When I speak about the **"New Nutrition",** I am, of course, talking about something called **nutrigenomics -** a topic I have spoken about before.

Let me start by giving you some background: All of you are probably familiar with the concept of genetic mutations - alterations in our DNA sequence that significantly disrupt the activity of a critical enzyme and cause a specific disease. **Cystic fibrosis and sickle cell disease are classical examples.**

But the concept of genetic polymorphisms is probably less familiar to most people. These are genetic alterations in our DNA sequence that cause more subtle changes in enzyme activity. They often increase the probability of certain diseases, but only under the right set of environmental conditions.

In some cases the environmental condition needed to trigger a disease involves the nutrients that we get in our diet. In this case, the enzyme activity is usually altered in such a way that it becomes more dependent on a specific nutrient for optimal activity. **As a result disease avoidance becomes more dependent on achieving optimal blood levels of that nutrient. This is what we refer to as nutrigenomics.**

Simply put, the science of nutrigenomics involves the identification of genetic polymorphisms that increase the need for one or more nutrients to prevent a particular disease.

Today's studies are a perfect example of nutrigenomics.
There is a genetic polymorphism of a gene called MTHFR that codes for an enzyme called methylenetetrahydrofolate reductase (There will be a quiz at the end of this "Tip").

Methylenetetrahydrofolate reductase requires a metabolite of riboflavin for full activity, and it turns out that the altered form of the enzyme has a lower affinity for this riboflavin metabolite. **Thus, full enzyme activity requires higher than normal blood levels of riboflavin.**

That might be inconsequential except that low methylenetetrahydrofolate enzyme activity is linked to high blood pressure and an increased risk of stroke. The exact mechanism by which this occurs is not known, but the correlation between low enzyme activity and high blood pressure is very strong.

The high-riboflavin polymorphism of MTHFR is not common. It occurs in about 10% of the US population (ranging from 4% to 18% depending on ethnicity), but it is important because it provides a low cost, low risk intervention for people with that polymorphism who have <u>developed high blood pressure.</u>

That brings us to the studies that I will be talking about today. The first study (Horigan et al., Journal of Hypertension, 28: 478-486, 2010) was a double blind, placebo controlled trial which showed that **1.6 mg/day of riboflavin given over a 16-week** period significantly lowered blood pressure in hypertensive patients with the high-riboflavin polymorphism of the MTHFR gene, but not in hypertensive patients with other polymorphisms of the MTHFR gene.

Surprisingly, the patients with the high-riboflavin polymorphism of the MTHFR gene were not put on riboflavin therapy when the trial ended (This fact will become significant in a minute). Instead, they were put on a newer form of drug therapy.

It turns out that the standard of care for patients with high blood pressure changed shortly after the first riboflavin intervention trial was concluded. Prior to 2006 the standard of care had been beta- blocker drugs for high blood pressure. In 2006 the standard of care for blood pressure was switched to a multi-drug approach.

So instead of recommending 1.6 mg/day of riboflavin (which had just been shown to work) to the hypertensive patients with the high-riboflavin MTHFR polymorphism, those patients were put on multiple drug therapy (with multiple side effects).

To me this is another example of "What were they thinking?"

The second study (Wilson et al, American Journal of Clinical Nutrition, 95: 766-772, 2011) was a follow-up four years latter to see if the multiple drug treatment was working and to see if riboflavin was effective in reducing blood pressure for patients who were already on multiple drug therapy to reduce blood pressure.

This was also a double blind placebo controlled 16-week trial with 1.6 mg/day of riboflavin. It utilized the same participants who had enrolled in the previous study four years earlier, but in this case the placebo and riboflavin groups were reversed. The group who had received riboflavin was put on the placebo this time around, and the placebo group was given riboflavin. So, in a sense, each patient served as their own control.

The scientists conducting this study also utilized a very sensitive red blood cell assay of riboflavin status for the patients enrolled in the study. Accordingly to the assay, the patients enrolled in this study started with suboptimal riboflavin status. Supplementation with 1.6 mg/day for 16 weeks was sufficient to bring their riboflavin status into the normal range. This showed that the level of supplementation was sufficient to reach optimal riboflavin status.

However, the most striking findings of this study were the following:

1) Multiple drug therapy (the current standard of care) was not terribly effective in bringing blood pressure under control for hypertensive patients with the high-riboflavin polymorphism of MTHFR.

Only 54% of the patients in this group were able to achieve the treatment goal of <140 mm Hg systolic blood pressure - compared to over 70% of the patients with other MTHFR polymorphisms.

2) Just as in the previous study, 1.6 mg/day of riboflavin reduced systolic blood pressure an average of 9 mm Hg in the group with the high-riboflavin MTHFR polymorphism, but had no significant effect on blood pressure in the groups with other MTHFR polymorphisms. This was often enough to bring the blood pressure within the normal range.

The authors concluded that 1.6 mg/day of riboflavin was sufficient to significantly lower blood pressure for hypertensive patients with the high-riboflavin MTHFR polymorphism - even those patients already on multiple drugs to lower high blood pressure. In fact, the authors concluded that "...the only time that blood pressure reached target levels in this genotype group was when riboflavin was introduced."

To put things in perspective the authors said that it would take a 22 pound weight loss or an exercise program that burned 4200 calories/week to achieve comparable decreases in blood pressure. They went on to point out that these interventions "...require considerable effort by both patients and health care staff...and long-term compliance is often poor."

So what does all of this mean to you?

1) Does this study mean that you should rush out and buy a "Super, Mega" high dose riboflavin or B Complex supplement? The answer is a clear no. 1.6 mg/day of riboflavin is actually a fairly modest dose. The RDA for riboflavin is 1.3 mg/day for men and 1.1 mg/day for women.

2) On the other hand, our flour has been enriched with riboflavin for years. Even Wonder Bread and donuts are enriched with riboflavin. Does that mean that we can assume that we don't have to worry about riboflavin intake? Again, the answer is a clear no. The people in this study were eating a typical American diet including riboflavin-enriched foods, yet their riboflavin status was sub-optimal unless it was supplemented.

3) If you have high blood pressure, should you rush out and get a test for MTHFR polymorphisms? Once again the answer is no. The cost of the test far outweighs the benefit of knowing your genetic polymorphism. As the authors point out riboflavin supplementation is a very low cost approach for lowering "...blood pressure in those genetically at risk...without causing harm to those who are not."

4) Is optimizing riboflavin status the only natural approach for lowering blood pressure? No. Other nutrients such as omega-3 fatty acids are effective at lowering blood pressure in a much larger segment of the population. In addition, the DASH diet (a holistic approach to healthy eating) was shown over a decade ago to be more effective than drugs at lowering blood pressure. And, as the authors mentioned, weight loss and exercise are also effective at lowering blood pressure.

5) And finally, should you abandon drugs in favor of natural approaches to lower blood pressure? Here the answer is absolutely not. For example, this study showed that riboflavin was effective in further lowering blood pressure in people already on medications. It did not show that riboflavin allowed people not on drugs to achieve normal blood pressure.

What I would suggest is that if you decide to use natural approaches to reduce your blood pressure, you have a conversation with your doctor so that he or she can reduce your medications (or even eliminate them) as the changes you are making begin to take effect.

To Your Health!
Dr. Stephen G Chaney