

August 2006 Issue | Neil Shulman, MD

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Welcome to *Functional Medicine Update* for August of 2006. In the July issue, we had an extraordinary visit with Dr. Wayne Jonas, director of the Samuelli Institute for Information Biology. He talked about the work they are doing on optimal healing environments. This research is important and can improve the effectiveness functional medicine programs.

This month, we are going to be speaking about two areas that I think have some direct implication on the healing environment. One of these is something we have spoken of extensively over the last 25 years of *Functional Medicine Update*, and that is how the nutrition and psychosocial environments translate (through the genes) into messages that ultimately influence an individual's function. The second area is new to *Functional Medicine Update*. We will be discussing the concept of humor and laughter in medicine, which is emerging to be important in this world of seriousness and time compression in which we live.

This month, let me start with a little poem that comes from 18th century English literature. The author is unknown, but this poem has been repeated over the last couple of hundred years. It goes something like this:

The best six doctors anywhere

And no one can deny it

Are sunshine, water, rest, and air

Exercise and diet

These six will gladly you attend

If only you are willing

Your mind they will ease

Your will they will mend

And charge you not a shilling.

This poem is insightful; it has to do with concepts we can modulate: sunshine, water, rest, air, exercise, and diet. These can be six friends to the gene-environment interaction, or they can be six enemies (depending on how the message gets translated).

How do we treat disease? We often treat disease by battling it ('winning the war' against it), or by treating it with a therapeutic agent. Possibly what we really need to do is construct an environment for a patient that is in harmony with the patient's genetic pluripotentiality, so that what emerges in the phenotype of the individual-or their outcome-are the characteristics we associate with good health. Some of those variables that are often not considered strongly in medicine as important tools (such as sunshine, water, rest, air, exercise, and diet) may represent some of the most important gene modulators of expression that can translate into improved function. When planning an optimal healing environment, one should look at these six variables and consider how they might be modified to improve outcome. Part of the outcome depends upon the response of the patient to environmental messages, as well as how the patient see him or her self as worthy or unworthy of getting better.

Compliance Relationships are Examined Following a Clinical Study on Candesartan

Last month, we talked at length with Dr. Jonas about the so-called placebo effect. I read a recent paper in the *Lancet* that reported on a double-blind, placebo-controlled trial of the drug candesartan cilexetil (which is approved for the treatment of chronic heart failure) that found that placebo adherence was therapeutically more valuable than the overall statistical treatment difference between the placebo and the active drug.¹ This study indicated that reduced mortality was similar among individuals who maintained good adherence to the program, whether on placebo or active.

How is this result rationalized in the face of what we know about pharmacology? A potential explanation is that those who complied were also more likely to comply with other drugs they may have been taking simultaneously, and the cornucopia effect of all drugs led to better management of their condition. The data inspection, however, does not seem to support this as the primary reason for the difference in outcome between compliers and non-compliers. Rather, the authors of the study propose that adherence may result in lower mortality, even if the treatment is placebo, and it might relate to expectations and beliefs that the therapy will work. It may also be that compliance defines a particular personality type that is more likely to demonstrate positive health habits-activities such as weight management, diet control, and exercise. Such habits can confer a positive outcome benefit regardless of whether a person is taking a placebo or drugs. The results of this study suggest that whatever these associated factors with compliance are, compliance may be more important than the specific drug in determining efficacy. That is a powerful concept.

Maximizing the Therapeutic Value of Patient Compliance

If we were to look at an assembly of published studies, we might theorize that the context of healing-the belief that a person is going to get better and the patient's willingness to comply with treatment-may be powerful therapeutic tools regardless of the specific agents that are being administered. The most important information with regard to clinical decision making may be related to how committed the patient is to getting well and what investment he or she is willing to make in the healing process.

How do we maximize the therapeutic value that resides in what we loosely term 'compliance?' A true understanding

Some of you probably recognize I am speaking with some degree of controversy because I am flying in the face of what most of us think with regard to pharmacology. We know that pharmaceutical products do work; the drugs that have been developed to specifically impact certain steps and physiological processes are well designed. But, although they certainly do the job of blocking, inhibiting, or modifying/modulating specific physiological processes, due to genetic polymorphisms and unique differences, drugs do not work the same on all people. The dark side of pharmacology has been the rejection of other things that are considered low-impact modifiers, such as dietary factors, lifestyle factors, environmental factors, and psychosocial factors-which are not considered to be the bailiwick of mainstream medicine. These things have not been thought to constitute an important part of the recovery or therapeutic process, as they are not part of treating a condition and winning the battle against a disease.

One topic that has been in the backwater of conversation for some time is the concept of dietary fats. We have had modified dietary fats, the partially hydrogenated vegetable oils, in our food supply system for the last 30 years. By partial hydrogenation, vegetable oils have been intentionally isomerized to form trans that are more stable to heat and oxygen. For many years, even in peer-reviewed medical and nutritional publications, individuals who raised concerns about trans fats in our diet were considered renegades who sensationalized something that had no clinical relevance.

