A NEW APPROACH TO METABOLIC SYNDROME

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Preface

Metabolic Syndrome (aka "Syndrome X"), with its four hallmark symptoms of obesity, hypertension, dyslipidemia, and hyperglycemia, is devastating North America, the US in particular. In March of 2005, the National Institutes of Health and the New England Journal of Medicine published a paper stating that because of this epidemic, the current generation is projected to have a shorter life expectancy then the previous one…for the first time in recorded history! Since then, things have become much worse. Worse, despite the fact we have changed the USDA "Food Pyramid," developed many new classes of pharmaceutical agents (especially for pre-diabetes and diabetes Type II), have taken soda machines out of schools, and even the First Lady's top priority is the obesity epidemic. This syndrome, with all of its comorbidities (cardiovascular disease, stroke, many cancers, kidney failure, blindness, amputations, etc.), accounts for the majority of healthcare dollars spent. If the tide is not turned, Metabolic Syndrome will bankrupt our country. This is a fact.

The Pathophysiology of Metabolic Syndrome

In 1987, the late Gerald Reaven, MD, Professor of Medicine at Stanford University's College of Medicine, first demonstrated that the four hallmark symptoms shared a commonality: hyper-insulinemia coupled with insulin resistance. He coined the term "Syndrome X" to illustrate the point: the four legs of the "X" represent the symptoms (hypertension, central obesity, hyperglycemia and dyslipidemia) and the nexus of the "X" being the causal agents of too much insulin along with insulin resistance (the cells do not respond to normal physiologic amounts of insulin). This is the standard, accepted medical model of this disease.

The Failure of Current Treatments

We are being ravaged by this syndrome due to the simple fact that we have ignored the model! Instead of focusing our attention on the root cause, we have decided to treat each of the symptoms as separate, unrelated diseases. Thus, we have new dietary recommendations and "diets d'jour," as well as a plethora of exercise regimens prescribed for obesity and of course, "diet pills." And then there are the myriad of prescription drugs to "control" the other three symptoms. If our focus is on "controlling symptoms," we have admitted, by default, that there is NOTHING WE CAN DO FOR THE CAUSATIVE FACTORS, and we will just have to LEARN TO LIVE WITH OUR DISEASE, i.e. "it will always be with us, we'll just control it." This attitude of acceptance is bad enough, and unaffordable in the long run, but that's the least of it.

If we understand the pathophysiology of this syndrome, we can readily see why many of these treatments actually make the other symptoms much worse! Hyper-insulinemia means the patient's pancreas is secreting an exaggerated amount of insulin in response to rises in blood glucose. This can easily be confirmed by doing a fasting insulin level or the standard glucose challenge test and ordering insulin levels along with glucose levels at time zero, one hour, and two hour intervals post challenge glucose administration. Sadly, the vast majority of practitioners do not even think about such an important marker. So we dwell on just the glucose level or Hemoglobin A1c (merely symptoms) and prescribe drugs such as the sulfonylureas (i.e. glyburide, glipizide, glimperide) which cause the pancreas to secrete EVEN MORE INSULIN or we actually give them INSULIN ITSELF in an aggressive attempt to control a symptom. If the model is correct, then this therapy should make the syndrome worse…and it does! This is the fundamental reason why we have failed to stem the tide (or actually reverse) this seemingly insidious malady.

The Concept of Homeostasis

If insulin just mediated glucose uptake by our cells and did nothing else, we likely would not have this problem. However, this is not the case, and when the amount of insulin remains consistently elevated it does other things…things that are NOT good. Before

discussing the effects of hyper-insulinemia, a review of the fundamental concept of homeostasis should be addressed. The body is an organism that strives to maintain a constant internal environment in the face of constantly changing, often hostile, external factors. Blood pressure, blood glucose, body temperature, acid/base balance, etc. must remain within a relatively narrow range in order for the body to survive. It does so by means of the action/reaction principle, or mechanisms that exert opposite effects so that a balance may be achieved. Examples are: vasodilation/vasoconstriction, oxidation/reduction, anabolism/catabolism, assimilation/elimination, etc. These systems are exquisitely regulated primarily by the nervous system and the endocrine (hormonal) system. So if the environmental temperature is 125° F, our internal temperature remains at 98.6°. Likewise, if the temperature drops to 20°, mechanisms are in place to ensure our internal temperature still remains a constant 98.6°. Glucose homeostasis is essential for life, as certain cells in the body only use glucose as an energy source (certain brain cells, the adrenal medulla, red blood cells, etc.). Whether in times of feast or famine, blood glucose must remain within a certain range, and insulin and glucagon are the master hormones that control this process. (Forget about ghrelin, leptin, incretins, and all the new "mini-hormones" in literature today…these are subservient to the two masters.) The body needs BOTH "master hormones" to maintain balance, as they have exactly the opposite physiological functions…if you know what insulin does, then you automatically know what glucagon does. If an imbalance occurs, dysfunction or "disease" will arise.

