April 2003 Issue | Scott Rigden, MD Family Preventive Medicine

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Welcome to *Functional Medicine Update* for April 2003, one month before our Tenth International Symposium on Functional Medicine. I hope you have made your reservations. We will have a great time together May 21-25 at La Paloma Resort in Tucson, Arizona. This meeting will focus on risk factors for vascular disorders beyond cholesterol. We will look specifically at inflammatory mediators and an array of other extended non-cholesterol-related risk factors.

This month in *FMU*, I would like to pave the way for my discussion with our Clinician of the Month. For 25 years, Dr. Scott Rigden has dealt with complex patients with a variety of cardiovascular and diabetic risk factors associated with altered body composition—or what we might call obesity. The word *obesity* is somewhat stigmatizing. It conjures up an image that may not reflect what the patient looks and feels like. Obesity might be used to describe someone who has increased body fat relative to muscle, or what we may call sarcopenic obesity, muscle loss with fat gain. As a consequence, he or she may have an altered physiological outcome, or phenotype, that increases the risk of vascular disorders and diabetes. Dr. Rigden will discuss his extraordinary approaches to managing this type of patient and his 25 years of clinical experience in doing so.

To set the tone for this discussion, I would like to consider weight problems apart from just excess calories. We spend a lot of time thinking about how to get a person to lose weight by tricking him or her in terms of calorie consumption. By “tricking” I don’t mean to imply deceiving; I mean finding ways to modify the diet to lower the individual’s calorie intake and/or increase his or her energy expenditure. Energy expenditure can be difficult to accomplish in a person who may have significant excess body weight, because the individual may have problems that prevent him or her from engaging in a heavy workout program. Such conditions might include esophageal reflux disorder, osteoarthritis, inflammatory foot problems, or plantar fasciitis.

Each pound of fat represents about 3500 stored extra calories. One might justifiably wonder how much exercise one needs to engage in to burn off a pound of fat. That calculation can be daunting, and it may detract from a person’s motivation to lose weight. For example, assuming a person expends about 100 calories of stored energy per mile, one would have to run 35 eight-minute miles to lose a pound of fat, or more than a marathon. Most people are not interested in doing that, and the suggestion dampens their enthusiasm for exercise.

The Role of Metabolism

The fallacy in that thermodynamic calculation, however, is that it overlooks that there is an effect of exercise, just as there is an effect of diet, at the moment of exercise or eating. That effect has to do with

influence of those variables on metabolism. Metabolism is the big black box between calories consumed and energy expended. The basic metabolic machine is controlled by neuro/immuno/physiological endocrine function that regulates the way calories are disposed of or distributed.

Calories may be converted to storage forms such as triglycerides that go into an adipocyte cell for a rainy day that may never come. Or they may be made available for use in the metabolic process of energy production through mitochondrial oxidation as triglyceride or carbohydrate or the carbon skeleton of amino acids in protein. That gives rise to the powering up of the energy economy of the cell and formation of reduced factor intermediates such as NADPH and FADH, which are involved in many functions in the body in terms of energy.

The Neuroendocrine/Immune Component of Metabolism

In designing weight-loss programs for patients, we often talk about ways to increase their energy expenditure through activity or ways to reduce their calorie intake through diet. We are apt to spend less time talking about the middle component, the regulation of metabolism, the black box that determines how those calories will travel through the body and either be stored as fat or used as energy. Numerous tested and proven programs can lower calorie intake, and exercise and activity programs can improve energy utilization. Not as well defined, however, is that intermediary neuroendocrine/immune component of metabolism that leads to weight gain.

This concept may seem strange at first because we are so used to the emphasis on the calories in/calories out argument, which is the first law of thermodynamics. Every calorie taken in must be converted to a calorie expended for energy conservation. What we are trying to do is regulate the number of calories taken in relative to calories expended.

Metabolism and the Kinetics of Energy Transfer

In the middle of that process is metabolism. It is true that in the end every calorie that comes in will go out as energy expended. If a person is morbidly obese, however, those calories may not leave his or her body until it decomposes and the energy departs as heat from microbial degradation. The person may have stored 100 or 200 pounds of those extra calories as fat, and those calories really are not lost to heat in any effective way in his/her lifetime. We are talking about improving the kinetics of energy transfer. We are trying to make sure that energy taken in and energy expended equal the energy need, so that the individual can function metabolically at a high level.

Let’s consider a hypothetical very overweight individual who has stored a tremendous number of extra calories as body fat. At 3500 calories per pound of fat, he may have 200 extra pounds of stored energy. On one level, he can be said to be suffering from too much energy because of all those extra pounds of calories, 3500 calories per pound. But that is not the way he behaves. He looks as though his level of energy is very low. He is tired, fatigued. He shuffles around without adequate energy to do things. He may be ravenously hungry, as if his body is saying it needs more fuel, but his energy performance looks as if he is running out of energy. He may be very depressed; his brain is not thinking clearly; his muscles aren’t functioning correctly; cardiovascular function is impaired.

Switched Metabolism

I call this “switched metabolism.” The individual’s body feels like its fuel tank is on empty, but his physiology keeps storing those calories for rainy days that never come. Why that is and what unique

properties or principles or triggering factors result in that condition are still an enormous area for future exploration and discovery within physiology.

With that caveat in mind, however, we are beginning to see tremendous progress in explaining why that may occur through alterations in the neuroendocrine immune system in individuals. Understanding that relationship helps us understand the kinetics of energy transport through the body and the availability of that energy we take in as potential energy in food. Each gram of carbohydrate or protein yields 4 calories; fat yields 9 calories per gram. Those calories must be converted into available energy for reproduction, immune function, cardiovascular function, muscle contraction, neuron firing, and all the functions that make up healthy physiology.

Obesity and Functional Physiology

In a sense, we can look at obesity, as I have defined it, as a functional medicine disorder associated with an imbalance between calories that come in, their metabolic conversion into utilizable functional units of energy, and the calories of energy expended. It is that middle area, the area of functional physiology, that we need to examine and ask what might go wrong in the person who says he never had a weight problem until he was 35 years old. Then, suddenly, his metabolism changed until it seems even thinking about food makes him gain weight. How did the metabolism change, and what does it mean?

The triggering factors that might change the metabolic conversion of potential energy in food into functional energy of activity, meaning physiological activity, may be vast and varied in type. They might cut across the neuroendocrine/immune systems. When you are dealing with a person whose history of weight problems began in midlife, it is no doubt the result of some unique factors in his or her neuroendocrine/immune systems.