In *The New England Journal of Medicine* (2006), an article appeared titled 'Trans fatty acids and cardiovascular disease.'² This article reminds us to not always believe what we read; that knowledge is an evolutionary process and there are new things to learn if we keep our mind open. In this particular article, the authors talk about trans fats being a very important part of an emerging understanding of cardiovascular disease risk and that they probably have greater relative risk contribution to cardiovascular disease than saturated fat themselves. This article (from Walter Willett and Meir Stampfer, et al. at Harvard) goes on to say that the average consumption of industrially produced trans fatty acids in the United States is about 2 to 3 percent of total calories consumed. Major sources of trans fats include deep-fried fast foods, bakery products, packaged snack foods, margarines, and crackers. These are shelf-stable foods that can sit around for months without going stale because they contain retardants to spoilage and these modified fatty acids are more stable from oxidative damage than the natural cis form of fats. These authors discuss the potential molecular mechanisms by which trans fatty acids can directly or indirectly modulate metabolic and inflammatory responses of the vascular endothelium, which include altering the secretion, lipid composition, and size of apolipoprotein B-100 (apoB-100) particles produced by hepatic cells. This alteration is paralleled in studies in humans by decreased rates of LDL apoB-100 catabolism, reductions in the size of LDL cholesterol particles to the atherogenic-dense LDLs, and increased rates of apoA-I catabolism, lowering the effects of HDL as a lipoprotein that causes cholesterol efflux from the artery wall.

These are not good things; these are risk factors. I lay this on top of the backdrop of 20 years of information suggesting that trans fats were benign and had no adverse effects on physiological function; this information came from good science and respectable investigators who were opinion leaders from whom we derived our clinical decision-making. We must be cautious about what we contextualize as facts, because as we learn more, ask different questions, and have the tools to examine those questions, new and important observations may emerge. I encourage you to read this article on trans fats and cardiovascular disease because it goes through the effects that trans fats have on hepatocyte lipid clearance and on endothelial cell dynamics at the vascular endothelium; their influence on the adipocyte cellular signaling and how trans fatty acids may encourage lipogenesis and lipodystrophy; and also the

effects on the immunological system. All of these mechanisms increase the risk of atherosclerosis, sudden death from cardiac causes, plaque rupture, and diabetes. Trans fatty acids are far from benign. This article argues very strongly that consuming trans fatty acids increases relative risk.

When you eat a diet that is very high in refined carbohydrate, trans fats, and overall fats, and low in omega-3 fatty acids and polyphenolic substances that come from fruits and vegetables, you have a much higher incidence of increased inflammatory markers. This was pointed out in an article authored by Dr. Jialal and his colleagues at the University of Texas Southwestern and the University of California at Davis, Division of Endocrinology³ In this particular work, the authors showed that humans have a very dramatic response to a diet that is high in processed carbohydrates and high in trans fats, in that it increases inflammatory markers, as measured by such markers as high sensitivity C-reactive protein and serum amyloid A protein. This is consistent with what Dr. Willett and Dr. Stampfer were talking about in their review article on trans fatty acids in *The New England Journal of Medicine*. The Jialal article is in the *American Journal of Clinical Nutrition*, and indicates that it is not just trans fats in and of themselves, but rather it is the complex way these are delivered in the diet that results in an amplified inflammatory influence.

When we talk about dietary signatures, and information coming from food that modifies function, the diet that we consume of shelf-stable, processed, convenience food is a diet that has shifted these inflammatory signals over into the state of alarm. The problem is not just too many calories; it is too many of the wrong types of calories that create information expressed by our genes through inflammation, which can induce physiological changes associated with an increased risk of cardiovascular disease, cancer, diabetes, and arthritis. We now know that these inflammatory responses to altered diet and physical inactivity associate themselves with many chronic diseases, including autoimmune disease.

Early-stage Autoimmune Disease of Unknown Etiology

An article by Dr. M.C. Gracia appeared recently in *Medical Hypotheses* that talks about how the immune system can be shifted in its balance between the thymus-dependent-1 and thymus-dependent-2 regulatory lymphocytes into a state of autoimmunity.⁴ Self-regulatory T-cells start to lose discrimination and start forming antibodies toward host tissue resulting in autoimmune disease. The endocrine organs appear to be particularly vulnerable to this. If we look at what happens in these inflammatory-mediating situations, it may lead us to recognize subclinical and early-stage autoimmune disease in the clinic. This early recognition may explain why we are seeing more systemic lupus erythematosus and more autoimmune thyroiditis, and why more and more men and women are being placed on medications to manage these inflammatory conditions.

In the Functional Medicine Clinical Research Center, we recently had a very dramatic example of this. It was so dramatic that it just stopped us in our tracks. This case is from Dr. Jacob Kornberg and Dr. Robert Lerman. A patient who came to the clinic had not worn shoes in some time. She was a woman who had young children and was basically incapacitated; she could not stand for long, and she could not walk due to a very serious and unusual type of autoimmune disease called erythromelalgia. This condition is characterized as being the opposite of Raynaud's syndrome. Raynaud's is a vasoconstrictive disorder; erythromelalgia is a vasodilation-related disorder, with the extremities becoming very hot and looking seriously sunburned. There is also a lot of pain with this condition.

This particular patient was on Neurontin three times a day-an extraordinarily high dose-and still was in

very serious pain. She was receiving standard of care from a very well-respected center of rheumatology, and certainly was getting what we might consider the best medicine. But she was still very seriously disabled.

Erythromelalgia: Understanding the Molecular Basis of a Pain Syndrome

Recently, in the journal, *TRENDS in Molecular Medicine*, there was an interesting article on the molecular basis for this pain syndrome.⁵ The authors of the article give a very detailed discussion of erythromelalgia: how the sympathetic ganglion neurons are influenced, what nociceptive dorsal root ganglions are influenced, how this relates to specific single nucleotide polymorphisms and genetic risks, why this tends to run in families, and why this results in inherited painful neuropathy. This is a complex genetic disease and a dramatic example of the exquisite uniqueness of a person's immune and neurological systems.

