional intervention product within the armamentarium of our tools--and that is essential fatty acids. I'm reminded of the Ames group in the New England area that was meeting with Dr. Donald Rudin and Dr. David Horrobin early on-this would have been probably the late 70s-to talk about the role that omega-3 fatty acid insufficiency had on increasing the relative risk to all sorts of health issues, including psychiatric disturbances, neurological disturbances, and cardiovascular, immunological, inflammatory disturbances. This was back in the late 70s. How long does it take for medicine to change a lightbulb? In this case, we are thirty years downstream and it's now become an "a-ha" for many people as they start to understand the role that omega-3 fatty acids play. But as with anything, a little is good and a whole lot more might not be better. In fact, a whole lot more might be not as good. This is the Tolman's Law of Pharmacology that says everything is toxic at some level.

With regard to omega-3 fatty acids, we have alpha-linolenic acid as the first member of the omega-3s, and then we have docosahexaenoic eicosopentaenoic acid (so that's DHA and EPA, respectively). Which of these are the best, and what roles do they play? What's the best dose response and are there any adverse side effects? There are a lot of questions, certainly, when we start supplementing or using therapeutic doses of these various substances that we need to properly address and answer.

One of the things that has been stated is that supplementation with DHA results in increased levels of LDL cholesterol. I've heard that being expressed in a number of places. DHA, as you know, is found in very high levels in various marine algae. In fact, EPA and DHA are not really manufactured primarily by fish. They come as a consequence of the fish consuming things within the food chain where the omega-3 fatty acids are already manufactured for them, and they get concentrated within the fish tissues as a consequence of them consuming foods that have it.

Certain forms of marine algae have high levels of DHA. You can start looking at the algal vegetarian supplementation of humans with high levels of DHA (when I talk about high levels, I'm talking about something on the order of, say, one-and-a-half to two grams per day of DHA-that's a very high level of DHA, specifically), and you can ask: what is the effect that that has on serum lipids? A paper was published in the *Journal of Nutrition* in which that intervention trial was done.[12] In this study what they found is that the consumption of DHA capsules did increase DHA serum levels and phospholipid levels by 246 percent, so it had a very remarkable effect in increasing DHA. It actually lowered the LDL-to-HDL ratio, and it also lowered serum triglyceride concentrations. This concept that DHA supplementation increases LDL...there may be those individuals who have a variant response, but at least in the case of use of algal form of DHA supplementation in humans, this study didn't find an elevation; they saw a reduction in LDL and an improved LDL-to-HDL ratio. This was further confirmed in another interesting paper published in the *American College of NutritionJournal*, looking at intervention in individuals who consumed up to 2.5 grams a day of DHA for six weeks, where it was found, once again, that triglycerides were significantly reduced, and HDL was increased.[13]

I think that we can say that there is generally a favorable trend towards cholesterol HDL ratios and LDL/HDL ratios, as well as a lowered triglyceride level in people that are supplemented with fairly high doses of DHA, and also its companion, EPA. I hope that's some help in kind of making sense of this information with regard to fatty acid supplementation. I look forward to being with you next month.

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