May 2005 Issue | Mehmet C. Oz, MD New York Presbyterian Hospital Columbia University

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Recently, in *The New England Journal of Medicine*, there was an article that discussed health care in the 21st century.[6] This was Dr. William Frist's Shattuck Lecture that was quite remarkable, particularly in the context of what Dr. Oz shared with us. Dr. Frist states:

"I would like you to meet a patient from the year 2015. He lives in a world in which years ago America's leaders made tough but wise decisions. They built on the best aspects of American health care and unleashed the creative power of the competitively driven marketplace. These changes resulted in dramatic improvements to the U.S. health care system-lower costs higher quality, greater efficiency, and better access to care."

This is an interesting perspective as to what we might see as we move forward from the lessons of the late 20th century. This lecture is based on work Dr. Frist has done in the area of health care in his role as Senate Majority Leader. He has both a physician's role and a legislative role. He believes that the high quality, rich information and common-sense efficiency inherent in the care of patients in 2015 are all within our grasp. He sees the medicine of the future being built upon a web-based mentality that will include much better access to medical information. He states:

"Today, however, we are saddled with glaring inefficiencies, high and rapidly rising health care costs, growing ranks of the uninsured, chasms in quality, and health care disparities. Health care spending in the United States is the highest of any industrialized country, making up nearly 15 percent of our gross domestic product. Today's average premium for an insurance policy for a family-$9,086 a year and rising-represents 21 percent of the national median household income of $42,409. We spend approximately $5,540 per person per year on health care in the United States."

There are some certainly some encouraging things that have come out of the application of medicine over the last 100 years. Remarkably, life expectancy has increased from 47 to 77 years of age. However, that is slightly skewed on the basis of lowered incidence of infant mortality. When infant mortality is reduced, the median average life expectancy is greatly increased. Nonetheless, we must take heed and give remarkable thanks for that improvement. Dr. Frist continues:

"Yet there are troubling signs that we are not getting a good return on our investment. We have uneven access to care, with the number of uninsured people climbing annually, most recently to about 45 million. The overall quality of care in the United States is not what it should be, especially in light of how much

we spend. According to a recent RAND study, Americans-even in the best of circumstances-receive only about 55 percent of the recommended care for a variety of common conditions.

"Although we have made massive investments in medical research, we clearly have underinvested in the research and infrastructure necessary to translate basic research into results."

This certainly applies to the chronically ill patient. As we have said in previous issues of FMU, these patients constitute about 78 percent of healthcare expenditures.

"For example, it takes our physicians an average of 17 years to adopt widely the findings from basic research. The health care sector invests dramatically less-some 50 percent less-in information technology than any other major sector of our economy."

Dr. Frist asks what we might focus on to make this view of a patient in the year 2015 become a reality. He says that first, we should focus on patient-centered health care. "The focus of the 21st-century health care system must be the patient." This has been a theme, a condition, and a primary under-riding principle of the Institute for Functional Medicine since its inception in 1991.

Secondly, Dr. Frist says we should allow the healthcare system to be consumer-driven and allow more consumer voice to be present in the decisions we make about procedures and therapies, and engage the patient more in the understanding of what they are getting for the money they are paying.

Third, we should make the healthcare delivery system more provider-friendly so that in the transformed healthcare system, we reestablish and promote the value of the doctor/patient relationship and get the third-party provider out of the exam room, which interferes with the sanctity of the relationship between the provider and the patient.

Fourth, Dr. Frist says we should go to universal electronic health records in order to capture information about a patient longitudinally so that over time, we have the information to paint a mosaic, or a picture of the individual's trajectory of health, rather than trying to make decisions on the run based on a specific crisis or incident. These people come with a history which is translated into their therapy and medical needs.

Next, he talks about healthcare coverage for children and low-income Americans, and making health care affordable by increasing personal responsibility, allowing people to know what their options are, stimulating them, encouraging them to participate in their own therapies, and providing therapies they can actually do something about. Rather than prescription dosing regimens, we need to look at lifestyle interventions, environmental changes, nutrition, and exercise programs. As this moves forward, Dr. Frist says we should be focusing on the security of long-term care. As people age, they suffer from more illness. We are more and more concerned about how the baby-boomer population will have proper care delivered at a time of economic deficiency. We can already see that starting to happen as it relates to the reframing of the Medicare system.

Last, we need to translate science into actual, palpable and demonstrable evidence-based cures.

"During the last decade, the practice of medicine will change dramatically through genetically based

diagnostic tests and personalized, targeted pharmacologic treatments that will enable a move beyond prevention to preemptive strategies."

I like that concept. I call it "personalized preventive medicine." Dr. Frist refers to it as "preemptive strategies" to personalize to the needs of the individual and prevent the need for high-technology and expensive intervention later on. You can see from Dr. Frist's Shattuck Lecture and his view of health care in the 21st century, that these have been the underlying principles of functional medicine since its inception, and they have also been part of this tape series for the past 20 years.

We are seeing an increased global burden of various types of chronic, degenerative, age-related diseases that, with the increasing demographic shift or transition of the population to older age, is putting a tremendous financial burden on the system. Hypertension is one of those diseases, as well as cardiovascular disease (CVD) and cancer. For the remainder of this month's FMU, I would like to focus on the cardiology connection that Dr. Oz so eloquently discussed, and move from that into type 2 diabetes and its implications for heart disease and cancer. Last, I would like to share a few thoughts on the malignant or oncogenic potential that results from some of the things that are occurring. That leads to a different frontier of how we might deliver the patient-centered medicine of 2015.

If we look at the global burden of hypertension as a marker for these major disease trends, we are taken with articles such as one that appeared recently in the *Lancet*, talking specifically about the global burden of hypertension from a worldwide perspective.[7] Overall, we are going to see an estimated total number of adults with hypertension increasing from 972,000,000 in the year 2000, to over 1.56 billion people by the year 2025, a nearly 60 percent increase. Delivering medical services to that need around what would be considered pharmacotherapy is a tremendous financial burden, not to mention the management issues related to patient visits with their physicians. This leads us into looking at what might be some of the lower technology, functional ways of approaching this problem.

Dietary Impact on Hypertension

I am talking about the delivery of functional medicine to major issues of chronic health management in the area of vascular disorders, which leads to how we might manage hypertension more effectively in its pandemic stage of growth. That takes us back to the DASH study and dietary approaches to the treatment and prevention of hypertension. The results of that study, which we shared with you in a number of previous issues of FMU, indicated that a diet higher in unrefined, complex carbohydrates, such as those found in fruits, vegetables, and whole grains, lower in refined animal products (which add saturated fat) and vegetable oils that have been altered by partial hydrogenation, as well as in salt and simple sugars, significantly reduced the incidence of hypertension. In many people, the effects on systolic and diastolic blood pressure can be comparable to those that would be achieved with a first-generation, antihypertensive drug, or a stage-1 antihypertensive drug, but would not involve the same risks to adverse side effects.

Folate Intake and Hypertension

Part of the story that is an interesting variation on a theme is, if you eat a minimally-processed diet, you are not only getting rid of things you don't want to consume, but you are also getting higher density and intake of things you do want to consume that may have been removed in the highly-processed diet, such as vitamins and minerals. One of the vitamins related to hypertension that has been in the news recently is folic acid. It may not be obvious how folic acid intake could have an effect on vascular tone and function

in the control of blood pressure, but if you have seen the recent paper in the *Journal of the American Medicine Association*, titled Folate Intake and the Risk of Incident Hypertension Among US Women,"[8] you know that folic acid may play a role in the maintenance of vascular tone, which is presumably as a consequence of its secondary effects on vascular smooth muscle reactivity. For example, this may involve nitric oxide (NO) output by the vascular endothelium.