The authors also point out, however, that this condition has sporadic onset and a dramatic phenotypic variability, so it is not a hard-wired, one-size-fits-all type of disease. They go on to say that there may be things that modulate the appearance of these particular processes. I quote, from this article, 'This suggests the involvement of other molecules in the form of the disease, possibly with modulation by other genetic and/or environmental factors that can trigger the appearance of disease symptoms.' That is obviously an entrée to our functional medicine thinking, because once you start saying gene-environment interactions, then you start seeing the situation as part of a web? How would we use the matrix in functional medicine to actually define the triggering points in a patient that might mediate what is ultimately seen as the cause of erythromelalgia and manage the symptoms associated with this condition?.

A Simple Approach to a Complex Syndrome?

With that in mind, let's go back to the patient that came to the Functional Medicine Research Center. She had a complex disease, but the treatment approach for the patient was actually quite simple. She was placed on a gluten-free diet to lower any potential immune stimulation. She was given a variety of low-antigen foods that were minimally processed. She was administered a mixture of EPA-DHA at about 6 grams per day, which provided about one-and-a-half grams of EPA. She was administered an anti-inflammatory medical food that has specific anti-inflammatory and immune-modulating phytochemicals/phytonutrients. Lastly, she was given a natural anti-inflammatory nutraceutical that contained selenium, zinc, and vitamin D.

You might think this particular treatment approach is too simple and too benign to really have an impact on such a very severe type of autoimmune disorder. The outcome of this story is very positive. Over the course of three to four months on this 'very simple' program, without any additional medications, the woman was able to lower, and ultimately reduce to zero the majority of the polypharmacy that she was taking, while improving her function throughout the whole treatment regime. At the end of three months, she was wearing shoes, walking through the mall, and standing up with little pain; the redness in her extremities was absent.

Here was a case of a complex disease and yet the treatment program was very simple. In this case, modifying the environment-the context of healing that was unique to the needs of this patient. We felt that gluten in this patient's diet was one of the precipitating factors of her illness. Prior to coming to the Functional Medicine Research Center, no one had ever asked this patient about her diet or her gut function. By appropriately balancing her environment through these dietary modifications and

augmentation of nutrients, the outcome was dramatic: lowering the signals that are associated with activation of inflammatory autoimmune responses and increasing immune regulation.

We have talked about gut function so many times in *Functional Medicine Update*, but we can really never say too much about this area. We know that the gut microbiota is a very important factor in energy regulation in the body. The gut is the second brain (as was described by Dr. Gershon in his remarkable book of that name) and signals through various trophic factors and hormones, through both the immune system and through systemic circulation. The gut influences activities in the rest of the body related to appetite, oxidative chemistry, anti-inflammation and/or proinflammatory cytokines, and trophic molecules that can enhance immune function.

Recently, Dr. George Wolf, from the University of California at Berkeley, authored a very interesting critical review on gut microbiota.⁶ In the article, Dr. Wolf says that if we really want to look at the role that intestinal bacteria play in immune function and in overall energy regulation, i.e. fat deposition, we only need to look at germ-free mice because they have no bacteria. These gnotobiotic animals have a very different response to diet in terms of increased body fat deposition. If we start modifying our gut flora, we can have a very dramatic change in the way our energy economy is managed by the body. It is hard to believe that gut bacteria can influence our appetite and our energy economy and regulation, but that is what is emerging from this work.

If we look at studies with *Lactobacillus acidophilus* and bifidobacteria supplementation we find a variety of interesting reports. One study looked at the role of oral pretreatment with lactobacilli and bifidobacteria to improve the efficacy of quadruple therapy in eradicating residual *Helicobacter pylori* infection. This study was performed with patients who had failed triple therapy alone. By administering triple therapy with probiotic supplementation, researchers found a significant decrease in *H. pylori* loads despite antimicrobial resistance, thus improving the efficacy of quadruple therapy in eradicating the residual *H. pylori* infection. This was work that was done at the Department of Internal Medicine at the Institute for Public Health at the Imperial Medical College in Taiwan and was published in the *American Journal of Clinical Nutrition*.⁷

We know that probiotics have a very powerful immuno-modulating effect, and they can be very useful for balancing TH1 and TH2 immunological systems. In a *Nutrition Reviews* article titled 'Probiotics: immunomodulation and evaluation of safety and efficacy,' authors Janine Ezendam and Henk van Loveren say that if a person has an imbalanced immunological system-autoimmunity or atopic disorders-the use of specific probiotic supplements can help to modulate immune system function by using the gut as a signaling agent to the rest of the body's immune system.⁸ These immunomodulatory effects of friendly bacteria may play an important role in helping to regulate immune function. Again, this leads to the concept of specific types of probiotic supplementation to regulate specific types of immune function, and that is certainly a theme that is starting to emerge in nutritional therapeutics.

We know that bifidogenic factors show promise for treatment of active ulcerative colitis. There are a number of clinical trials that have been published recently on this, one of which is found in the journal *Nutrition* in 2006.⁹ We are starting to witness dramatic opportunities for improved outcomes in patients with ulcerative colitis using probiotic supplementation.