The Hormone Connection

We used to hear weight gain described as a “hormone problem,” or, more specifically, a “thyroid problem.” Now we know that thyroid function is only a part of the equation. The neuroendocrine/immune function I am describing is much more complex than any single component. We cannot look only at thyroid-stimulating hormones, T4, T3, and reverse T3. We have to look at their interaction with adrenal steroidogenesis and gonadosteroids and how those factors interrelate with neurotransmitters and neuromodulators.

Then we must examine the relationship to immune factors like the thymus-dependent 1 and thymus-dependent 2 cytokines and inflammatory mediators and neuromodulators. These substances may be produced in the gut as cholecystokinin, in the fat cell itself as leptin, or through the lateral nucleus of the hypothalamus as neuropeptide Y (NPY), or melanocyte-stimulating hormone. The interaction of this variety of mediators then ultimately controls the expression of appetite, calorie regulation, and the way metabolism converts calories into energy units for utilization

Let’s discuss how this strategy could be applied in the clinic. Many women first experience problems controlling their weight about the time of metabolic change at perimenopause or menopause. That is when estrogen and progesterone levels move rapidly up and down in wide fluctuations.

Many women gain weight during this period of time. We used to think putting a patient on hormone replacement therapy (HRT) would correct the problem. However, we have recently seen from the results

of the Women's Health Initiative (WHI) that intervention with conjugated mixed equine estrogens and synthetic progestin does not produce the benefit and outcome we might have liked. In fact, according to the authors of a recent article in the *New England Journal of Medicine*, "Rethinking Postmenopausal Hormone Therapy," the WHI trial of daily combined therapy with estrogen and progestin was terminated early, in May of 2002.[1]

> "The reason for stopping was an increased risk of breast cancer (and evidence of greater overall risk than benefit) in the hormone-therapy group. Far more surprising, however, was the associated increase in the risk of myocardial infarction.

> "Several observational studies involving women without coronary disease had shown roughly a halving of the risk of myocardial infarction among hormone users."

Reevaluating HRT

The WHI findings were unexpected. They caused considerable consternation and a reevaluation of our presumption about the benefits of HRT. The hormone formulations in the WHI were 0.625 mg of conjugated equine estrogen and 2.5 mg of medroxyprogesterone.

> "In reality, the absolute risks associated with a daily combined estrogen-progestin therapy are small. For example, the 29 percent increase in the risk of coronary heart disease and the 26 percent increase in the risk of invasive breast cancer associated with hormone therapy in the WHI translate to 4 additional coronary events and 4 additional breast cancers for every 1000 women followed for an average of 5.2 years."

HRT Concerns

If you are one of those women, however, that is a major concern. The argument against using postmenopausal HRT for the prevention of chronic disease is not that the likelihood of harm is high. It is that the potential harm outweighs the potential benefit, based on the new WHI data.

One of the major applications of equine estrogens and progesterones was modification of vasomotor symptoms—night sweats and hot flushing—but other treatments may be available for those symptoms. Some use of the selective serotonin reuptake inhibitors has been found effective, for example. Potentially beneficial natural interventions employ various types of plant hormone modulators of estrogen receptivity, estrogen reactivity, and the interrelationship between progesterone and estrogen.

Natural Modulators of Hormone Function
Natural substances such as soy isoflavones, red clover isoflavones, kudzu isoflavones, and lignans from flax modulate estrogen cross-talk and influence estrogen reception and activity. Other natural products, such as indole-3 carbinolfrom crucifers and resveratrol from grapes, influence the metabolism of estrogen into the hydroxylated and methylated estrogens.

Black cohosh has also received considerable attention since the publication of clinical trials showing it ameliorated menopausal symptoms.

If we only look at flushing and night sweats, estrogen/progestin probably would not be justified as a singular treatment from a risk/benefit perspectiv

The authors of a review article on drug therapy in the *New England Journal of Medicine*, titled “Selective Estrogen-Receptor Modulators—Mechanisms of Action and Application to Clinical Practice,”[2] discuss the selective estrogen-receptor modulators (SERMs) as a major therapeutic advance in clinical practice.

> “Unlike estrogens, which are uniformly agonists, and antiestrogens, which are uniformly antagonists, the SERMs exert selective agonist or antagonist effects on various estrogen target tissues.”

Natural Adaptogens
From a traditional botanical medicine perspective, we might call these adaptogens. In one case, in a certain tissue, they can stimulate estrogen activity; in another tissue they can inhibit it. Many natural SERMs are much more moderate in their action than the synthetic SERMs. Examples of synthetic SERMs are tamoxifen and raloxifene. The reactivity of tamoxifen and raloxifene is different in different tissues. Tamoxifen is very strong in the breast; raloxifene is much stronger as an estrogen modulator in the bone. Tamoxifen may reduce the risk of breast cancer in high-risk women by as much as 50 percent, but it may increase the risk of uterine cancer. One is faced with this kind of juggling act with tamoxifen.

Some of the natural SERMs, although they are much milder in activity than the synthetic SERMs, may have much different safety profiles and much different tissue specificity or agonist/antagonist activity.

Adaptogenic Activity

An adaptogen has agonist/antagonist specificity. In certain cases it may upregulate and activate a process, and in other cases that same molecule or collection of molecules may suppress activity as an antagonist. It can do so in a tissue-specific way. There are many cases in which this mechanism is emerging. An adaptogen may facilitate binding of a ligand to its receptor, like estrogen through the estrogen receptor-α, or it may work away from that receptor to communicate a message to the receptor that may up- or downregulate the expression of the receptor or its activity toward the ligand. These are advances in our understanding of the way substances like SERMs may work in modulating activity.

According to the authors of the review paper on SERMs:

> "Because of their selective estrogen-agonist properties, SERMs can be used to prevent or treat diseases caused by estrogen deficiency, such as osteoporosis, without most of the undesirable actions of estrogen. Conversely, because of their selective estrogen-antagonist properties, they can be used to prevent or treat diseases, such as breast cancer, in which estrogen-agonist activity is undesirable for a given tissue."

The Role of Hormones in Physiology

Our understanding of the ways hormones may influence physiology is improving. A hormone may have effects beyond serving as a classic receptor. It may play a role that is outside the normal cell receptor-to-gene mechanism. This was recently found to be the case with estrogen, which has a traditional estrogen receptor activity and may also have an effect away from the estrogen receptor through other cell signaling.