NO, released by the vascular endothelium, is manufactured by way of the conversion of the amino acid arginine into its byproduct citrulline through the enzyme activity of endothelial NO synthase (eNOS). That process is facilitated by a coenzyme called tetrahydrobiopterin. Tetrahydrobiopterin is a substance manufactured in the body as a biopterin molecule, a Pter molecule. The biopterin is ultimately connected to folate chemistry. There is a folate-scavenging, or biopterin-scavenging pathway that requires 5-methyltetrahydrofolate for tetrahydrobiopterin to be synthesized in the body. Folate may play a role through the biosynthetic pathways in the manufacture and control of tetrahydrobiopterin levels, which regulate the activity of eNOS and have an important function in monitoring or controlling vascular smooth muscle tone and blood pressure.

This is not just all speculation coming only from epidemiological associative studies. In intervention trials, high-doses of 5-methyltetrahydrofolate or folic acid were associated with decreased blood pressure and improved vascular reactivity in humans. There is an emerging recognition that nutrients present at higher doses in an unrefined diet may have a favorable effect upon vascular function and blood pressure control beyond that of reducing salt and saturated fats. Many new reasons are likely to emerge over the years to explain how phytochemicals and various nutrients found in a minimally-processed diet have dramatically different effects on vascular function than similar calories in highly processed foods.

Does this relate to genetics? Are we just measuring a genetic susceptibility factor? That is the wild card that is changing the face of medicine that Dr. Frist talks about in his Shattuck Lecture. How will we personalize medicine based on individual characteristics? In the absence of looking at cohorts of reactivity, we may be led to false assumptions looking at the class effect of the group at large. Recently, in *Nature Genetics*, there was an article which discussed the genetic control of disease and whether race matters.[9] In this article, the authors come up with a pretty remarkable concept that there is greater diversity of function at the cellular level among people of any single race than there is between members of different races. We are seeing the end of the concept of race. It may be more important to know your biochemistry than your skin color, eye color, hair color, height, or gender. These are important concepts, because we have often classified individuals just based on age, structure, or gender, not looking at how we would classify them on the basis of their genotypic control of cell function. That is what is described in this article. The authors state:

"Now, a new study reviewing 43 disease-associated gene variants suggests that the effects of gene variants may be largely consistent across different racial' or ethnic' groups."

This leads us to recognize that race or ethnicity is not as important as genotypically-controlled biochemistry. I think Dr. Roger Williams, who developed the theory of genetotrophic disease, published in 1950, would be applauding if he were still with us.

If we look at the takeaways from the model, such as hyperhomocysteinemia and its relationship to vascular disease, not everyone has a polymorphism that requires high doses of B6, B12, folic acid, and

betaine in order to enhance homocysteine metabolism. Individuals who carry certain nucleotide polymorphisms are those who may, therefore, depend on higher levels of these nutrients for proper function. In some cases, if the frequency distributions of these polymorphisms is fairly small, and they are not taken into account in a trial design, their effects may get lost in the "noise" of a randomized, double-blind, placebo-controlled trial, in which one regresses to the mean and is able to define the average results of a population that may be highly stratified and polymorphic.

As we learn about the differences among people at the genotypic, metabolomic, and phenotypic levels, we begin to see that stratification of research to different genotypes might lend different outcome variables for their management. Regarding homocysteine, if a person has the methylenetetrahydrofolate reductase polymorphism, the non-wild type, they may require higher doses of folic acid and B12. However, there may be many other different polymorphisms related to homocysteine metabolism that have different sensitivities. In a study in the *American Journal of Clinical Nutrition,* individuals with trisomy 21 were monitored with respect to homocysteine metabolism and the need for higher levels of nutrient intake relative to improving function in Down syndrome children who may have altered homocysteine metabolism.[10]

The genetic relationships to the major chronic, age-related diseases are being examined. We begin to see that the name of the disease is not as important as understanding the etiology of the disease. It's a little bit like the discussion I just had on race. Perhaps we have seen the end of the term "race"; perhaps we are also seeing the end of the term "disease." It's more important to know the mechanism and the individual characteristics leading to the cluster of signs and symptoms that we call a disease, than being able to name it, assuming that it's an independent variable shared in common by all people that present with those signs and symptoms.

This is taken from an interesting paper on genetic factors in type 2 diabetes that appeared in *Science* magazine. [11] The authors state:

"The intensive search for genetic variants that predispose to type 2 diabetes was launched with optimism, but progress has been slower than was hoped."

It has been assumed that we would find just a few genes that might regulate the function of an individual who would, in the absence of proper regulation, present with the symptoms of type 2 diabetes. However, the more this is evaluated, the more genes are found that interrelate as a family, and that may couple together in their function to give rise to the expression of what we call type 2 diabetes. They start looking at the PPAR gene variants, mitochondrial genome variants, and the insulin signaling genes and their variations. There is tremendous variation in the different types of metabolic principles that cluster together with similar signs and symptoms that we call a disease. The proper treatment for those individuals may, however, be better served by focusing on their individual genetic and metabolomic needs, rather than just on the class of disease management.

As we go from complex to simple, the interesting thing about this, as Dr. Oz stated, is that there is a difference between complexity and making something simple. Simple doesn't mean that you lose all the facts; it means that you make them clear. This is the same as it pertains to the concept of using genomic information. That is what the authors speak about at the beginning of their article, "Genetic Factors and Type 2 Diabetes."

I was talking about type 2 diabetes. One of the genetic families of characteristics that appears to modify insulin sensitivity, giving rise to type 2 diabetes, are those genes found in the mitochondrial genome-extra nuclear DNA that has come principally from our mothers. Mitochondrial dysfunction and its association with type 2 diabetes is ever-increasing. Agents in the environment, drugs, excess alcohol, chemicals, or even radiation that would damage mitochondrial DNA, have been associated in animal and human studies with the onset of insulin resistance, hyperinsulinemia, and type 2 diabetes.

Mitochondrial Dysfunction and Type 2 Diabetes
Perhaps there is a connection between mitochondrial toxicity, mitochondrial energy, or mitochondrial oxidative damage and the relationship of lowered insulin response, lowered bioenergetics, and what we later call type 2 diabetes. This has been well defined in a number of studies and reviews that have been published over the last few years. One you might want to look at is titled, "Mitochondrial Dysfunction in Type 2 Diabetes," that appeared in *Science*magazine.[12] The authors state:

"Maintenance of normal blood glucose levels depends on the complex interplay between the insulin responsiveness of skeletal muscle and liver and glucose-stimulated insulin secretion by the pancreatic β cells. Defects in the former are responsible for insulin resistance, and defects in the latter are responsible for progression to hyperglycemia."

That is where we get the varying forms of metabolic syndrome that finally result in frank type 2 diabetes.

"Emerging evidence supports the potentially unifying hypothesis that both of these prominent features of type 2 diabetes are caused by mitochondrial dysfunction."

That is both the skeletal and liver non-responsiveness to the insulin message, and a loss of function of the endocrine β cells in the pancreas. Agents that would cause destruction of mitochondria in those tissues will contribute to the onset of diabetes.