It is also recognized that the use of probiotics is often amplified in clinical effectiveness when administered simultaneously with prebiotic substances. These are substrates that preferentially support symbiotic bacteria at the expense of starving the parasitic bacteria. These prebiotics then are substrates that are selectively fermented (or used as food) by the friendly bacteria. A recent paper that appeared in *Nutrition Reviews* is titled, 'A Prebiotic Substance Persistently Enhances Intestinal Calcium Absorption and Increases Bone Mineralization in Young Adolescents.'¹⁰ This article described the use of substances that are fermented by friendly bacteria and also improve calcium absorption and bone mineralization.

I have talked about gut-immune function associated with enteric bacteria, and the effects this has on systemic immunity. I have talked about calcium mobilization. I have talked about vitamin D chemistry that goes on within the gut mucosal system that is activated by specific bacteria. These are all very important therapeutic tools in setting up the context of healing. If the gut bacterial flora are not appropriately composed to modulate immune system function, then the individual may have an ongoing immunological imbalance that triggers systemic effects. We are starting to recognize that gut function is one important arm of the therapeutic opportunity in managing these inflammatory processes.

This is why in functional medicine we constantly emphasize the 4R Program, which is our gut restoration algorithm. The first 'R' is remove the offending agents-the toxins, the allergens, etc.; the second 'R' is replace (where necessary) stomach acid through betaine hydrochloride or hydrochloric acid or pancreatic enzymes (if the person is pancreatic enzyme insufficient); the third 'R' is the reinoculate phase, which is the use of the prebiotics and probiotics to stimulate proper enteric bacterial species and to normalize gut immune function; and the fourth 'R' is the repair phase, which is to add nutrients that are needed for proper gut mucosal repair (L-glutamine, arginine, zinc in a non-irritating form, pantothenic acid, vitamin E-these are all agents that support gut tissue and repair).

The Reappearance of β -Glucans in Grains

When I talk about prebiotics, I want to emphasize that this concept of nondigestible carbohydrates that are substrates for the fermentation of friendly bacteria is a very important part of getting the most out of the third 'R,' the reinoculate phase. An interesting article that just appeared in *Science* magazine talks about β -glucans-a 'dietician's delight.'¹¹ In this paper, the authors point out that β -glucans in grains have been historically considered to be the bane of brewers because they do not allow proper fermentation of beer. They have often been selected out by plant breeding, resulting in lower β -glucan content in certain grain products. We know that barley grain has historically contained β -glucans, but it has been genetically selected to lower the β -glucan content. Now people are beginning to recognize the importance of β -glucans as prebiotics, and so there is a trend toward going back to genetically hybridized grains to form specific types of high-glucan-containing grains for therapeutic application, such as improving gut fermentation and proper bacterial proliferation.

Inducing Higher Levels of Equol Production

When you have the proper bacteria in your gut, it helps in the secondary metabolism of various types of phytochemicals in food, such as soy isoflavones, which are converted by favorable bacteria into secondary substances like equol. Equol, we know, is very important as a hormone modulator-as an estrogen regulator in women-and is associated with lowered incidence of breast cancer and other estrogen-related cancers. In a recent interesting paper that was published in the journal *Nutrition*, a group of investigators from Ghent University, headed by Dr. Willy Verstraete (head of the department in the medical microbiology area), found a mixture of bacteria that can convert isoflavones into equol.¹² We are

starting to see that it might be possible to stimulate proper gastrointestinal microbial ecology to induce higher formation of these secondary metabolites from phytochemicals, which then may have a favorable effect on hormone modulation. This has been a long-standing question, and I think that Dr. Verstraete's work will help us to actually start to develop a specific microbial culture that can induce higher levels of equol formation in women and/or men who are low-equol producers. This may help us to understand more about the interrelationship between soy intake and breast cancer.

A Meta-analysis of Soy Intake and Breast Cancer Risk

Women may have differing effects to a soy-based diet depending upon their individual gut flora and how it converts the isoflavones into estrogen-modulating substances. In reviewing soy intake and breast cancer risk a paper in the *Journal of the National Cancer Institute* reports results from a meta-analysis that used many studies performed from 1978 to 2004, including 18 epidemiological studies, 12 case-controlled studies, and 6 cohort (or nested case-controlled) studies.¹³ The authors came to the conclusion that soy intake is associated with a modest reduction in breast cancer risk.

We now come back to where I started this whole discussion-the little poem talking about the best six doctors anywhere (sunshine, water, rest, air, exercise, and diet). From that, let's talk about the concept of humor and laughter in medicine, another contextual aspect that is associated with the optimal healing environment.

In this issue of *Functional Medicine Update* we want to talk about a concept that does not receive much attention in medicine (and certainly not in traditional medical education). But this concept can be a powerful tool. It was first brought to my attention by the book, *Anatomy of an Illness*, written by Norman Cousins.

Many years ago, back in the late 70's or early 80's, Dr. Cousins, at UCLA, got us thinking about his own personal experience with healing from a very serious, chronic, life-threatening illness. He rented versions of *The Three Stooges* and *Laurel and Hardy*, and watched these laugh-filled comedies of a slapstick nature while he was in the throws of a very serious crisis situation (life-threatening). He recovered (he had a 'spontaneous remission'), and he later talked about how important humor and laughter is as a therapeutic tool in medicine.

Humor Can Reduce Tension and Create Connections

Since then, many investigators have been looking at humor as a tool or a technique that enhances the healing experience. Rachel Sobel, who is a fourth-year medical student, just recently authored an article in *The New England Journal of Medicine* titled, 'Does laughter make good medicine-'¹⁴ In the article, she discusses her experience as a UCSF medical student, working at the Moffit-Long Hospital in the bay area of California, and talks about how humor breaks pressure, stress, and tension, and creates the space for clarity and for improving the connection between the doctor and the patient at times when things are 'very serious.'