Many women respond adversely to the perimenopause/menopause period. They experience numerous symptoms, including weight gain and changes to vascular risk such as cholesterol/HDL ratios and high-sensitivity C-reactive protein. These women may have unique metabolic genotypes with certain sensitivities to the effects of various hormonal modulators. Although not every person may have these reactions, some women have a unique propensity to do so.

Let me give you an example. Some women have altered methylation characteristics. Estradiol and estrone molecules are hydroxylated by three potential pathways in their conversion to excretory byproducts. One is by 2-hydroxylation, which goes on to be methylated to its 2-hydroxy form. The next is 16-hydroxylation, which goes on to be glucuronidated or sulfated before excretion.

The last is the 4-hydroxylation, which results in methylation to the 4-methoxy compounds, which are also important in mediating and preventing some of the adverse effects of the 4-hydroxylated compounds. The 4-hydroxylated compounds can become potentially genotoxic and can injure DNA through conversion to

3,4 quinone derivatives. These quinones are very reactive with DNA and produce mutations. We want to be sure to get proper methylation.

Catechol-O-Methyltransferase (COMT)
Methylation of the 2- and 4-hydroxyestrogens occurs as a consequence of an enzyme called catechol-O-methyltransferase (COMT). COMT requires the availability of a substance called S-adenosyl-methionine (SAM) for its activity. SAM is subsequently manufactured through the tetrahydrofolate cycle, the folic acid cycle, the proper integrity of which requires the remethylation of homocysteine to methionine. That remethylation pathway is dependent upon availability of 5-methyltetrahydrofolate.

Scientists have identified a number of unique genetic polymorphisms in this pathway. Those polymorphisms may alter the availability of methylated steroids, either as a consequence of changes in the production and availability of SAM, or changes in the availability and production of the methylated hormones by altered enzyme activity of the methylating enzyme, COMT. Drugs that block COMT may also block the production of methylated estrogens, which may increase the carcinogenicity of various estrogens, particularly those in the 4-hydroxy family.

Genetic Variability of COMT
The COMT family of enzymes has a high degree of genetic variability, or great frequency of different alleles of single nucleotide polymorphisms. One recently published study on this topic appears in *Human Reproduction.*[3] It examines the influence of the COMT polymorphism 158 on estrogen levels in women. In this study, researchers demonstrated that COMT is the principal enzyme in the conjugation pathway for the 2- and 4-hydroxylated estrogens. Blood levels of 17-β-estradiol and estrone in postmenopausal women receiving an oral estradiol preparation are dependent on the enzyme activity of COMT. Various polymorphisms, such as the 158 polymorphism of COMT, lower the methylation rate and alter estradiol levels.

The researchers concluded that serum estradiol levels significantly correlate with the COMT genotype, and differences in COMT genotype might be involved in causing variable effects of estrogens on diseases such as hormone-dependent cancers and coronary heart disease, and on the efficacy of HRT.

Managing Estrogen Metabolism
Appropriate estrogen metabolism may be blocked in some women as a consequence of a COMT polymorphism, coupled with a poor-quality diet, which may be lower in folate or the other folate-dependent nutrients. In this case, the woman's ability to detoxify her estrogens may be impaired, and she may be at higher risk to her estrogens, both the hydroxylated derivatives and estradiol itself. Estradiol is mitogenic and increases cell cycling and cell replication rate in specific cells.

In such a case, that woman might require higher levels of the B-complex nutrients to help support proper methylation. She might even require adjunctive SAM to assist in proper methylation. In any case, folic acid, 5-methyltetrahydrofolate, methyl cobalamin (a form of vitamin B12), pyridoxine, riboflavin, and vitamin B2 are important in these women.

Women with hyperhomocysteinemia might be among those at highest risk. These women have an imbalance in their folate cycles. If you see elevated homocysteine above 8 picograms per ml on a blood chemical profile, that person might be a candidate for methyl support using various nutrients. You might

also want to determine if she is methylating her hormones appropriately by activity of COMT. The range of need may vary by a factor of 100 from one moment to another based on genetic uniqueness.

Hormones and Weight Gain

How does this hormone story relate to the question of weight gain in women going through these changes? A number of metabolic changes may be occurring with changes in estrogen/progesterone levels and the relative ratio of the estrogen metabolites that create a different internal milieu of the cell, leading to water retention and different energy economy which can create fat gain and muscle loss. All of these are related to postmenopausal weight gain.

Not every woman going through menopause gains weight. In fact, some women sail through menopause with no change in body composition. Why do some women experience serious problems with weight gain? Complex changes in signaling molecules associated with rhythmic changes in the endocrine system may be part of that story. That is different from looking at calories alone. We are looking at the metabolic balance

Gastroenterological effects on endocrine and immune system balance may also have something to do with weight. An interesting story has emerged concerning the possible effect of immunization in certain children, and its potential influence on conditions like autism. It is quite a stretch of the imagination to go from a discussion on autism to one on weight gain, but I want you to think about the implications of Dr. Andrew Wakefield's work reported in the *Lancet* 1998.

You may recall that in a previous issue of *FMU*, we reviewed that Wakefield paper, titled "Ileal-Lymphoid-Nodular Hyperplasia, Nonspecific Colitis, and Pervasive Developmental Disorder in Children."[4] In this paper, Wakefield proposed that an MMR vaccination could, in certain genetically susceptible children, precipitate or be a trigger to later-stage injury of their immune system and a brain/gut connection that alters neurological development and function and produces the symptoms we call the autistic spectrum.

Autism Studies

We have talked about some of the subsequent studies on this topic published in the *Lancet*and other journals that have strongly challenged the Wakefield hypothesis. Recently, in the*American Journal of Gastroenterology*, Dr. Wakefield and his colleagues published a follow-up study, titled "Enterocolitis in Children with Developmental Disorders,"[5] showing once again a very high correspondence between the presence of autistic spectrum disorders in these children and developmental disorders or neurological alterations. This is not proof of cause, but the association was very high.

In a more recent paper, D'Eufemia et al. looked at abnormal intestinal permeability in children with autism. They showed that autistic spectrum disorders increased what we might call "leaky gut syndrome," or at least abnormal intestinal permeability, with more absorption of larger molecular-weight molecules across the gastrointestinal tract.[6] In the *Journal of Paediatrics*, Horvath et al. also reported gastrointestinal abnormalities in children with autistic disorders.[7]

Fecal Calprotectin Levels and Inflammation

Bjarason et al. (one of the first groups to discover the concept of altered gut permeability in the 1970s), in a paper published in 2000 in the journal *Gut*, described fecal calprotectin levels that correlate with acute inflammation in autistic enterocolitis.[8] This is an interesting study because calprotectin is a measure in the feces of an inflammatory mediator produced by gut wall immunological upregulation.