What could do that? At first level, you could have things like autoantibodies against endocrine glands that could cause damage to tissues. Secondly, you could have chemical injuries, such as in chemically-induced diabetes, such as streptozotocin in animals and many other drugs and chemicals that are injurious to hepatic cells. The most classic example is the medication used to treat acquired immunity deficiency disease syndrome (AIDS), in which there is injury to mitochondrial function, which results in lipodystrophy, type 2 diabetes, and cardiopathy. This is a secondary manifestation of the drug. This may be a time-compressed example of what occurs to people who, over life, continue to be exposed to low-grade mitochondrial toxins, oxidative injury, toxic xenobiotics, toxic stress, molecules such as oxidized catecholamines, and under-nutrition. We need to bring the mitochondrial connection to type 2 diabetes up on the radar screen, and begin to examine how one defends against injury to the liver, skeletal muscle, and the β cells of the pancreas.

Obesity and Type 2 Diabetes
How does obesity play a role in the onset of type 2 diabetes? In the past, we thought that obesity caused diabetes, but there is more and more evidence indicating that the onset of type 2 diabetes occurs through a process that involves altered adipocyte fat cell physiology that leads to accumulation of lipid and hypertrophic adipocytes, ultimately leading to obesity. It may be some underling mechanism that couples the two of them together, and may also connect to endothelial injury, such as from oxidative stress at the

endothelium, and altered arterial cell wall dynamics that we call atherogenesis and cerebrovascular disease. A series of metabolic changes from different genomic signaling connects to many of these age-related disorders.

This is discussed in an article in *Science* magazine, titled "How Obesity Causes Diabetes: Not a Tall Tale."[13] The author states:

"The epidemic of obesity-associated diabetes is a major crisis in modern societies, in which food is plentiful and exercise is optional.

The biological basis of this problem has been explored from evolutionary and mechanistic perspectives."

In an appropriate signaling environment, the adipocyte cell upregulates the expression of inflammatory mediators that cause white cells to stick to the vascular endothelium. Injury to the vascular bed alters endothelial nitric oxide (NO) production, then uncouples NO and produces things like peroxynitrite, which leads to oxidative injury to the vascular bed. All of these are atherogenic risk factors and can be coupled together with certain lipid risk factors, but may be partially independent from those lipid risk factors, or at least associated, not directly related.

The question is, what triggers the adipocyte fat cell so it evolves into a personality of inflammation that leads to the production of adipocytokines? Could it be that the information molecules that the adipocyte is exposed to such as from an altered diet, lifestyle, or environment, are creating gene modification? Is there a certain set-point-a calorie intake-to the point where we trip the adipocyte into alarm physiology, which is like a dog chasing its tail?

These questions have not yet been answered, but we know that many of the things that are triggered after the adipocyte cell accumulates a certain threshold level of fat are related to increasing insulin resistance, increasing oxidative injury, and increasing risk to heart disease. These particular conditions were built into our genes to help protect against the most significant risk to human survival throughout our history, which was starvation, not excess calories. In states of deprivation, these pathways were advantageous to help to store glucose in the right places for support of crucial tissues, such as the immune system. Perhaps the peripheral cells were made insulin resistant intentionally as an evolutionary benefit to salvage glucose or allow for energy generation even when glucose was at a minimum, in order to drive the immune system to maintain defense against infection and help the individual to survive to the next period in time.

The question of what we consider disadvantageous as genetic characteristics has to be put through the lens of exactly what the environment of choice is. At one time, what might have been very advantageous, such as thrifty genes in the Pima Indians, may now be considered disadvantageous, given our current "Super-size Me" opportunities.

We ought not to jump to the conclusion that the solution to this problem is starvation, and that by just taking calories away from people, we're going to solve the problem. If the wrong types of calories are taken away, and people continue to eat a lower level of the wrong foods, we still have the problem of inappropriate signaling that can initiate inflammatory processes. Once this occurs, the adipocyte triggers inflammatory messages and the inflammation doesn't stay localized. It is not "think locally, act locally"; it is "think locally, act globally," because inflammatory mediators have impact on many other tissues, and

this connection can account for such diverse relationships as those seen with type 2 diabetes, metabolic syndrome, and dementia. The mechanisms by which these are connected are becoming better understood.

Diabetes, Obesity and the Brain
There is a good discussion of diabetes, obesity, and the brain in *Science* magazine.[14] The authors talk about the dysregulation of insulin and glucose and how it interrelates with inflammatory mediators coming from the adipocyte, which creates an environment that precipitates brain oxidative injury, neuronal apoptosis, and dementia. It is not just localized type 2 diabetes; it is not just coronary artery disease; and it is not just cerebrovascular disease. It is metastatic changes, oncogenic insult, angiogenesis, and things like dementia that are all connected together by these mechanisms.

It is now known that inflammation is an important progenitor marker in CHD. It is correlated, in part, with serum lipids, but it also has its own independent risk factor. A number of papers have been published in *The New England Journal of Medicine* go into this topic in greater detail, looking at inflammatory markers and the risk of CHD in men and women. In one report, it was shown that elevated levels of inflammatory markers, particularly high-sensitivity C-reactive protein (hsCRP), are associated with increased risk of CHD. [15] Lipids (such as dense LDL particles and total serum cholesterol) were still found to be important indicators, but hsCRP levels above 3 mg/L were also important to consider.

In secondary prevention trials, where individuals have already sustained a heart attack and are on aggressive statin therapies, it has been shown that the patients who do the best are those who maintain a low level of CRP. Even if their serum lipids come down remarkably, if their hsCRP levels remain elevated, they have a much higher incidence of secondary heart attack and sudden coronary death. A paper by Paul Ridker and his colleagues at Harvard discussing this issue was published in *The New England Journal of Medicine*.[16] In a companion paper, by Steven Nissen and his colleagues at the Cleveland Clinic, ultrasonography was used to observe the progression of atherosclerosis. It was demonstrated that patients on secondary prevention who maintained lower levels of hsCRP after aggressive intervention with statins had a significant reduction in the rate of thickening in their arterial lumen. [17]

When we look at comprehensive nutrition and lifestyle variables, we find that these factors can affect inflammatory burden, and management of these variables may have a positive effect on lowering the incidence and risk of many of the age-related diseases that constitute the majority of medical expenditures.

How does that relate to things like postmenopausal heart disease? That is a big question that has been sitting in the literature for some time. Why is it that women who lose their ovarian estrogen secretion show an incidence of heart disease that is comparable to men of the same age? This has been an active area of investigation for the last several years, particularly in light of the HERS Trial and the Women's Health Initiative trials, which did not find positive roles for Premarin and Provera in lowering the incidence of vascular disease risk. People have been asking exactly what is going on.

In previous discussions in FMU, I talked about the role that estrogen has in modifying inflammatory processes, and that it is seen as a kind of anti-inflammatory by a woman's gene response elements. As she loses estrogen secretory ability, the inhibiting molecule for expression of various inflammatory genes is taken away. These genes may then become expressed, particularly if they are triggered by

proinflammatory agents, which suggests that estrogen may be related to heart disease by its influence on inflammation.

A paper in the December 2004 issue of *Science* magazine titled, "COX-2-Derived Prostacyclin Confers Atheroprotection on Female Mice" addresses this inflammation connection.[18] The authors looked at the prostacyclin molecule (i.e., PGI_2,),which is principally derived from vascular endothelial COX-2 activity. This is the same COX-2 that is blocked by selective COX-2 inhibitors and commonly used for arthritis pain. I'll come back in a few moments to discuss that implication.