The doctor may be sleep-deprived and working under multiple demands; there is a sense of overload. By bringing in humor as a clear beacon, there is suddenly a space to reconnect to the purpose, and to be involved in a process of reestablishing the context of healing for the patient and for the doctor

'Why in those few seconds of juvenile hilarity did I not feel an ounce of guilt-' she questions in this

article. 'Perhaps it was simply that being with a group of other medical 'professionals' made it seem okay. Or maybe it was justified because laughing brought us together as a team in an important bonding moment, which would ultimately benefit our patients. Or perhaps laughing was less about making fun of patients and more about coping, finding humor in a day filled with suffering.' You need to find those oases to create the context for the healing experience.

Humor is a very important part of the process of developing a style by which one can find a path of enlightenment, and maybe even the opportunity for a learning experience that opens the door to healing and recovery. Healing may be-in the broadest sense of the term-more than just getting over the disease; maybe it is feeling good about where that person is.

The Science of Laughter: A Variety of Clinical Studies and Articles

When we go back and look at the history of the science of laughter and its relationship to medicine, we are reminded that there are many very interesting studies that have been published. In the journal, *Oncologist*, in 2005, an article was published titled, 'Laughter: the best medicine-' which talked about the application of laughter, even in the field of oncology.¹⁵ We might think that in cancer treatment (being one of the most serious and moribund types of disciplines, with gravity of the situation being present at all times) humor can build the connection between the caregiver, patient, and family. However, as they point out in this article, insensitive joking is offensive and distressing, and therefore you have to find the right way to use humor in the context of healing-one that allows for it to be a positive rather than a negative force.

There are other review articles on this subject. 'Laughter really is the best medicine: the use of humour in therapy,' was published in the journal, *Perspectives* in the spring of 2005.¹⁶ There is a series of articles that go back to 2000, 2001, and 2002 on laughter and medicine and how humor can help the patient heal, including publications in the *Mayo Clinic Womens Healthsource* in 1999.¹⁷ I was very interested to find an article in the *Nursing Journal of India* in 2003 that is titled, 'Laughter is the best medicine: the value of humour in current nursing practice.'¹⁸ And in the *Journal of Oncology* in 2005, 'Humor and oncology,' and how, again, cancer therapy, being this very serious business, may be contextualized in a different way by bringing humor appropriately into the relationship of the clinic.¹⁹ It is interesting to note that the *Tennessee Medical Journal* actually has had articles on the use of humor and laughter in medicine going back almost 25 years.²⁰

Nursing, oncology, cardiology, internal medicine-there are articles in all of these areas. There is even an interesting article in *Australian Family Physician* from 2001 titled, 'Happiness and humour: a medical perspective,' in which the author, at the Monash Institute of Public Health, Faculty of Medicine at Monash University in Victoria, talks about how the medical profession's focus on dealing with negative mental states has led to the suggestion of classifying happiness as a major affective disorder.²¹ Maybe what we need to do is recast this to demonstrate that happiness and laughter during conditions of illness is a desirable attribute to bring into the healing process and even into the therapeutic encounter with the patient. The author goes on to say that epidemiological data suggests that happiness is related to personality factors such as high self esteem, feelings of personal control, and is a very important part of mounting an appropriate immune response. Recapturing the optimistic enchantment with life that is part of our childhood may be a key to happiness and health, even in patients who have disease. These are very interesting concepts that I think fit into trying to define the status of an optimal healing environment.

As we go through this discussion, we are very touched with the fact that there are some individuals in the field who have been the standard bearers for bringing laughter and humor into medicine. One is Dr. Patch Adams at the Gesundheit! Institute, and also the extraordinary work of Dr. Neil Shulman, who is our clinician of the month. Dr. Shulman, a medical school professor at Emory University School of Medicine, has been involved in finding ways to bring humor and laughter into health care in a positive way to contextualize the healing process. I think when you hear from Dr. Shulman about his experiences, you will find that this is another tool, another technique, another skill that we can actually learn. Many of us don't think of ourselves as comedians, but yet we might have that sense of knowing when the comedic moment is present. It can help to break down barriers and reconnect the patient to their healing process.

Is Humor Applied Biochemistry at the Whole-organism Level?

Those who have been listening to *Functional Medicine Update* for many years may wonder why we are talking about humor when we have so heavily focused on biochemistry, but the affective influence of disease on behavior, which ultimately then influences immune-system function and the healing process, is, in some way, applied biochemistry at the whole-organism level. I think we are dealing with things that really can make differences. I think it is appropriate to talk about laughter and humor and how we contextualize it, how we integrate it within medical practice, and how it can become part of the skill-building bag of tools that we have to help in patient management. With that in mind, let's move to the interview with our clinician of the month.

INTERVIEW TRANSCRIPT

Clinician/Researcher of the Month

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JB: Once again we are here at that portion of Functional Medicine Update that I am always excited to engage in because we have the privilege of talking with some of the most remarkable creative thinkers-people who are really creating change in health care. That is the case in this issue with our guest, Dr. Neil Shulman.