The investigators found a strong correlation between fecal calprotectin levels and inflammation associated with enterocolitis in autistic children. None of these studies, in and of itself, unequivocally demonstrates cause and effect, but there certainly are strong associations among gut function, immunological function, and neurological sequelae.

Statistics: Averages versus Individual Cases

The most recent paper in this series, from the work of Bjarason and his colleagues at the Guy's, King's, St. Thomas' Medical School in Denmark and the Bessemer Road, Department of Medicine, Guy's Hospital in London, appeared in the journal *Gut.* This paper is titled "Effect of Pentavac and Measles-Mumps-Rubella (MMR) Vaccination on the Intestine."[9] In this study, after failing to demonstrate MMR vaccine caused an intestinal inflammatory response, the authors conclude this provides evidence against the gut-brain interaction that is central to the autistic "enterocolitis" hypothesis.

If you read this paper carefully, however, you will notice the ranges of data they looked for in fecal calprotectin in MMR-treated children before and after immunization are very broad. Thus, although there may be not an average change, there might be individual changes within the data set. If we looked at small frequency penetration of this characteristic, we might see it. We almost have to look at the data on a case-by- case basis because of the wide range in variability from person to person.

MMR and Autism Connection Possible in Some Children

This story is still open to discussion regarding whether an MMR vaccination in certain genetically susceptible children does, in fact, create a gut/brain connection that could lead to neurological developmental disorders, or what we call the autistic spectrum disorders. As Bjarason says, "The lack of a detectable intestinal inflammatory response suggests that the measles vaccine virus itself is not enterotoxic in healthy infants, which argues against the MMR-induced autistic 'enterocolitis' theory. This does not, however, rule out the possibility that vaccination might have an adverse effect on susceptible infants that are perhaps immune compromised or with an immunological makeup that predisposes them to autoimmune disease."

I believe the Wakefield concept deserves more attention and evaluation. We should ask who the susceptible children are that might be candidates for an adverse response to their immunological system.

This research is also of interest when we start looking at adult conditions of the gastrointestinal tract that involve the immune system beyond autistic disorders. Examples include gastrointestinal disorders like Crohn's disease or inflammatory bowel disease (IBD). Intestinal permeability increases in patients with Crohn's disease, and relapse can be predicted on the basis of how permeable the gut is after patients have undergone treatment for Crohn's disease.

With increased gut permeability, there is a much higher level of relapse. In fact, if you use the lactulose/mannitol challenge test to evaluate gut mucosal integrity, individuals with compromised gut mucosal integrity shown by intestinal permeability on a challenge test have at least 80 percent probability

of relapse within one year. Individuals with a gut mucosal integrity that was much less permeable upon treatment had less than a 10 percent probability of relapse within one year. This information was reported in the *Lancet.*[10]Studies published in the *European Journal of Gastroenterology and Hepatology* support these findings.[11]

We are starting to recognize that the interrelationship between our diet and our gut mucosal immune system may influence the immunological message that is received by our body. That message then could influence systemic vectors associated with inflammation that then can change metabolism. Is there a food allergy component to altered body composition through altered metabolism? Does an effect occur in relation to altered gastrointestinal sufficiency, such as pancreatic insufficiency or chronic maldigestion? All of these are much more complicated questions than just evaluating the number of calories in and the number of calories out in an individual.

In programs to manage that, we might reinoculate the gut with friendly bacteria, add digestive aids to improve digestion, get food-sensitivity agents out of the diet, and get rid of chronic infection of the gut with parasites or parasitic bacteria. I am describing what we call the 4R Program—Remove, Replace, Reinoculate, Repair. Remove the agents in the diet that are potentially immune hypersensitizing, and get rid of the chronic infections or parasites. Replace them with stomach acid or pancreatic enzymes where necessary. Reinoculate with friendly bacteria like acidophilus and bifidobacteria and prebiotics like fructans or larch arabino galactans.

We can help to repair the gut with nutrients like glutamine, zinc in a non-irritating form, and vitamin E to try to rebuild gut mucosal integrity.

Benefits of Nutritional Factors in Gut Healing

A number of studies show this can be very helpful. We might also consider lowering inflammatory potential in the gut to assist in gut mucosal recovery by the administration of omega-3 fatty acids, or fish oil. Enterically coated fish oils deliver their contents in the small bowel and can be helpful in the healing and recovery of Crohn’s disease lesions and increased permeability. An interesting paper appeared in the *Journal of Parenteral and Enteral Nutrition* on the use of omega-3 fatty acids and attenuating systemic disease sequelae in experimental pancreatitis.[12]

Vitamin E plays an important role in this recovery process as well. The total mixed tocopherols, not just α-tocopherol, but γ-tocopherol also seem to play an important role in reducing the immune-induced inflammation through nitric oxide upregulation and peroxynitrite formation. As the authors of a paper in *Free Radical Medicine & Biology* showed, γ-tocopherol, a component of mixed tocopherols, plays an important role in reducing these activations of the immune system.[13] Vitamin E, essential fatty acids, the amino acid glutamine, zinc in a non-irritating form such as zinc glycinate, *Lactobacillus acidophilus*, and prebiotics may all help to balance the immune system in individuals who have alterations in immunological activity.

Controlling the Signaling Process

A number of variables control the signaling process that leads ultimately to the control of calorie utilization and the way the metabolism functions. I have used the extreme example of autistic spectrum disorders and their relationship to the gut, but clearly, we may take less extreme examples and look at

overall metabolic function and signaling through the immune system, of which 60 percent is clustered around the gut.

With that in mind, our Clinician of Month, Dr. Scott Rigden, is going to tell us more about how to apply this complex algorithm for management of the patient who has weight difficulties and increased cardiovascular and diabetic risk. Let's turn to side II

INTERVIEW TRANSCRIPT

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JB: It is time for our Clinician/Researcher of the Month interview. This month, we are fortunate to have a clinical expert with 25 years of experience in the area he will be discussing. A longstanding member of the Functional Medicine Steering Group, Dr. Rigden was on hand when the Institute for Functional Medicine was in its planning stages, with development of our first models and our patient-centered assessment and treatment methodology. He is also a good friend and one of my closest professional colleagues. Dr. Rigden is a family practitioner from Tempe, Arizona. He specializes in lifestyle management, weight-related issues, and management of chronic disease, particularly chronic fatigue syndrome.