What would COX-2 have to do with atheroprotection in a female mouse? By keeping COX-2, which is a housekeeping enzyme, alive and well in the vascular endothelium, one activates production of prostacyclin, which robs platelets of their coagulation ability so they don't adhere or stick together as readily, they don't form thrombi as easily, and there are favorable effects on smooth muscle function. Prostacyclin has an important role in the housekeeping activities of the vascular system.

If there was any relationship between estrogen and COX-2, it could have an effect on the balance between prostacyclin, which prevents platelets from sticking together, and thromboxane A2, which is produced by the platelets and causes them to stick together. It's the equilibrium between these agents that gives rise to proper coagulation and proper wound healing or clotting.

In this study, the investigators looked at female mice that had relative protection from cardiovascular disease. They reported that estrogen acts on an estrogen receptor subtype A5; to upregulate the production of the atheroprotective prostacyclin (PGI_2) by activation of COX-2. This suggests that chronic treatment of premenopausal women with selective inhibitors of COX-2 could, therefore, undermine the protection from CVD. Blocking COX-2 activities with a selective COX-2 or an NSAID drug may further increase the risk of thrombus formation.

In light of what has recently happened with the withdrawal of rofecoxib from the marketplace and the shadow that has been cast on celecoxib, there is an interesting paper that appeared in the *Journal of the American Medical Association,* titled "Arthritis Medicines and CVD Events-'House of Coxibs.'" The "House of Cards" concept, according to Eric Topol, was built on the idea that something very unstable could fall over. He says the "House of Coxibs" is a little like the "House of Cards."

Dr. Topol is at the Cleveland Clinic, and has done quite a bit of work on the mechanisms of selective COX-2 inhibitors.[19] He points out that it is not just rofecoxib (Vioxx), and valdecoxib, but also celecoxib (Celebrex) these may all be showing a class effect because of blocking COX-2 in all tissues that could result in increased risk to heart disease. In his article, he discusses data from a large intervention trial for celecoxib. Results of the trial demonstrated that, at 400 mg and 800 mg a day of celecoxib, there were statistically significant increases in the incidence of cardiovascular events as compared to placebo.

Dr. Topol points out that specifically blocking COX-2 in all tissues, (which downregulates the production of proinflammatory mediators like prostaglandin E2), also blocks the production of things like prostacyclin (PGI_2) in the vascular endothelium, which increases the risk of platelet adhesion and thrombus formation. Again, this shows us how all these things fit together in a web. If we ask if statins are the right choice for the prevention of atherosclerosis, we see that they may have pleotr9phic affects, serving both as antiinflammatories and hypocholesterolemic agents. Dietary and lifestyle interventions

focused on the same principles of modulating the signaling related to inflammation, as well as lowering lipids, could have dramatic pleotrophic effects in lowering the incidence of CHD and stroke, as well as type 2 diabetes and other manifestations of dysinsulinism.

Anything that increases inflammation might be considered problematic. That could be chronic infection or inflammation from chronic trauma. What about dietary variables in refined and processed diets? One of those on the list of candidates for concern is partially hydrogenated vegetable oils that can alter cellular fatty acid composition and structure. Up to 40 percent of some solid vegetable fats that have been partially hydrogenated are found as *trans*configured double bonds, which are not the natural cis form of double bonds found in edible oils.

If we look at the relationship between *trans* fatty acid intake and systemic inflammation in apparently healthy people, we find that there is an interesting strong association between the two. I am now quoting from a paper in the *American Journal of Clinical Nutrition*.[20] This work was done by a group from the Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School. They expanded this observation by investigating the effect of *trans f*ats in patients with established heart disease and found a strong association between *trans* fats consumed in the diet and systemic inflammation. Dietary intervention should remove the bad things, as well as increase the good things.

The good things, as I mentioned earlier, are those that have gotten on the list of problematic foods. These are the complex carbohydrate-rich whole foods and whole grains, which now, in this age of "protein is good and carbohydrates are bad," have been forgotten. We want to bring them back. Intake of whole grains, bran, and germ is strongly associated with a reduced risk to CHD and a reduced incidence of inflammatory conditions. This has been demonstrated in many papers. There have been studies recently published in *The New England Journal of Medicine* on the Mediterranean Diet, inflammatory markers, and CHD risk. A paper in the *American Journal of Clinical Nutrition* talks about support for the reported beneficial association of whole-grain intake with CHD.[21] It suggests that bran components of whole grains could be a key factor in this association.

That leads to the conundrum of this month's FMU-vitamin E. Vitamin E has a long, interesting history. It goes back to the work of the Shute brothers in London, Ontario, and to the early work at the University of California Berkeley where, in a laboratory, it was found that vegetable oils, when stripped of certain unsaturates, would no longer be able to support reproduction in animals. The family of molecules that had been stripped out by processing the vegetable oil was called the birth-giving molecules, tocopherols0 or vitamin E. The common chemical name for vitamin E tocopherol-was coined in 1924 from the Greek words "tokos" meaning childbirth and "pherin" meaning to bring forth.

In the early 1940s, vitamin E gained a reputation for being an aphrodisiac vitamin because it had a positive effect on sexual vitality. That evolved from the concept that if vitamin E was not present in the diets of animals, they could not have proper offspring. It really had little to do with libido, but it was promoted and overly-advertised from that standpoint. It did appear to be an important agent in the diet, and it eventually became listed as a vitamin, a life-necessary substance that our body cannot produce.

In early studies on the chemistry and biology of vitamin E, it was found to be a family of many molecules, not as simple as vitamin C, ascorbic acid. It was a member of different isomeric and conjugate

forms of a phenolic molecule-alpha, beta, gamma, and delta forms, with a phytyl side chain in the chromane ring-and existed as a natural enantiomer of the RRR form as the chiral, or optically isomeric pure form.

The first studies on vitamin E, such as those by the Shute brothers, were done with semi-purified mixtures of vegetable oil that contained a mixture of tocopherols and tocotrienols. However, as we moved forward in technology, a bioassay was developed to determine potency of vitamin E preparations, because these were semi-pure concentrates and extracts of vegetable oils and researchers wanted to define the specific potency and necessary molecules. From that research, the exudative diathesis bioassay and the rat fetal resorption assay were developed. One was in chicks and the other in rats.

Obviously, people don't take vitamin E to prevent rat fetal resorption. There is no direct connection between this bioassay and why humans take vitamin E. However, it was found that of the various forms of vitamin E used in the rat fetal resorption assay, the alpha form of the RRR tocopherol was the most potent, so it was given the nomenclature of highest potency. Everything that was less effective in preventing rat fetal resorption was given a lower potency, based on its designated units. This would be the beta, gamma, and delta forms of tocopherol. We have gone through many years thinking that the alpha form was the most potent (meaning "important") form of vitamin E. In reality, we don't know that to be a fact. There is now evidence to suggest that it is not necessarily the most "important" form, and that perhaps the beta, gamma, and delta forms are more active in specific ways. In plant oils, the alpha form is generally lower in composition than the gamma tocopherol form. If you eat a natural mixture of oils, you will get alpha, beta, gamma, and delta, only a small percentage of which would be the alpha form, which we now say is the most 1otent form, and the one used in various natural vitamin E preparations.

