Genetic Bypass: Using Nutrition to Bypass Genetic Mutations

This is an excerpt from:

Part 1: General Background

The Basics

We have reached a point in today's society where every illness needs to be viewed from the standpoint of multifactorial disease. Many factors influence our susceptibility to disease. These include our stress load, our environment and the toxins we absorb from it, the total number of infectious agents we are exposed to as well as our underlying genetic susceptibility to these diseases. The precise combination of components that interact to cause multifactorial diseases may be different in every individual. There may be slight or enormous changes in the relative contributions of each of these components to disease.

Multifactorial diseases are caused by infections and environmental events occurring in *genetically susceptible individuals*. Basic parameters like age and gender, along with other genetic and environmental factors, play a role in the onset of these diseases. Infections combined with excessive environmental burdens only lead to disease if they occur in individuals with the appropriate genetic susceptibility.

It is important in this day and age to address all of the contributing factors to these diseases. One clear, definitive way to evaluate the genetic contribution of multifactorial disease is to take advantage of new methodologies that allow for personalized genetic screening. Genetic testing gives us a way to evaluate and address the genetic component of multifactorial disease. Currently, tests are available to identify a number of underlying genetic susceptibilities based on allelic variations that are found in the DNA. Unfortunately, the use of this testing has fallen short of expectations. Perceive impediments to the use of genetic screening to identify underlying susceptibilities to disease include concerns of job discrimination, loss of insurance coverage and the ability to address diagnosed disease states.

While 79% of Americans surveyed responded that they would take a genetic test to assess the risks of inherited diseases, and 41% said they had a family history of genetic or inherited health problems, the reality is that genetic testing is severely underutilized. Genetic screening should be the wave of the future for both alternative healthcare as well as allopathic medicine. Both disciplines (alternative and allopathic medicine) should be taking advantage of the stride made in the Human Genome Project that allow us to utilize simple genetic tests to look at our genetic weaknesses.

The goal of the Human Genome Project was to identify all the approximately 30,000 genes in human DNA and to determine the sequences or "spelling" of the 3 billion chemical base pairs that make up human DNA. This project was completed in June of 2000. As a direct consequence of having the complete sequence of the human genome, research first focused on identifying particular genes that were involved with specific diseases. The next step has been to use this information to look for the presence of these identified disease causing genes in an individual person. Rather than looking at complete gene profiles, it is also possible to look at particular changes in the "spelling" of your DNA in only specific areas of interest. In this way, you can more quickly get a sense of known genetic weaknesses. In order to find relationships between genetic changes and the susceptibility to disease, this testing is done utilizing single nucleotide polymorphisms, otherwise known as SNPs (pronounced snips). This process systematically compares genomes of those individuals with a disease or an imbalance in a nutritional pathway to the corresponding DNA of a "normal" population.

If the potential of genetic testing is so great, and most Americans feel that they would be willing to take genetic tests, and that genetic issues affect their family's health, then why has this technology not been used to its full potential?

The answer is *FEAR*.

For most people a great fear exists that genetic screening will uncover a serious, fatal or life threatening condition. As a result, individuals are fearful of the results of genetic screening. This points to the need to have a way to address the results of genetic screens so that we not only diagnose genetic susceptibility but also have a way to respond to it.

The lack of use of this powerful diagnostic technology highlights the need for adequate means to address the results of personalized genetic testing. It is a travesty to have the ability to specifically identify genetic weakness, yet have this technology underutilized out of fear. It points to a dire need for therapeutic technologies that take advantage of this same genetic information with an eye toward personalized treatment or nutritional supplementation, rather than simply personalized diagnosis. It is essential that we take advantage of the strides that have been made in the human genome project not only to understand our underlying genetic susceptibilities but also to successfully deal with chronic health issues.

The beauty of nutrigenomic testing is that it focuses on weaknesses in known, characterized nutritional pathways. Knowledge of these pathways lends itself to providing nutritional "bypasses" for genetic mutations.