It’s with great enthusiasm that I welcome you back to FMU, Scott. Many things have happened in the field and in your life since January of 1994, the last time you were our Clinician of the Month.

SR: Thank you. Good morning. It’s great to be with you, Jeff.

Heart Disease and Obesity

JB: You have been a model for me in a lot of things that have happened over the past 25 years, in translating the biomedical sciences into clinical practice, particularly in the complex area of weight management. You will provide a workshop at our Tenth International Symposium on Functional Medicine in May, focusing on obesity as a cardiovascular-related risk factor. I thought we might review, from your perspective, the history of the relationship between heart disease and obesity. You have certainly seen many changes in this field. Would you give us a historical review?

SR: Historical and hopefully not too hysterical. Sometimes, it’s a little overwhelming for all of us, but the Surgeon General recently proclaimed obesity and closely related issues, such as sedentary lifestyle, as two of the key things that have to be altered in our society by the year 2010.

We now know that 320,000 premature deaths occur each year in the U.S. due to obesity. That’s 900 people every day, or 38 per hour. It’s an incredible problem. Second only to smoking, it’s the leading preventable cause of death.

Obesity-Related Research

You have covered in FMU the plethora of research that has occurred in the past year or two. An article in the American Journal of Clinical Nutrition in March of last year pointed out the interrelationship among high glycemic load, obesity, and C-reactive protein.14 An article in JAMA in January of last year pointed out the incredible relationship of cardiovascular disease to obesity and the metabolic syndrome, or syndrome X.15 We have seen all kinds of articles describing the relationship of the waist-to-hip ratio, the so-called "apple configuration" of obesity. We know this ratio predicts vascular endothelial dysfunction, in addition to things like insulin resistance, lipid abnormalities, and increased left ventricular mass.

The Nurses Health Studies that have been published in several journals in past years include long-term studies showing how obesity directly relates to coronary artery disease and stroke. We know from a New England Journal of Medicine article you covered several years ago that a weight loss of even 8 kilos in an obese person can significantly decrease left ventricular mass and decrease blood pressure.

We could go on and on with the research, but there's no question that the American Heart Association has listed obesity as an independent, very significant coronary risk factor. I love this quote from Dr. Walter Willett's book, Eat, Drink and Be Healthy: "A healthy diet teamed up with regular exercise and no smoking could eliminate 80 percent of heart disease." He says that next to whether or not you smoke, the number that stares up at you from the bathroom scale is the most important measure of your future health. I think there's a mandate for us in functional medicine to get involved with this. Surely, we are all seeing it virtually every day in our practices.

Measuring Obesity

JB: Would you discuss how we medically assess and define words like "obesity," "morbid obesity," "marginal obesity," and "overweight"? We've heard of body mass index (BMI), waist-to-hip relationships, and body composition using bioimpedance. At what point does the patient go from modest risk to greater risk?

SR: There are three ways our listeners might want to assess their patients beyond just height and weight. Certainly, body mass index is becoming the gold standard. That is weight in kilograms divided by height in meters squared. That might be a little bit beyond my calculation skills, but nomograms are readily available from the Surgeon General, the National Institutes of Health, and other groups.

Basically, we know that at a BMI of 30, there is a rapid escalation, a very steep increase on a graph of risk factors related to obesity, various cancers, diabetes, cerebral vascular and cardiovascular disease, sleep apnea, anesthetic risk, blood clots, and other problems. The escalation is quite steep at a BMI of 30, which generally correlates in a lot of people with roughly 30 pounds overweight. At a BMI of 27 to 30, there is moderate increase in those risk factors, and in many people that would be approximately 20 pounds of excess weight.

Healthy BMI and Body Composition

At a BMI of 25, most people have pretty minimal coronary risk factors and associated risk factors to their weight. Our goal with BMI is generally to try to get it down to 23 to 25, although we recognize that in some cases, it's an achievement just to get the person out of that high-risk zone and below 30. If you're starting at 300 pounds and are 150 pounds overweight, certainly that would be a far more realistic goal than worrying about a BMI of 23.

We also do body fat composition analysis. Most people in our practice are not young adults who are jocks. Our goals are a little more liberal than those published in the physiology journals. We like to see our men come in around 19 to 22 percent body fat as a goal, and our women at 22 to 25 percent. We think that for most of the population, that would be a tremendous upgrade.

Waist-to-Hip Ratio

If we look at the waist-to-hip ratio, a lot of the research says that 0.9 in females and certainly a 1 in males can be a very significant problem, but more and more, we're just looking at waist circumference per se. We can all have a tape measure in our offices without investing a lot of money.

There are two magic numbers our listeners can key in on. If women have a waist circumference of 36 inches or more, and men 40 inches or more, this highly correlates with insulin resistance and the risk factors of a BMI of 30 or more. These are some things we can implement in our assessment in the office.

Calculating Weight: Clothes or No Clothes?

JB: This is a simple question, but I've had it asked of me so I want to clarify it. When we look at the BMI and measuring weight, is that weight without clothes, or is it weight normally dressed? We don't want to get the wrong kind of weight data to put into our BMI calculation.

SR: In our office, it's with normal clothing without shoes. If you go to weight loss meetings, you'll get a lot of controversy about this, but I think you just need to be consistent and weigh patients in the same way on the same scale with the standard that you decide upon. In our office, it's with their regular clothing on, without shoes. That way, everybody is pretty comfortable as you track results and look at your relative data points.

NIH Therapeutic Lifestyle Changes Concept

JB: Within the last two years, the National Institutes of Health has published a document they call the Therapeutic Lifestyle Changes Concept. It outlines for physicians how to approach a patient who is at risk to heart disease or in the early stages of type 2 diabetes. As I recall, according to this document, before you introduce drugs or other pharmaceutical agents, the patient should first undertake a lifestyle, exercise, and diet intervention program. This program includes things like a lowered lipid diet, improved unrefined complex carbohydrate, and increased neutral plant sterols like beta-sistosterol-containing foods such as soy.

This position is very different from that of the NIH in the past. Do you think that document has had any impact in medicine? How do you view this whole NIH concept?

SR: I'm excited about these changes. For example, in January of this year, for the first time in its history, the American Heart Association endorsed a nutritional supplement—fish oil—(eicosapentaenoic acid, [EPA] and docosapentaenoic acid [DHA]). When groups that used to think Jeff Bland and Scott Rigden were way out on the fringe begin endorsing fish oil capsules, it's really exciting.