That is the backdrop for a recent paper in the *Journal of the American Medical Association*, titled "Effects of Long-term Vitamin E Supplementation on Cardiovascular Events and Cancer,"[22] in which the results of the Heart Outcomes Prevention Evaluation Trial (HOPE) and HOPE-TOO Trials are discussed. These are the intervention trials using 400 IUs of vitamin E as natural RRR tocopherol. The HOPE Trial was an international, multi-centered, double-blind, randomized, two-by-two, factorial designed trial, evaluating either an ACE inhibitor versus placebo or vitamin E versus placebo, in patients at high risk for cardiovascular events. These patients were eligible for the study if they were at least 55 years old, had a history of coronary or peripheral artery disease, stroke, diabetes, had not had previous heart failure, and did not have an injection fraction lower than 40 percent. It was a large trial-9541 patients, randomized into two groups, one receiving 400 IUs of vitamin E per day and the other group a placebo.

The results were not at all encouraging. In fact, it was found there was no cardioprotection or cancer protection afforded by the vitamin E intervention. In the editorial that follows this paper, the authors state:

"In the past decade, a number of prospective, randomized, placebo-controlled, 3- to 6-year clinical trials have been published, testing the effect of vitamin E and other antioxidant vitamins or their combinations on clinical manifestations of cardiovascular disease and cancer. These trials have surprisingly yet consistently shown that commonly used antioxidant vitamin regimens (vitamins E, C, beta, or a combination) do not significantly reduce overall cardiovascular events or cancer."[23]

We would come to the conclusion that perhaps vitamin E is not all we thought it was. The point I would like to make is quite significant relative to everything we have discussed in this issue of FMU. That is, is

it a single molecule of purity that produces good outcome? In other words, is it alpha tocopherol that is presumed to have the highest potency, but that potency comes from rat fetal resorption? Or, is it a combination of vitamin E molecules found in natural sources?

I'd like to quote from a remarkable paper that appeared in the *Journal of Nutrition*, titled "Potential Synergy of Phytochemicals in Cancer Prevention: Mechanism of Action."[24] The author states:

"The additive and synergistic effects of phytochemicals in fruits and vegetables have been proposed to be responsible for their potent antioxidant and anticancer activities. The benefit of a diet rich in fruits and vegetables is attributed to the complex mixture of phytochemicals present in these and other whole foods. This partially explains why no single antioxidant can replace the combination of natural phytochemicals in fruits and vegetables in achieving the observed health benefits. Thousands of phytochemicals are present in whole foods. These compounds differ in molecular size, polarity, and solubility, which may affect the bioavailability and distribution of each phytochemical on different macromolecules, subcellular organelles, cells, organs, and tissues. The balanced natural combination of phytochemicals present in fruits and vegetables cannot simply be mimicked by pills or tablets."

That is consistent with a recent review, titled "Vitamin E: Underestimated as an Antioxidant," in which the author discusses the natural mixture of vitamin E, not a single molecule-D-α-tocopherol-taken out of the mixture.[25] I hope this provides you with some interesting food for thought" as we close this month's FMU.

INTERVIEW TRANSCRIPT

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It's time for our Clinician of the Month. Over the last more than 20 years, I have had the pleasure of interviewing some remarkable clinicians and researchers who are cutting a new swath to the future of health care. It has been a major part of my education to listen to them and to read their work. I have been deeply affected by their perspectives, what they have done, and how they have done it.

Our clinician this month is an individual who, from his years of life, has achieved remarkable accomplishments. As testament to that, and as you will learn throughout the course of our discussion, not only does he represent an academic medical success story, but he is a tremendous clinician/technician who has integrated many unique concepts into his practice (at some peril, I'm sure) that are different from those of his colleagues. On top of all that, he has also managed to raise a marvelous family. He has been married for 19 years and has a wonderful wife whom I have known for many years. She is the daughter of one of our previous FMU Clinicians of the Month, Dr. Gerald Lemole, a cardiologist at the University of Pennsylvania. Dr. Lemole was our guest on FMU in November of 1998.

It is with great privilege that I introduce Dr. Mehmet Oz, Vice-Chair of the Department of Surgery and Professor of Surgery at Columbia University. He also directs the Cardiovascular Institute in complementary medical programs at New York Presbyterian Hospital. He is the author of a wonderful book, most fitting for the general public, titled Healing from the Heart (Dutton Penguin Putnam; 1998).

He also has a new book, published in April of this year, which I can hardly wait to read. It's titled, You: The Owner's Manual (Harper Collins; 2005.)

The best way to introduce Dr. Oz is to cite a few of his papers. They demonstrate the breadth of his contributions and experience. In 1998, he co-authored an article that appeared in The New England Journal of Medicine titled, "Implantable Left Ventricular Assist Devices,"1 which demonstrated his scope of expertise in the area of heart transplant surgery and the pioneering of new surgical techniques in vascular medicine. In 1999, in The New England Journal of Medicine, he co-authored a paper titled, "Alternative Medicine-The Case of Herbal Remedies."2 He published an article in Circulation in 1998 titled, "Evidence for Unconscious Memory Processing during Elective Cardiac Surgery,"3 showing the mind/body connection that has been part of the multiple things he has looked at related to improving effectiveness in medicine and vascular biology. In the Journal of Thoracic and Cardiovascular Surgery in 2000, he and his colleagues published an article titled, "Use of Alternative Medicine by Patients Undergoing Cardiac Surgery,"4 a topic I would like to discuss with him during this interview. Dr. Oz also published an interesting report in JAMA in 1998 titled, "Complementary Medicine in the Surgical Wards."5

We are remarkably fortunate in capturing Dr. Oz for this interview. He has just come out of surgery. With that introduction, Mehmet, it's wonderful to have you on FMU, and thanks for joining us. Would you tell us a little bit about your background and what led you to some of these remarkable life experiences?

MO: You asked me how I got started. I was raised in a fairly traditional household, learning about medicine the way most folks do-through the eyes of a child being taken care of by a pediatrician with the same indoctrination that most folks have when going into the medical profession. Several things happened along the path that changed my life. One was the fact that I was raised partly in Turkey and I saw the world from a very different perspective. As a son of Turkish immigrants, I appreciated how differently things look when you're not looking from the same vantage point as is everyone else in your community.

I distinctly remember meeting my wife's parents. You mentioned that my father-in-law was a great cardiac surgeon at Christiana Medical Center. Even more impressively, my mother-in-law is a caregiver. Now, what does being a caregiver mean? She's one of the almost 50,000,000 people in our country who take care of other people. We all know who they are. They're the people we go to when we need advice. Those folks play the role of a primary caregiver in most communities. I watched her raise herbs in the garden and give advice on micronutrients and mind/body techniques. She had a network. She knew who would go where and she understood a lot about the functional medicine that you speak so beautifully of.

I watched that transition. When I was in medical school, I remember being dragged off to a conference in Washington, DC, where the keynote speaker was Jeffrey Bland. At the time, I was still quite timid about my exploration into integrated approaches, but I heard you speak, and I don't pay you false kudos-it was remarkable. I was a young scientist, going through medical school indoctrination, and you expressed your vision so beautifully from a scientific perspective-that we don't take enough advantage of the body's biochemistry. We don't look at how food, medicines, herbs, micronutrients, and even the mind, influence how the body functions. It reawakened me to the fact that health and disease are not binary processes. You are not one or the other; you are a spectrum. That, together with other leaders in our field, took a generation of folks like myself, graduating from medical school, to change the way we viewed what

medicine was going to do for our patients.

You mentioned one interesting paper in The New England Journal of Medicine about mechanical hearts and left ventricular assist devices (LVADS). These are mechanical pumps placed into the hearts of folks who are dying, to keep them alive. These folks are desperate. They will do anything it takes, and they will experiment with their lives. They're trying to crawl back from the precipice of death. Those folks, for me, created the practice of using some alternative approaches, because they were out there looking for solutions and teaching me. From that educational process, we created the integrative medicine center. I think that's a pretty robust, but straightforward discussion of why I got interested in what you do so well.