Dr. Shulman-on the pedigree, you might say-sounds like a very diligent professional in the medical research area: associate professor of medicine at Emory University School of Medicine, 20-plus years of experience in the cardiovascular/hypertension area of research, and multiple publications (over 50 of them in this area). He was co-investigator of an eight-million-dollar study in NIH-funded cardiovascular clinical research. But when you go a little bit deeper, you find that Dr. Shulman is a remarkable person to have developed a concept from his own experiences (that he will discuss), which is to bring humor into medicine. Dr. Shulman is a comedian, par excellence; he is an author, and has written extensively in the area of medical humor. I have had the privilege of reading a couple of his books. Dr. Shulman was principally responsible for writing the movie, *Doc Hollywood*, which starred Michael J. Fox. You may recall that this humorous movie was about a doctor who was going to go seek his fame and fortune as a cosmetic surgeon in California, but got waylaid along the way in rural America, and decided maybe that was where he wanted to stay. It was a very humorous-but also very poignant-story that came from the ideas and pen of Dr. Shulman.

In the context of what we are discussing in this issue of Functional Medicine Update, which is the optimal healing environment as it relates to humor, I can think of no one better than Dr. Shulman to represent this concept. Dr. Shulman, we welcome you to Functional Medicine Update. I guess the first question that everyone probably asks you is, how did a medical researcher/academic clinician get to where you are today?

NS: I was giving a lecture on blood pressure some place in the world, and I heard somebody snoring, and it was me. I decided I should change my course a little bit. Seriously, I was always blessed to have a lot of humor around me as I was growing up. My parents both had a great sense of humor. My grandmother was very funny. She was a matchmaker; she had come over from Belarus in 1905. So, it was being around a lot of humor, and I think the other thing was that I was a klutz growing up. I couldn't throw a baseball very well, and kids would laugh at me when I was five-, six-, seven-, eight-years old, and it made me very self-conscious. And then one day it just dawned on me: whether they are laughing at me or with me makes no difference-I'm making them happy. When I went on stage and did comedy, I was still the same klutz, but people actually paid to laugh at me.

JB: I have that same thing except mine isn't considered humor. It is considered seriousness, but I still get that laughter, so I can appreciate this.

NS: There's nothing like exploiting your own disabilities. I've got plenty to exploit.

Humor as a Teaching Mechanism

JB: I read one of your recent books, 101 Ways to Know if You're a Medical Services Professional. I thought it contained some great insights. You have used humor as a remarkable tool for introspection and for self-evaluation in a non-threatening way. Can you tell us a little bit about how humor comes to be a teaching mechanism and how you contextualize it? I think you do it in a very interesting way.

NS: In the teaching arena, you've got one person who is supposed to be sort of the know-it-all and the other person who is supposed to be learning from the know-it-all. That can be pretty intimidating. No matter what the topic, whoever you are talking to might have unique or interesting insights that can be valuable, that you haven't thought about. I think when we're talking about humor and using it in that process of teaching, it makes that person who is learning more comfortable (particularly if it is the appropriate type of humor), and more receptive to what you are saying and not putting you on a pedestal, but seeing you as another human being. Then they open up more, and you can learn from them. I think, for instance, any time you create something, you don't know what you create until you get responses from people. It is the same in teaching-you don't know what you're teaching until you hear back, and you want to make the other person comfortable.

JB: I notice that in your book-I think it may be your most recent book-Your Body, Your Health, Jane Fonda wrote a very glowing forward. I worked with Jane, myself, a number of years ago and I have a great admiration and respect for her. She obviously was touched by the way that you are contextualizing your information and motivating people to change. What was the nature of the relationship you had with her?

NS: I first met Jane Fonda when I was performing for a comedic fundraiser. It had to do with eating disorders, actually-a fundraiser for an organization dealing with that issue. She was the co-host with me

and we hit it off. After that, we got together for a number of other activities that had a humorous slant. I did a comedy performance called 'What's in a Doctor's Bag-' with the instruments in a doctor's bag-Otis the otoscope, Lubb and Dubba, Ms. Kneeknocker-for her grandson at a birthday party. Then we went and did a bunch of other similar types of activities.

Dr. Patch Adams and the Gesundheit! Institute

JB: When you originally met Patch Adams-I know you have had some engagement with the Gesundheit! Institute and I've also known Patch for probably 20 years, as well-you two must have hit it off very quickly, sharing a common view of how humor can be brought into healing.

NS: Yes. Patch actually called me when he had just spent time with Robin Williams doing clowning at a hospital. It was before they shot the movie, Patch Adams, but Robin was getting a flavor of Patch, and then Patch called me and said this movie was going to be coming out and he was wondering what my experience was because I had a movie come out and I was a doctor involved in humor. I gave him some insight and then I said, 'Patch, why don't you come down to Atlanta and let's do a fundraiser for Gesundheit!, your nonprofit, on the coattails of the promotion of the movie when it's about to come out?' He agreed to do that, and we had about 1500 people at Symphony Hall in Atlanta, and we did the real Doc Hollywood and the real Patch Adams. We then did a number of other events in Atlanta, and we were able to write him a check for seventy-five or eighty thousand dollars for his nonprofit and he called back and asked if I would be on his Board. I ended up getting on his Board of Directors and now I'm President of the Gesundheit! Institute. I think Patch has a really good message and we've connected a lot, and we've done other humorous performances around the country, as well as workshops on humor and health.

Doc Hollywood

JB: Tell us a little bit about the Doc Hollywood experience. That sounds like a fascinating chapter. It is one of-I think-the great medical comedies. It really has, as I said, a very poignant underlying message. How was it working with Michael J. Fox and what response did you get to the movie, not just from an entertainment value, but also from kind of an 'aha' experience?