New Food Guide Pyramid

A totally new Food Guide pyramid will be released this year. The base of the pyramid will be regular exercise and weight control instead of 6-11 servings of high glycemic index carbohydrates, starches, and grains. I think we all have good reason to be very optimistic. I hope the new Food Guide Pyramid will

make a real impact on our education process when it's presented to our educators and students. It says a daily multiple vitamin is recommended in most cases, and if women of a certain age aren't getting enough daily calcium they should consider a calcium supplement, and other things that were never addressed.

The old Food Guide Pyramid tended toward "all fat is bad." The new Food Guide Pyramid is going to emphasize the role of healthy oils, healthy fats, and monounsaturates. The new things that are coming out really support your teachings and the views you have held through the years. I think they are encouraging for all functional medicine practitioners. We are no longer going to be considered on the edge. I think this is going to be more and more the mainstream thinking.

Early AMA Thinking about Fats and Heart Disease
JB: In 1980 I was invited to a major American Medical Association meeting to present some of the early work on fish oils and heart disease. My observations were based on my discussions with Drs. Bang and Dyerberg in Denmark about their 15 years of work in Greenland. I had also talked with Dr. Hugh Sinclair from the University of London School of Medicine.

Dr. Sinclair was one of the first to do studies on the blood of Greenland Eskimos, looking at the high intake of seal oil and its relationship to platelet stickiness and cardiovascular risk factors. When he first went to Greenland in the late 1940s, they didn't even have enough electricity available for centrifuges. When he got blood samples, he had to use a mechanical centrifuge. He and his students turned a big crank, the arms would fly around, and they centrifuged the blood that way.

That was some of the early work that led us to recognize that the Greenland Eskimos were consuming a diet that was very high in fat and yet they had a very low incidence of coronary heart disease. When I presented that data in 1980, I was considered a heretic.

SR: It's a good thing you weren't tarred and feathered!

Good Fats/Bad Fats
JB: It is very interesting to watch what has happened in this field over the last 23 years. Nathan Pritikin wasn't totally wrong when he said less fat was desirable. Many people tended to throw the baby out with the bath water, however, when they recommended elimination of all fats rather than just the wrong fats, the partially hydrogenated trans fats and the highly saturated solid fats.

SR: I remember when you discussed trans fats in the late 1970s and 1980s. I took some of your papers and presented them to the local medical society. To say my presentation did not go over well is an understatement. Obviously, now there is a consensus on trans fats that validates your presentation some 23 years ago. Again, congratulations on being way ahead of the curve.

Adipose Tissue and Cell Signaling
JB: Sometimes the leading edge can seem like the bleeding edge. Let's move on to the emerging story that body fat is not what we thought it was for the past 30 or 40 years in physiology. It is not a very stable storage tissue that is just there to suck up excess lipids in the form of triglyceride. It's a contractile tissue. The adipocyte stores calories for rainy days that often never come in people.

Now, suddenly, a new revelation says the adipocyte is actually a very important cellular communication elaborating tissue, or cell, and that it produces not just leptin, but inflammatory mediators and a series of neuroregulators. Now we need to reexamine the whole concept of the fat mass from a different perspective around cellular signaling.

SR: It has been amazing. Not only is it an endocrine disorder and perhaps at times a hypersensitivity disorder and a disorder related to problems with hepatic detoxification, but it's also an inflammatory disorder in and of itself. Obesity independently correlates with elevated C-reactive protein levels and subtle changes that can be measured in sophisticated immune system studies. For example, 10 years ago, when we saw women with infertility, ovarian cysts, uterine hyperplasia, or fibrocystic disease, we didn't consider that they would have insulin resistance. Now we are seeing those kinds of relationships very much in the forefront in some of the research areas.

I think it takes a functional medicine perspective to start integrating all of these relationships. Certainly, if you drink enough beer and eat enough pizza, your unhealthy lifestyle can be a condition, but I think we have to start integrating and synthesizing all these potential areas of impact.

Taking the Message to Patients

JB: The media message continues to be that all fat is bad, that we should diet ourselves to thinness so we won't look cosmetically unattractive. Those messages are probably antithetical to what we're trying to achieve with patients in terms of their health. Understanding how complicated and detailed these emerging mechanisms are, how do you discuss the issue with patients? How do you get them to go beyond the impact of advertisements in the media to view weight management in the proper context?

SR: First of all, we try to establish at the outset which of these five categories are their main issues. We find that with the exception of congenital disorders like Prader-Willi syndrome and those unfortunate people who have been abused or molested, most of our patients fall into one or more of five categories. Two of those categories are lifestyle and endocrine issues. That could include thyroid and/or adrenal and/or testosterone or estrogen issues, or metabolic syndrome (syndrome X). According to a report in JAMA last year, 47,000,000 American adults have metabolic syndrome.15 That is more than one in five, which represents a very significant portion of everyone's practice. Food hypersensitivity is another category. This is another area in which some of your pioneering has been most helpful. We feel there is a subgroup of people that get missed on the radar screen with this as a major etiologic factor. And finally, some people's obesity is related to chronic illness that can affect hepatic detoxification and perhaps contribute to medications they've had to take that promote the obesity.

We start out by trying to help them understand that these are areas they may not have explored or discovered in working with other physicians. We explain that we have effective programs for each of these areas. We are developing algorithms and more effective tests to pinpoint if they have metabolic syndrome (syndrome X) or if they have endocrine, food hypersensitivity, or hepatic detoxification problems.

Weight Management Is a Marathon, Not a Sprint

After we work on the nuts and bolts of that, we have to establish the right attitude. We emphasize three things right from the start. The first is that this will be a marathon and not a sprint. If you're going to change your relationship with food, and if you're going to change your physiology dramatically and turn

your health around, there are no shortcuts.

All kinds of unscrupulous ads out there imply you're a dunce if you don't lose 30 pounds in a month. In our office, we tell them we don't care how long it takes as long as we get the job done. If you're the tortoise that beats the hare, that's just fine. You're the little engine that could. We recommend long, slow, distance (the LSD approach). We're very comfortable with that and keep emphasizing it.

No Total Deprivation; Slumps Are Normal

The second thing is that we don't believe in total deprivation. Most of our patients have been desperate. They've tried the grapefruit diets, soup diets, and various crazy things. I know when I was obese, I was tempted to get involved with those. We assure them that is not the way to go. With diets like that the best they can do is quickly lose some counterfeit weight, but they will regain it just as quickly. It is just fool's gold. At their worst, these diets can make them quite ill.