JB: That's a marvelous introduction to several of the questions I hope to touch upon. I'd like to codify our discussion into three areas and hopefully, we can discuss each one during this interview. One area relates to your perspective on medical technology and cardiology. That gets back to what you just mentioned-LVAD implants-and how patients define function in their lives differently than a person who is looking for optimal performance in a marathon. It's all part of the continuum-function relates to everyone. I'd like to discuss how technology interfaces with life decisions and alternative opportunities for improving function at all stages.

Second, I'd like to talk about the concept of what complementary and alternative medicine is, as applied to cardiology. Does it have a useful role, and how do you manage the risk/benefit equation so that people are not put at undue risk?

Third, I didn't mention in my introduction that you have an MBA from Wharton Business School in Health Care Finance. I want to ask some questions about your perspectives on financing in the healthcare reimbursement system. Those are the three areas I hope you will feel comfortable discussing.

Medical Technology and Cardiology
MO: Let's start with technology. The amazing thing about health care, and I'll bring a little finance into this, is what drives costs is not inefficiencies, and not just errors, although I think many would agree that the most expensive thing to do is deliver bad health care. But technology does usually deliver value. Because it does, people want to pay for it, and they see that investment as saving years of life. Ventricular assist devices, defibrillators, and different stents in coronary bypass surgery, are examples of that. But they are not where we should be investing most of our effort. They provide a continuance of life and they improve quality of life quite dramatically, but they're the wakeup call, and we need to get that wakeup call to occur earlier.

Much of what you've taught, and I want to applaud you for it, is the need to get folks to realize earlier in the course of life that there are challenges occurring in their bodies and often, they don't have the insight they need to be aware of what the challenges are. That was the reason we wrote the book, You: The Owner's Manual. We wanted to provide an expos on your own body so that you feel comfortable making some of the minor adjustments (and sometimes, major checkups), that one would have to get, because things just didn't sound, look, or feel right.

The technology we use in medicine is cool, fun, and hip, and I've been proud to be involved in developing some of it, especially the minimally invasive approaches. It solves the problem for folks who have fallen off the tightrope of life. But we need to take a step back. Some of the newer technologies, like 64-slice

CT scanners, provide remarkable insights into what the heart, lungs, and brain are doing in the body. These are useful because they show us earlier that there are problems, but they're also potentially dangerous because sometimes they show us too much. By that, I mean they have a high false-positive rate. We become nervous about things that are not important. Nonetheless, when used appropriately, they're wonderful wakeup calls, resulting in folks starting to take the necessary proactive steps to avoid some of the major interventions down the road.

JB: One of the interesting things you've touched upon is how people make changes, which reminds me of the Stages of Change model that James Prochaska talks about-going through the stages of enlightenment into putting a plan into action. It appears that you have to get people's attention. I recall an illustration of that when my executive assistant came in to my office one day and told me she had seen an unbelievable TV show on which a doctor from New York had been the guest. She said he showed human organ pathology on national TV and that it had been very gripping. She said she'd never known what your insides look like if you didn't take care of yourself. Well, that was you on that TV show and I've since had a chance to see a video of it. It was very effective at getting people's attention. Would you tell us how you get people to look seriously at, or to think about these things when they can't see inside their bodies?

Life-Changing Imagery Techniques

MO: Advertising 101 is, don't take the intelligence of your audience for granted. People are smart. They can see through makeup stories and dumped-down versions of what reality is. Unfortunately, we have spent a lot of time doing that. We create these images. For example, for coronary artery disease, it shows your sink blocked up with a hairball and, just like you'd pour Drano down there to clear out the blockage, we need to do the same thing to your heart. That imagery, besides being false, is misleading and makes folks think about their disease in a different way than they should be visualizing it. I've tried to move away from simplifying to just making it simple. There's a big difference. To me, making it simple means that I'll show you what an aorta looks like in someone who has abused his or her body. It has plaque distributed throughout the entire aortic system, blocking off the blood supply to the kidneys, thus causing hypertension and kidney failure. That's reality. That's what it really looks like.

I can also draw you a cartoon of it, but if I've lost the element of reality, you're not going to believe it, because it's not as tangible; it's not up close. What we did on that TV show, and we have others planned along the same vein in the future, was to get folks to change their lives. I've received so many kind notes, some to the effect that many people had been advised to stop smoking, but when they saw me show the lung cancer and the lungs with emphysema of people who had died, that hit home for them. We need to move outside the ivory towers of academia where we have a lot of this knowledge, and move it into the mainstream, but we can't do it by just mainlining information. We need to put the information in context, and the reality of disease does that quite effectively.

JB: Do you find that your colleagues are receptive to opening the slit and allowing different wavelengths of enlightenment to come through? Do they ask about sick hearts and sick environments in a different way?

Complementary and Alternative Medicine

MO: I'm seeing more of that, and it probably takes us to the second major area of discussion-complementary and alternative medicine. The problem is that being a doctor is a religion, as if you were

indoctrinated into the priesthood. You understand the way the body works, and if you work your tail off for four years in college, four years in medical school, and for seven years of residency, you think you know it all. If you don't know it, it's not out there. It's not true; it's not real. You tend to pooh-pooh some of the findings being made by folks who came from very different disciplines. The paper we published in Alternative Medicine about patients undergoing heart surgery brought light from my specialty as to the huge credibility gap occurring in medicine between doctors and their patients.

We ask patients, for example, whether they have spoken to their doctors about the use of alternative medicine. Seventeen percent of people said yes. Then we asked, if their doctor wanted to know, would they tell him? Only a third of the people said they would. Why? Because some of them were nervous about destroying that precious covenant they have with their doctors, and I understand that. But others felt that their doctors didn't know anything about this, anyway. If he's going to pooh-pooh it, why bother asking? We need to reestablish that connection. For me, complementary and alternative medicine, or integrative medicine, is really the globalization of medicine. Think about that. We've got banks; they're global. All of our financial institutions are pretty much global. We've got global media setups. But we don't have global medicine. Medicine has remained remarkably provincial. When we start to bring in therapies that work in other parts of the world and bring them into our own system, we call them alternative or complementary or integrative. But, in fact, it's the globalization of our field.

JB: That's a magnificent perspective and very interesting. That opens up some extraordinary opportunities for discovery. For instance, when you ask that question, you start to look at papers such as the one you co-authored, titled "Evidence for Unconscious Memory Processing during Elective Cardiac Surgery," in which you asked a question about whether there are certain auditory imprints that occur during the time of anesthesia that may have an effect on either the patient's memory or experience, or even how they may travel out of the experience in terms of recovery, based on the fact that the mind/body connection is pretty strong.

Memory Patterns and Anesthesia

MO: It worked beautifully for some of us, but let me take that one step further. What that paper did, which was the study on what happens to the brain waves and subsequently to memory patterns, especially implicit memory, in other words, conditioned memory, on patients undergoing heart surgery. What it did was to study why we have anesthesia. Now, think about that. Many of your listeners have had anesthesia. Everyone knows someone who's had anesthesia. We all know how it works. That's startling isn't it? We don't really know why it is you fall asleep when we administer inhalation gas anesthesia. We use it, and we assume the patients are asleep because after all, when they wake up, they don't have any recall, but is that the same thing? Not having recall is different from not having any input. We studied what happens to brain waves and we found that, in fact, when people hear sounds in their ears in the operating room, their EEG readings reflect that there's a level of awareness. It's throughout the operation, even when we're operating on their heart with their chest open. When we stop their heart, it's still present. So, we know they're aware. By the way, I had lots of wonderful collaborators-psychologists, psychiatrists, and criminologists (they're very good at looking at memory and implicit memory). We got together and created some word pairs.