NS: The experience was great. I got some great help and collaboration from somebody who is recognized in the book, Carl Hiaasen (Carl has a movie coming out on a book of his own called Hoot in the next couple of weeks). That book, which was originally called, What Dead...Again?, became Doc Hollywood ten years after it was published. Michael J. Fox was absolutely delightful to work with on that project. I was associate producer, so I worked with the screenwriters. There were lots of different screenwriters until Michael agreed to the final script. When we were shooting in Okeechobee, Florida, it was Thanksgiving time and there were a bunch of homeless people around. Michael just took money out of his pocket and threw a big party for Thanksgiving for the homeless people there. He is a really wonderful caring individual; unfortunately that is when he found out he had Parkinson's.

Saluting Healthcare Providers in Underserved Areas

One of my hopes with the movie, Doc Hollywood, is that it had impact on drawing attention to the issue of shortages of doctors and saluting the doctors who do work in underserved areas. There is actually a 'Doc Hollywood Day' that is starting. You can go to www.dochollywodday.com. The president of the Indiana Rural Healthcare Association is starting this and hopefully there will be a national day that doctors and nurses and other healthcare providers in underserved areas can be saluted for their work-maybe put apple pies at their front doors and have parades and put them on floats and tell them we're glad

they are practicing where they are needed.

As for the experience of actually making the movie, Hollywood is a really interesting place; there are a lot of interesting characters who I became friends with. I got a lot of experience which then led to me independently co-directing a movie that I actually acted in that we've just finished called Who Nose- It is sort of a reality comedy about a desperate man looking for a life, and I play that desperate man.

JB: Well, we can hardly wait to see the 'desperatism;' it sounds exciting. It is a legacy of our lives, right, that we don't often know-in fact maybe we never know-exactly where the journey will take us. We may have a premonition, but then it unfolds. Through this remarkable history-this journey-how have you seen humor (in the way that you have described it through your medical allegories and metaphors) integrating itself into healthcare? Do you have any sense that people are starting to see this as a tool and that there are places where it can be introduced, contextually, within medicine in an appropriate way? Or in health care?

Helping People Through Laughter

NS: Absolutely. There is a guy who has dedicated his life to that very issue named Steve Wilson. He went over to India and met a doctor who used to get together every week with his patients and tell jokes. And then eventually they ran out of jokes, so they just started laughing. Steve Wilson came back to the US and started this laughter club, and he goes all over the country certifying people in becoming laughter leaders. They do all sorts of laughter-with people who are disabled, people in nursing homes, Alzheimer's patients, and then just everyday people to help them. I wrote a paper-sort of a review article-with Zoe Haugo, on the area of the science and practice of humor, and there is a lot that has been published: studies looking at the immune system, looking at improvement of the cardiovascular system, the psychologically positive impact of humor.

Incorporating Humor into Curriculum

Unfortunately, the resources to get humor taught in medical schools as a serious topic is very difficult and that is because medical education is very much driven by money, sometimes money that is tied to patented products. If you have a patented product, you can sell it at a premium price and use that extra money to give grants to medical schools and get professors to do additional research on that particular product, whether it be a pharmaceutical drug or some device. You can have a tremendous number of detail reps going and knocking on the doors of doctors, giving out brochures and having dinners and events and so forth. If you don't have a patented product and you are just trying to promote the humor, you are not going to have anything-anything-like those resources. So, even though it may be very helpful-and free, you can laugh for free-it is going to be very hard to get an established curriculum. The only place I know of was Washington University in St. Louis where they had month-long rotation in pediatrics in humor and clowning for the residents.

I lecture a lot on humor, in a hopefully humorous way; I was just at the University of South Florida for the Dean's Lecture Series and I just did it at Emory for the Department of Internal Medicine residents, medical students, and faculty. Intermittently, I have even gone to medical school graduations where I addressed the issue of humor, but I do it in a humorous way so it is sort of like a stand-up comedy act. I got up at Oklahoma, at the medical school there, a couple of years ago, and I said, 'This is going to be the longest graduation speech known to mankind.' There were 3000 people in the audience and they started booing and hissing. And then I said, 'I'm just fooling. It's the shortest.' I sat down and got a standing ovation. I did get back up.

Humor is something I think should be incorporated not only into medical school education, but into the education all health providers, nurses, and physicians' assistants. It should be incorporated into primary and secondary school. I think that humor is a serious enough matter, and just like reading, writing, and arithmetic, it should be part of education. It is very, very important. In my opinion, life is the dash between two numbers on a tombstone. You should enjoy your dash and help others enjoy it. We all won the lottery-it takes 250 million sperm to fertilize an egg and we are all winning sperm. If you are a winning sperm, you get a dash-why not enjoy it? And why shouldn't enjoying it be considered an integrated part of the processes of education?

We are the only animal creatures I know of that laugh. We have this wonderful ability to laugh, and I think we have to exploit it. Kids, up to the age of puberty, laugh maybe 20, 30, 40 times a day. But adults only laugh maybe 5 or 6 times a day. I think before puberty the whole human race enjoys laughter and spontaneity. It does seem to come back around after menopause. I think before puberty you have a good time because you don't know any better and after menopause you have a good time because you don't care anymore.

Engaging Laughter in Alzheimer's Patients

JB: You said something that I want to pick up on that I thought was quite insightful. I know you do a lot of work with older-age segments in various types of environments like nursing homes and care centers. You mentioned that in Alzheimer's patients you can engage laughter, and often we have this stereotype that humor and laughter are high-cerebral functions and that people who may have some cognitive dysfunction can't laugh. I'd like to come back and revisit that with you. Do you have experience with Alzheimer's patients who can see humor and can engage in laughter?