The third thing, right at the start, is that we assure them it is normal to have slumps. They are going against the flow of society, and they may be trying to reprogram years of behavior. We understand that everybody, no matter how committed he or she is, will have a bad day or a bad week. When that happens, it is easy to get angry, discouraged, and frustrated. Rather than taking the fork in the road that says, I quit, we encourage them to remember this conversation, take a deep breath, remember they can get a grip on things, and get back on track the next day. If they have 25 good days out of 30, they're still going to have a great month. If they have 48 good weeks out of 52 in the upcoming year, they're going to be very excited about where their health and their body is a year from now.

That's the perspective we want them to have. It's not about perfection; it's about resiliency and the ability to bounce back. We will encourage and support them through those slumps, and our agenda won't change. We'll just keep grinding it out.

Dr. Rigden's Program in Practice

JB: The combination of the five-point program you've described (lifestyle, endocrine, metabolic syndrome X, food hypersensitivity, and chronic illness factors), along with a support program, patient education, motivation, and being there as a part of their team, represents a unique and innovative program. To how many patients have you had the opportunity to apply this program in your 25 years of practice?

SR: One time I counted and it was over 2000, but that was quite a while ago. We are talking about a real commitment over a long period of time. I'm sure at this point I have probably worked with more than 3000 weight management patients through the years, and it's been a labor of love for me. Thanks to functional medicine and the things I've learned in association with our group, we really are getting unprecedented results.

That isn't to say that everybody who walks in is successful, because this is a very challenging field. But we now have tools we just didn't have before. Now we can really understand that somebody can have a normal TSH and still have a significant thyroid situation that needs to be addressed through functional medical evaluation. Or somebody can have a fairly decent-looking chem screen with perhaps just a little elevated triglycerides and low HDL, and if that ratio is a little over 4, we can see we have a subtle syndrome X problem brewing. Or, if somebody has the allergic shiners and a history of chronic sinusitis,

we might be able to extrapolate to the point where we determine food allergies are really affecting their weight-loss metabolism.

I want to encourage our listeners. We weren't taught much in medical school about this field, and we weren't given the tools we now have. I think the information coming out at the functional medicine meetings and, again, looking at this subcategorization, will help them gain a new sense of empowerment. They can reach out to patients and give them programs and tools they've never heard of or tried before. In many cases, I find it's a key to a whole new perspective.

The Transformation Process

JB: I applaud what you've done. I know it's not always easy in this area. There are a lot of forces working on that patient for simple fixes, such as the latest drug for weight loss or bypass surgery to get it over with once and for all. Working together with patients requires a dedicated clinician. I presume the payoff for you is that you must have an extraordinary sense of bringing about a transformation in the patient. You're working together in a real way, rather than just writing a prescription. You are walking the patient through each of the steps, and it must be a real celebration for everyone.

SR: Just an hour ago, we saw a woman I'll call Kathy, who started working with us 2 ½ years ago. Her BMI was well over 50; her weight was well over 300 pounds. This morning when I saw her, she had lost 162 pounds over a 2 ½ year period of time. She is no longer diabetic; she is no longer hypertensive; she is no longer taking any medication; and she walks three miles a day. She was slated to have a knee replacement, which was cancelled and will not now be required. It's so exciting to see lives change. Of course, it has done fantastic things for her self-esteem and her overall psychological outlook.

When you have a few stories like this, it inspires you to keep going, It shows you what the human spirit can do if we all pitch in and work together. We can give them a chance to understand they really do have unique biochemical and metabolic challenges, and we, as functional medicine doctors, are starting to get into the position where we can figure this out much better and provide them the guidance they need.

A Reason for Optimism

JB: Dr. Rigden, thank you. We could continue this conversation for hours to learn more about some of the tricks of the trade that you've learned over the years. I encourage listeners who want to follow up to attend your workshop at the upcoming May symposium and/or get copies of the tapes that will come out of that workshop. You are a master clinician who speaks from years of experience. Thank you for giving us a glimpse at what you do, along with some optimism. This very complicated problem really does include options and opportunities for remediation.

SR: Thank you, Jeff. I appreciate the opportunity and I look forward to talking with our listeners in Tucson.

Reviewing Dr. Rigden's Five-Point Program

I want to emphasize the importance of Dr. Rigden's program as a different way of approaching patients with weight-related risk factors with vascular and diabetic consequences. That program goes beyond looking at calories taken in and energy expended, to look at the metabolic component in the middle of that conversion cycle.

To summarize, the five-point program involves the following:

1)A lifestyle evaluation that has to do with exercise and diet considerations;
2)An endocrine-balancing component;
3)Evaluation for signs of metabolic syndrome (syndrome X);
4)Management of food sensitivities;
5)Assessment and management of chronic illness factors.

Balancing Estrogens

I talked on side I about the estrogen component in perimenopause and the importance of balancing estrogen metabolism and estrogen receptivity with a diet rich in phytonutrients that help promote estrogen balance. This includes such things as soy isoflavones, lignans from flax, cruciferous vegetables that promote estrogen detoxification, and the glucosinolates they contain, such as indole-3 carbinol. To give you a reference range, two portions of fresh broccoli provide about 200 mg of glucosinolates as indole-3 carbinol.

Last, I talked about the methylation pathway—the folate cycle requiring 5-methyltetrahydrofolate—that produces SAM, which provides the methyl group for proper methylation of hormones. That was just an example of the way we would use the news I described in a clinical setting. We might look at a perimenopausal or menopausal woman who is gaining weight and get her on an appropriate hormone-balancing program. An appropriate hormone metabolic management program would provide the necessary dietary support with estrogen modulators and agonists/antagonists like isoflavones from kudzu and red clover to stabilize her estrogen receptivity systems.

The Gut as an Immune Modulator

We also talked about immunological factors on side I. These factors include the gut as an immune modulator and the possible role of food allergy in this process by sensitizing the gut. I used a pretty extreme example of the influence that immunization could have on genetically susceptible children, the gut/brain connection, the gut as the second brain, and how that interrelates with autistic spectrum disorders.

I went on to discuss conditions we observe in clinical medicine, such as Crohn’s disease (or IBD). In those conditions the relationship between the gut and the immune system could affect function. That could affect the balance within the cellular compartment of energy economy, including mitochondrial function, muscle function, and fat cell function. Again, we might look at allergy and gut function.

The “4R Program”

I talked about the “4R Program” as a therapy, along with getting rid of the foods that are problematic. You might begin by eliminating dairy and gluten-containing grain products from the diet, to see how the patient responds. Then you could introduce friendly bacteria and prebiotics and give the patient proper glutamine levels for gut repair, and vitamin E and zinc for the defense of the mucosal integrity of the gut. That was another part of the story we touched upon with Dr. Rigden.