Jeff, I'll ask you a question. What color comes to your mind if I say the word black?

JB: Red.

MO: Most people will say white. Black/white is a typical color pattern that most people will gravitate to. After I put you to sleep, if I play the word pairs black/brown in your ear, and you awaken from surgery; you never hear it again. The day you're going home, I ask you what color comes to mind if I say the color black. People will almost always answer brown. So, we can actually change how you would respond to a question, or perhaps even a stress, by conditioning you during the course of anesthesia. These are insights that are profoundly important to a field that took anesthesia for granted and assumed because we didn't study it as well as we could have, the impact of the head-on memory.

JB: Now we go back and interface with complementary and alternative medicine. How do you prepare a patient for surgery during the preoperative period, the surgery period, and the postoperative period? Clearly, that may have some impact, along with the procedure itself.

Preparing Patients for Surgery

MO: There are several companies that now make audiotapes that I find very useful. Peggy Huddleston has written on these, and Belleruth Naparstek has published a series of tapes. We have taken some of these tapes and modified them for our patients, but the Naparstektapes are wonderful guided-imagery tapes; they can focus on sleep, if you desire, or pain, or anxiety, or there's an interoperative tape. We provide these to our patients. They're relatively inexpensive; we actually subsidize it to make it very inexpensive, in order to help them be proactive in getting ready for their procedures. This is a logistically simple technique to deliver so we do it frequently, but there are other examples. In fact, on these tapes, I try to get patients to take deep breaths after a procedure to feel confident, and to not sense the pain as much-get them to take charge of the recovery process that we have for too long ignored.

JB: Let me bear on your thoughts about a few things that I'm sure come across your radar screen periodically when patients are using what might be called alternative or botanical medicines. I'm sure there are a variety of potential interactions that many of these substances might have with traditional cardiac drugs. Do you worry about botanical medicines in cardiology? Are there those you feel fairly comfortable with? Do you take it on a case-by-case basis? How do you deal with that issue?

Botanical Medicines

MO: There are some things I fear with patients. The first is, herbs are drugs. You need to know what you're doing with them. There are folks who know what these drugs do, and they can use them effectively. It's not that I'm against using herbs; I just want to know what they are so I can help you. For example, we know that many of the "Gs," ginkgo biloba, ginger, ginseng, and garlic change either lipid function or inhibit coagulation factors. If I'm going to thin your blood with some of my drugs, and you're self-medicating effectively because you're taking high doses of garlic, then you're not going to have the kind of coagulation profile that I want you to have. You're likely to bleed. So, let's have this discussion. Let's talk about which botanicals do what. I promise you that I will not make decisions because I don't know; I'll make decisions because I've thought about it and have asked around. That's quite effective.

Coenzyme Q10

There are some guidelines. For example, I give coenzyme Q10 to patients routinely prior to surgery, because we have done our own work on this. There's also published data from other institutions showing that hearts tolerate the procedures we do better if patients have been taking coenzyme Q10. I'm very quick to give patients fish oils following surgery, in part because we think they may play a role in reducing the amount of depression that patients have, and the duration of the depression after surgery. In fact, there is a

nice study looking at postpartum depression, demonstrating the value of 2 grams of fish oils post-partum. We're in the middle of a randomized trial looking at the same thing in adults undergoing heart surgery. There are things that offer a lot of opportunity and potential. We offer those when we can, but we definitely want to know what patients are on. That's one of the big challenges we have in American medicine, because we weren't trained in botanicals so we don't know. Then, we look at the usual cheat booklets to try and figure out who does what and when. If patients don't mention these to us, we start to build a big credibility gap.

JB: Let me address an issue that is obviously very controversial and I'm sure you're getting questions about it, and that's vitamin E. Do you have a position, or is this still open for further discussion?

Vitamin E

MO: With vitamin E, I'm telling patients that the most recent study that was done that argued that it actually may hurt patients, was one that looked at whether vitamin E allowed Lipitor or cholesterol-lowering drugs to do what they're supposed to do. It wasn't a study looking at vitamin E as sole therapy. I'm coming away with the belief that if you're already taking a drug for cholesterol management, a lipid-lowering drug, a statin, then your vitamin E dosing probably shouldn't be as high as it was in the past. I'm not going to completely change how we manage vitamin use in our patients based on a single study, but there's a cautionary note there. If you're not on a lipid-lowering drug, I don't believe that vitamin E has a negative profile that would mandate its stoppage. What do you think?

JB: This has been an interesting evolution, with the various epidemiological and intervention trials. The March 16 JAMA papers have probably created another stage of controversy because the HOPE trials were controlled intervention trials with vitamin E, looking at 400 IUs in patients to prevent cardiovascular events and cancer. That study is a prospective, randomized, clinical trial of fairly good size and the data looks real. I have a long-standing affiliation with vitamin E, going back to the early 1970s with some of my first research, but I think we need to take a look at where these confounders may be coming from and do some cohort analysis to see if there are subtypes of individuals on whom, for reasons that we don't understand, vitamin E is not having a favorable effect.

MO: When your aunt calls you and says she's on Lipitor and they want to reduce her vitamin E, what do you tell her?

JB: I would say, given the studies that have now been published, that keeping the intake of vitamin E (a combination of diet plus supplement), between 100 and 400 IUs a day is probably the safe, prudent approach for today.

JB: As you have broadened your scope of thinking and your communication of these concepts, you can influence people with a sense of a different reality than they may be familiar with. What about the criticism, controversy, and scrutiny that often affects people's ability to communicate to their colleagues? Has that been an issue for you?

MO: It has been an issue, in that sometimes we're not as open as we should be about true motivation. Some folks have criticized me about some of our research and I sometimes feel that the criticism is perhaps harsher than it would have been if it had been a paper on a more mundane, less inflammatory topic. On the other hand, I must give my colleagues credit because overwhelmingly, they have been

supportive in letting me do what we're supposed to do in an academic center, which is research. As long as we're actually studying what we're doing, my colleagues have been very supportive. That's the reason we offer clinical services such as massage to almost every patient who comes to the heart center. In fact, about 96 percent of patients are offered massages. We teach yoga. We have some guided imagery classes. We can do some of the things that I want to do. We don't have full range-for example, with acupuncture. But it's a reasonable start for Columbia University, which is an institution that has a strong tradition and has people in it who have strong beliefs.

This brings us to the third topic you brought up, which is what am I doing in healthcare policy, and what's going on in that arena. In many ways, what I'm seeing in medicine and in the behavior of my colleagues, is a concern about where the field is going and, particularly, a beginning sense of nihilism about how we're going to deal with some of the challenges in health care in this nation. I'm not a pessimist. I think we can fix the problems, because there's one root cause of most of the challenges we face-an implosion of trust in the system. The solutions we should be coming up with to deal with challenges ranging from affordable health insurance for all to health information systems that are functional, and even to malpractice and health justice systems that are useful, is to make sure they build trust in the system.