NS: Yes. I was medical director of a nursing home for about 23 years, but I really didn't understand Alzheimer's until my mother got it. I remember in the early stages I brought her this big bouquet of flowers. She lived in Washington, DC and I lived in Atlanta, and I'd go home and visit intermittently and I brought her this big bouquet of flowers. She got all excited and gave me all these kisses. I came back two minutes later with the same flowers, did the whole thing again, and she was really excited. And I said, 'Mom, I only have to buy these flowers once, but I get credit five times.' She laughed, and we laughed about it. That was in the early stages, but in the latter part of her life, when the disease was really difficult and she was very agitated and wasn't communicating much at all, if you got really close to her and just started laughing, it was like everything disappeared and she would just start laughing and it was magic.

There are other things with Alzheimer's patients-hugging them, for example. I did go and do humorous performances for Alzheimer's patients and also for some fundraisers for Alzheimer's. With the Alzheimer's patients, I found that they responded very well, but more to the slapstick sort of thing. There are all kinds of humor, and slapstick humor was one that they could enjoy and appreciate more, and that is also the type of humor that little kids seem to enjoy the most-2-, 3-, 4-, 5-year-olds. When I perform with them I am Dr. Neil, the banana peel; they like that much more than the real Doc Hollywood.

JB: Can you actually engage humor into healing by projecting humor to patients so that it becomes infectious in their own response? In other words, do you have to be more assertive about getting humor into the relationship so they'll imprint that or can you subtly encourage humor and laughter in that individual?

NS: The safest humor for me is self-deprecating-when you make fun of yourself-because you're not making fun of somebody else, and then they laugh and then they see you as not being this person on a pedestal, but somebody who is connecting with them as a friend. With patients I find that is the case. I had a doctor once who said he did not want to just walk in a room and have the patient be intimidated by his white coat and stethoscope, but he didn't feel he was a funny person. So what he did was he started telling his patients that he was giving them a homework assignment: every time they were to see him they were to bring a joke. He did this so he could set up some humorous rapport. But he said that people started canceling their appointments because they didn't have jokes...

JB: So he needed to have some jokes in the waiting room that he could give them in case of an emergency...

Laughing at Yourself

NS: That's right! I have found that some of the best humor comes from real life experiences and, particularly, when you have had embarrassing moments. I was once in front of 250 cardiologists and I was trying to get them to loosen up and I said, 'I'd like one cardiologist to come up and tell me the most embarrassing thing that ever happened to you.' So they were sort of an uptight group and this guy comes up and he says, 'Well, I was examining a woman who had a lump in her breast and I thought it was totally benign, but I wanted to explain to her husband what was going on. So I went out to the waiting room, got this gentleman, brought him into the examining room, where the woman was lying on the examining table. I took his hand and put it on the woman's normal breast. I moved it around and said, 'This is a normal breast.' Then I took his hand and put it on the other breast and moved it around and said, 'This is the lump, do you understand now-' And the gentleman said, 'Yes, I do, but this is not my wife.' He had gotten the wrong man. The woman thought it was another doctor. She did calm him down and the doctor did make it through the visit. I find that in times of stress, if you can rewire your brain by throwing in some humor, either for yourself or if you are in an argument with somebody, just throw in some humor and get things rerouted.

Humor and Professionalism: Finding the Right Balance

JB: Let me ask one last question because your experiences are remarkable. I think a lot of doctors feel that if they brought humor into their practice it might lower their professionalism and create a lack of confidence in their patients. Could you speak to that? I think that is one of the reservations that many docs have about showing their personalities. They have been trained to have this austere demeanor that connotes-supposedly-professionalism.

NS: You want people, obviously, to have confidence in you. But I haven't found that confidence is associated with somebody feeling as though you are on a pedestal. Frequently you are thought to be egocentric if you are standoffish. Obviously, you want to be honest with patients about what you know and what you don't know. I think you want them to see you as a human being who has flaws, but you are self-critical about those flaws. I think most of the population is smart enough to realize nobody is perfect.

I was once on a plane, sitting next to a pilot, and he said, 'Doctors are just like pilots. If we make mistakes, we can lose a lot of lives.' I said, 'There's a big difference. A doctor is not on a plane.' I think the patients know that. I will say, by the way, we have a website, which is www.neilshulman.com, and on that website there are links to other websites that have humorous things, like the spots we're doing on public TV now. There is a program called 'Second Wind Dreams' to give wishes to people in nursing

homes. And there are also some serious things, like warning signs of disease for consumers. There is a lot of stuff there to demystify medicine that might be useful or helpful for people in this area who have interest in that.

JB: Dr. Shulman, I want to thank you. I think you've given us some really important messages about the optimal healing environment and bringing humor and laughter into that environment and making it joyful. As you said, this experience we have is fairly short. All of us will ultimately encounter health challenges, sometime throughout this process, and somehow finding the levity that is associated with this unknown experience called life puts it in the proper context, and, as you said, can activate that immune system in a very positive way. In terms of contextual healing, this is a pretty good therapy. I really thank you for helping us to understand that.

NS: I really enjoyed this conversation a lot. I will say that I think life does have three phases. The first part of life, you follow grades so you will do well; the second part of life, you follow money so you will make a living; and the third you follow doctors, so you can stay alive.

JB: And hopefully you can have some laughter with them through the process and create a good outcome. Thanks a million and we wish you the best and keep spreading the message.

NS: Thanks a lot. This was really fun.

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