These nutritional pathways can be viewed as complex roadways. Any mutations in the pathways can be visualized as road blocks. If we are familiar enough with the roadways and the maps we can design detours to get around the road blocks. The field of nutrigenomic testing and the supplementation of nutrients should take the fear out of genetic testing, at least for these well characterized nutritional pathways.

Nutrigenomics integrates concepts in molecular biology and genomics to study the ability of foods and nutritional supplements to interact with genes to influence our health and lower the genetic risk component for multifactorial disease. This field of nutrigenomics is perhaps best described by the group that is dedicated to promoting this new science of nutritional genomics. According to the National Center of Excellence in Nutritional Genomics at UC Davis, "The science of nutrigenomics seeks to provide a molecular understanding for how common dietary chemicals (i.e., nutrition) affect health by altering the expression and/or structure of an individual's genetic makeup. Just as pharmacogenomics has led to the concept of "personalized medicine" and "designer drugs", so will the new field of nutrigenomics open the way for "personalized nutrition." In other words, by understanding our nutritional needs, our nutritional status, and our genotype, nutrigenomics should enable individuals to manage better their health and well-being by precisely matching their diets with their unique genetic makeup."

The nutrigenomic test results that are analyzed in this book focus on genetic weaknesses in a particular pathway in the body that is involved in generating and utilizing methyl groups in the body. This central pathway in the body is particularly amenable to nutrigenomic screening for genetic weaknesses. Defects in methylation lay the appropriate groundwork for the further assault of environmental and infectious agents and result in an increased risk for additional health conditions including diabetes, cardiovascular disease, thyroid dysfunction, neurological inflammation, chronic viral infection, neurotransmitter imbalances, atherosclerosis, cancer, aging, neural tube defects, Alzheimer's disease and autism.

As a result of decreased activity in the methylation pathway due to mutations, there is a shortage of methyl groups in the body for a variety of important functions. Methyl groups are "CH3" groups that are moved around in the body to turn on or off genes. There are several particular sites in this pathway where blocks can occur as a result of genetic weaknesses. Supplementation with appropriate foods and nutrients will bypass these mutations to allow for restored function of the pathway.
By looking at diagrammatic representations of the methylation pathway and relating the effects of genetic polymorphisms to biochemical pathways, we are able to draw a personalized map for each individual's imbalances which may impact upon their health. By identifying the precise areas of genetic fragility, it is then possible to target appropriate nutritional supplementation of these pathways to optimize the functioning of these crucial biochemical processes.

> *"With the completion of the Human Genome Project, we have a nearly complete list of the genes needed to produce a human. However, the situation is far more complex than a simple catalogue of genes. Of equal importance is a second system that cells use to determine when and where a particular gene will be expressed during development. This system (DNA methylation) is overlaid on DNA in the form of epigenetic marks that are heritable during cell division but do not alter the DNA....The importance of DNA methylation is emphasized by the growing number of human diseases that are known to occur when this epigenetic information is not properly established and /or maintained..."*
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> Keith Robertson, Nature Review Genetics, August 2005.

The Methylation Cycle for Nutrigenomic Analysis

The methylation cycle is the ideal pathway to focus on for nutrigenomic analysis and supplementation because the function of this pathway is essential for a number of critical reactions in the body. As a consequence, genetic weaknesses (mutations) in this pathway are risk factors for a number of serious health conditions including heart disease, stroke, cancer, diabetes, MS, Alzheimer's disease, ALS, Parkinson's disease, Huntington's disease, CFS/FM, mitochondrial disease, SLE, neural tube defects, miscarriages, Down's syndrome, bipolar disorder, schizophrenia, repair of tissue damage, proper immune function, the aging process as well as autism. In the field of autism, which is my major area of study at this time, I have genetic data on almost 200 individuals. Thus far 100% of the children show one or more mutations somewhere in this pathway. Even if this percentage does not hold up over time, I would expect that a statistically significant number of children with autism will harbor mutations in this pathway.