The Issue of Lawsuits

For example, the issue of lawsuits. A lot of folks want to put caps on lawsuits. That doesn't really build trust. It may cut costs, but to build trust, you want to, for example, have health courts. Instead of having a malpractice lottery, where one person wins and so many others are hurt by a mistake, let's make the mistake public so people can learn from it and it's not being hidden. At the same time, let's make the settlements fast, so people who are hurt are given compensation quicker, and physicians aren't laid out for months trying to defend themselves. Medical information is perhaps a better example for this tape. We have so much information in the system, but we don't share it. We have rules that restrict us from sharing it and we have a reticence, for malpractice reasons and also in terms of being open, about what's really going on in our practices. We should break those barriers down. We should be using this data to drive evidence-based solutions. Even if we don't have randomized trials, at least we'd know from large groups of patients and doctors, what happens in reality when certain things are being done. Patients ought to have access to that, as well. Folks, like the bright ones who listen to your tapes, ought to be able to look at the data and see that such and such a heart center has a higher mortality and here's 15 other things I know about them that could change my decision to go there or not go there, and here's what happens when they use ginkgo biloba in surgery and here are the results of coenzyme Q10 and heart failure. They can begin to pull some of this data to the forefront, even though we don't have the larger-scale, randomized trials that we so much desire.

JB: That was eloquently stated. In August of 1998 on FMU, I interviewed Regina Herzlinger from the Harvard University School of Business. She had just published her book, Market Focused Health Care, in which she advocated that if we allowed people to really understand what they were paying for indirectly in the healthcare system, and used the same market forces that we have in any other competitive field, that we might see a leveling of the playing field and actually improve cost effectiveness and patient recruitment into the program. I think this is the theme you are leading us to-put the light of day on the whole system and get away from self-reinforcement of the double-blind, placebo-controlled, randomized clinical trial, which really focuses on one molecule against one endpoint. That loads the dice in favor of pharmacology. Let's look at everything on the same playing field from a true evidence-based perspective.

Looking at Things from an Evidence-Based Perspective
MO: Absolutely, and it comes back to one overarching concept which is, being a professional involves always putting the patient first. It involves having a body of knowledge that we will advance, and it involves policing each other, unfortunately, but that's what professionals are supposed to do. There's also a fourth element to professionalism. That is, you have to have a civic responsibility that you acknowledge and act upon. It would be a tragedy if we lost our voice.

We've got to regain our voice. I drafted something called The Covenant for America, which is an effort by physicians to regain their voice by stating clearly not self-interest issues, but broadly, what do we think ought to be happening in health care? Just get it out there, so that folks who don't spend their whole life thinking about health, like our political leaders, and like many of our civic leaders can read this document. A lot of doctors who looked at this think this is good for us, so maybe we ought to move toward affordable health care for all. They feel strongly about having better health information systems. Let's make that capital investment. Folks like you and me and others, ought to out there hammering the message that this is what doctors think is best for America. It's not about us; it's about America.

JB: I'd like to acknowledge something. I know it's the end of your day, and that's it's been one filled with technology, emotion, and other things that required your full attention, both from a humanistic and professional perspective. The answer to the question, what is functional medicine, or what is function, comes down to the kind of abilities you have demonstrated in this interview to bring the full sense of who you are as a human being to these questions. They are not always easy questions, and we don't have all the answers. We need to interface them with the real aspirations, fears, and desires of people and try to be a little better with service each day, and do it in such a way that you feel you're part of the system-not above or separate from it. You've conveyed that beautifully. It's quite remarkable to know about the things that have gone on throughout your day and the different types of regimentation you've had to face, and then see you center yourself and be present for this discussion, That embodies what functional medicine is all about. I want to thank you.

MO: You're very kind. I'm a big fan. Keep up the great work.

JB: You do the same, and we'll be in touch soon.

What a great pleasure to talk with Dr. Oz and get his sense of where we are going, where we have come from, and how we can improve the healthcare system.

Bibliography

1 Goldstein DJ, Oz MC, Rose EA. Implantable left ventricular assist devices. N Engl J Med. 1998;339(21):1522-1533.

2 Oz MC, Rose EA, Lemo2e GM. Alternative medicine-the case of herbal remedies. N Engl J Med. 1999;340(13):1056.

3 Adams DC, Hilton HJ, Madigan JD, et al. Evidence for unconscious memory processing during elective

cardiac surgery. Circulation. 1998(98);II-289-II-293.

4 Liu EH, Turner LM, Lin SX, et al. Use of alternative medicine by patients undergoing cardiac surgery. J Thorac Cardiovasc Surg. 2000;120:335-341.

5 Oz MC, Whitworth GC, Liu EH. Complementary medicine in the surgical wards. JAMA. 1998;279(9):710-711.

6 Frist WH. Health care in the 21st century. N Engl J Med. 2005;352:267-272.

7 Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005;365:217-233.

8 Forman JP, Rimm EB, Stampfer MJ, Curhan GC. Folate intake and the risk of incident hypertension among US women. JAMA. 2005;293:320-329.

9 Goldstein DB, Hirschhorn JN. In genetic control of disease, does 'race' matter? Nature Genetics. 2004;36(12):1243-1244.

10 Fillon-Emery N, Chango A, Mircher C, et al. Homocysteine concentrations in adults with trisomy 21: effect of B vitamins and genetic polymorphisms. Am J Clin Nutr. 2004;80:1551-1557.

11 O'Rahilly S, Barroso I, Wareham NJ. Genetic factors in type 2 diabetes: the end of the beginning? Science. 2005;307:370-373.

12 Lowell BB, Shulman GI. Mitochondrial dysfunction and type 2 diabetes. Science. 2005;307:384-387.

13 Lazar MA. How obesity causes diabetes: not a tall tale. Science. 2005;307:373-375.

14 Schwartz MW, Porte D. Diabetes, obesity, and the brain. Science. 2005;307:375-379.

15 Pai JK, Pischon T, Ma J, et al. Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med. 2004;351:2599-2610.

16 Ridker PM, Cannon CP, Morrow D, et al. C-reactive protein levels and outcomes after statin therapy. N Engl J Med. 2005;352:20-28.

17 Nissen SE, Tuzcu EM, Schoenhagen P, et al. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. N Engl J Med. 2005;352:29-38.

18 Egan KM, Lawson JA, Fries S, et al. COX-2-derived prostacyclin confers atheroprotection on female mice. Science. 2004;306:1954-1957.

19 Topol EJ. Arthritis medicines and cardiovascular events-House of Coxibs." JAMA. 2005;293(3):366-368.

20 Mozaffarian D, Rimm EB, King IB, Lawler RL, McDonald GB, Levy WC. trans Fatty acids and systemic inflammation in heart failure. Am J C0in Nutr. 2004;80:1521-1525.

21 Jensen MK, Koh-Banerjee P, Hu FB, et al. Intakes of w1ole grains, bran, and germ and the risk of coronary heart disease in men. Am J Clin Nutr. 2004;80:1492-1499.

22 The HOPE and HOPE-TOO Trial Investigators. Effects of long-term vitamin E Supplementation on cardiovascular events and cancer. JAMA. 2005;293:1338-1347.

23 Brown BG, Crowley J. Is there any hope for vitamin E? JAMA. 2005;293:1387-1390.

24 Liu RH. Pote6tial synergy of phytochemicals in cancer prevention: mechanism of action. J Nutr. 2004;134:3479S-3485S.

25 Pfluger P, Kluth D, Landes N, Bumke-Vogt C, Brigelius-Flohe R. Vitamin E: underestimated as an antioxidant. Redox Report. 2004;9(5):249~-8254.p>