"Envirogenomics" Looks at Individual Detoxification Profiles

All of these factors are related to the detoxification of endogenous and exogenous substances. This topic appears in the news with greater and greater frequency. I found an interesting first-page discussion in the *Wall Street Journal* in January 2003, titled "Poisons Aren't Toxic to Everyone Equally, Creating a Dilemma."[16] This article used a new word—"envirogenomics," a term that relates to alteration in the way an individual detoxifies environmental substances based on his or her own unique genetics. The author discusses how envirogenomics has turned up common polymorphisms that affect the specific risks that an individual has to a health problem associated with exposure to a specific chemical. The answer is related to the unique detoxification processes of that individual.

Individual Differences in Detoxification

This is an important point that is emerging. Different individuals may detoxify a substance in ways that differ by a factor of as much as 100 times, based on the individual's detoxification profile and unique genetics for detoxification. The effect is through the phase I cytochrome P450s and the phase II conjugation enzymes that regulate metabolic detoxification.

This is both genetically determined and environmentally modulated through things like diet. If a person eats a poor-quality diet, those genetic uniquenesses might be further amplified to result in poor or imbalanced detoxification outcomes.

Individual Response to Pharmaceutical Products

As we look at the way this applies to pharmaceutical products and the patient's response to them, we can consider a paper that appeared in the *New England Journal of Medicine*.[17] According to the author of this paper, which is titled "Pharmacogenetics in the Laboratory and the Clinic":

> "One of the most striking features of modern medicines is how often they fail to work. Even when they do work, they are often associated with serious adverse reactions. Indeed, adverse reactions to drugs rank as one of the leading causes of death and illness in the developed world. How can we improve the success rate?"
>
> "The Human Genome Project and other advances have generated expectations that medicines can be customized to match the genetic makeup of patients, thereby dramatically improving efficacy and safety."

The Importance of Proper Diet

These are very laudable objectives. In today's world, however, the most effective way to influence how both exogenous and endogenous chemicals travel through the body may be by providing a proper diet that

contains the nutrients necessary to support phase I and phase II detoxification. A poor-quality diet does not necessarily accomplish that goal, particularly in individuals who may have specific SNPs that make them already imbalanced or poor detoxifiers.

Alteration of detoxification capability may make the internal and external environment more "toxic" to a person. This may have an effect on metabolic function that can translate into a difference of intra- and extracellular water, different electrolyte balance, different oxidative stress mechanisms, different muscle cell physiology, and different adipocyte physiology, which we can see in terms of altered body composition. These unique concepts have not been considered historically in evaluating patients with obesity. However, historically, if we look at the effect these factors have on reduction/oxidation, energy economy, energy utilization versus energy storage, we are going to see more examples of how they adversely influence body function in terms of energy economy

Metabolic Disruption in Obesity
The body is put into a metabolically poisoned state, to use that term metaphorically. It stores fat for a rainy day that never comes, rather than utilizing the calories for energy of action. The patient gets into what I would call a store-and-hibernate model of physiology. You will notice this in many patients as they start to gain weight; their metabolic presentation is one of inflammation coupled with storage and metabolic hibernation. Their metabolism seems to "slow down; they appear to start storing calories of energy they formerly used for functional energy; and they become more inflammation-prone.

This is a dog-chasing-its-tail argument, because the adipocyte itself—the fat cell—produces its own inflammatory mediators. The more fat-cell activation, the more potential for the production of tumor necrosis factor-α, interleukin-6, and high-sensitivity C-reactive protein, which activates its own inflammatory signaling process, and around the cycle goes. That alters metabolism, increasing the relative tendency to gain weight as fat, and decreasing metabolic efficiency in the functional cell, like the sarcomere, the muscle cell.

A State of Hyperinflammation
We are beginning to understand the transition that occurs in some people. (Dr. Rigden talked about it with people who have BMIs above 30.) Something different happens in their bodies. They shift over into a different physiological state of function, and it is very hard to get them back. It is like a dog chasing its tail. Individuals with a modest weight gain can generally pull it back fairly quickly because they still have the metabolic underpinnings to manage it. They are not in a hyperinflamed state; they are not in a metabolic resting state; they are able to regulate what some people call the thermogenics; they are able to regulate metabolic function much more easily by diet and lifestyle intervention.

Once one tips over into an endocrine/immune/neurological imbalanced system, where the neurochemistry is changed, the endocrine system is changed, and the endocrinological balance has changed into one of inflammation, it is much more difficult to get back. That is why we have to employ interventions that are much more heroic.

Clinical Steps in Managing the Metabolically Poisoned Patient
The solution is not simply to put the person on a weight control deprivation diet and give him or her an appetite control agent (which basically kills their appestat center). It is to try to deal in a comprehensive fashion with the five areas Dr. Rigden talked about. We need to look at the hypersensitivity relationship,

underlying chronic illnesses, associated alterations in the endocrine system, and an underlying potential for insulin resistance and hyperinsulinemia

We should examine the patient's 2-hour postprandial insulin and blood sugar levels after a glucose load. Is there a significant increase in area under the curve, showing that the patient has hyperinsulinemia? Does he or she show a triglyceride-to-HDL ratio greater than 4.5, suggesting insulin resistance/hyperinsulinemia? What about endocrine balance? What about the relationship of the patient's sex steroid hormones and inflammatory mediators to the endocrine hormones which regulate aspects of metabolism?

One needs to look at all of these variables to develop a comprehensive picture, rather than just put a person on an appetite suppressant and a calorie-deprived diet. By the way, a calorie-deprived diet, in some genotypes, just forces the individual back into an alarm reaction. He or she stores more fat and fights back with more inflammatory molecules.

Treating the Complex Obese Patient

In summary, the next time you see a patient with excess body fat, you should examine the complex series of events that may have led to a state of altered body composition. Look at the relationship to altered metabolism that tracks risk to heart disease, diabetes, and other metabolic problems such as kidney difficulties, neurological problems, and ocular problems with cataracts. All of these issues are related to changes in the physiological state of function. They are not solely related to calories ingested. We have to look at the type of calories, the type of lifestyle, signals to the genes, and the complex relationship to the endocrine, nervous, and immune systems. Therefore, we should be looking at a comprehensive program using a functional medicine weblike approach to treat this type of patient.

Dr. Rigden has done an excellent job with his 25 years of experience in helping to paint that picture for us and to open that door. We thank him and look forward to visiting with you next month.

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