Methylation is related to neurotransmitter levels; methylation of intermediates in tryptophan metabolism can affect the levels of serotonin; intermediates of the methylation pathway are also shared with the pathway involved in serotonin and dopamine synthesis. Consequently, imbalances in the methylation pathway will also affect the neurotransmitter dopamine. In addition to its direct role as a neurotransmitter, dopamine is involved in methylating phospholipids in the cell membranes to increase membrane fluidity. Membrane fluidity is important for a variety of reasons including proper signaling of the immune system as well as protecting nerves from damage. A number of serious neurological conditions site reduced membrane fluidity as part of the disease process including MS, ALS, and Alzheimer's disease. In addition, phospholipid methylation may be involved in modulation of NMDA (glutamate) receptors, acting to control excitotoxin damage.

Increases in certain inflammatory mediators of the immune system such as IL6 and TNF alpha lead to decreases in methylation. Chronic inflammation would therefore exacerbate an existing genetic condition of undermethylation. The inability to progress normally through the methylation pathway as a result of this methylation cycle mutation, could lead to a build-up of precursors of the methylation pathway, including the excitotoxin glutamate.

The building blocks for DNA and RNA require the methylation pathway. Without adequate DNA and RNA it is difficult for the body to synthesize new cells. This would result in a decreased level of new cells including critical cells of the immune system, the T cells. De novo T cell synthesis is necessary to respond to bacterial, parasitic and viral infection, as well as for other aspects of the proper functioning of the immune system. T cells are necessary for antibody producing cells in the body (B cells) as both T helpers and T suppressors are needed to appropriately regulate the antibody response.

In addition, decreased levels of methylation can result in improper DNA regulation. DNA methylation is necessary to prevent the expression of viral genes that have been inserted into the body's DNA. Loss of methylation can lead to the expression of inserted viral genes.

Proper levels of methylation are also directly related to the body's ability to both myelinate nerves and to prune nerves. Myelin is a sheath that wraps around the neuronal wiring to insulate and facilitate faster transmission of electrical potentials. Without adequate methylation, the nerves cannot myelinate in the first place, or cannot remyelinate after insults such as viral infection or heavy metal toxicity. A secondary effect of a lack of methylation and hence decreased myelination is inadequate pruning of nerves. Pruning helps to prevent excessive wiring of unused neural connections and reduces the synaptic density. Without adequate pruning the brain cell connections are misdirected and proliferate into dense, bunched thickets. All of these changes, when they occur in utero or in very young children, can alter brain development and can also set up metabolic changes that cause ongoing compromise of brain function. These metabolically caused changes in brain function can, however, be mitigated if the underlying nutrigenomic weaknesses that are causing these changes are identified and supplemented nutritionally.

We are used to talking about single biomarkers serving as indicators for specific disease states. However, I believe that for a number of health conditions, including autism, we may be looking at the entire methylation pathway (as it is drawn on the diagrams presented in this book) as representing "the biomarker" for underlying genetic susceptibility for a number of disease states. We may then need to expand our view of a "biomarker" beyond the restriction of a mutation in a single gene to a mutation somewhere in an entire pathway of interconnected function.

This does not mean that every individual with mutations in this pathway will be autistic or will have one of the health conditions listed above. It may be a necessary but not a sufficient condition. As described in the Preface and The Basics section of this book, most health conditions that we see today are multifactorial in nature. There are genetic components, infectious components and environmental components. A certain threshold or body burden needs to be met for each of these factors in order for multifactorial disease to occur. However, part of what makes the methylation cycle so unique and so critical for our health, is that mutations in this pathway have the capability to impair all three of these factors. This would suggest that if an individual has enough mutations or weaknesses in this pathway it MAY be sufficient to cause mutlifactorial disease, as methylation cycle mutations can lead to chronic infectious diseases, increased environmental toxin burdens and have secondary effects on genetic expression.