The Physiological Effects of Insulin

Insulin's primary function is mediating glucose uptake to muscle cells, and in this way, helps regulate blood glucose homeostasis. However, insulin binds to many other receptors in the body and affects MANY other physiological parameters, so here is the problem: if insulin receptors on the muscle cells become resistant to insulin's effect (and do not uptake glucose in an effective manner), the pancreas will produce more to ensure glucose uptake will occur. But if we increase insulin levels, what happens to receptors that modulate OTHER bodily functions and are not "resistant"? The scenario becomes much more complicated, in that these receptors become insulin resistant at different times. A typical "Syndrome-Xer" presents to the physician with some central obesity, slightly elevated blood pressure, slightly elevated blood glucose, and a less than stellar lipid panel. He is told to lose some weight by eating more fruits and vegetables, cut down on fats and cholesterol (have oatmeal instead of bacon and eggs) and do some light exercise. This standard, first line therapy of lifestyle changes sounds very reasonable. This compliant patient makes these changes and returns in two months, shocked and disappointed that his symptoms have become worse! Now he is given a low dose ACE inhibitor coupled with a diuretic for his hypertension and placed on metformin and glyburide to help control hyperglycemia. The glyburide tells the pancreas to secrete even more insulin and he gains more weight. Insulin also "ramps up" the enzyme HMG-Co A reductase which basically tells the body to produce even more cholesterol. Excess insulin also drives the kidneys to retain sodium and waste magnesium, which is an essential element for insulin receptor sensitivity. Hypertension and insulin resistance worsen. Usually at this point, if not sooner, a statin is added along with niacin and another oral hypoglycemic and we "start the march" to insulin therapy. This is why many of these patients will find themselves on six to nine prescription drugs… the current "standard of care" for this syndrome.

Let Your Food Be Your Medicine

Let us now suppose that the above patient first visited a physician is skilled in the use of a "muscle-sparing" protein diet (NOT a hyper-protein diet alá Atkins. This diet is also low in fat, particularly saturated fat, and is carbohydrate restrictive (providing about 40 grams of carbohydrates daily, mainly from fibrous vegetables). The physician explains the "medical model" of Syndrome X and relates how the overproduction of insulin can contribute to all his symptoms. Correcting hyperinsulinemia is very straightforward: all carbohydrates (with the exception of fiber) will eventually be converted to glucose…sometimes quickly, sometimes slowly. As the glucose is absorbed, the pancreas begins to secrete insulin (in this case, too much insulin). By restricting the carbohydrates, the production of insulin is immediately reduced. The patient is interested, but confides that he can be hypoglycemic at times and is afraid of such a restrictive protocol. The physician relates that hypoglycemia is usually the consequence of insulin overproduction, not a lack of carbohydrates. He further explains that the body has "three tanks of energy" from which to draw. Glycogen (stored glucose), muscle, which can be broken down via gluconeogenesis to supply glucose, and fat (triglycerides), which can be turned into glucose (from the glycerol) and ketonic bodies which most of the cells In the body can use for fuel. But the body draws on these compartments in a very specific order. It will always use the glycogen first, and only when that tank is empty, will it begin to simultaneously burn muscle and fat. The physician tells the patient if he keeps "putting fuel in the glycogen tank," he will never be able to access his fat reserves, thus the restriction of carbohydrates. He also says that we never want to lose muscle, thus the inclusion of the adequate amount of protein to replenish what is lost to gluconeogenesis.

During the first three days of this protocol, the patient may feel a little tired or weak as the body depletes its glycogen, but once this is gone and the body switches over to burning stored fat, he will have plenty of energy, and hypoglycemic episodes will be a thing of the past. His patient is interested but asks: "Ketonic bodies?" Does that mean ketosis…I thought that was bad?" Again, the physician explains that *ketoacidosis* is bad and that is why a Type I diabetic would never be placed on this program. In this case, ketosis just mean "living off your reserves" and is the reason human beings were able to survive times of famines. His concerns allayed, the patient begins the program.

Under The Influence Of Glucagon

Six weeks later, the elated patient returns to his physician, thirty pounds lighter, and discovers that his blood work is fantastic! The physician tells him: "Well, you have actually reset your pancreas. It is no longer is pumping out too much insulin, so now you can start to put fruits, grains, and dairy back into your diet." After this patient's glycogen reserves were depleted and carbohydrates continued to be restricted, the body had to ensure proper blood glucose levels were maintained. Under these conditions, the pancreas produces more glucagon (which raises blood sugar) and much less insulin (whose primary function is to lower blood sugar). But there is more to glucagon than this primary function. Glucagon stimulates two adipocyte (fat cell) enzymes (HSL and ATGL) and inhibits a third (Lipoprotein lipase). The result is the release of trigylcerides from the fat cell (to be used as fuel), as opposed to insulin's effect, which is to store fat. Glucagon enhances the entry of free fatty acids across the mitochondrial membranes so they can be used as fuel (insulin inhibits this). Glucagon also greatly inhibits the action of HMG-CoA reductase (along with all the other enzymes necessary for cholesterol synthesis) and forces cells to pull cholesterol from the blood stream via "ramping-up" LDL receptors (1983 Nobel Prize in Medicine). This is why the patient's lipid panel came back stellar. Finally, in the kidneys, the retention of sodium caused by excess insulin has now been corrected and his hypertension has resolved. The pathophysiology of Syndrome X is predictable. The reversal of this syndrome is also predictable and repeatable! As a matter of fact, this exact method is being employed by thousands of medical practices in the United States and Canada. Tens of thousands of patients have experienced same benefits described here. Physicians of all backgrounds and specialities can become a leading force in helping to reverse this terrible syndrome. Let this article be a call to action!

